Vol. 27. N.º 6. Noviembre-Diciembre 2012

Nutrición Hospitalaria

ÓRGANO OFICIAL DE LA SOCIEDAD ESPANOLA DE NUTRICIÓN PARENTERAL Y ENTERAL
ÓRGANO OFICIAL DEL CENTRO INTERNACIONAL VIRTUAL DE INVESTIGACIÓN EN NUTRICIÓN
ÓRGANO OFICIAL DE LA SOCIEDAD ESPANOLA DE NUTRICIÓN
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ISSN 0212-1611

ÍNDICE COMPLETO EN EL INTERIOR DE LA REVISTA

Nutr Hosp. 2012;(6)27:1751-???? • ISSN (Versión papel): 0212-1611 • ISSN (Versión electrónica): 1699-5198 • CODEN NUHOEQ • S.V.R. 318

Incluida en EMBASE (Excerpta Medica), MEDLINE (Index Medicus), Chemical Abstracts, Cinahl, Cochrane plus, Ebsco, Indice Médico Español, preIBECS, IBECS, MEDES, SENIOR, SciELO, Science Citation Index Expanded (SciSearch), Cancerlit, Toxline, Aidsline y Health Planning Administration

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Nutrición Hospitalaria

Vol. 27
N.º 6 • NOVIEMBRE-DICIEMBRE 2012
ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

Nutrición Hospitalaria

IMPACT FACTOR 2011: 1,120 (JCR)

www.nutriciónhospitalaria.com

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N.º 6

Noviembre-Diciembre 2012 • Vol. 27
Periodicidad bimestral

Edición y Administración
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Tel.: 913 576 609 - Fax: 913 576 521
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Dep. Legal: M-34.850-1982
Soporte válido: 19/05-R-CM
ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

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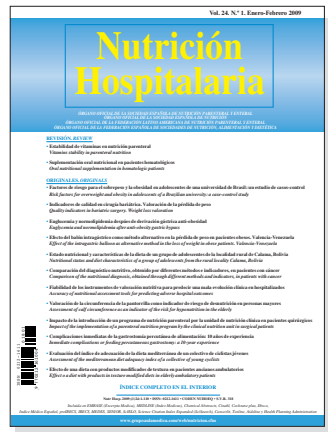
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Nutrición Hospitalaria

Vol. 27
N.º 6 • NOVIEMBRE-DICIEMBRE 2012
ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

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NUTRICIÓN HOSPITALARIA ES PROPIEDAD DE SENPE

Vol. 27
N.º 6 • NOVIEMBRE-DICIEMBRE 2012
ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

Nutrición Hospitalaria

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La Sociedad Española de Nutrición Parenteral y Enteral, que tiene como objetivos desde su fundación el potenciar el desarrollo y la investigación sobre temas científicos relacionados con el soporte nutricional, agradece su ayuda a los siguientes socios-entidades colaboradoras.

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Nutrición Hospitalaria

Vol. 27
N.º 6 • NOVIEMBRE-DICIEMBRE 2012
ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

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Vol. 27
N.º 6 • NOVIEMBRE-DICIEMBRE 2012

ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

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ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

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N.º 6 • NOVIEMBRE-DICIEMBRE 2012

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Vol. 27
N.º 6 • NOVIEMBRE-DICIEMBRE 2012

ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

IMPACT FACTOR 2011: 1,120 (JCR)

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ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

Vol. 27
N.º 6 • NOVIEMBRE-DICIEMBRE 2012

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Vol. 27
N.º 6 • NOVIEMBRE-DICIEMBRE 2012

ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

IMPACT FACTOR 2011: 1,120 (JCR)

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ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

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ISSN (Versión electrónica): 1699-5198

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ISSN (Versión papel): 0212-1611
ISSN (Versión electrónica): 1699-5198

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1751-1757
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Artículo especial

El factor de necrosis tumoral-α, la resistencia a la insulina, el metabolismo de lipoproteínas y la obesidad en humanos

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Resumen

En la obesidad el tejido adiposo produce moléculas proinflamatorias como el Factor de Necrosis Tumoral-α, que tiene efectos locales en la fisiología del adipocito y efectos sistémicos en otros órganos. Muchos estudios relacionando TNF-α, obesidad, resistencia a la insulina y metabolismo lipídico se han realizado en ratas, conejos y perros, pero los resultados observados en varios de estos estudios han sido contradictorios y muchos de ellos no se han logrado reproducir en humanos, lo que hace difícil la interpretación del efecto del TNF-α sobre el metabolismo humano.

Objetivo: **Realizar una revisión sistemática de los estudios realizados en humanos donde se relacione TNF-α, obesidad, resistencia a la insulina y metabolismo de las lipoproteínas.**

Metodología: **Se realizó una búsqueda en la base de datos PubMed de estudios realizados en humanos, tejidos humanos y líneas celulares humanas, relacionando TNF-α, obesidad, resistencia a la insulina y lipoproteínas.**

Resultados: **Existe una mayor producción de TNF-α en tejido adiposo de sujetos obesos. El TNF-α disminuye la respuesta celular a la insulina en adipocitos, hepatocitos y células musculares humanas. Hay un aumento de TNF-α en pacientes con dislipidemia, y la inactivación del TNF-α afecta el metabolismo lipídico. En hepatocitos humanos, el TNF-α inhibe la expresión de APO AI, lo cual puede disminuir la secreción de las lipoproteínas de alta densidad. El TNF-α afecta la excreción de colesterol al inhibir en hepatocitos a la enzima colesterol-7α-hidroxilasa.**

Conclusión: **El TNF-α disminuye la respuesta celular a la insulina, y tiene efectos sobre el metabolismo del colesterol y las lipoproteínas en humanos. Un mayor conocimiento de los mecanismos de la respuesta inflamatoria inducida por la obesidad en humanos, puede llevar a identificar nuevos blancos terapéuticos que permitan prevenir las complicaciones asociadas a la obesidad.**

(*Nutr Hosp.* 2012;27:1751-1757)

DOI:10.3305/nh.2012.27.6.6004

Palabras clave: *Factor de necrosis tumoral-α. Resistencia a la insulina. Lipoproteínas. Colesterol.*

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Recibido: 13-VI-2012.
Aceptado: 7-VIII-2012.

TUMOR NECROSIS FACTOR-α, INSULIN RESISTANCE, THE LIPOPROTEIN METABOLISM AND OBESITY IN HUMANS

Abstract

In the obese adipose tissue produces proinflammatory molecules as tumor necrosis factor-α, which has local effects on adipocyte physiology and systemic effects in other organs. Many studies linking TNF-α, obesity, insulin resistance and lipid metabolism have been conducted in rats, rabbits and dogs, but the results observed in several of these studies have been conflicting and many of them have not been able to reproduce in humans, which on human makes difficult the interpretation of the effect of TNF-α on human metabolism.

Objective: **To conduct a systematic review of human studies which relates, TNF-α insulin resistance and lipoprotein metabolism.**

Methods: **We searched the PubMed database for studies in humans, human tissue and human cell lines linking TNF-α, obesity, insulin resistance and lipoprotein.**

Results: **There is a increased production of TNF-α on adipose tissue of obese. TNF-α decreases the cellular response to insulin in adipocytes, hepatocytes and human muscle cells. There is an increase of TNF-α in patients with dyslipidemia, and inactivation of TNF-α affects lipid metabolism. In human hepatocytes, TNF-α inhibits expression of APO AI, which may decrease the secretion of high density lipoproteins. TNF-α affects the excretion of cholesterol by inhibiting the enzyme cholesterol-7α-hydroxylase in hepatocytes.**

Conclusion: **TNF-α decreases the cellular response to insulin, and has effects on the metabolism of cholesterol and lipoproteins in humans. A better understanding of the mechanisms of the inflammatory response induced obesity in humans, can lead to identifying new therapeutic targets that can prevent the complications associated with obesity.**

(*Nutr Hosp.* 2012;27:1751-1757)

DOI:10.3305/nh.2012.27.6.6004

Key words: *Tumor necrosis factor-α. Insulin resistance. Lipoproteins. Cholesterol.*

Introducción

La obesidad se define como un acúmulo de grasa corporal que se traduce en un aumento de peso. La obesidad es un factor de riesgo para enfermedades cardiovasculares, enfermedades pulmonares, enfermedades metabólicas, enfermedades osteoarticulares y para varios tipos de cáncer[1-3]. La obesidad, además de tener una fuerte asociación con la ocurrencia de condiciones médicas crónicas, tiene una asociación con el deterioro de la calidad de vida relacionada con la salud, y con un incremento en la atención sanitaria de los países.

La obesidad está relacionada con cambios en importantes parámetros fisiológicos como la presión arterial, sensibilidad a la insulina y la concentración sérica de lípidos. Se ha descrito una correlación positiva entre el grado de obesidad y ciertos desordenes asociados a la obesidad como la hipertensión arterial, dislipidemia e intolerancia a la glucosa[2,4,5]. Las causas de la obesidad y sus consecuencias a nivel fisiológico son objeto de estudio actualmente.

Recientemente, las dislipidemias, la resistencia a la insulina, la aterosclerosis y la obesidad han sido relacionadas con un estado de inflamación crónica. Las citoquinas no sólo son producidas por las células del sistema inmunológico, si no también por otros tipos celulares como lo adipocitos y las células no grasas del tejido adiposo. Además, estas citoquinas pueden actuar de manera local (autocrina/paracrina) y a nivel sistémico, y han sido implicadas en la disfunción del tejido adiposo y están relacionadas bioquímicamente con la resistencia a la insulina, la alteración en la liberación de ácidos grasos libres y el desarrollo de alteraciones del metabolismo hepático asociadas con la obesidad. Adicional a esto, el adipocito expresa receptores que le permiten responder a diferentes señales de regulación del metabolismo celular de las citoquinas[6-8].

La demostración de que el tejido adiposo puede producir citoquinas tales como IL-6, IL-8, TNF-α y moléculas proinflamatorias como la proteína C reactiva (PCR), sugiere que los obesos pueden presentar un estado inflamatorio subclínico[9-11]. Existen evidencias que soportan la hipótesis que afirma que la obesidad es una condición inflamatoria que lleva a una activación crónica del sistema inmunológico innato lo cual conduce a las distintas condiciones clínicas que se observan en la obesidad. Estudios experimentales y la evidencia de estudios prospectivos y longitudinales en humanos son consistentes con el rol etiológico de la inflamación subclínica en la patogénesis de muchas de las enfermedades asociadas a la obesidad, como la aterosclerosis, donde la inflamación juega un papel clave en el inicio y progreso de la placa aterosclerótica[12].

Muchos estudios relacionando TNF-α, obesidad y metabolismo se han realizado en ratas, conejos y perros, pero los resultados observados en varios de estos estudios han sido contradictorios y muchos de ellos no se han logrado reproducir en humanos. Por ejemplo, el tratamiento de la rata genéticamente obesa Zucker *(fa/fa)* con anticuerpos monoclonales neutralizantes anti-TNF-α revirtió el estado de resistencia a la insulina en estas ratas[13], pero la administración de una sola dosis de anticuerpos anti-TNF-α neutralizantes a humanos obesos con diabetes tipo II[14] o del receptor recombinante del TNF-α[15] no produjo ningún efecto en la sensibilidad a la insulina. Este estudio tiene por objetivo hacer una revisión de los estudios que relacionen TNF-α, obesidad y metabolismo realizados en humanos, en tejidos humanos, así como en líneas celulares humanas.

Hipertrofia e hiperplasia de los adipocitos

La principal función de los adipocitos es el almacenaje de los ácidos grasos en forma de triacilgliceroles (TAG). En sujetos obesos, el desbalance crónico entre las calorías consumidas y las gastadas causa un aumento de almacenamiento en forma de TAG en tejido adiposo, lo que se manifiesta de las siguientes formas: incremento de los lípidos intracelulares, aumento del tamaño de los adipocitos (hipertrofia), incremento del número de adipocitos (hiperplasia)[16].

El incremento de lípidos dentro del adipocito, unido a la hipertrofia e hiperplasia del tejido adiposo, lleva a una disfunción celular que se manifiesta con anormalidades como la secreción de citoquinas y moléculas proinflamatorias por parte del tejido adiposo tales como TNF-α, IL-6, la proteína quimiotáctica de monocitos-1 (MCP-1), Factores Estimuladores de Colonia (CSF) y la sintetasa inducible de oxido nítrico (iNOS), generando el estado proinflamatorio descrito y reconocido en obesos. Sin embargo, estudios en los últimos años han puesto de manifiesto que los adipocitos no son la única fuente de secreción de citoquinas inflamatorias en el tejido adiposo. Las células no adiposas, que constituyen la fracción del estroma vascular, que incluye preadipocitos, células endoteliales, los fibroblastos, los leucocitos y macrófagos tienen parte de importante en la responsabilidad del desarrollo de la respuesta inflamatoria crónica observada en la obesidad[17,18].

El TNF-α en la obesidad

El TNF-α es una citoquina proinflamatoria secretada en el sistema inmunitario por monocitos y macrófagos, por linfocitos T y B, células NK y por leucocitos polimorfonucleares. El TNF-α también puede ser secretado por otros tipos celulares como los adipocitos. El TNF-α tiene un amplio rango de efectos biológicos que incluyen inducción de apoptosis, citotoxicidad de células tumorales, activación y diferenciación de monocitos, inducción de la diferenciación de precursores inmaduros a monocitos, aumento de la actividad parasiticida y bactericida de los macrófagos al inducir las vías del superóxido y del óxido nítrico, inducción

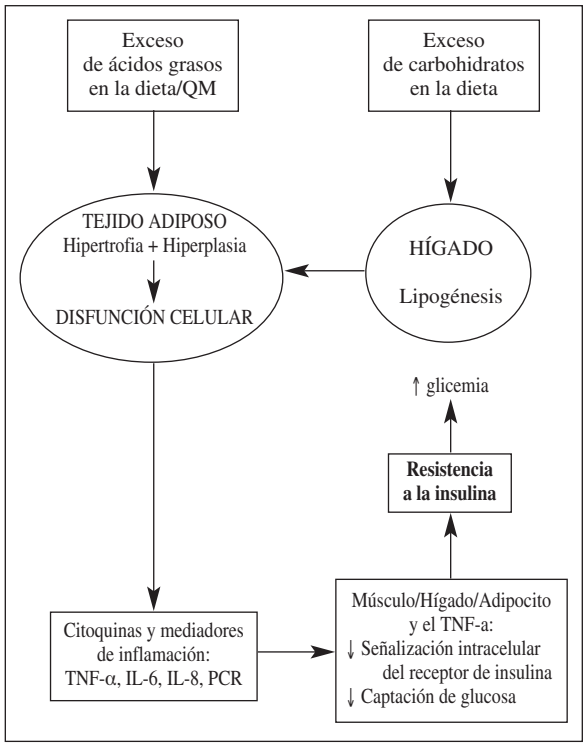


Fig. 1.—Secreción de adipoquinas en el tejido adiposo y la resistencia a la insulina. QM: quilomocrones; AG: ácidos grasos.

de la expresión de moléculas de adhesión en células endoteliales favoreciendo la migración local de leucocitos, aumento del receptor de IL-2 en linfocitos T y por consiguiente aumento de la respuesta proliferativa a IL-2, aumento de la respuesta de los linfocitos B estimulados. Por otro lado, el TNF-α tiene efectos fisiopatológicos al ser secretado en grandes cantidades en enfermedades agudas y crónicas, sepsis, infecciones crónicas, inflamaciones crónicas y cáncer. El TNF-α es sintetizado como una proteína transmembrana no glicosilada de 26 kDa que contiene una secuencia hidrofóbica. Tras una proteólisis se produce un fragmento de 14 kDa y un fragmento de 17 kDa que es la forma circulante como homotrímero unido de forma no covalente. La enzima encargada de la proteólisis es una metaloproteasa llamada TACE *(TNF-alpha converting enzyme)*. El TNF-α tiene dos tipos de receptores, tipo 1 y tipo 2 que son expresados en muchas células, incluyendo los adipocitos[19-21].

El primer estudio que relacionó la obesidad con el TNF-α fue publicado por Hotamisligil y cols.[22], este estudio estableció el inicio de los estudios de TNF-α/inflamación en la obesidad. La expresión de las citoquina proinflamatoria TNF-α esta incrementada en adipocitos de sujetos obesos y de sujetos con resistencia a la insulina[23]. Además del incremento de la expresión del TNF-α en tejido adiposo de sujetos obesos, se ha descrito que los sujetos obesos presentan mayores niveles séricos de TNF-α[24], y que la pérdida de peso en obesos reduce los niveles séricos de TNF-α[25] y la expresión del mRNA del TNF-α en tejido adiposo[26].

El TNF-α y la resistencia a la insulina

La insulina es una hormona liberada por las células beta pancreáticas en respuesta a niveles elevados de glucosa en sangre, controlando funciones energéticas críticas en el metabolismo de los glúcidos, de las proteínas y de los lípidos, además, promueve el crecimiento celular. La insulina actúa en el metabolismo lipídico promoviendo el anabolismo e inhibiendo el catabolismo: regula al alza la lipoproteína lipasa (LPL) y estimula la expresión intracelular de enzimas lipogénicas como Acetil-CoA carboxilasa y ácido graso sintetasa, además, la insulina inhibe la lipasa sensible a hormonas (LSH) inhibiendo de esta manera la lipólisis.

Las acciones de la insulina son mediadas por cascadas de señalización intracelular, en las cuales la fosforilación inicial del receptor en residuos de tirosina lleva a una serie de eventos de fosforilación/desfosforilación de cinasas de tirosina y serina/treonina. Estas cinasas son las responsables de transmitir la señal de la insulina para la regulación de eventos metabólicos dentro de la célula. La incapacidad de las células blanco de responder a la insulina, genera un estado conocido como resistencia a la insulina.

La expresión de TNF-α en los adipocitos se correlaciona positivamente con la obesidad y con la resistencia a la insulina. El TNF-α tiene múltiples efectos en el metabolismo, debido a un efecto paracrino sobre los adipocitos y a efectos en el metabolismo hepático. El TNF-α disminuye la señalización intracelular del receptor de insulina en adipocitos[26,27], en células HepG2 (línea celular humana de carcinoma hepatocelular)[28] y en células de músculo esquelético humano[29], a través de la inhibición de IRS-1 (substrato del receptor de insulina-1) haciendo a esta molécula un pobre sustrato para fosforilación de los residuos de tirosina mediada por el receptor de insulina, y por tanto disminuyendo la amplificación intracelular de la señal del receptor insulínico, generando un estado de resistencia a la insulina, que trae consecuencias sobre el metabolismo celular.

El transporte de glucosa a través de la membrana celular se lleva a cabo por una familia de moléculas llamadas transportadores de glucosa (GLUT). El GLUT4 se encuentra almacenado en vesículas en el citosol de las células en el tejido muscular estriado, tejido muscular cardíaco y adipocito, siendo movilizadas las vesículas a la membrana celular por acción de la insulina, favoreciendo el movimiento de glucosa desde la sangre al interior de las células. Este comportamiento representa un mecanismo de regulación del metabolismo de la glucosa que sólo permite la entrada de glucosa al tejido muscular cuando es lo suficientemente elevada como para estimular la secreción de insulina y que en última instancia favorecerá la entrada del excedente de glucosa al interior celular. Se ha descrito que el tratamiento de adipocitos humanos en cultivo con TNF-α disminuye la expresión del mRNA de GLUT4[30]. Los tejidos sensibles a la acción de la insulina, tales como el tejido adiposo, músculo esquelético y cardiaco, mues-

Tabla I
Alteraciones en la regulación del metabolismo celular inducido por el TNF-α en humanos

Molécula/Proceso	*Alteración en la regulación*	*Consecuencias*
Receptor de insulina en adipocito[26,27], hepatocito[28] y músculo[29].	Disminuye la señalización intracelular del receptor de insulina	Resistencia a la insulina
GLUT4[30]	Disminuye la expresión de GLUT4. Disminuye el transporte de glucosa a través de la membrana celular	Disminuye captación de glucosa Mecanismo inductor de hiperglicemia
Sortilina[31]	Disminuye la expresión de Sortilina, por lo que disminuye el transporte de GLUT4 a la membrana celular	Disminuye captación de glucosa Mecanismo inductor de hiperglicemia
LPL[43,44]	Disminuye la actividad de la enzima	Incapacidad para degradar los triacilglicéridos de VLDL y QM. Hipertrigliceridemia.
Síntesis de HDL[47-51]	Disminuye la síntesis en hepatocitos y células intestinales	Bajos niveles de HDL, incremento del riesgo cardiovascular
Colesterol-7α-hidroxilasa[53], esterol-27 hidroxilasa y oxiesterol 7α-hidroxilasa[54]	Inhibe en hepatocitos la expresión y la actividad de estas enzimas	Disminuye la excreción de colesterol al inhibir la producción de sales biliares
Receptor de LDL en hepatocitos[55,56]	Aumenta la expresión del receptor de LDL	Favorece el acúmulo de colesterol en hepatocitos, lo que juega un papel importante en el desarrollo de Hígado Graso-No Alcohólico

GLUT4: Transportador de glucosa 4; LPL: Lipoprotein lipasa; QM: Quilomicrones; HDL: Lipoproteína de alta densidad; LDL: Lipoproteína de baja densidad; VLDL: Lipoproteínas de muy baja densidad.

tran incremento en la entrada de la glucosa a la célula cuando se estimula mediante insulina, debido a la activación del GLUT4. Esta activación está alterada debido a la exposición de las células al TNF-α, con disminución en la función de GLUT 4, el cual es un mecanismo inductor de hiperglicemia.

La sortilina es una proteína implicada en el trasporte de GLUT4 hacia la membrana citoplasmática. Los niveles de mRNA de la sortilina se encontraron disminuidos en tejido adiposo de pacientes diabéticos obesos, además, el tratamiento de adipocitos humanos en cultivo con TNF-α disminuye la expresión del mRNA de la sortilina, lo que se traduce en una menor translocación de GLUT4 hacia la membrana citoplasmática[31]. Estos resultados sugieren que la resistencia a la insulina en sujetos obesos se debe en parte, a la interferencia del TNF-α en expresión del gen y en la actividad de GLUT4 inducida por la insulina.

El TNF-α y su relación con el colesterol sérico total y las lipoproteínas

Existe una clara relación entre el TNF-α y los lípidos séricos, basados en estudios realizados en humanos. Primero, se ha descrito un aumento de TNF-α en pacientes con dislipidemia. En pacientes con hipercolesterolemia, se ha reportado elevados niveles séricos de TNF-α y acompañados de niveles elevados de triglicéridos (TG) y colesterol de lipoproteínas de baja densidad (LDL-C)[32]. Además, en pacientes hiperlipidémicos, los niveles séricos de TNF-α se correlacionan positivamente con los niveles de lipoproteínas de muy baja densidad (VLDL), TG y colesterol total (CT), y negativamente con el colesterol de lipoproteínas de alta densidad (HDL-C)[33]. En pacientes con hipercolesterolemia familiar hereditaria y con hiperlipidemia familiar hereditaria, afecciones que se caracterizan por niveles elevados de CT, LDL-C y un incremento significativo del riesgo de sufrir enfermedad coronaria prematura, se ha descrito un elevado nivel sérico de TNF-α[34,35].

Segundo, la inactivación del TNF-α puede afectar el metabolismo lipídico. El boqueo de la unión del TNF-α a su receptor celular por medio de Ac. monoclonales o receptores solubles, es un tratamiento utilizado en enfermedades como la artritis reumatoide. El boqueo de la unión del TNF-α a su receptor celular provee evidencia directa del rol del TNF-α en el metabolismo lipídico. La administración de anticuerpos monoclonales anti-TNF-α humano (Infliximab) a pacientes con artritis reumatoide, aumenta los niveles de HDL-C y disminuye el índice aterogénico[36,37], pero este es un efecto que sólo se mantiene en el corto plazo. Estudios más recientes, indican que la administración de Ac. anti-TNF-α monoclonales a largo plazo produjo un incremento de las concentraciones plasmáticas de CT y LDL-C y el índice aterogénico luego de 6 meses y 1 año desde el inicio de la terapia. Durante la terapia, los cambios en el estado inflamatorio se correlacionan negativamente con los cambios en los niveles de HDL-C y positivamente con la

variación del índice aterogénico. Los autores concluyen que un año de tratamiento con Infliximab es probable que conduzca a un modelo más pro-aterogénico en las concentraciones de lípidos plasmáticos[38]. En otro estudio similar, la administración de Ac. anti-TNF-α a pacientes con AR durante dos años produjo un incremento del CT, LDL-C y de los índices LDL/HDL y CT/HDL, y luego de 3 meses de tratamiento el HDL-C disminuyó significativamente[39]. Todo parece indicar que el TNF- regula los lípidos séricos por medio de mecanismos complejos, por lo que se debe continuar estudiando el efecto del bloqueo del TNF-α sobre las concentraciones séricas de lípidos, con especial énfasis en los efectos a largo plazo de este bloqueo.

Tercero, la administración de estatinas a pacientes hipercolesterolémicos disminuyen los niveles séricos de TNF-α lo cual se ha descrito como un efecto no lipídico de las estatinas que juega un rol importante en la disminución del riesgo cardiovascular del paciente. Las estatinas son fármacos inhibidores de la enzima 3-hidroxi-3-metilglutaril-coenzima A reductasa (HMG-CoA reductasa), que bloquean la síntesis endógena de colesterol, lo cual disminuye los niveles séricos de colesterol. La simvastatina y la atorvastatina disminuyen los niveles séricos de IL-6 y de TNF-α en pacientes hiperlipémicos[40]. En otro estudio donde se determinó el efecto de la dieta y de la simvastatina sobre los marcadores serológicos de estrés oxidativo e inflamación, se obtuvo como resultado que comparado con la dieta sola, el tratamiento de los pacientes con dieta y simvastatina disminuyó significativamente los niveles de TNF-α de la molécula de adhesión intercelular tipo-1 (ICAM-1), de la PCR y del fibrinógeno[41]. También se ha reportado que el tratamiento con atorvastatina disminuye los niveles séricos de TNF-α, IL-1, IL-6, ICAM-1 y PCR en pacientes hipercolesterolémicos[42].

Cuarto, el TNF-α inhibe la actividad de la LPL. La LPL es una enzima clave en la hidrólisis de los TAG de los quilomicrones (QM) y de las VLDL, ya que descompone los TAG a ácidos grasos libres y glicerol, liberándolos en músculo y tejido adiposo. En un estudio se determinó el efecto del TNF-α sobre la actividad de LPL en tejido adiposo humano en cultivo. La adición de TNF-α al medio de cultivo causó una inhibición dosis-dependiente de la actividad de la LPL, causada por una inhibición de los niveles de mRNA de la LPL y una inhibición en la síntesis proteica de esta enzima[43]. Este resultado ha sido confirmado por otros estudios[44], e indica que el TNF-α es un potente inhibidor de la expresión del gen de LPL en tejido adiposo.

En estudios realizados en sujetos en un amplio rango de IMC, se determinó la relación entre la expresión del TNF-α y la actividad de LPL en el tejido adiposo. Los resultados indicaron que los sujetos obesos presentaron mayor expresión del TNF-α en comparación con las controles normopeso, y la expresión del TNF-α se correlacionó negativamente con la actividad de la LPL[45,46]. En muchos estudios se ha relacionado la obesidad con un estado de hipertrigliceridemia. La disminución de la actividad de la LPL puede explicar en parte la hipertrigliceridemia observada en obesos, debido a la incapacidad para degradar los triacilglicéridos de las VLDL y los QM.

Quinto, el TNF-α inhibe la expresión de APO AI y APO E en hepatocitos, interfiriendo en la síntesis de HDL. Las HDL son sintetizadas en hígado e intestino, siendo su función transportar el colesterol de los tejidos del organismo hasta el hígado para ser eliminado. Las APO AI y APO E son apolipoproteínas presentes en la estructura de las HDL. La APO AI participa activamente en el transporte reverso del colesterol y activa la lecitina-colesterol acil transferasa (LCAT), que cataliza la hidrólisis de un ácido graso de la fosfatidilcolina (lecitina) presente en las partículas de HDL en su estado naciente o discoidal y lo esterifica con el colesterol dando lugar al colesterol esterificado que pasa al interior de la partícula de HDL discoidal. El tratamiento con TNF-α de células humanas HepG2 en cultivo suprimió la expresión de la proteína APO AI y la secreción de APO E de una manera dosis-dependiente, además, también suprimió los niveles de mRNA de APO AI[47,48]. Estos resultados indican que el TNF-α puede estar implicado en la disminución de los niveles séricos de HDL al disminuir la síntesis de las apoproteínas que forman parte estructural de las HDL.

Sexto, el TNF-α disminuye la síntesis de HDL en células intestinales humanas. El tratamiento con TNF-α de las células Caco-2 en cultivo (línea celular de carcinoma de colon humano) inhibe la síntesis de HDL y de APO AI[49], modulando el metabolismo lipídico intestinal.

Por otra parte, el transporte reverso del colesterol se ve facilitado por un transportador de la superficie celular llamada ABCA1 *(ATP-binding cassette transporter A1)*. Este transportador media el paso limitante en la formación de HDL, promoviendo el flujo de colesterol y los fosfolípidos hacia la APO AI en las HDL[49]. Las mutaciones en ABCA1 son responsables del fenotipo de la enfermedad de Tangier. Este trastorno se caracteriza por una deficiencia severa de HDL, la acumulación de ésteres de colesterol en los macrófagos en diferentes tejidos, y aterosclerosis prematura[50,51]. Así, es evidente que ABCA1 es crítico para la síntesis de las partículas de HDL y desempeña un papel protector en la prevención de la aterosclerosis. Se ha descrito que el TNF-α disminuye la expresión de ABCA1 en las células Caco-2 en cultivo[52], lo cual puede disminuir los niveles de HDL e interferir en el flujo de colesterol hacia las APO A1. La disfunción en la síntesis de HDL en hígado e intestino inducida por el TNF-α puede llevar a bajos niveles de HDL y a un incremento del riego cardiovascular, lo cual es de particular importancia en obesos.

Séptimo, el TNF-α puede afectar el metabolismo y le excreción de colesterol al inhibir en hepatocitos la expresión y la actividad de la enzima colesterol-7α-hidroxilasa, enzima clave de la síntesis de sales biliares a partir del colesterol en el higado[53]. Además, el TNF- disminuye la actividad de las enzimas esterol-27 hidroxilasa y oxiesterol 7α-hidroxilasa, las enzimas clave en

la vía alternativa de síntesis de sales biliares[54]. El colesterol se elimina del organismo al ser convertido en ácidos y sales biliares las cuales son secretados en la bilis hacia el intestino para desecharse por heces fecales. Estos resultados indican que el TNF-α puede disminuir la excreción de colesterol al inhibir la producción de sales biliares, favoreciendo un acúmulo de colesterol que finalmente estará disponible para una mayor síntesis de lipoproteínas en el hígado.

Octavo, el TNF-α aumenta la expresión del receptor de LDL (LDL-r) en hepatocitos humanos, favoreciendo el acúmulo de colesterol en hepatocitos, lo que juega un papel importante en el desarrollo de la afección clínica Hígado Graso-No Alcohólico[55,56].

Por lo hasta ahora descrito, se sugiere que el TNF-α tiene un profundo efecto sobre la respuesta celular a la insulina y sobre el metabolismo lipídico. Esto hecho es de particular importancia en los sujetos obesos, que presentan una mayor producción de TNF-α y un estado inflamatorio subclínico que juega un papel principal en el desarrollo de las enfermedades asociadas a la obesidad. Las investigaciones a realizar deben ir conducidas a determinar los distintos factores que inducen el estado de inflamación subclínica en sujetos obesos, lo cual puede llevar a nuevos blancos terapéuticos para prevenir las complicaciones relacionadas con los niveles elevados de TNF-α y con la obesidad.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(5):1758-1771
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Calcium ingestion and obesity control

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Abstract

Introduction: **Obesity is a risk factor for other non-transmissible chronic diseases. It has been suggested calcium intake helps to control obesity, but there is no consensus about this.**

Objective: **Analyze the studies published on this topic in order to highlight issues to be further explored in future studies.**

Methods: **A literature review was conducted using the PUBMED, Science Direct, Scielo, Scopus, Medline and CAPES electronic scientific basis. Studies, which evaluated the effect of calcium ingestion in energy metabolism, body weight, and body composition, published from 2000 through 2011, were analyzed.**

Results and discussion: **The results of most of the interventional studies selected suggest that calcium ingestion may favor the reduction of the anthropometric measures and improve body composition. The discrepancy in the results of the observational studies is probably due to methodological differences. It seems that the benefits are only detected when a low calcium habitual ingestion (≈ 700 mg/day or lower) is increased to about 1,200-1,300 mg/day.**

Conclusion: **When assessing the effect of calcium derived from supplements, the investigators should test higher bioavailability compounds. If the calcium source is the dairy product, it is necessary that to consider and isolate the impact of other nutrients present in these foods. Longer term studies should be conducted to assess the effect of calcium on energy metabolism.**

(*Nutr Hosp.* 2012;27:1758-1771)

DOI:10.3305/nh.2012.27.6.5977

Key words: *Calcium. Energy metabolism. Body weight. Body composition.*

INGESTA DE CALCIO Y CONTROL DE LA OBESIDAD

Resumen

Introducción: **La obesidad es un factor de riesgo para otras enfermedades crónicas no transmisibles. Se ha sugerido que el consumo de calcio ayuda a controlar la obesidad, pero no hay un consenso al respecto.**

Objetivo: **Analizar los estudios publicados sobre este tema con el fin de destacar los aspectos a investigar en estudios futuros.**

Métodos: **Se realizó una revisión bibliográfica utilizando las bases de datos electrónicas PUBMED, Science Direct, Scielo, Scopus, Medline y CAPES. Se analizaron los estudios que evaluaban el efecto de la ingesta de calcio sobre el metabolismo energético, el peso corporal y la composición corporal, publicados desde 2000 a 2011.**

Resultados y discusión: **Los resultados de la mayoría de los estudios intervencionistas seleccionados sugieren que la ingesta de calcio podría favorecer la reducción de las medidas antropométricas y mejorar la composición corporal. La discrepancia de los resultados de los estudios observacionales probablemente sea debida a diferencias metodológicas. Parece que los beneficios sólo se detectan cuando una ingesta habitual de calcio baja (~ 700 mg/día o menor) se incrementa hasta cerca de 1.200-1.300 mg/día.**

Conclusión: **Cuando se evalúa el efecto del calcio derivado de los suplementos, los investigadores deberían evaluar la biodisponibilidad de los preparados. Si la fuente de calcio son los productos lácteos, es necesario que consideren y aíslen el impacto de otros nutrientes presentes en estos alimentos. Deberían realizarse estudios a largo plazo para evaluar el efecto del calcio sobre el metabolismo energético.**

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DOI:10.3305/nh.2012.27.6.5977

Palabras clave: *Calcio, Metabolismo energético, Peso corporal, Composición corporal.*

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Recibido: 1-VI-2012.
Aceptado: 3-VII-2012.

Abbreviations

NTSD = Non-Transmissible Chronic Diseases.
PTH = Parathyroid Hormone.
RDA = Recommended Dietary Allowance.
NHANES = National Health and Nutrition Examination Survey.
FAS = Fatty Acid Synthase.
UCP2 = Uncoupling protein 2.
BMI = Body Mass Index.
WC = Waist Circumference.
EAR = Estimated Average Requirement.
DEXA = Dual Energy X Ray Absorptiometry.

Introduction

Non-transmissible chronic diseases (NTSD) are a global health problem.[1] It causes serious impacts on health, leading to several adverse effects on life quality of people, favoring the occurrence of premature deaths and high costs for society.[2] Cardiovascular diseases, cancer, chronic respiratory diseases and diabetes are responsible for 60% of deaths around the world.[3] If effective prevention and control measures are not taken, it is estimated that 41 million people will die from a NTSD by 2015.[2]

Obesity stands out among the NTSD because it is a risk factor for other diseases such as dyslipidemia, cardiovascular diseases, diabetes, hypertension, câncer.[1,2,4-6] Overweight and obesity are responsible for 2.6 million deaths per year.[2] Regardless of its complex and multifactorial etiology,[7] the decrease in the levels of physical activity and the increase in energy intake are strong environmental determinants for this situation.[2,7,8] Many researchers have focused on the identification of the combination of macronutrients capable of regulating body weight, but the effect of micronutrients still needs to be further explored.[9-12] Minerals participate in the energy metabolism and in the secretion and action of insulin,[13] and may interfere in the control of obesity.

Calcium, the most abundant mineral in the human body, is involved in various physiological processes: muscle contraction, cell adhesion, hormones and neurotransmitters release, glycogen metabolism, cell proliferation and differentiation, blood clotting, nerve or synapthetic impulse transmission and structural support of the skeleton.[14, 15] In addition, it has been suggested that it may assist body weight control. Two possible mechanisms of action have been proposed to explain this effect. It seems that when high quantities of calcium is consumed, it binds to dietary fat forming insoluble compounds, reducing fat absorption and hence the amount of calories generated from this absorption.[16,17] Calcium ingestion is also important to maintain normal blood calcium levels, preventing the increase of $1,25(OH)_2D_3$ and parathyroid hormone (PTH), which in turn can promote increased levels of intracellular Ca^{2+}, activating lipogenic routes.[18]

However, there is no consensus in the results of studies evaluating the effects of calcium intake on body weight and body composition,[11,19-29] and in energy metabolism.[11,17,30-32] It is possible that the outcomes may be affected by the source of calcium tested. Although the results of some studies suggest that calcium originated from the supplements has no effect,[20,22,24,27,29] others demonstrate positive effects in controlling obesity.[21,33,34] It has been suggested that dairy products may have a stronger effect than supplements.[18,33] However, exact the reason why this occurs is not known.[17,27,35,36]

The new recommendation for calcium intake (Recommended Dietary Allowance (RDA) = 1000 mg/day) is based on its effects on bone health, since there is no consensus on its effects on NTSD.[38] According to some authors, to obtain the beneficial effects on body weight and NTSD calcium intake should range from 1,000 to 1,200 mg/day.[39] It is unclear whether the effects are dose dependent, but the knowledge of the minimal dosage capable of resulting in positive effects is important to improve adherence and effectiveness in response to the mineral intake and to minimize the costs with NTSD.[29]

Due to the increase in obesity prevalence, the effect of diet in its etiology and the limited number of longitudinal clinical studies publish about this topic so far, it is necessary to conduct well-designed studies to assess the effect of high calcium intake on resting energy expenditure, body weight, and body fat control.[12,19] Therefore, the purpose of this review is to highlight issues to be further explored in future studies to clarify the possible effect of calcium intake on anthropometry, body composition and energy metabolism.

Methodology

Articles published from 2000 to 2011, in which the effects/association of calcium intake on/with body weight, body composition and energy metabolism were selected. A literature review was conducted in order to find articles in the electronic databases PUBMED, Science Direct, Scielo, Scopus, Medline and CAPES Journals.

Using the following indexing terms in English or in Portuguese: "calcium intake and obesity", "calcium intake and weight control", "calcium intake and weight loss", "calcium intake and body composition", "calcium intake and energy metabolism," "calcium intake and fat oxidation", "calcium intake and energy intake".

Possible mechanisms through which calcium may favor obesity control

The inverse relationship between calcium intake and body weight was observed since the 1st National Health

and Nutrition Examination Survey (NHANES) in 1984.[40] However, due to the lack of a possible mechanism of action to explain this association made this topic was not explored at that time. Today, the mechanisms by which calcium may control body weight and the magnitude of this effect are not well understood.[22] However, two possible mechanisms of action have been suggested. These mechanisms will be presented below.[30,41,42]

Increased fat excretion

It has been postulated that the interaction of calcium with fatty acids forming insoluble soaps can reduce the absorption and increase the excretion of these fatty acids, contributing to body weight reduction.[16,17,43]

In a crossover study, the effect of two treatment types on fat excretion in adult men was assessed. One of the treatments contained ≈ 410 mg/day of dietary calcium. The other contained 1,800 mg of calcium citrate malate plus 400 mg/day of dietary calcium (total of ≈ 2,200 mg/day). Calcium citrate malate, a soluble form of calcium, was administered together with fatty acids. Saturated fatty acids excretion doubled after the high calcium treatment compared to the low content one.[43] In another study, the effect of the consumption of a diet containing calcium-free chocolate (≈ 950 mg/day) and of another containing chocolate supplemented with calcium (calcium carbonate) was compared (≈ 1,855 mg/day). Once again, the excretion of saturated fatty acids was increased approximately two times after the consumption of the chocolate supplemented diet.[16] The results of these last two studies suggest that fatty acids should be consumed with calcium in the same meal so that fat excretion increase can take place.

Fecal fat excretion was 2.5 times higher after the consumption of a diet containing 1,800 mg/day of calcium and 15% protein compared to two other test diets (500 mg/day of calcium + 15% of protein and 1,800 mg/day of calcium + 23% of protein). According to the authors, a higher protein intake may favor calcium binding to phosphorylated proteins. Therefore, fatty acids would be free to be absorbed in the intestine, reducing the effects of calcium intake on fat excretion.[17]

The results of these studies suggest that calcium consumption ≥ 1,800 mg/day may be effective to reduce fat absorption, and that the joint ingestion of that mineral with fatty acids is important for that effect to occur. It should be noted, however, that this amount is higher than the recommended daily intake of calcium.[38] It has been shown that in some populations calcium intake is less than what is recommended.[41,42,44-48]

It should be emphasized that in two of the previously mentioned studies[17,43] there was an increase in urinary calcium excretion in response to the higher calcium intake, suggesting that the amount of the ingested

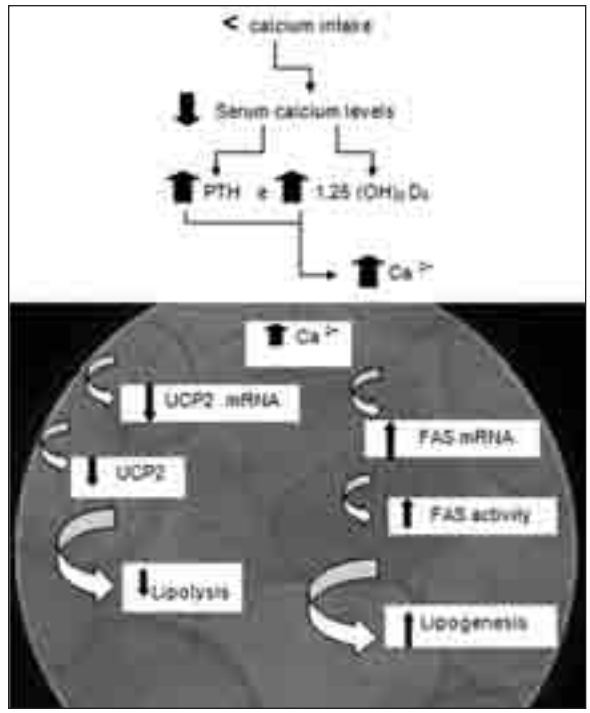


Fig. 1.—Mechanism of action of calcium proposed by Zemel et al., 2000.[18] The low intake of the mineral, reduces the serum calcium levels by stimulating the increase of PTH and 1,25(OH)$_2$D$_3$ levels. As a result there is an incrase in the intracellular levels of Ca^{2+} that can stimulate lipogenesis and distributive lipolysis.

calcium capable of increasing fat excretion may be lower than the ones tested. However, in one of these studies,[17] the higher urinary excretion was observed only when the high calcium intake was associated with high protein intake (1,800 mg/day + 23% protein). It has been demonstrated that an increase in protein consumption may increase calcium urinary excretion.[49]

Increased levels of intracellular Ca^{2+}

Some authors suggest that the effect in response to calcium consumption would be small to explain the magnitude of the observed effects on body weight and body composition. Besides that the amount to be consumed to possibly lead to these effects is very high.[33,50] Therefore, the mechanism proposed by Zemel et al. (2000)[18] (fig. 1) has been pointed out as the more consistent one to explain how low calcium intake would contribute to excess weight.[42]

The analysis of human adiposities indicated that the levels of 1,25(OH)$_2$D$_3$ and PTH can increase the intracellular levels of Ca^{2+} and inhibit lipolysis.[18] The results of human adipose tissue culture studies showed that the treatment with 1,25(OH)$_2$D$_3$ induced an increase of intracellular Ca^{2+} in a dose dependent form, increased by 40% the activity of fatty acid synthase (FAS), increased from 2 to 2.5 times the expression of mRNA FAS and inhibited the lipolysis in 35%,[51] reducing in

40% the expression of mRNA of uncoupling protein (UCP2), which is involved in the regulation of thermogenesis and energy metabolism and the levels of UCP2 in 50%.[52]

On the other hand, a higher consumption of calcium is capable of preventing weight gain, reducing body fat and increasing thermogenesis. These effects were observed in an animal study, which ate one of the four types of diet. 1) 0.4% of calcium diet, 2) 1.2% of calcium (0.4% dietary calcium + 0.8% from $CaCO_3$ supplement), 3) 1.2% of calcium (0.4% non-dairy source + 0.8% derived from dairy) and 4) 2.4% (0.4% non-dairy source + 2% derived from dairy). Although in terms of quality the effects of calcium from supplement were equivalent to dairy, the effects of calcium from dairy were stronger.[18]

Animal studies also support this evidence.[35,53,54] The consumption of a low calcium (0.4%), high fat, and sucrose diet doubled the concentration of intracellular Ca^{2+}. On the other hand, the consumption of diets containing 1.2 and 2.4% of calcium reduced the concentration to 50%, besides leading to greater reduction on body weight, body fat, mRNA FAS expression, FAS activity, and increased lipolysis, UCP2 expression, and body temperature. A greater increase body temperature, and a greater reduction in body weight, body fat, activity and expression of FAS was observed in response to the consumption of dairy calcium compared to calcium carbonate.[35] Parra et al. (2008)[54] verified that the consumption of a calcium supplemented diet reduced body weight and body fat in laboratory animals. But no changes were observed in the levels of UCP2. The effect of the consumption of a diet enriched with milk serum protein, calcium and vitamin D to that of a diet with low content of these nutrients were tested. Both test diets had high fat and sucrose content. Although food intake and body weight were not affected, it was observed that the animals that were fed the enriched diets had less body fat, and there was an increase in lean body mass.[53] However, the results of this study cannot be attributed to any specific nutrient (protein, vitamin D or calcium).

The consumption of a calcium-rich diet by laboratory animals led to less body weight and body fat gain, increased UCP2 expression, higher lipolysis rates, and higher body temperature than those that consumed a diet with low calcium content. These results suggest that calcium and dairy products may modulate adiposity independently of caloric restriction. In quantitative terms, the consumption of the high calcium derived dairy products diet resulted in the greatest effects than the diet continuing calcium from fortified cereal.[37]

This is useful for explaining the effect of calcium in adiposities and in rodents, but there it is necessary to conduct studies involving human beings to test this mechanism.[19] Although investigations in animals support this hypothesis, there is no homogeneity in the results of the studies in terms of some parameters assessed; for example the expression of UCP2.[35,52,53,54] There is also a study involving animals in which body fat was not affected after the ingestion of diets with low, normal amount of calcium and supplemented with calcium.[55]

The reasons why the effects of dairy products could exert more striking effects, quantitatively, than calcium supplements are not clear.[17,35,50] In animals similar effects were observed in reducing the concentration of intracellular Ca^{2+}. It has been suggested that other dairy products components may act by a route independent of that concentration. However, neither the mechanism of action nor the responsible components of dairy products have been identified,[35] and future studies are needed to determine the effect of these components.[50]

In human studies, the effects of calcium in body weight and body fat are not consistent either.[32] If we think about the proposed mechanism[18] it is important to find out not only the possible effects of calcium but also the role that PTH and $1,25(OH)_2D_3$ may play in humans body weight and body fat regulation.[11]

Effect of vitamin D ingestion and serum levels

There is no consensus on the relationship between serum levels of vitamin D and adiposity. The results of an intervention study indicated that there is no difference between serum levels of vitamin D between obese and normal weight people.[56] However, after being submitted to UV-B, obese subjects showed a more attenuated response to changes in the levels of $1,25(OH)_2D_3$ than the normal weight subjects, regardless of the absence of a significant difference in the production of $1,25(OH)_2D_3$.[56] This result suggests that obese individuals release less vitamin D from the skin to the circulation.[56] It has been claimed that vitamin D is stored in the adipose tissue, and that the higher the fatty tissue, the lower the serum levels of 25(OH)D.[57] In the previously mentioned study,[56] it was verified a negative correlation between body mass index (BMI) and serum levels of $1,25(OH)_2D_3$ only after UV-B radiation treatment. Obese patients had lower serum levels of 25(OH)D. BMI was negatively correlated with 25(OH)D concentrations only after the ingestion of 50000 IU of that vitamin.[56]

These results have been corroborated in other studies. Parikh et al. (2004) verified lower levels of 25(OH)D and $1,25(OH)_2D_3$ in obese compared to normal weight adults.[36] Vitamin D deficiency (levels of 25(OH)D < 20 ng/ml) was considered a predictor of metabolic syndrome in obese patients with BMI > 40 kg/m^2. It was observed a higher occurrence of deficiency between obese patients presenting metabolic syndrome.[58] The levels of 25(OH)D were negatively correlated with body fat,[57,59] BMI,[59,60] waist circumference (WC) and skinfolds.[59]

These data contradict what has been claimed by Zemel et al. (2000),[18] that is high serum levels of

vitamin D would increase the body weight and adiposity. Therefore, further studies are needed to evaluate the influence of serum levels of vitamin D on body weight, body composition and energy metabolism.

Thus, there has also been evaluated the possible influence of the ingestion of this vitamin on body weight and body composition. In the fourth Tromso Study, the usual intake of vitamin D by adults was negatively correlated with BMI. The odds ratio for obesity was equivalent to 2.24 in men and 1.51 in women. These participants were in the lowest quartile of intake of the vitamin. However, the authors report that cod liver oil the cod fish itself were the highest source of vitamin D habitually consumed by the subjects of that study. Therefore, the effect observed may have been caused by other substances present in these foods.[61] In the Women's Health Study, the usual intake of vitamin D was negatively associated with BMI and WC. However, this association was independent of calcium intake.[62] These results suggest that habitual intake of vitamin D alone has little influence on body weight and body composition.

The effect of vitamin supplementation on body weight, body fat and anthropometric indicators was also evaluated. The addition of 400 IU/day of vitamin D and 1,200 mg/day of calcium associated with caloric restriction (700 kcal/day) did not affect BMI, body weight, body fat and WC in women with excess body weight and obese, which had a habitual calcium intake < 800 mg/day.[63] However, when among women with habitual calcium intake < 600 mg/day, there was a reduction in body weight, BMI and body fat percentage.[64]

In women with lower calcium intake than the recommendations, it was verified that the supplementation with 400 IU of vitamin D associated with 1,000 mg of elemental calcium for seven years reduced the risk of body weight gain.[65] However, weekly supplementation of 20,000 IU (≈ 2,857/day) and 40,000 IU (≈ 5,714/day) of vitamin D associated with 500 mg of calcium/day, did not promote a significant reduction of BMI, body weight, body fat percentage, waist circumference and hip circumference, compared to a placebo containing 500 mg of calcium/day.[60] In another study, the supplementation of 2,000 IU of vitamin D for seven days did not change serum calcium levels, resting metabolic rate and the expression of genes related to lipogenic and lipolytic process such as FAS and UCP2.[66] Despite the increased vitamin D serum levels and reduced PTH concentrations obtained as a result of the daily 3,332 IU vitamin D supplementation for 12 months associated with a body weight reduction program it did not affect the body weight compared to placebo.[67]

These results suggest that the supplementation in higher dosages than the RDA (600 IU)[38] does not result in body weight control. However, the intake of vitamin D in amounts equivalent to the Estimated Average Requirement (EAR = 400 IU)[38] may exert a beneficial effect when combined with calcium supplementation and applied to people with low habitual dietary calcium intake. This data raise questions about which nutrient would be responsible for such benefits (vitamin D or calcium). It is possible that the benefits are due to the combined effect of these nutrients and they are conditioned to the habitual intake of the population evaluated.

Human prospective intervention studies assessing the effect of the adequacy of vitamin D status for NTSD treatment and prevention are still scarce. Therefore, the impact of vitamin D nutritional status in these diseases should be evaluated in future studies.[68]

Effect of PTH serum levels

Some studies have shown higher levels of PTH in obese individuals compared to normal weight individuals.[36,56,59,69] There has been observed a positive association between BMI and PTH levels, PTH and body fat in adults,[37] and between PTH levels and body fat, BMI, waist circumference and skinfold sum in elderly.[59] In the fifth Tromso Study it was observed that each increase of 1 pmol/l in PTH caused an increase of 0.17 kg/m^2 in men and 0.26 kg/m^2 in women in terms of BMI. The relative risk for obesity was 1.40 for men and 1.48 for women, who were in the highest PTH levels quartile.[69] These studies are consistent with the mechanism proposed by Zemel et al. (2000).[18]

In adiposites and skeletal muscles PTH stimulates phospholipids C resulting in an increase in intracellular Ca^{2+}. This increase can impair the ability of catecholamine to activate lipolysis and stimulates cAMP phosphodiesterase, which suppresses lipolysis. The increase in calcium concentration in adiposities can increase the expression of fatty acid synthase and increase lipogenesis.[70]

Although some studies show that both calcium and vitamin D intake and their serum levels may influence the levels of PTH,[69,71] studies involving young adults in Brazil, showed no association between PTH levels versus serum calcium levels and 25(OH)D and calcium intake.[72] Studies involving the supplementation of vitamin D (40,000 IU vitamin D + 500 mg of calcium)[60] and dosage of 3,332 IU of that vitamin caused a reduction of PTH concentrations.[67] These results highlight the controversy as to the triggering factor responsible for the increase in PTH levels. With respect to vitamin D, supplemented quantities capable of reducing the PTH levels are higher (40,000 IU) or close (3,332) to the upper intake levels for this vitamin (4,000 IU).[38]

Observational studies

The results of some studies have suggested the occurrence of possible effects and relationships dosage/effect of calcium intake on body weight and body composition. It has been claimed that calcium intake may explain 3 to 10% of body weight varia-

tion.[73,74] Analyzing the data from NHANES III, it was observed that an increase in calcium intake from 400 mg to 1,000 mg for a year in obese American subjects caused a reduction of 4.9 kg.[18] In middle aged women it was observed that the probability of overweight is reduce from 14.6% to 4.1% and of becoming obese reduces from 1.4 to 0.2%, when calcium intake increases from 10 to 20 mg calcium/g of protein. Besides that the weight gain/year reduces from 0.425 to -0.011 kg when the ingestion increases from 9 to 20 mg calcium/g of protein.[74] According to Eagan et al. (2006), in young normal weight people it is expected a body fat gain of 1.26 kg in 18 months in response to the ingestion of 500 mg of calcium from dairy products/day while in response to an ingestion of 1,200 mg/day it is expected a weight loss of 0.631 kg.[57]

The main features of these observational studies can be seen in table I. Despite the suggestions of the existence of a possible ratio dosage/effect previously mentioned, he analyses of a larger number of observational studies show a non-conclusive scenario in terms of: the existence of effects, dosages and source of calcium (dairy products or supplement). This can be attributed to methodological differences among these studies in term of how the anthropometric data, body composition, and dietary intake were obtained, and even with regards to types of analyses used in these studies.

Anthropometric and body composition data have been obtained by self-reports, electrical bioimpedance and anthropometry (weight, height, BMI, WC), computed tomography and dual energy x ray absorptiometry (DEXA). It is clear that the use of some of these methodologies may affect the accuracy of the measurements. It has been shown, for example, that self-report data may differ from the measured data, which may interfere in the nutritional status classification.[75,76] Some authors have reported that bio-impendence may underestimate body fat percentage compared to DEXA in overweight people.[77,78] These methods have different capabilities and applicability of measuring body fat and its distribution.[79]

Food intake data have been obtained through dietary recalls and food frequency questionnaires. The number of recalls and frequency in which they were used vary between studies. The 24-hour recall and food record only represent the habitual diet if applied for several nonconsecutive days.[80,81] The accuracy of these methods depends on the number of days in which they are repeated. According to Willett et al. (1998),[80] these dietary recalls should be applied from 3 to 10 times.

Another important factor to be considered is the need to adjust the statistical analyses regarding the consumption of nutrients such as proteins and vitamin D that may affect results.[23,37,64,82-88]

Nevertheless, the results of these studies suggest that calcium derived from dairy products or from supplements and even the dairy products themselves are associated with body weight and body composition, and that a low calcium intake (≈ 600-700 mg/day) is related to a higher body weight and adiposity. Due to methodological differences and to the fact that observational studies do not prove causality it is necessary to analyze the results obtained in the existing intervention studies.

Intervention studies

Effect of calcium intake on anthropometry and body composition

The characteristics of some intervention studies on the effect of calcium on body weight and body composition are shown in table II. The results of sudies that evaluated the effects of the calcium intake derived from the supplements,[20,22,27] mostly suggest that calcium does not affect body weight and body composition. However, there are some common points in these studies that need to be better explored. It is observed that the tested dosage of the supplements was higher than 1,000 mg/day, which added to the habitual food intake lead to a daily ingestion higher than the recommendation.[38] If calcium affects anthropometry and body composition, there may be a threshold level after which this effect does not occur. Another issue is that in these studies the average habitual intake of the participants was higher than 800 mg/day and results of observational studies[19,25] suggest that there is a strong association when the habitual intake is lower than ≈ 700 mg/day. Therefore, there must be a lower intake threshold where the association can be detected. The administration different forms of supplements can also interfere in the results. According to one of the proposed mechanisms of action of calcium, the ingestion of supplement in association with food is important for the mineral to cause the expected effect.[16,43] Furthermore, the ingestion in association with certain types of foods may increase the calcium bioavailability.[49]

The results of intervention studies[28,33,83] reinforce the assumption that when participants have low habitual intake < ≈ 700 mg/day, calcium seems to really affect body weight and body composition.[19,25] In the study conducted by Kabrnová-Hlavatá et al. (2008)[84] there was no significant effect of calcium. However, in the treatment groups fat free mass was preserved compared to placebo. Furthermore, it is likely that the absence of effects may be attributed to the amount of calcium consumed (850 mg/day), which was lower than the RDA (1,000 mg),[38] or to the short duration of the study.

In a study conducted by Zemel et al. (2004),[33] the effect of calcium derived from dairy products was quantitatively higher than that derived from calcium supplements. The possible reason for this possible superiority remains unexplained. This difference may be due to the bioavailability of the mineral in the supplement. Therefore, it becomes interesting to conduct studies to test the effect of supplements having higher bioavailability such as calcium citrate.[49,89,90] It is

Table I

Characteristics of the observational studies that evaluated the effect of calcium intake on anthropometric measures and body composition

Reference	*Subjects characterisics (number of participants/ gender/age/BMI*	*Observation period*	*Daily habitual calcium intake (mg/day)*	*Results*
Jacqmain et al. 2003[19]	235 ♀ and 235 ♂ 20-65 years old ≈ 25-31 kg/m²	–	< 600 600-1,000 > 1,000	There was a correlation between calcium intake and body fat %, fat mass, BMI, WC in women. Body weight, BMI, fat %, fat mass, WC, and abdominal fat were significantly higher in women with calcium intakes < 600 mg
González et al., 2006[21]	10,591 ♂♀; 53-57 years old	8-12 years (retrospective)	♀ 1,094 ± 558 ♂ (1,115 ± 557) (diet + supplement)	Women who used supplements had lower weight gain than those who did not use. Dosage of supplements > 500 mg was associated with less weight gain.
Rajpathak et al. 2006[24]	19,615 ♂ 40-75 years old ≈ 25 kg/m²	12 years	Baseline-Total: 791 diet: 736 End-total: 899, diet: 765	Increase in calcium intake was not associated with changes in body weight; even when dietary calcium, dairy products, supplements was evaluated separately
Eliat-Adar et al. 2008[25]	2,975♂♀; 47-79 years old ♀ 31.7 ± 0.1 kg/m² ♂ 29.9 ± 0.2 kg/m²	–	♀ 610 + 8.56 ♂ (680 ± 14.11)	BMI (0.80 kg/m² lower) and body fat (1.28% lower) in the highest quintiles of calcium intake (> 1,200 mg) compared to the lowest (≈ 300 mg)
Vergnaud et al. 2008[26]	2,267 ♀♂; ♀ 50.8 ± 4.3 years old; ♂ 51.5 ± 4.4 years old; ♂ 25.2 ± 3 kg/m²; ♀ 23.5 ± 3.7 kg/m²	6 years	♂ 1,048 ± 354 ♀ 909 ± 319	Consumption of milk and yogurt was inversely associated with changes in body weight and WC in men who where overweight at baseline. In women who where normal weight yogurt consumption was positively associated with weight change and changes in WC was positively associated with the consumption of milk in the ones that were overweight. These associations were not explained by calcium intake.
Azadbakht et al. 2005[23]	827 (357 ♂ and 470 ♀); 18-74 years old; 24.9 ± 4-26.8 ± 4.1 kg/m²	–	< 1.7 servings dairy; 1.7-< 2.3 servings; 2.3-< 3.1 servings; > 3.1 servings	Subjects with higher dairy products ingestion had lower BMI and WC. After adjusting for calcium intake this association became weaker. However, when protein intake was adjusted, the associations were not affected
Esteves, Rodrigues & Paulino, 2010[48]	50 ♀; ≥ 25 a ≤ 44 years old; 26.30 ± 6.20 kg/m²	–	438.7	There was no negative correlation between BMI, fat %, WC

BMI: Body mass index; WC: Waist circumference.

Table II

Characteristics of intervention studies that assessed the effect of calcium intake on anthropometric measures and body composition

Reference	*Subjects characterisics (number of participants/ gender/age/BMI*	*Study duration*	*Habitual calcium intake (mg/day)*	*Treatment*	*Results*
Shapses et al. 2004[22]	100 ♀ pre and post-menopausal ≈ 40-60 years old; ≈ 33 kg/m²	25 weeks	600-1,000	1) 500 kcal + Placebo. 2) 500 kcal + 1,000 mg of calcium (source calcium citrate malate or calcium citrate).	There was no difference in body weight and body fat between treatments.
Reid et al. 2005[20]	1,471 ♀ post-menopausal; ≈ 74 years old, ≈ 26.5 kg/m²	30 months	Placebo = 878 ± 430 Ca = 861 ± 390	1,000 mg of calcium (source calcium citrate). Placebo.	Body weight, BMI, body fat and lean mass did not differ between the groups.
Yanoski et al. 2009[27]	340 ♀♂; 38.8 years old; 33.2 ± 6.8 kg/m² (Ca) and 33.6 ± 6.8 kg/m² (placebo)	2 years	Placebo = 878 ± 430 Ca = 887 ± 350	1,500 mg (source calcium carbonate). Placebo.	Body weight, body fat, BMI, WC, hip circumference did not differ between the groups.
Faghih et al. 2011[83]	85 ♀; ≈ 38 years old; ≈ 31 kg/m²	25 weeks	Control: 512.85 ± 72.71 Ca: 532.29 ± 149.77 Milk: 484.58 ± 131.07 Soy: 509.61 ± 101.19	1) 500 kcal; 500-600 mg of calcium. 2) 500 kcal; 1,300-1,400 mg of calcium (800 mg = source calcium carbonate). 3) 500 kcal; 1,200-1,300 mg of calcium (source milk). 4) 500 kcal; 1,200-1,300 mg of calcium (source soy extract fortified with calcium).	Changes in WC were higher in groups 3 and 4. Changes in body weight and BMI wew higher in the group that ingested calcium from milk.
Zemel et al. 2004[33]	32 ♀♂; 49 ± 6 years old; 34.9 ± 4.3 kg/m²	24 weeks	500-600	1) 500 kcal; 400-500 mg of calcium, placebo. 2) 500 kcal; 1,200-1,300 mg of calcium (800 mg = source calcium carbonate). 3) 500 kcal; 1,200-1,300 mg of calcium (source dairy).	Body weight and body fat, including in the trunk region, reduced after the consumption of the diets with high calcium content. Such effects were higher in the diet in which the calcium was derived from dairy products.
Kabrnová et al. 2008[64]	67 ♀; 49.1 ± 12.1 years old; 32.2 ± 4.1 kg/m²	4 weeks	Not specified	1) 600 kcal; diet with 350 mg of calcium + placebo. 2) 600 kcal; diet with 350 mg of calcium + 500 mg of calcium (calcium carbonate). 3) 600 kcal; diet with 350 mg of calcium + 500 mg of calcium (calcium citrate + phosphate + lactate).	There were no differences between the groups in terms of anthropometric measurements and body composition. In the placebo group, there was reduction in free fat mass, tending to be significant compared to the groups treated with calcium.
Wennersberg et al. 2009[28]	76 ♀ 37 ♂; ♀♂: 56.7 ± 7/51.2 ± 8.1 years old; 30 ± 3.3 kg/m² (control) 30.1 ± 3.6 kg/m² (milk)	6 months	Control: 644 ± 252 mg Milk: 815 ± 364 mg	The participants included in the milk group were instructed to increase 3-5 servings of dairy products daily intake.	Weight, BMI, WC, body fat did not change in the course of the study. When evaluating only the people who had basal ingestion lower than 700 mg there was reduction of WC in the milk group.
Gunther et al. 2005[12]	135 ♀; 18-30 years old; 22.1 ± 3.1 kg/m² (control); 23.3 ± 3.9 kg/m² (average) 22.4 ± 2.6 kg/m² (high)	1 year	Control: 695 ± 263 Average 727 ± 269 High: 693 ± 281	1) Control: keep usual intake. 2) 1,000-1,100 mg of Ca (source dairy). 3) 1,300-1,400 mg of Ca (source dairy).	There was no differents in the group as to weight, BMI, and body composition between treatments.
Reid et al. 2010[29]	323 ♂; ≈ 57 years old; ≈ 26 kg/m²	2 years	1) 800 ± 360 mg 1) 870 ± 470 mg 1) 930 ± 510 mg	1) Placebo. 2) 600 mg of Ca (source calcium citrate) 3) 1,200 mg of Ca (source calcium citrate) divided into two daily doses	There was an increase in fat mass in the groups and reduction in the lean mass with no difference between the groups.

BMI: Body mass index; WC: Waist circumference.

also necessary to consider the way in which the supplement is administrated, that is if it is administrated in association with food or not.

Some authors attribute the stronger observed effect to other nutrients present in dairy products such as vitamin D[64] and proteins (branched chain amino acids, such as leucine).[23,37,82-88] It has been claimed that proteins could increase satiation, thermogenesis and avoid muscular mass loss.

Leucine would lead to greater fat mass loss, would stimulate the recovery of muscle protein synthesis thus reducing the loss of lean body mass.[85-88] In the culture of cells, leucine stimulated fat oxidation in muscular cells and inhibited FAS in adiposites.[82] On the other hand, in the elderly, the ingestion of 1g of protein /kg of body weight, containing 7.5 g of leucine/day did not change body composition.[91]

In general, it is suggested that a high protein intake is required to exert the effect. In a recent review study it was shown that in most studies, there is a reduction in energy intake when 30% or more of total energy intake derives from protein.[87] The comparison of the effect of the consumption of isocaloric and isoglycidic diets containing 15% and 30% of protein showed no difference in adults resting metabolic rate. However, there was a reduction in hunger sensation and energy intake, and an increase in satiety in the group that consumed the diet containing 30% of protein.[92] In contrast, in another study, obese subjects consumed diets containing 30% of protein (1,600 mg of calcium) x 15% of protein (600 mg calcium) and the same fat content (30%). There was no difference in energy intake, body weight and body composition. Only in women who consumed 1.4 g of protein/kg body weight lean body mass was preserved. Furthermore, in the group that consumed 30% of protein there was lower ingestion of fiber and higher ingestion of cholesterol. One cannot distinguish if the observed effects are related to increased intake of protein, calcium or reducing carbohydrate ingestion.[93] Similarly, in studies in which there is great change in the percentage of macronutrients, the effects can perhaps be attributed to these changes.

Besides confirming the effectiveness of increased protein intake on obesity control, future studies should assess how this type of dietary intervention effects renal function, calcium balance, cardiovascular diseases risk and other adverse effects associated with chronic high protein consumption before high protein diets are recommended for weight loss,[87,92] once there is currently no Tolerable Upper Intake Level for protein.[85]

These facts can lead to discussion about the most appropriate distribution of macronutrients to maintain healthy body weight. The current recommended distribution of macronutrients considering the total energy expenditure is: protein - 10 to 15%, carbohydrate - 45 to 65%; fat - 20 to 35%.[94] The distribution of macro nutrients tested by some authors, that is (protein: 16%, fat: 35%, carbohydrates: 49%),[33] (protein: 25,3%, fat: 28,7%, carbohydrate: 46%),[84] and (protein:18%, fat: 27%, carbohydrate: 55%)[83] differ from the current healthy diet recommendations and the ones recommended for weight loss (protein: 15%, fat: 30%, carbohydrate: 55%).[5,95-97] Therefore, the effect of increased calcium ingestion associated with the consumption of a diet presenting the recommended macronutrient distribution is not known.

The results of these intervention studies suggest that a daily intake of about 1,200-1,300 mg/day can affect body weight and body composition.[57] On the other hand, the results of the studies that assessed the association between increased fat excretion versus body composition and anthropometry it seems that the ingestion of large quantities of calcium has no effect, suggesting the existence of an upper threshold quantity capable of controlling obesity.

Effect of calcium intake on energy expenditure and substrate oxidation

The main characteristics of the studies that evaluated the effect of calcium on energy expenditure and substrate oxidation are presented in table III. Although the results of the studies indicate that the highest consumption of calcium or dairy products might increase lipid oxidation, this topic is still controversial.[34]

In the study conducted by Teegarden et al. (2008),[34] there was an increase in fat oxidation only in the group treated with supplement. The authors report that other components of dairy products might prevent the increase in fat oxidation induced by calcium. In that study,[34] the protein content was higher (16% SEV) than the recommendations.[5,94-97] The results of that study[34] contradicts the idea that protein could increase thermogenesis and lipid oxidation.[85,86,88,98] In other studies, the consumption of diets containing 20%[30] and 23%[17] of total energy intake derived from proteins did not affect energy expenditure and fat oxidation. But this aspect should be further explored because in two other studies[17,32] the consumption of a diet containing 15% of protein did not change such parameters. However, in that second study, the percentage of carbohydrate in the diet (60% of total energy intake) may have inhibited fat oxidation, since the carbohydrate is the preferred source of energy.[99] This reinforces the importance to assess how the distribution of macronutrients affects the results of such studies.

In terms of the effects of calcium intake on body weight and body composition a minimum and maximum consumption seems to be necessary for the effects to be detected. It is not known whether these assumptions can be extrapolated in terms of the effects on energy expenditure and substrate oxidation. It has been observed that there is an increase in calcium urinary excretion in participants that are used to consuming that mineral above the RDA (1,000 mg),[17,30] which start consuming a higher calcium dose.[31,32] In a study conducted by Jacobsen et al. (2005),[17] it was

Table III

Characteristics of intervention studies that evaluated the effect of calcium intake on substrate oxidation and energy metabolism

Reference	*Subjects characterisics (number of participants/ gender/age/BMI*	*Study duration*	*Habitual calcium intake (mg/day)*	*Treatment*	*Results*
Jacobsen et al. 2005[17]	2 ♂, 8 ♀; 24.2 ± 2 years old; 26.5 ± 2 kg/m²	1 week each diet	1,214 ± 264	1) 500 mg of calcium; 15% protein. 2) 1,800 mg of calcium; 15% protein. 3) 1,800 mg of calcium; 23% protein.	The treatments did not promote significant changes in energy expenditure, metabolic rate at rest and energy balance for 24 hours. Protein oxidation higher in the diet with 23% protein.
Boon et al. 2005[30]	12 ♂; 28 ± 2 (20-40 years old): 25.2 ± 0.6 kg/m²	7 days each stage	1,027 ± 82	1) Low Ca/Low Lat = 300-400 mg of Ca. 2) Alto Ca/Low Lat = 1,200-1,300 mg Ca (source calcium carbonate). 3) Alto Ca/High Lat = 1,200-1,300 mg of Ca (source diary).	Energy expenditure in total for 24 hours and at differente times (sleep, at rest, during exercise) did not differ. There was no difference between balances of substrates and in the expression of RNA of genes related to lipid metabolism.
Teegarden et al. 2009[34]	24 ♀; Control/calcium/dairy: 23.3 ± 3.2/22.4 ± 3.7/21.0 ± 2.6 years old; 28.8 ± 2.9/27.1 ± 1.59/ 27.2 ± 1.09 kg/m²	12 weeks	C = 690 ± 85 Ca = 592 ± 104 Lat = 688 ± 85	1) C = 500 mg of Ca/(-500 kcal). 2) Ca = 500 mg + 900 mg of Ca (source: calcium carbonate)/(-500 kcal). 3) Lat = 500 mg + 800 mg of Ca (source: dairy/(-500 kcal).	No differences were observed as to total energy expenditure. There was an increase in fat oxidation in the calcium group.
Bortolotti et al. 2008[31]	3 ♂, 7 ♀; 22.2 ± 1.2 years old; 28.5 ± 1.4 kg/m²	5 weeks each session	586 ± 137	1) Placebo. 2) Supplement = proteins, minerals, lactose and 800 mg of calcium (source: calcium phosphate).	No changes were observed in energy expenditures and significant changes in macronutrients oxidation. No changes were found in the turnover of glycerol and markers of lipid metabolism in fat tissue.
Sampath, Havel & King, 2008[32]	15 ♀; 29 ± 8 years old; 27.8 ± 2.7 kg/m²	12 weeks	616 ± 211	Supplementation with 1,500 mg of calcium (source calcium carbonate).	No changes were observed at the levels of glycerol and in oxidation.
Gunther et al. 2005[11]	19; Low/high calcium: 20.3 ± 2.5/19.4 ± 2.6 years old; 20.2 ± 2.4/24.0 ± 3.3 kg/m²	1 year	1) Low calcium; 643 ± 167 2) High calcium: 663 ± 242	1) Keep usual calcium ingestion. 2) Consume 1,000-1,400 mg/day meals were served with high (> 500 mg) and low (< 100 mg) of calcium on test days.	The acute increase did not affect fat oxidation after low chronic ingestion of calcium. Chronic increase of calcium ingestion increased fat oxidation.
Melanson et al. 2003[9]	21 ♂, 14 ♀; 31 ± 6 years old; 23.7 ± 2.9 kg/m²	24 hours	1,222 ± 116 (485-4,109)	The individuals could select the foods. Average ingestion = 1,046 ± 55 (477-1,768) mg/day.	Acute calcium ingestion was positively correlated with fat oxidation and inversely related to respiratory quotient. Acute calcium ingestion from dairy products was also positively associated with fat oxidation. Total calcium ingestion was a higher predictor than the ingestion of dairy products calcium. Habitual calcium ingestion was not correlated to fat oxidation.

observed an increase in urinary excretion of calcium only when the diet was high in protein content (23%). However, Farnsworth et al. (2003)[93] did not detect differences in excretion when comparing the effect of the consumption of a diet containing 30% of protein (1,600 mg calcium) versus a 15% of protein (600 mg calcium) diet. Data available in the literature are insufficient to define the minimum amount of dietary calcium required to induce a change in energy expenditure and substrate utilization.[32]

The number of human studies in which energy expenditure and substrate oxidation was assessed is small and the duration of these studies is short compared to the number of studies that anthropometry and body composition were evaluated. For example, Boon et al. (2005)[30] tested the effect of the consumption of 1,200-1,300 mg of calcium /day for a period of seven days. On the other hand, it has been suggested that acute changes in calcium ingestion can modify fat oxidation rates. However, these modifications tend revert within a relatively short period of time.[32]

Thinking about the relationship between the effects of calcium intake and study duration, Melanson et al. (2003)[9] and Gunther et al. (2005)[11] obtained different results. In the first study,[9] the authors observed that an acute increase in calcium intake leads to an increase in fat oxidation, whereas if the usual intake of calcium is already high that parameter is not affected. According to Gunther et al. (2005),[11] fat oxidation is only affected when a higher calcium ingestion occurs for longer periods of time. The duration of these two studies and the usual ingestion of the participants were quite different. In addition, both involved normal weight participants. It is not known if the response would differ in overweight people. It has been argued that in normal weight people, the increase in calcium ingestion may cause alter substrate oxidation, without, however, affecting energy expenditure. That would happen as a mechanism to maintain body weight and prevent excessive weight loss due to the increase in fat oxidation.[11]

Final considerations

The results of the studies published so far suggest that the consumption of calcium derived from supplements and dairy products can reduce the anthropometric measurements and favor the achievement of an adequate body composition. However, there is no homogeneity in the results of the observational studies probably due to the differences in the methodologies used. It appears that the benefits of calcium ingestion are only detected in individuals with low habitual consumption of the mineral, and there may be an upper threshold amount of calcium from which this effect is no longer observed. Further studies are needed to confirm this fact and to determine what these values are. It should be emphasized that higher availability supplements should be tested and the administration form must be considered. In the case of dairy products, it is necessary to isolate the effect of other nutrients also present in these foods. It should also be taken into consideration the interference of the distribution of macronutrients in the possible effects of calcium. To better understand the consequences of calcium intake on energy expenditure and substrate oxidation in addition to these factors, longer duration studies should be conducted.

Acknowledgements

To CAPES for the master's scholarship grant and to FAPEMIG for the support (CDS-APQ-01677-10).

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1772-1781
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Importancia del género *Alternaria* como productor de micotoxinas y agente causal de enfermedades humanas

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Resumen

***Alternaria* es un género fúngico muy común, donde se incluyen numerosas especies saprofitas, endofíticas y patógenas ampliamente distribuidas en el suelo y la materia orgánica en descomposición. Incluye especies patógenas que pueden invadir los cultivos vegetales antes y después de la recolección y es responsable de considerables pérdidas económicas, debido a que reduce el rendimiento de las cosechas y produce alteraciones en los vegetales durante su almacenamiento. Las especies del género *Alternaria* sintetizan más de 70 metabolitos secundarios tóxicos para las plantas (fitotoxinas), algunos de los cuales afectan también a personas y animales, por lo que se consideran micotoxinas. La exposición a las toxinas de *Alternaria* spp. se ha relacionado con la aparición de efectos adversos para la salud en personas y animales y, en muchos casos, se ha demostrado que tienen capacidad genotóxica, mutagénica, carcinogénica y citotóxica. Las micotoxinas de *Alternaria* spp. se han aislado de frutas (manzana, pera, melón, albaricoque, uvas, uvas pasas, fresa, aceituna, cítricos e higos desecados), hortalizas (tomate, pimiento y zanahoria) y tubérculos (patata), así como de numerosos alimentos procesados elaborados con materias primas contaminadas (zumos, conservas, salsas, etc.). Además, determinadas especies de *Alternaria* están implicadas en infecciones y alergias humanas, hasta el punto de que *Alternaria* se considera uno de los principales géneros fúngicos causantes de alergias.**

(*Nutr Hosp.* 2012;27:1772-1781)

DOI:10.3305/nh.2012.27.6.6017

Palabras clave: *Micotoxinas. Alternaria spp. Toxicidad. Alimentos. Enfermedad humana.*

THE IMPORTANCE OF GENUS *ALTERNARIA* IN MYCOTOXINS PRODUCTION AND HUMAN DISEASES

Abstract

***Alternaria* is a cosmopolitan fungal genus that includes saprophytic, endophytic and pathogenic species, widely distributed in soil and organic matter in decomposition. Plant pathogenic species affect cereals, vegetables and fruit crops in the field and during storage. *Alternaria* spp. contamination is responsible for some of the world's most devastating plant diseases, causing serious reduction of crop yields and considerable economic losses. *Alternaria* species produce more than 70 secondary metabolites which are toxic to plants, and some of these phytotoxins have been chemically characterised and reported to act as mycotoxins to humans and animals. Exposure to *Alternaria* spp. toxins has been linked to a variety of adverse effects on human and animal health, including genotoxic, mutagenic, carcinogenic and cytotoxic effects. *Alternaria* spp. mycotoxins have been isolated from fruits (apple, pear, melon, apricot, grapes, raisins, strawberry, olive, citrus fruits and dried figs), vegetables (tomato, pepper and carrot) and tubers (potato), as well as from several processed foodstuffs manufactured with damaged raw materials (juices, preserves, sauces, etc.). Moreover, *Alternaria* spp. are frequently associated with allergic reactions in sensitized individuals.**

(*Nutr Hosp.* 2012;27:1772-1781)

DOI:10.3305/nh.2012.27.6.6017

Key words: *Mycotoxins. Alternaria spp. Toxicity. Food. Human disease.*

Abreviaturas

ALT: Altenueno.
AOH: Alternariol.
AME: Alternariol monometil éter.
TeA: Ácido tenuazónico.
ATX: Altertoxina.
SEE: Síndrome del Edificio Enfermo.

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Recibido: 17-V-2012.
1.ª Revisión: 22-VI-2012.
Aceptado: 17-VII-2012.

Introducción

Los mohos son microorganismos cuya presencia en los alimentos puede tener consecuencias diversas y en ocasiones son de gran utilidad en la industria alimentaria. Determinadas especies de géneros fúngicos como *Aspergillus, Penicillium, Rhizopus, Mucor* o *Geotri-*

chum participan en la maduración de quesos, productos cárnicos crudos madurados y alimentos orientales a base de soja y cereales. Además, se emplean para la producción de metabolitos usados como aditivos en diferentes tipos de alimentos como zumos, licores o productos lácteos[1]. Sin embargo, también tienen consecuencias negativas, ya que la contaminación fúngica es una de las principales causas de alteración de los alimentos y la presencia de determinadas especies de géneros como *Fusarium*, *Penicillium*, *Aspergillus* o *Alternaria* constituye una amenaza para la salud de los consumidores debido a la producción de compuestos tóxicos para el ser humano (micotoxinas).

Las autoridades sanitarias europeas han establecido niveles máximos permitidos de determinadas micotoxinas como las aflatoxinas B_1, B_2, G_1, G_2 y M_1, ocratoxina A, patulina, deoxinivalenol, zearalenona y fumonisinas B_1 y B_2, y toxinas T-2 y HT-2 en los alimentos[2,3,4,5]. Sin embargo, son cada vez más frecuentes los casos de productos hortofrutícolas y sus derivados en los que se demuestra la presencia de especies del género *Alternaria,* muchas de ellas productoras de micotoxinas como el altenueno (ALT), alternariol (AOH), alternariol monometil éter (AME), ácido tenuazónico (TeA) y altertoxinas (ATX). Este aumento en la incidencia de alimentos contaminados con *Alternaria* spp. y/o sus micotoxinas, causa especial preocupación por la repercusión que puede tener su presencia en la salud de los consumidores, debido a su elevado poder toxicológico[6,7]. Además, determinadas especies de *Alternaria* también se encuentran relacionadas con la aparición de infecciones y alergias en personas[8,9].

Micotoxinas producidas por el género *Alternaria*

Las micotoxinas son metabolitos secundarios de bajo peso molecular (Pm < 700 kDa) producidos por determinadas especies fúngicas al final de la fase exponencial de crecimiento y durante la fase estacionaria. La ingestión, inhalación o absorción cutánea de estos compuestos provoca efectos adversos en la salud de animales y personas. Las micotoxinas pueden contaminar los alimentos, los piensos o las materias primas utilizadas para su elaboración, originando un grupo de enfermedades o trastornos, denominados micotoxicosis[1,10,11].

Las especies del género *Alternaria* sintetizan más de 70 metabolitos secundarios tóxicos para las plantas (fitotoxinas), pero solo una pequeña parte de ellos se han caracterizado químicamente e identificado como compuestos tóxicos para personas y animales, por lo que se consideran micotoxinas (tabla I)[7,12,13]. Atendiendo a sus efectos sobre las plantas, las toxinas de *Alternaria* spp. se agrupan en toxinas no específicas de hospedador y toxinas específicas de hospedador. Las toxinas no específicas de hospedador afectan a una a una amplia variedad de especies vegetales, aunque en muchos casos su modo de acción no se ha identificado. Sin embargo, si se ha determinado la actividad fitotóxica de toxinas como el zinniol, el TeA y la tentoxina. El TeA inhibe la síntesis proteica, mientras que el zinniol afecta a la permeabilización de la membrana y la tentoxina inhibe la fosforilación debido a que se une a la cloroplasto ATP sintetasa[14]. Además, algunas de estas toxinas no específicas como el AOH, AME, ALT, TeA y ATX se han relacionado con la aparición de enfermedades en personas y animales[13].

Tabla I
Toxinas producidas por las principales especies toxigénicas del género Alternaria

Especie	*Toxina*[a]
Alternaria alternata	AOH, AME, ALT, Altenusina, ATX-I, ATX-II, ATX-III, Tentoxina, AAL toxinas, AS toxina, AF toxina, ACR toxina, ACTG toxina
A. arborescens	AOH, AME, ALT, ATX-I, TeA
A. brassicae	AOH, AME, TeA
A. brassicicola	AOH, AME, TeA, ATX-I
A. citri	AOH, AME, ALT, TeA
A. cucumerina	AOH, AME, Macrosporina
A. dauci	AOH, AME, Macrosporina, Zinniol
A. gaisen	AOH, AME, ALT, Altenusina, TeA, ATX-I
A. infectoria	Infectopironas, Novae-zelandinas
A. longipes	AME, TeA, ATX-I
A. mali	TeA, ATX-I, ATX-II, ATX-III, Tentoxina, AM-toxina
A. porri	AOH, AME, ALT, TeA, Altersolanol, Tentoxin, Macrosporina, Zinniol
A. radicina	ALT, TeA, ATX-I, Radicinina, Radicinol
A. solani	AOH, AME, Altersolanol, Macrosporina, Zinniol
A. tenuissima	AOH, AME, ALT, TeA, ATX-I, Tentoxina

[a]AOH: Alternariol; AME: Alternariol monometil éter; ALT: Altenueno; TeA: Ácido tenuazónico; ATX: Altertoxina; TEN: Tentoxina.

Las toxinas específicas de hospedador afectan a un menor número de especies vegetales. Por lo general, causan alteraciones severas en determinadas plantas donde se desarrolla la especie de *Alternaria* productora de estas toxinas. Aunque se han determinado los mecanismos de acción de algunas toxinas específicas de hospedador, como las AAL toxinas, ya que desempeñan un papel crucial en la patogenicidad de la especie que colonizan, todavía existen pocos estudios sobre su toxicidad en animales[12].

El estudio de la síntesis de micotoxinas se realiza mediante el cultivo de las especies productoras en condiciones y medios de cultivo óptimos. Sin embargo, para que se produzcan las micotoxinas, además de la presencia de la especie productora, influyen las condiciones ambientales y la composición del sustrato. En la tabla I se muestran las especies productoras de las principales toxinas de *Alternaria* spp. descritas. Toxinas como el AOH, AME, ALT, TeA, ATX, TEN o altenu-

sina pueden sintetizarlas diferentes especies del género[15,16]. Por el contrario, otras toxinas como el altersolanol, la macrosporina o el zinniol, solo las producen las especies del grupo de *A. porri*, al que pertenecen *A. porri, A. dauci, A. solani* y *A. cucumerina*[17,18], mientras que las especies englobadas en el grupo de *A. infectoria* son las únicas productoras de infectopironas y novaezelandinas[19,20]. Por último, existen toxinas que solo las sintetizan determinadas cepas patógenas. En ese grupo se incluyen las AAL toxinas *(A. alternata* f. sp. *lycopersici)*, AS toxina *(A. alternata* patotipo del girasol), AF toxina *(A. alternata* f. sp. *fragariae)*, ACR toxina *(A. alternata* patotipo del limón rugoso) y ACTG toxina *(A. alternata* patotipo de las mandarinas). La AK toxina y la AM toxina se han detectado en peras y manzanas contaminadas con cepas patógenas de *A. gaisen* y *A. mali*, respectivamente[14,21,22]. Sin embargo, no todas las cepas pertenecientes a estos grupos producen siempre dichas toxinas, ya que la síntesis está determinada por las condiciones ambientales en que se desarrolla el moho.

Las especies de *Alternaria* pueden producir micotoxinas en intervalos de temperatura muy amplios, pero siempre con actividades de agua superiores a 0,90. Young et al.[23] determinaron que la máxima producción de TeA en semillas de algodón inoculadas con *A. tenuissima* tiene lugar a 20 ºC y con un 37,5% de humedad del grano. Magan y Lacey[24] identificaron una producción máxima de AOH, AME y ALT en granos de trigo contaminados con *A. alternata* a 25 ºC y 0,98 a_w, mientras que en pulpa de tomate contaminada con varias especies de *Alternaria*, las condiciones óptimas para la producción de AOH, AME y TeA identificadas por Pose et al.[25] fueron de 21 ºC/0,954 a_w, 35 ºC/0,954 a_w y 21 ºC/0,982 a_w, respectivamente. Por último, Oviedo y et al.[26], observaron máximos de producción de AOH y AME a 0,98 a_w, aunque la temperatura óptima dependía de la cepa de *A. alternata* que inoculaban en granos de soja irradiados.

Diversos estudios demuestran que la composición del sustrato en el que se desarrolla el moho influye en la producción de micotoxinas. En este sentido, aunque no existen datos sobre su influencia en la síntesis de micotoxinas de *Alternaria* spp., se ha descrito el efecto estimulante de determinados aminoácidos, ácidos grasos o metales como el zinc en la producción de aflatoxinas[27]. También se ha observado el efecto inhibidor de determinados compuestos fenólicos en la producción de varias micotoxinas[28,29].

Propiedades físicas y químicas de las micotoxinas de *Alternaria* spp.

Las toxinas de *Alternaria* spp. se clasifican en cinco grupos atendiendo a sus estructuras químicas:

- Dibenzo-α-pironas: AOH, AME y ALT.
- Perileno quinonas: ATX-I, -II, -III.
- Ácidos tetrámicos: TeA.
- AAL toxinas: AAL-TA1, AAL-TA2, AAL-TB1, AAL-TB2.
- Otras estructuras: TEN.

En la tabla II se muestran las propiedades bioquímicas de las principales toxinas de *Alternaria* spp. Estas micotoxinas se aislaron, caracterizaron e identificaron entre los años 1953 y 1986[7]. El estudio de las rutas de biosíntesis y el metabolismo del AOH, AME y ALT, demostró que se pueden conjugar con otras moléculas más polares como la glucosa, aminoácidos y sulfatos, presentes en los sustratos vegetales donde se producen. La formación de conjugados en los alimentos dificulta el desarrollo de métodos analíticos para su detección, debido a los cambios de polaridad que presentan respecto a las micotoxinas precursoras[30,31,32]. En cuanto al metabolismo de las toxinas, la hidroxilación del AOH, AME y el ALT y su conjugación con el ácido glucurónico y sulfatos se ha demostrado en estudios *in vitro*. Sin embargo, no se dispone de datos suficientes sobre la absorción, la distribución y excreción de las toxinas de *Alternaria* spp. en personas y animales.

Toxicidad de las micotoxinas producidas por *Alternaria* spp.

La exposición a las toxinas de *Alternaria* spp. se ha relacionado con la aparición de una gran variedad de efectos adversos en la salud de personas y animales. Determinados cultivos de *Alternaria* spp. son tóxicos en ratas, embriones de pollo y cultivos celulares humanos, y también son teratogénicos y fetotóxicos en ratones[33,34,35,36]. Además, los extractos de cultivos de *A. alternata* son mutagénicos en varios sistemas *in vitro* y cancerígenos en ratas alimentadas con piensos contaminados[37,38,39,40]. Por otra parte, Liu et al.[41] relacionaron el consumo de alimentos contaminados con *A. alternata* con una elevada incidencia de cáncer de esófago. Los efectos tóxicos que los cultivos de *Alternaria* spp. producen en los diferentes modelos *in vitro* e *in vivo* son muy variables, ya que dependen del tipo de micotoxinas sintetizadas (tabla III).

Dibenzo-α-pironas

AOH y AME son mutagénicos, genotóxicos, carcinogénicos y citotóxicos en cultivos celulares animales y bacterianos. Presentan una actividad mutagénica elevada tanto en cultivos de *Bacillus subtilis*[42], como de *Escherichia coli*[43,44], y baja en cultivos de *Salmonella* Typhimurium[40,45]. Los estudios de genotoxicidad demuestran que el AOH tiene mayor actividad que el AME[38,46,47,48,49]. En cuanto al poder carcinogénico de estas micotoxinas, no existen estudios exhaustivos en animales. Sin embargo, en ratones alimentados con 50-100 mg de

Tabla II
Propiedades bioquímicas de las principales microtoxinas producidas por Alternaria *spp.*

Toxina	*Nombre bioquímico*	*N.º CAS*	*Pm (Da)*	*Fórmula*
Alternariol (AOH)	3,7,9-Trihidroxi-1-metil-6*H*-dibenzo[*b,d*]piran-6-ona	641-38-3	258	$C_{14}H_{10}O_5$
Alternariol monometil éter (AME)	3,7-Dihidroxi-9-metoxi-1-metil-6*H*-dibenzo[*b,d*]piran-6-ona	23452-05-3	272	$C_{15}H_{12}O_5$
Altenueno (ALT)	(2*R*,3*R*,4a*R*)-rel-2,3,4,4a-Tetrahidro-2,3,7-trihidroxi-9-metoxi-4a-metil-6*H*-dibenzo[*b,d*]piran-6-ona	29752-43-0	292	$C_{15}H1_6{}^{o}{}_6$
Altertoxina I (ATX-I)	(1*S*,12a*R*,12b*S*)-1,2,11,12,12ª,12b-Hexahidro-1,4,9,12a-tetrahidroxi-3,10-perilenodiona	56258-32-3	352	$C_{20}H_{16}O_6$
Altertoxina II (ATX-II)	(7a*R*,8a*R*,8b*S*,8c*R*)-7a,8ª,8b,8c,9,10-Hexahidro-1,6,8c-trihidroxi-perilo[1,2-b]oxireno-7,11-diona	56257-59-1	350	$C_{20}H_{14}0_6$
Altertoxina III (ATX-III)	(1a*R*,1b*S*,5a*R*,6a*R*,6b*S*,10a*R*)-1a,1b,5a,6a,6b,10a-Hexahidro-4,9-dihidroxi-perilo[1,2-*b*:7,8-*b*‘]bisoxireno-5,10-diona	105579-74-6	348	$C_{20}H_{12}O_6$
Ácido tenuazónico (TeA)	(5*S*)-3-Acetil-1,5-dihidro-4-hidroxi-5-[(1*S*)-1-etilpropil]-2*H*-pirrol-2-ona	610-88-8	197	$C_{10}H_{15}O_3N$
Tentoxina (TEN)	Ciclo[*N*-metil-L-alanil-L-leucil-(*Z*)- , -didehidro-*N*metilfenilalanilglicilo]	28540-82-1	414	$C_{22}H_{30}O_4N_4$
AAL TA1 toxina	Ácido (2*R*)-1,2,3-Propanotricarboxílico, Éster 1-[(1*S*,3*S*,9*R*,10*S*,12*S*)-13-amino-9,10,12-trihidroxi-1-[(1*R*,2*R*)-1-hidroxi-2-metilbutil] -3-metiltridecilo]	79367-52-5	521	$C_{25}H_{47}O_{10}N$
AAL TA1 toxina	Ácido (2*R*)-1,2,3-Propanotricarboxílico, Éster 1-[(1*R*,2*S*,4*S*,10*R*,11*S*,13*S*)-14-amino-2,10,11,13-tetrahidroxi-4-metil-1-[(1*R*)-1-metilpropil]tetradecilo]	79367-51-4	521	$C_{25}H_{47}O_{10}N$
AAL TB1 toxina	Ácido (2*R*)-1,2,3-Propanotricarboxílico, Éster 1-[(1*S*,3*S*,10*R*,12*S*)-13-amino-10,12-dihidroxi-1-[(1*R*,2*R*)-1-hidroxi-2-metilbutil] -3-metilltridecilo]	176590-32-2	505	$C_{25}H_{47}O_9N$
AAL TB2 toxina	Ácido (2*R*)-1,2,3-Propanotricarboxílico, Éster 1-[(1*R*,2*S*,4*S*,11*R*,13*S*) -14-amino-2,11,13-trihidroxi-4-metil-1-[(1*R*)-1-metilpropil]tetradecilo]	176705-51-4	505	$C_{25}H_{47}O_9N$

Nº CAS: Chemical Abstracts Services Registry Number; Pm: Peso Molecular.

Tabla III
Principales efectos tóxicos provocados por las micotoxinas de Alternaria *spp.*

Micotoxina	*Efectos tóxicos*	*Referencias*
AOH	Actividad mutagénica en cultivos bacterianos	40, 42, 44, 45
	Actividad genotóxica en cultivos animales	38, 46, 47, 48, 49
	Actividad citotóxica en cultivos de camarón (*Artemia salina*)	51
AME	Actividad mutagénica en cultivos bacterianos	40, 42, 43, 44, 45
	Actividad genotóxica en cultivos animales	38, 47, 48
	Alteraciones precancerosas en mucosa esofágica de ratones	50
	Actividad citotóxica en cultivos de camarón (*Artemia salina*)	51
ALT	Actividad citotóxica en cultivos de camarón (*Artemia salina*)	51
TeA	Hemorragias internas en perros y aves	52
	Alteraciones precancerosas en mucosa esofágica de ratones	50
	Desorden hematológico en personas (Onyalai)	7, 53
ATX	Actividad mutagénica en el test de Ames	39, 40, 54, 55, 56, 57
	Actividad genotóxica en cultivos celulares de ratón (ATX-I y ATX-III)	58

AME por kg de peso durante 10 meses, se desarrollaron alteraciones precancerosas en la mucosa esofágica[50]. Por otra parte, los estudios de toxicidad del ALT en larvas de camarón *(Artemia salina)* en salmuera, pusieron de manifiesto que las dosis letales medias de ALT (375 g/mL) son muy superiores a las del TeA (75 mg/mL) y AOH (200 mg/mL)[51].

Ácido tenuazónico

La toxicidad del TeA se ha demostrado en plantas, embriones de pollo y en otras especies animales[52]. En perros, la ingesta de dosis diarias de 10 mg/kg de peso, provocó la aparición de hemorragias en diversos órganos. En las aves domésticas, una dosis de 10 mg/kg en

Tabla IV
Identidad y concentración de las micotoxinas de Alternaria *spp. detectadas en diversos alimentos*

Alimento	*Micotoxinas detectadas*[a]	*Concentración máxima (µg/kg)*	*Referencias*
Granos de cereales y derivados	AOH	2.320	Abd el-Aal[59]
	AME	7.451	Azcarate et al.[52]
	ALT	1.480	Abd el-Aal[59]
	TeA	8.814	Azcarate et al.[52]
	TEN	38	EFSA[13]
Semillas oleaginosas	AOH	1.800	Bottalico y Logrieco[6]
	AME	440	EFSA[13]
	TeA	5.400	EFSA[13]
	TEN	880	Kralova et al.[63]
	ALT	9	EFSA[13]
	ATX-I	80	EFSA[13]
Aceites de semillas	AOH	18	EFSA[13]
	AME	85	EFSA[13]
	TeA,	390	EFSA[13]
	TEN	67	EFSA[13]
Legumbres	AOH	290	Ostry et al.[66]
	AME	1.153	Barros et al.[65]
Hortalizas y derivados	AOH	8.756	Terminiello et al.[71]
	AME	1.734	Terminiello et al.[71]
	ALT	2	Noser et al.[76]
	TeA	4.021	Terminiello et al.[71]
	TEN	9,2	EFSA[13]
Frutas y derivados	AOH,	151	EFSA[13]
	AME,	42	EFSA[13]
	TeA	8.700	EFSA[13]
Bebidas alcohólicas	AOH,	7,59	Asam et al.[67]
	AME,	1,5	EFSA[13]
	TeA	175	Siegel et al.[62]
Alimentos infantiles	AME	3,3	EFSA[13]
	TeA	1	EFSA[13]

[a]Las concentraciones mínimas detectadas en todos los casos fueron de 0,01 µg/kg para el AOH y el AME, 1 µg/kg para el ALT, 2 µg/kg para el TeA y la TEN y 10 µg/kg para la ATX-I[13] , excepto en el caso del AME en legumbres que fue de 16 µg/kg[65].

el pienso disminuyó tanto la eficiencia alimenticia como la ganancia de peso e incrementó las hemorragias internas en las canales. Sin embargo, no se ha demostrado efecto mutagénico del TeA en cultivos bacterianos[39,40]. Al igual que con el AME, los ratones que consumieron pienso contaminado con TeA durante 10 meses, desarrollaron alteraciones en la mucosa esofágica, pero en este caso, la dosis diaria fue de 25 mg/kg[50]. Además, el consumo de sorgo contaminado con TeA, se ha relacionado con la aparición de un desorden hematológico en personas conocido como Onyalai[7,53].

Altertoxinas

Las ATXs presentan actividad mutagénica en el test de Ames[40,54,55,56]. La actividad mutagénica de las ATXs (ATX-I, II, III) en ratones es superior a la del AOH y AME, siendo la ATX-III la de mayor actividad[39,57]. El potencial mutagénico de la ATX-III es 10 veces inferior al de la aflatoxina B_1, que es la micotoxina con mayor actividad mutagénica en la especie humana[55,56]. También se ha demostrado que la ATX-I y la ATX-III son genotóxicas en cultivos celulares de ratón[58].

Presencia de micotoxinas de *Alternaria* spp. en alimentos y piensos

Las toxinas de *Alternaria* spp. se aíslan con frecuencia de una gran variedad de productos vegetales frescos y procesados (tabla IV). La presencia de micotoxinas de *Alternaria* spp. en cereales es muy común, debido al almacenamiento de los granos en condiciones favorables para el crecimiento del moho. En este sentido, se ha detectado AOH, AME, ALT, TeA o TEN en granos de trigo, cebada, avena, centeno, arroz y maíz. El procesado de los granos de cereales no evita la presencia de micotoxinas, como lo demuestra el hecho de que las

muestras de cereales de desayuno, harina, pasta o cerveza analizadas por diversos investigadores, contenían AOH, AME o TeA[13,52,59,60,61,62]. También se ha detectado la presencia de AME en papillas infantiles y TeA en alimentos infantiles que contenían cereales en su composición, lo cual causa especial preocupación, ya que estos alimentos son la base fundamental de la alimentación en las primeras etapas de la vida[13].

En semillas oleaginosas como la colza, girasol, sésamo y linaza también se ha determinado la presencia de AOH y AME. En las semillas de colza y linaza se ha detectado además ALT y en las de girasol y sésamo TeA. La TEN solo se ha aislado a partir de semillas de girasol y la ATX-I de semillas de sésamo. Por otra parte, las mismas toxinas que contaminaban las semillas se detectaron en las muestras de aceite de semillas de girasol y sésamo[13,63,64]. Asimismo, se ha encontrado AOH y AME en legumbres como las lentejas y la soja[65,66].

En numerosas frutas (manzana, pera, melón, albaricoque, uvas, uvas pasas, fresa, aceituna, cítricos e higos desecados), hortalizas (tomate, pimiento y zanahoria) y tubérculos (patata) se ha puesto de manifiesto la presencia de AOH, AME, ALT, TeA y TEN[6,61,67,68,69,70,71]. El consumo directo de frutas y hortalizas con putrefacción fúngica visible es improbable. Sin embargo, no es infrecuente aislar toxinas de *Alternaria* spp. a partir de alimentos procesados como salsas de tomate, ketchup, tomates desecados, conservas, mermeladas, vino o zumos de frutas (manzana, tomate, uva, naranja)[70,72,73,74,75,76,77,78]. La presencia de micotoxinas en alimentos procesados puede ser consecuencia de la utilización de materias primas con alteraciones fúngicas cuyos síntomas afectan solo a la parte interna, como ocurre en la putrefacción de las manzanas y los cítricos. Además, aunque se eliminen las zonas visiblemente alteradas, las toxinas de *Alternaria* spp. se pueden transferir a los tejidos circundantes[79]. Por otra parte, las industrias transformadoras no siempre disponen de métodos eficientes para detectar y eliminar completamente las materias primas afectadas con algún grado de alteración fúngica.

La presencia de micotoxinas de *Alternaria* spp. también se ha investigado en piensos. En este sentido, se han detectado cantidades elevadas de AOH, AME, ALT, ATX-I, TeA, TEN y AAL toxinas, en granos de cereales y semillas oleaginosas destinadas a la alimentación animal. Por lo general, las muestras que contenían mayores cantidades de micotoxinas tenían contaminaciones visibles de *Alternaria* spp., posiblemente debido a las condiciones de almacenamiento de los granos y semillas en las granjas, donde la elevada temperatura y humedad favorecen el crecimiento de determinadas especies de *Alternaria* y la producción de micotoxinas[61,65,80,81,82].

Exposición humana a las micotoxinas de *Alternaria* spp.

La Autoridad Europea de Seguridad Alimentaria ha publicado recientemente los resultados de un estudio nutricional realizado para evaluar la exposición diaria a AOH, AME, TeA y TEN en los grupos de población comprendidos entre los 18 y 65 años[13]. En este estudio se determinó que los niveles diarios de ingesta eran de 1,9-39 ng/kg de peso para el AOH, 0,8-4,7 ng/kg de peso para el AME, 36-141 ng/kg de peso para el TeA y 0,01-7 ng/kg de peso para la TEN. Aunque la exposición a las micotoxinas de *Alternaria* spp. no se ha estudiado en la población infantil, se estima que su ingesta es dos o tres veces mayor que en la población adulta. Las estimaciones realizadas en este estudio se han establecido teniendo en cuenta únicamente alimentos de origen vegetal, puesto que no se ha demostrado la presencia de micotoxinas de *Alternaria* spp. en alimentos de origen animal.

Control y prevención de micotoxinas en alimentos

La contaminación de los alimentos con micotoxinas se produce de manera natural y su concentración puede aumentar como resultado de las condiciones ambientales o de operaciones inadecuadas de recolección, almacenamiento y elaboración de los productos alimentarios. Por ello, es necesario disponer de programas de control que eviten la contaminación con mohos toxigénicos. Asimismo, se deben aplicar medidas preventivas que minimicen el desarrollo fúngico en los alimentos, tales como el almacenamiento en condiciones idóneas de temperatura, humedad relativa y atmósfera. En este sentido, las autoridades oficiales de control de los alimentos están estableciendo programas preventivos y procedimientos para minimizar los riesgos asociados a la contaminación de los alimentos con micotoxinas. Dentro de estos programas se incluyen las buenas prácticas agrícolas (GAP: *"Good Agricultural Practice"*) e industriales (GMP: *"Good Manufacturing Practice"*) y la aplicación del sistema de Análisis de Peligros y Puntos de Control Crítico (APPCC).

El sistema APPCC identifica y evalúa, mediante un enfoque estructurado y sistemático, los peligros que hay que controlar para garantizar la inocuidad de los alimentos desde la granja hasta la mesa. Para llevar a cabo la aplicación efectiva del sistema APPCC con relación a los peligros derivados de la presencia de mohos toxigénicos en los alimentos, es necesario disponer de técnicas rápidas para la detección de mohos productores de micotoxinas tanto en materias primas como en alimentos elaborados. Esto permitiría adoptar las medidas necesarias para apartar de la cadena alimentaria los productos que puedan suponer un riesgo para la salud del consumidor, impidiendo de esta forma la presencia de micotoxinas en los alimentos elaborados. En este sentido es necesario contar con herramientas capaces de detectar de una forma rápida y precoz la presencia de *Alternaria* spp. en alimentos, debido especialmente a que no existe una normativa que regule los niveles máximos permitidos de las micotoxinas de *Alternaria* en alimentos.

Tabla V
Alérgenos producidos por A. alternata aprobados por el Comité de Nomenclatura de Alérgenos de la OMS/IUIS

Alérgeno	*Tipo de proteína*	*Peso Molecular (kDa)*	*N.º de acceso (UniProt)*
Alt a 1	Glicoproteína dimérica	29 (14,5/16)	P79085
Alt a 3	Proteína de choque térmico	70	P78983
Alt a 4	Disulfuro isomerasa	57	Q00002
Alt a 5	Proteína ribosomal P2	11	P42037
Alt a 6	Enolasa	45	Q9HDT3
Alt a 7	Proteína YCP4	22	P42058
Alt a 8	Manitol deshidrogenasa	29	P0C044
Alt a 10	Aldehído deshidrogenasa	53	P42041
Alt a 12	Proteína ácida ribosomal P1	11	P49148
Alt a 13	Glutatión S-transferasa	26	Q6R4B4

El género *Alternaria* como agente causal de enfermedades humanas

Aunque el género *Alternaria* incluye principalmente especies patógenas de plantas, algunas especies también se encuentran relacionadas con la aparición de infecciones humanas. *A. alternata* y *A. tenuissima* producen la alternariosis cutánea, que se manifiesta con lesiones únicas o múltiples en forma de placas pardo-rojizas papulonodulares, pustulosas o ulcerocostrosas, localizadas en superficies corporales expuestas, siendo rara la diseminación sistémica. La alternariosis cutánea se considera una infección oportunista que aparece en personas inmunodeficientes, debido a que padecen síndrome de inmunodeficiencia adquirida (VIH), síndrome de Cushing, algún proceso tumoral, o que han recibido trasplantes de órganos[9,83,84]. Además, *A. alternata* y *A. infectoria* se han relacionado con la aparición de queratomicosis y endoftalmitis en personas que han sufrido un traumatismo o cirugía ocular[85,86,87].

La incidencia de *Alternaria* spp. en infecciones humanas no es muy elevada, ya que solo ocurre en casos de personas inmunodeficientes. Sin embargo, *Alternaria* es, junto con *Cladosporium,* uno de los principales géneros fúngicos causantes de alergias[8]. La incidencia de personas sensibilizadas frente a alérgenos fúngicos alcanza hasta el 30% de los pacientes analizados, aunque depende en gran medida de las condiciones geográficas y climáticas. *A. alternata* es la principal especie productora de alérgenos del género, causando reacciones cutáneas positivas en el 70% de los pacientes alérgicos a antígenos fúngicos[88]. La fracción alergénica producida por *A. alternata* es muy heterogénea. El Comité de Nomenclatura de Alérgenos de la OMS/IUIS ha secuenciado y aprobado diez alérgenos de esta especie (tabla V)[89,90,91,92]. El principal alérgeno es el Alt a 1, al que reconocen los anticuerpos IgE de más del 90% de los pacientes alérgicos a *A. alternata*. La respuesta alérgica es mayor frente a las esporas fúngicas que frente a los restos micelares u otras células fúngicas. En el caso de *Alternaria* spp., la respuesta alérgica se presenta clínicamente como reacciones asmáticas de tipo inmediato mediadas por IgE[91].

La abundancia relativa de conidios de *A. alternata* en el aire y su presencia en las casas con humedades convierte a este microorganismo en una fuente alergénica importante. La exposición a esporas fúngicas se diferencia de la exposición al polen en que las cantidades de esporas fúngicas por metro cúbico son mayores que las de granos de polen. Además, la exposición es más duradera, puesto que puede durar meses, mientras que la exposición a pólenes suele durar semanas. Esta exposición intensa y prolongada a *A. alternata* se asemeja a la exposición a restos epidérmicos de animales o a los ácaros del polvo y contribuye a la cronicidad y severidad del asma en las personas sensibilizadas frente a *Alternaria* spp.[93]. Por otro lado, la presencia de esporas de *Alternaria* spp. en el interior de los edificios se ha identificado como uno de los factores causantes del Síndrome del Edificio Enfermo (SEE). Se denomina así al conjunto de síntomas diversos que presentan los ocupantes de un edificio, y cuyas causas radican en el propio edificio[94,95]. La sintomatología relacionada con el SEE es muy variada, pudiendo llegar a ser compleja, ya que suele ser el resultado de la combinación de distintos efectos. Los síntomas más significativos incluyen:

- Irritaciones de ojos, nariz y garganta.
- Sequedad de la piel.
- Síntomas generales: dolor de cabeza, fatiga mental, y pérdida de capacidad de memoria a corto plazo.

Conclusiones

Muchas especies del género *Alternaria* producen micotoxinas, aunque solo se ha demostrado la producción natural en alimentos y piensos del TeA, AOH, AME, ALT, TEN, ATX-I y toxinas AAL. En estudios

realizados *in vitro*, se ha demostrado la capacidad genotóxica, mutagénica, carcinogénica y citotóxica del AOH, AME, ATX o TeA. Por el contrario, no existen datos relevantes sobre la genotoxicidad y carcinogenicidad en estudios *in vivo*, aunque si se han demostrado alteraciones precancerosas en la mucosa esofágica de ratones. Actualmente, la UE no tiene establecidos límites máximos para ninguna de las micotoxinas de *Alternaria* spp. aisladas en alimentos. Sin embargo, teniendo en cuenta los datos sobre toxicidad y la creciente presencia de estas toxinas en alimentos, determinados organismos de la UE como el Instituto Federal de Evaluación de Riesgos de Alemania[96], el Comité de Científicos Alimentarios de la República Checa[97] y la Autoridad Europea de Seguridad Alimentaria[13], consideran necesario realizar nuevos estudios sobre la toxicidad de las micotoxinas producidas por *Alternaria* spp. y su presencia en alimentos, con el fin de disponer de datos objetivos que permitan evaluar la situación actual con vistas a establecer límites máximos permitidos. Por último conviene señalar que, además de su importancia como productor de micotoxinas, el género *Alternaria* es uno de los principales mohos causantes de alergias y se encuentra implicado en la aparición de infecciones en personas inmunodeficientes.

Agradecimientos

Este trabajo ha sido financiado por el Ministerio de Ciencia e Innovación (proyecto AGL2006-07659) y por la Comunidad de Madrid (proyecto Vigilancia Sanitaria 2009/AGR-1489).

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1782-1802
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Propuesta de perfil de ácidos grasos omega 3 en nutrición enteral

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Resumen

Revisamos las recomendaciones internacionales de ingesta oral de ácidos grasos n-3.y su contenido en las fórmulas de nutrición enteral. Sus acciones metabólicas dependen de su metabolización a EPA y DHA. La actividad de las 5D y 6D desaturasas, que catalizan este proceso, aumenta con el ejercicio, insulina, estrógenos de mujer fértil y proliferadores peroxisómicos, mientras que disminuye con el ayuno, déficit de proteínas y oligoelementos, edad > 30 años, sedentarismo, tabaco, alcohol, colesterol, ácidos grasos trans y saturados, insulinopenia y hormonas de estrés (adrenalina y glucocorticoides). La mayoría de las guías recomiendan 20-35% de la energía total en forma de grasas, repartidas en saturadas 7-10%, poliinsaturadas 6-10% y monoinsutaradas en España 20%. El de AG n-3 es de 0,5-2 g/día o bien 0,5-2% de la ingesta calórica total, con un límite superior de 3 g/día. El de AG n-6 es del 2,5-10% del aporte calórico total y el cociente recomendado n-6/n-3 no está bien definido pero la mayoría recomienan 5/1. El contenido en EPA y DHA, debe ser de al menos los 500 mg diarios. Por último, la ratio EPA/DHA en la mayoría es de 2/1. Las fórmulas de nutrición estándar presentan un contenido en grasas adecuado, pero la mayoría de los productos que contienen EPA y DHA exceden el límite de los 3 g/día. De los productos hiperproteicos y/o concentrados por vía oral sólo un producto de este grupo contiene EPA y DHA. Las del anciano frágil no todas aportan EPA y DHA y las que los contienen, su concentración puede ser incluso excesiva y en una relación poco parecida a la del aceite de pescado.

(*Nutr Hosp.* 2012;27:1782-1802)

DOI:10.3305/nh.2012.27.6.6023

Palabras clave: *Ácidos grasos omega 3. EPA. DHA. Nutrición enteral.*

PROPOSED PROFILE OF OMEGA 3 FATTY ACIDS IN ENTERAL NUTRITION

Abstract

We review the international recommendations on oral intake of n-3 fatty acids and their content in the enteral nutrition formulas. Their metabolic actions depend on their metabolization to EPA and DHA. The activity of desaturases catalyzing this process increases with exercise, insulin, estrogens in the fertile women, and peroxisomal proliferators, whereas it decreases with fasting, protein and oligoelements deficiencies, age < 30 years, sedentary lifestyle, cigarette smoking, alcohol, cholesterol, trans and saturated fatty acids, insulin deficiency, and stress hormones (adrenalin and glucocorticoids). Most of the guidelines recommend that 20-35% of the total energy comes from fat, being 7-10% saturated fats, 6-10% polyunsaturated, and 20% monounsaturated, in Spain. The recommendation for n-3 FA is 0.5-2 g/day or 0.5-2% of total caloric intake, with an upper limit of 3 g/day. For n-6 FA, 2.5-10% of total caloric intake, the n-6/n-3 ratio not being well established although most of the guidelines recommend 5:1. The EPA and DHA content should be at least 500 mg per day. Finally, the EPA/DHA ratio is 2:1 in most of them. Standard nutrition formulas present an appropriate fat content, although most of the products containing EPA and DHA exceed the limit of 3 g/day. Among the products with hyperprotein and/or concentrated, only of them contains EPA y DHA. Not all the formulas used for the frail elderly contain EPA or DHA, and in those containing them their concentration may be excessive and with a proportion very dissimilar to that of fish oil.

(*Nutr Hosp.* 2012;27:1782-1802)

DOI:10.3305/nh.2012.27.6.6023

Key words: *Omega 3 fatty acids. EPA. DHA. Enteral nutrition.*

Abreviaturas

AG: Ácidos grasos.
AGPI: AG poliinsaturados.
n-3: Omega 3.
n-6: Omega 6.
EPA: Ácido eicosapentaenoico.
DHA: Ácido docosahexaenoico.
LA: Ácido linoleico.
ALA: Ácido linolénico.
DHGL: Ácido dihomo-γ-linoleico.
DPA n-6: Ácido docosapentanoico.
DEHP: di-(2-etilhexil)ftalato.
COX: Ciclooxigenasa.
LOX: Lipooxigenasa.
CYP: Citocromo P450.

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Recibido: 24-VI-2012.
Aceptado: 15-VII-2012.

PGH_2: Prostaglandina H_2.
TXA_2: Tromboxano A_2.
HETEs: Ácidos hidroxieicosatetranoicos.
EETs: Epoxieicosatrienoicos.
AHA: American Heart Association.
DRI: Recomendaciones diarias de ingesta.
FNB-IOM: Food and Nutrition Board of the American Institute of Medicine.
GISSI: Gruppo Italiano per lo Studio della Sopravivenza nell'Infarto miocardio.
AGMI: Grasas monoinsaturadas.

Introducción

Los ácidos grasos (AG) son moléculas de naturaleza lipídica que presentan un grupo carboxilo terminal unido a una cadena hidrocarbonada. Pueden clasificarse de distintas maneras en función del número de átomos de carbono de su cadena o en función del número de dobles enlaces que presenten. De entre todos ellos, es bien conocido que los AG poliinsaturados, (AGPI) es decir, aquellos que contienen dos o más dobles enlaces en su cadena, juegan un papel importante dentro de nuestro organismo. Son dos las principales familias de AGPI: los omega 3 (n-3) y los omega 6 (n-6). Aunque se trata de familias estructural y funcionalmente diferentes, ambas tienen vías metabólicas muy interrelacionadas, como revisaremos posteriormente. En esta revisión nos centraremos en los AG n-3. En la tabla I reseñamos la nomenclatura que nos podemos encontrar de estos AG en la bibliografía.

El organismo humano sintetiza numerosos AG denominados no esenciales, pero hay otros que deben ser incorporados por medio de la dieta, ya que el cuerpo no es capaz de sintetizarlos, por lo que se conocen como esenciales. George y Mildred Burr, en 1929, observaron que la alimentación de ratas con una dieta carente en grasas producía un crecimiento muy pobre de los animales, dermatitis grave, perdida de pelaje, emanciación y a veces la muerte. No fue hasta 1963 cuando Hansen y sus colaboradores demostraron en humanos la clara necesidad del aporte de ciertos AG en la dieta[1].

Los AG n-6 y n-3 son muy importantes para mantener la estructura de las membranas celulares, facilitar la absorción de vitaminas liposolubles y regular el metabolismo del colesterol, lo cual hace que tengan una función primordial en el desarrollo del sistema nervioso y visual. Además en los últimos años ha aumentado el interés científico en relación a su capacidad de producir eicosanoides (prostaglandinas, prostaciclinas, leucotrienos y tromboxanos) y la regulación de múltiples procesos celulares, entre ellos el control de la homeostasis vascular, coagulación sanguínea y fenómenos inflamatorios[2].

El interés por el estudio de los AG n-3 surgió a partir de los años 70 tras la observación de Bang y Dyberg quienes detectaron en la población esquimal de Groenlandia una baja mortalidad por enfermedad cardiovascular a pesar de una dieta rica en grasas. Los autores propusieron la dieta rica en n-3 proveniente de una fuente marina (pescados, focas y ballenas) como causa de este hallazgo[3].

Desde entonces, numerosos estudios experimentales, epidemiológicos y de intervención han demostrado que la ingesta de una dieta rica en AG n-3 reduce la mortalidad coronaria y la muerte súbita cardíaca y que en las zonas geográficas donde estos AG predominan en la dieta la incidencia de enfermedad cardiovascular

Tabla I
Nomenclatura de los AG de las familias omega 3 y omega 6

Nombre	*IUPAC*	*Según el carboxilo*	*Según el omega*	*Abreviatura*
Ácido linolénico	9,12,15-ácido octadecenoico	$18:3\Delta^{9,12,15}$	18:3 n-3 18:3 (ω-3)	ALA α-LA LNA α-LNA
Ácido docosahexaenoico	4,8,12,15,19-ácido docosahexaenoico	$22:6\Delta^{4,8,12,15,19}$	22:6 n-3 22:6 (ω -3)	DHA
Ácido docosapentaenoico	7,10,13,16,19-ácido docosapentaenoico	$22:5\Delta^{7,10,13,16,19}$	22:5 n-3 22:5 (ω-3)	DPA
Ácido eicosapentaenoico Ácido icosapentaenoico Ácido timnodónico	5,8,11,14,17-ácido eicosapentaenoico	$22:5\Delta^{5,8,11,14,17}$	20:5 n-3 20:5 (ω-3)	EPA
Ácido araquidónico	5,8,11,14-ácido araquidónico	$20:4\Delta^{5,8,11,14}$	20:4 n-6 20:4 (ω-6)	AA
Ácido linoleico	9,12-ácido linoleico	$18:2\Delta^{9,12}$	18:2 n-6 18:2 (ω-6)	LA

IUPAC: International Unión of Pure and Applied Chemistry.

disminuye. Se ha demostrado que los AG n-3 reducen las concentraciones plasmáticas de triglicéridos, tienen propiedades antiarrítmicas, antiaterogénicas, antitrombóticas y antiinflamatorias[4].

Ciertas enfermedades crónicas de base inflamatoria podrían entonces ser susceptibles de ser tratadas con AG n-3. Destacaríamos patologías como enfermedad de Crohn, colitis ulcerosa, pancreatitis aguda, artritis reumatoide traumas de origen múltiple, asma, fibrosis quística, enfermedad de Alzheimer y neuropatía por inmunoglobulina A, entre otras[5].

Por otra parte, la importancia del aumento del cociente n-6/n-3 ha sido estudiado repetidamente en los últimos años. En la sociedad industrializada se observa un incremento del consumo de hidratos de carbono refinados, grasas saturadas, AG n-6 y grasas trans, mientras que ha disminuido la de AG n-3, hidratos de carbono de absorción lenta y fibra. Esto ha hecho que mientras que la ratio n-6/n-3 en los países industrializados es de 15-20/1, la de los animales salvajes y la que suponemos de los hombres prehistóricos es de 1/1[6]. Este cambio en el esquema de AG consumidos ha dado lugar al aumento de la prevalencia de enfermedades crónicas como aterosclerosis, hipertensión arterial esencial, obesidad, diabetes mellitus, artritis y algunas enfermedades autoinmunes, así como diferentes tipos de cánceres, como el de mama, colon y próstata[7].

La posible utilidad clínica de este tipo de AG en gran cantidad de patologías ha hecho que aumentara el interés por la composición de estos nutrientes en las fórmulas de nutrición enteral específicas[8]. El siguiente paso será el valorar el cociente n-6/n-3 más que la composición total de AG n-3 a la luz de los últimos estudios. Y por último, en un tercer paso se ha revisado el aporte de EPA y DHA en estos productos de nutrición enteral.

Todas estas consideraciones nos llevan a estudiar el metabolismo de estos AG n-3, para conocer sus metabolitos intermedios y los mediadores inmunitarios de los que son sustratos, además de las interacciones existentes de los enzimas que participan en el paso de un metabolito a otro. Esta será la primera parte de nuestra revisión.

En la segunda parte revisaremos las recomendaciones dietéticas de las diferentes sociedades científicas. Estas nos podrán servir de referencia para proponer un perfil de AG n-3 para las fórmulas de nutrición enteral, dada la escasez de estudios y ausencia de consenso sobre los niveles óptimos de estos nutrientes en las fórmulas de nutrición enteral, nos obliga a basarnos en las recomendaciones en la dieta oral.

Enzimas y factores que inciden en el metabolismo de LA y ALA

Tanto el ácido linoleico (LA) como el ácido linolénico (ALA) son AG esenciales, es decir, el ser humano no es capaz de sintetizarlos por sí mismo. Una vez ingeridos, pueden metabolizarse dando lugar a otros ácidos grasos con mayor grado de instauración y mayor tamaño de cadena: los llamados AGPI de cadena larga.

Así, el LA es precursor del AA mientras que el ALA lo es del EPA. Estos AG compiten por los enzimas encargados del proceso de desaturación (las desaturasas D5 y D6) y por las encargadas de alargar la cadena hidrocarbonada (las elongasas). El mayor nivel de competición enzimática se produce a nivel del AA y del EPA. Aunque las dos vías de síntesis de AGPI de cadena larga utilizan las mismas enzimas, no hay reacciones cruzadas entre ambas.

Se sabe que esta conversión enzimática es bastante ineficaz, principalmente en lo que se refiere a la producción de DHA[9]. En concreto, se estima que la eficacia de conversión de ALA a EPA es 0,2%, a DPA n-3 del 0,13% y a DHA del 0,05%[10].

El LA, a través de la D6 desaturasa, da lugar al ácido-γ-linoléico, que a través de una elongasa produce el ácido dihomo-γ-linoleico (DHGL). Éste se desatura por la acción de la D5 desaturasa para formar AA. El AA, mediante distintas reacciones enzimáticas de elongación, desaturación y un último paso de β oxidación, se convierte en ácido docosapentanoico (DPA n-6).

Por su parte, el ALA, a través de la D6 desaturasa, da lugar al ácido estearidónico (18:4), que por acción de la elongasa se transforma en el ácido eicosatetraenoico (20:4). Éste, a su vez, por la acción de la D5 desaturasa, produce EPA (20:5). El EPA, mediante una elongasa, se transforma en ácido docosapentanoico (DPA, 22:5), que mediante varias reacciones enzimáticas dará lugar al ácido docosahexanoico (DHA, 22:6). El DHA, por oxidación perixosomal, se vuelve a reducir hasta EPA. Todas estas reacciones enzimáticas tienen lugar en el reticulo endoplásmico a excepción de la última reacción de formación del DHA que se produce en el peroxisoma.

La ingesta de ALA aumenta los niveles de EPA y DPA n-3. Sin embargo, influye mínimamente en los de DHA. Además, si esta ingesta de ALA está aumentada de forma crónica, existe un aumento de la conversión a EPA, con un aumento de los niveles de EPA en plasma y en los depositos celulares. Sin embargo, el grado de conversión a DHA es insuficiente para aumentar la concentración de este AG y los niveles de DHA pueden llegar a disminuir[11]. La figura 1 resume el metabolismo de LA y ALA.

Estos AG n-3, principalmente el DHA, se incorporan en los fosfolípidos de las membranas celulares como componentes estructurales, formando parte de tejidos como la retina, el cerebro o los espermatozoides, por lo que son esenciales en el desarrollo de una óptima función visual, reproductora y cerebral. La cantidad de AGPI en las membranas celulares (principalmente el AA y DHA) se mantiene gracias a un mecanismo de retroalimentación que tiene la propia ruta metabólica[5]. Cuando el EPA se produce como metabolito del ALA, da lugar a DHA. Sin embargo, cuando el EPA procede de la dieta, termina produciendo eicosanoides. Estos eicosanoidos antagonizan la acción de los eicosanoides derivados de AA. Además también tienen

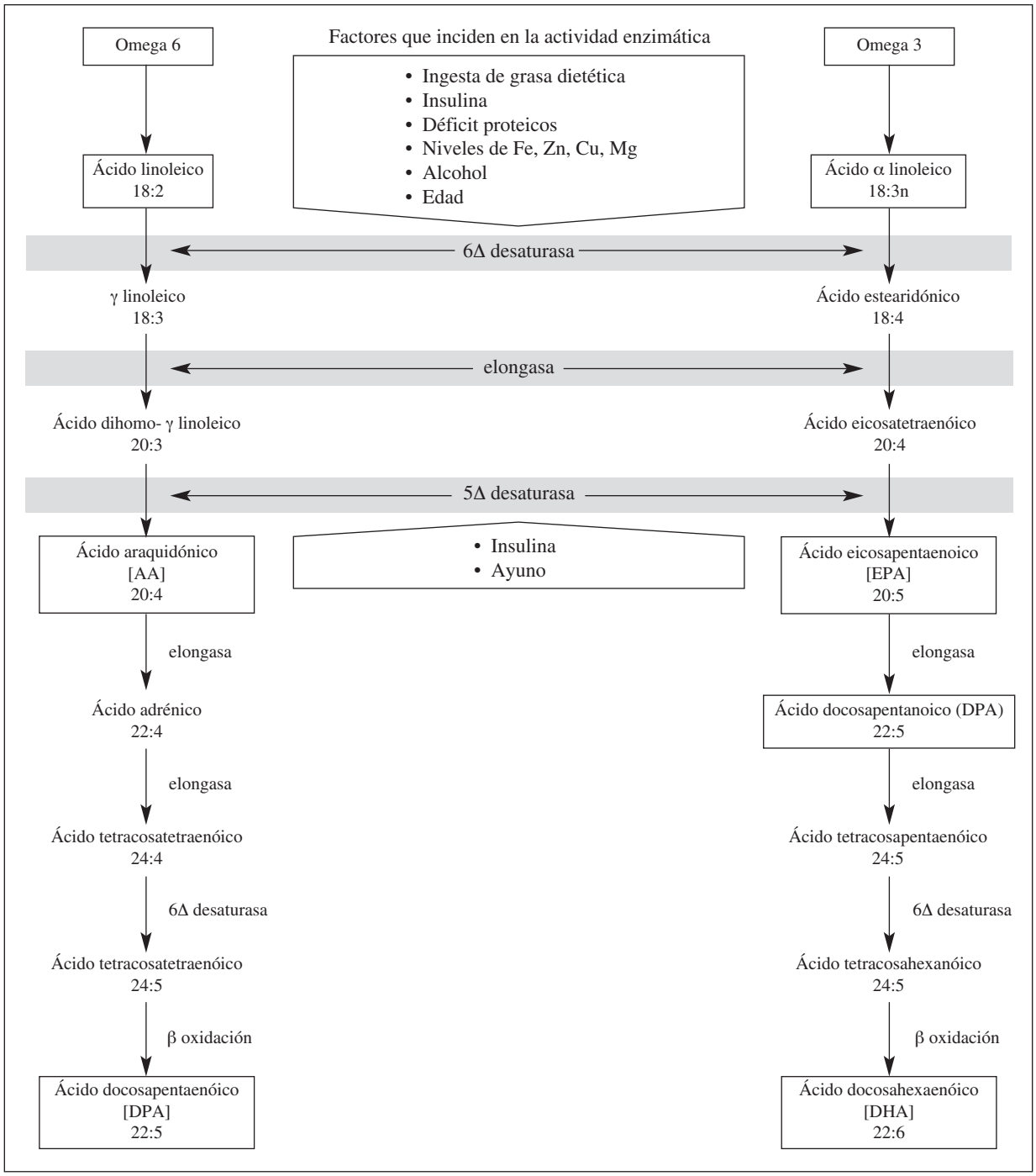


Fig. 1.—Metabolismo de los AGPI: LA y ALA.

efecto en la reducción de los valores de triglicéridos, colesterol, vasodilatación y efectos antitrombóticos.

La D6 desaturasa constituye el primer paso limitante de la ruta metabólica[12]. Su actividad, junto con la de la D5 desaturasa y la producción de AGPI de cadena larga, se encuentra regulada por múltiples factores[5,13] Es interesante estudiar estos factores ya que se ha descrito que la actividad de las desaturasas se ha asociado al desarrollo de enfermedad cardiometabólica, como el infarto agudo de miocardio[14] o el síndrome metabólico[15]. En otro artículo de Warensjo et al.[16] se cuantifica el riesgo de desarrollar sobrepeso según modificaciones de la actividad enzimática: se detectó que por cada desviación estándar de incremento de la actividad de la D9 y la D6, el riesgo de desarrollar sobrepeso se aumentaba en un 60%. Por el contrario, cada desviación estándar de incremento de la actividad de la D5 reducía el riesgo de sobrepeso en un 30%.

Cabe resaltar la dificultad para calcular la actividad de las desaturasas en humanos, por lo que en múltiples

estudios se calcula la actividad estimada de estas enzimas utilizando una ratio entre producto AG/y su precursor. La actividad estimada de la D5 desaturasa se expresa generalmente como el ratio entre AA/DHGL mientras que la actividad estimada de la D6 desaturasa se expresa como ácido-γ-linoléico/LA.

Entre los factores que afectan a la actividad de estas enzimas destacan los siguientes:

La ingesta de grasa dietética

Es bien conocido el efecto que produce en el desarrollo de eventos cardiovasculares y endocrino-metabólicos tanto la cantidad como sobre todo la calidad de las grasas que ingerimos diariamente. Pero a su vez, esta grasa dietética influye de forma significativa en la actividad enzimática. Ya Garg et al.[17] en los años 80 apuntaban la disminución de esta actividad en dietas ricas en grasas y posteriormente Huang et al.[18] con la ingesta de colesterol. Diferentes estudios indican que la actividad de la D6 desaturasa se induce por *dietas bajas en ácidos grasos esenciales* mientras que disminuye con *dietas ricas en aceites vegetales o marinos*[19].

Por otro lado, el *aumento de la ingesta de AG trans* y *un aumento de AG n-6* también reducen esta actividad, como lo hace el propio DHA. Sin embargo, cuando se suplementa con AG n3 se detecta una reducción en la actividad de la Δ6 desaturasa y un aumento de la Δ5 asociado a un aumento de EPA y DHA plasmático[20].

En un estudio de intervención publicado por Warensjö E. et al.[21] se observó un aumento de la actividad estimada de la Δ6 desaturasa y una baja actividad estimada de Δ5 desaturasa en aquel grupo de individuos que seguían una *dieta rica en AG saturados* comparados con aquellos que seguían una dieta rica en AG insaturados. Este cambio en la actividad enzimática se ha vinculado al desarrollo de síndrome metabólico[15]. La síntesis de AG n-3 a partir del ALA es más efectiva cuando la ingesta es rica en AG saturados y pobre en LA. Este autor fue el primero en mostrar el cambio en la actividad estimada de las desaturasas según la calidad de la grasa ingerida.

En general inhiben la acción de ambas desaturasas las grasas saturadas, el colesterol y las grasas trans[22,23]. La ingesta de los AG n-3 y n-6 producen un mecanismo de contrarregulación de las desaturasas hepáticas[24].

Factores endocrinos

En pacientes diabéticos se ha detectado un descenso en la actividad de la Δ5 desaturasa[25] y de la Δ6 desaturasa[25]. Sin embargo se encuentran diferencias según el tipo de diabetes desarrollada.

En concreto, varios autores han detectado este descenso en la actividad enzimática (de la 5Δ desaturasa particularmente) en pacientes diabéticos tipo 1 y la restauración de esta actividad con el inicio de la insulinoterapia[26,27]. Además en estos pacientes cuando se detecta un mal control metabólico, por ejemplo cuando el paciente se encuentra en estados de cetosis, esta disminución se mantiene[28]. Sin embargo, estos hallazgos descritos en pacientes con diabetes mellitus tipo 1 son opuestos a los que se detectan en pacientes con diabetes tipo 2. En ellos, esta actividad desaturasa aumenta[29] y tras el inicio de la insulinzación no se altera su actividad[20]. También se ha descrito que la actividad de la 5 desaturasa se correlaciona de forma positiva con los valores de la hemoglobina glicosilada en situaciones de mal control metabólico, pero no se correlaciona cuando se da un buen control metabolico[29].

El interés de estudiar la actividad de estas desaturasas viene definido por su posible papel en el desarrollo de insulino-resistencia tanto en los estudios realizados en humanos como en animales[30]. Recientemente se ha detectado en varios estudios prospectivos una fuerte asociación inversa de la actividad estimada de la 5Δ desaturasa con respecto al riesgo de desarrollo de diabetes y una asociación directa de la 6Δ desaturasa. Es decir, a mayor actividad estimada de la 5Δ desaturasa menor riesgo de diabetes, mientras que un aumento de la actividad de la 6Δ desaturasa se asocia a un aumento manifiesto del riesgo[31].

Otras hormonas implicadas en el control del estrés, con efecto opuesto a la insulina, como son la *adrenalina* y *glucocorticoides,* han demostrado inhibir la acción de ambas desaturasas[22].

Factores nutricionales

Los déficits de algunos *oligoelementos* como el *hierro, zinc, cobre o magnesio*, que pueden observarse en situaciones de desnutrición, disminuyen la actividad de la Δ6 desaturasa y secundariamente la formación de AGPI de cadena larga[25] . *Piridoxina, zinc, ácido nicotínico* y *magnesio* son co-factores de la acción de la Δ6 desaturasa, por lo que sus déficits se asocian a una disminución de su actividad.

El *ayuno total*, la *ingesta proteica deficitaria* y la *dieta rica en glucosa* reducen la actividad de las desaturasas, mientras que la *restricción calórica parcial* la estimula[23].

Factores tóxicos

Los estudios experimentales in vitro realizados en microsomas hepáticos de ratas alimentadas con *etanol* en los años 80 describieron la disminución de la actividad de la Δ6 y 5 desaturasa[32]. Posteriormente Nakamura et al.[33] también corroboraron estos resultados in vitro en cerdos alimentados durante meses con una ingesta rica en grasas y alcohol.

La aportación posterior de Narce et al.[34] describió la actividad enzimática *in vivo* en cultivos celulares hepáticos de ratas a distintas concentraciones de etanol: a mayor concentración de alcohol la actividad enzimática disminuía, pero aumentaba con concentraciones de

alcohol mínimas. Además de alterar la acción de las desaturasas, el consumo de alcohol disminuye las concentraciones tisulares de AGPI de cadera larga[35].

Otro factor que influye en esta actividad enzimática es el *tabaco*[36]. En el estudio de Marangoni et al.[37]realizado *in vitro* con células epiteliales de la glándula mamaria que estaban expuestas al humo del tabaco se detectó una inhibición de la conversión de ALA en AG n-3 y un bloqueo de acción enzimática de la 5Δ desaturasa.

Factores constitucionales

La *edad* puede afectar también a las desaturasas, de hecho se sabe que esta actividad disminuye a partir de la tercera década de la vida manteniéndose esta disminución en la ancianidad. De ahí la importancia de incorporar en la dieta de nuestros mayores la ingesta de pescados grasos como fuente de AGPI. Por otro lado, la acción enzimática se encuentra disminuida durante los primeros 6 meses de vida. Por ejemplo, en niños prematuros o con bajo peso al nacer, esta menor actividad de la Δ6 desaturasa, puede conllevar un riesgo para la síntesis de AG, con el consecuente compromiso en el desarrollo de una óptima función neurológica. De ahí la importancia de la lactancia materna que aporta estos AG o de la ingesta de formulaciones lácteas para los prematuros enriquecidas en estos AG.

En cuanto al *sexo* también podemos encontrar diferencias tanto en la ruta de desaturación/elongación como en la proporción de ALA que se dirige a ser oxidado. Los estrógenos parece que incrementan la actividad de esta ruta y además producen un aumento de conversión de ALA con el consecuente incremento de EPA y DHA. También se detecta en mujeres una mayor tasa de conversión de DPA n-3 a DHA. Se sabe que la concentración de DHA es mayor en mujeres comparado con hombres. Parece ser que la razón de este hallazgo se debe a un aumento de la expresión hepática de 5Δ y 6Δ desaturasa en mujeres en edad fértil que les confiere mayor capacidad de sintetizar DHA a partir del ALA dietético[38]. Este estudio corroboraría la hipótesis sobre la regulación hormonal de la síntesis de AGPI. Otra diferencia entre hombres y mujeres es la menor proporción de ALA destinada a la oxidación en mujeres en comparación de hombres de la misma edad[39].

Proliferadores peroxisómicos

Los proliferadores peroxisómicos son aquellos agentes o sustancias que tienen la capacidad de proliferar, no sólo los peroxisomas sino también otras organelas celulares como las mitocondrias o el reticulo endoplásmico. Algunos fármacos se incluyen dentro de esta definición. Distintos estudios en los años 80 describían el aumento de la actividad enzimática de algunos enzimas hepáticos implicados en la biosíntesis de fosfolípidos tras la administración de estas moléculas[40].

Estas sustancias son inductores de la actividad de la D6 desaturasa. Los primeros que describieron el efecto de los fibratos (incluidos dentro de los proliferadores peroxisomicos) como inductores de esta actividad enzimática fueron Kawashima et al.[41] El tiadenol y el DEHP (di-(2-etilhexil)ftalato), que son estructuralmente diferentes al fibrato ácido clofibrico, son también capaces de incrementar esta actividad enzimática[41]. Y por último destacar como potente inductor el Wy 14,643, otro proliferador peroxisómico y PPAR alfa ligando[42].

Otros factores

Se ha descrito que los *virus oncogénicos* y la *radiación* inhiben la Δ6 desaturasa. Esta situación tiene interés especial en los pacientes oncológicos.

Cabe destacar que, dado que estas reacciones enzimáticas tienen lugar en el hígado (que es el órgano con mayor actividad Δ5 y Δ6 desaturasa), todas las patologías que conllevan *alteración en la función hepática* pueden afectar a la actividad enzimática. De hecho, en pacientes cirróticos se ha constatado un descenso en los niveles de EPA y AA[43].

Por último, hay que destacar la influencia de la *actividad física* en la actividad enzimática. Andersson et al describieron cómo los pacientes más activos físicamente mostraban mayor actividad de la Δ5 desaturasa que los más sedentarios. Entre todos los sujetos estudiados no se encontraron diferencias en cuanto al aporte graso de su dieta[44].

En condiciones fisiológicas, la Δ6 desaturasa tiene mas afinidad por el ALA que por el LA. Pero, como en nuestra alimentación hay mayor cantidad de LA que de ALA[45], la vía del ALA se activa poco y por tanto la producción de EPA y DHA es escasa. Esto hace que las concentraciones plasmáticas y tisulares de los AGPI de cadena larga, de la familia n6 son mayores que los de la familia n-3. De hecho, el porcentaje de ALA presente en los lípidos tisulares y en plasma supone el 0,5% de todos los AG[46].

En conclusión, nos encontramos con diferentes situaciones en las que parece existir una disminución de la actividad las desaturasas (tabla II). Por mucho

Tabla II
Factores que inciden en la actividad de las 5Δ y 6Δ desaturasas

Aumento de actividad	*Disminución de actividad*
Dieta baja de AG esenciales	Ayuno, deficit proteinas, oligoelementos
Mujer en edad fértil	Edad > 30 años Edad: los primeros 6 meses de edad
Ejercicio físico	Sedentarismo
Insulina, Diabetes tipo 2	Insulinopenia, Diabetes tipo 1, cetoacidosis
Proliferadores peroxisómicos	Hepatopatías Tabaco, alcohol AG trans, AG saturados, colesterol Adrenalina, glucocorticoides (estrés)

ALA que administremos, su metabolización a EPA y DHA es escasa, porque su conversión es ineficaz, y además porque el aumento crónico de ALA disminuye los niveles de DHA. El consumo de pescado aporta AG n-3, pero también es rico en EPA y DHA, por lo que no depende de su transformación a partir del precursor. Además, las propiedades antiinflamatorias, antitrombóticas y reductoras del nivel de colesterol, es decir de protección cardiovascular, proceden del EPA dietético y no del EPA producido a partir del ALA, que dará lugar al DHA.

La ingesta de AG n-3 disminuye la actividad de la Δ6 desaturasa (la primera enzima limitante) por lo que se podría pensar que aumentar la ingesta de AG n-3 no conseguiría aumentar los niveles de EPA y DHA. Sin embargo esta ingesta de AG n-3 estimula la actividad de la Δ5 desaturasa (la segunda enzima), por lo que el efecto final parece ser de aumento de producción de EPA y DHA. Van der Meij[47] observa que después de 4-7 días de la administración de AG n-3 mediante nutrición enteral se consigue la incorporación de EPA (y en algunos casos de DHA) en el plasma, las membranas celulares de las células sanguíneas y de los tejidos mucosos, aunque no llega a determinar la duración de este cambio tras suspender la administración de AG n-3. Burdge es el autor que mejor ha estudiado estos efectos e indica que la ingesta de ALA aumenta los niveles de EPA y DPA n-3, pero influye mínimamente en los de DHA[11].

Mediadores de la respuesta inmune

Los eicosanoides son moléculas con 20 átomos de carbono que actúan modulando la función renal[47], vascular[48] y la inflamación[49] de forma paracrina o autocrina. Se incluyen en este grupo las prostaglandinas, prostaciclinas, los leucotrienos y tromboxanos entre otras moléculas. Las prostaglandinas se producen en la mayoría de los tejidos, las prostaciclinas en el endotelio vascular, los leucotrienos principalmente en los leucocitos y por último los tromboxanos en las plaquetas. Estos mediadores de la respuesta inmune derivan principalmente del metabolismo del AA y del EPA. De hecho, la principal función del AA es la de ser precursor de la síntesis de estas moléculas.

Las células inflamatorias humanas presentan grandes cantidades de AA y pequeñas de AG de la familia n-3. La proporción de ambas familias varía según el tipo celular. La presencia de mayor cantidad de AA en las membranas celulares hace que pueda ser metabolizado dando lugar a sustancias potencialmente inflamatorias. Sin embargo, esta proporción se puede modificar a través de la administración oral de EPA y DHA. Es decir, que aumentando el aporte de EPA dietético, se puede reducir la proporción de AA de las membranas celulares y aumentar la de EPA, disminuyendo así la producción de los metabolitos lipídicos nocivos[50]. Esto se conoce como la función inmunomoduladora de los AG n-3, dado que el cambio en la composición grasa de las células inflamatorias modifica su función.

Eicosanoides derivados del metabolismo del AA

El AA de las membranas celulares, a través de la activación de las fosfolipasas y en especial de las fosfolipasa A2, es capaz de ser liberado a plasma. Así, se convierte en sustrato para las rutas enzimáticas, de entre las que destacan tres: Ciclooxigenasa (COX), Lipooxigenasa (LOX) y citocromo P450 (CYP). Los eicosanoides que derivan de la ruta de la COX tienen mayor actividad biológica que aquellos que lo hacen de la LOX.

Eicosanoides de la ruta COX

Las prostaglandinas, los tromboxanos y las prostaciclinas son las principales sustancias que se derivan de esta ruta enzimática. Tras un primer paso de conversión en prostaglandina H_2 (PG H_2) por la acción del enzima COX, se producirán *PG* de la serie 2, entre las que se incluyen PGD_2, PGE_2, PG I_2, (que es una prostaciclina), PGF $_{2\mu}$ y tromboxano A_2 (TX A_2) . Mientras que las PG D_2, E_2, I_2 son vasodilatadores, el TX A_2 es un potente vasoconstrictor e inductor de la agregación plaquetaria. Además del poder vasodilatador de la prostaciclina PG I_2, esta molécula es capaz de inhibir la agregación plaquetar y la activación de los leucocitos. Estas prostaciclinas son antagonistas fisiológicos de los tromboxanos. El balance que existe entre estos dos grupos de moléculas con efectos fisiológicos antagónicos es clave para el mantenimiento de la homeostasis vascular.

Eicosanoides de la ruta LOX

Por la ruta de la LOX se generarán los leucotrienos y los ácidos hidroxieicosatetranoicos (HETEs) principalmente. El enzima LOX se clasifica según la localización del grupo hidroperóxido; así, encontramos la 5-LOX, 8-LOX, 12-LOX y 15-LOX[51]. Por la activación de la 5-LOX se producirán los leucotrienos (LT) de la serie 4, destacando el LT B4 que facilita la quimiotaxis y la adhesión celular. El efecto de estos mediadores es claramente inflamatorio. Por la vía de la 12-LOX se generarán los HETEs. Y por último, a través de la 15-LOX se producirán unas moléculas con propiedades antiinflamatorias conocidas como lipoxinas, entre las que destacan la A_4 y B_4 con efectos vasodilatadores, inhibidores de la quimiotaxis de los neutrófilos y estimulador de la adherencia de los monocitos. Estas moléculas tienen un papel clave en el control y resolución del proceso inflamatorio.

Eicosanoides de la ruta CYP 450

Entre los eicosanoides derivados de esta ruta se encuentran los ácidos epoxieicosatrienoicos (EETs) y los HETEs. Destacan los EETs por su actividad antinflamatoria y angiogénica. Estas sustancias, productos de un proceso de epoxigenación, desempeñan un papel decisivo en la regulación de la función renal y cardiovascular, por ello son diana terapéutica para enfermedades como la hipertensión arterial o el ictus.

Eicosanoides derivados del metabolismo del EPA

El enzima COX-2

Convierte el EPA en las PG y TX de las series 1 y 3. Destaca entre ellos el TX A_3 que es un débil agente plaquetario y vasoconstrictor, con poca actividad biológica. También por la acción de la COX se producirá en las células endoteliales la prostaciclina $I_{3,}$ agente vasodilatador y antiagregante plaquetario.

Por la acción de LOX

Se formaran en los leucocitos los LT de la serie 5. De entre ellos hay que destacar el LT-B_5, que presenta efecto antiinflamatorio e inhibidor de la adhesión celular. Todos estos mediadores son significativamente menos inflamatorios, es decir tienen menor actividad biológica.

La epoxigenación

La epoxigenación del EPA da lugar a unas sustancias denominadas resolvinas, en concreto la resolvina E1, con propiedades antiinflamatorias, que después describiremos.

Eicosanoides derivados de otros AGPI

Además de los eicosanoides que derivan del AA y del EPA también pueden producirse otros mediadores lipídicos a partir de otros AGPI como son el DHGL o el DHA

El DHGL, que es una sustancia intermediaria en el metabolismo del AA como explicamos anteriormente, es fuente de producción de sustancias con propiedades antinflamatorias. Destacan algunas PG y TX de la serie 1 que inhiben la producción de coágulos.

A partir del DHA también se producen moléculas con propiedades antinflamatorias denominadas resolvinas o docosanoides. Se encuentran presentes en la sangre, en los leucocitos y en el tejido encefálico. Podemos destacar la resolvina D1 y la protectina D1. Estas sustancias se han visto involucradas en la protección de algunos tejidos como el sistema nervioso, pulmón o hígado así como en la resolución del proceso inflamatorio. La figura 2 ilustra esta cascada de producción de eicosanoides.

Recomendaciones dietéticas internacionales de ácidos grasos esenciales

La escasez de estudios y ausencia de consenso sobre los niveles óptimos de estos nutrientes en las fórmulas de nutrición enteral, nos obliga a basarnos en las recomendaciones en la dieta oral. En el apartado siguiente revisaremos las recomendaciones dietéticas de las diferentes sociedades científicas. Éstas nos podrán servir de referencia para las fórmulas de nutrición enteral.

Las recomendaciones dietéticas de los AGPI es un tema a debate, no habiéndose establecido todavía unos niveles máximos de ingesta de AG n-6 y n-3. Además las cantidades a recomendar van a depender de las diferentes enfermedades. No existe tampoco acuerdo sobre la mejor proporción de aporte de DHA y de EPA, si es mejor darlos de forma separada o combinada y si existen otros AG n-3 de cadena larga que pueden tener un efecto beneficioso. Otras razones que dificultan establecer claras guías en cuanto a las recomendaciones de los AG n-3 son la gran variabilidad interindividual en cuanto a su metabolismo, basado en determinantes genéticos, sexo, edad y enfermedad de base. Por lo tanto los requerimientos para sus efectos fisiológicos necesitarían ser ajustados de forma individual[52].

Las recomendaciones de las sociedades científicas sobre la ingesta de grasa y AG en particular, se han hecho tanto para personas sanas como para la prevención y el tratamiento de enfermedades crónicas. Se recomienda generalmente una disminución en la ingesta de grasa saturada y AG *trans*, con una ingesta total de grasa que oscile entre un 20-25% a un 35% del total del aporte energético[53]. Aunque en una revisión reciente de Aranceta et al.[54]. Se considera que no hay una recomendación estándar, que varía según países y sólo las recomendaciones más recientes establecen la importancia de un adecuado aporte de AG n-3.

Las primeras recomendaciones se basaban en estudios en los que relacionaban los efectos beneficiosos de los AG n-3 con el consumo de pescado, pero no con el propio n-3 directamente[55]. En posteriores estudios se utilizan sólo AG n-3, demostrando que estos AG son los mas importantes para la prevención primaria cardiovascular de todos los nutrientes que aporta el pescado[56-58].

Otra forma de enfocar las recomendaciones de ingesta de AG n-3 es el cociente n-6/n-3. El aporte de AG a través de la dieta ha ido evolucionando, siendo totalmente diferente el contenido y la relación de n-6/n-3 en nuestros días comparado con la de los primeros humanos. La dieta de los cazadores-recolectores de la era paleolítica era abundante en carnes magras, peces, vegetales verdes y frutas, con un bajo aporte de grasas

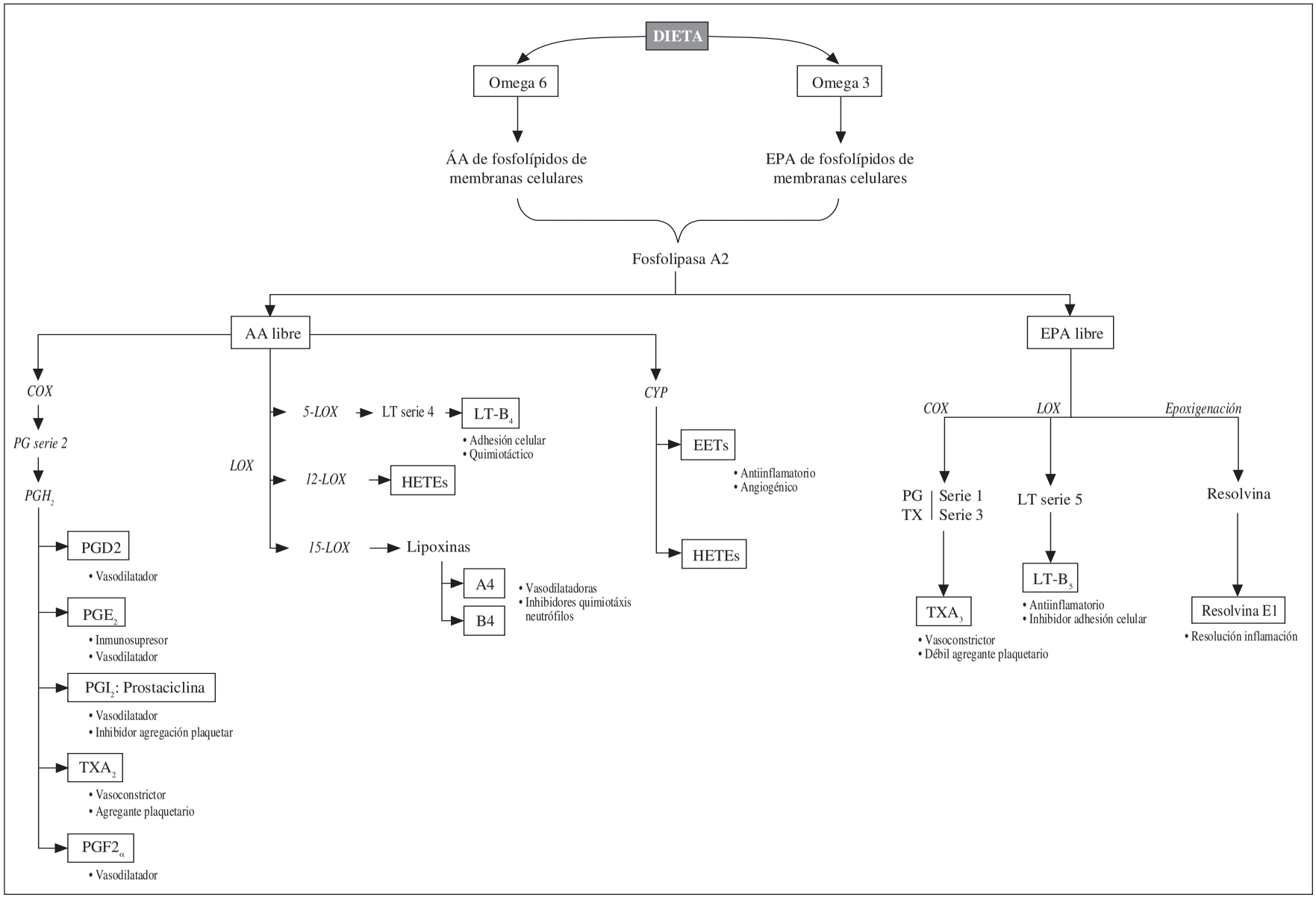


Fig. 2—Cascada de producción de eicosanoides a partir de AA y EPA.

totales (20%) y de grasa saturada (< 6%), y prácticamente sin grasa saturada y la relación entre los AG n-6 y n-3 consumidos era 1/1. La carne de los peces y otros productos marinos les aportaban AG n-3 y los vegetales verdes LA y ALA.

El comienzo de la agricultura, aunque modificó el perfil nutricional del hombre, ya que se incorporaron los cereales a la alimentación, no produjo grandes cambios en la disponibilidad y la cantidad de AG y la cantidad de la grasa total de la dieta. Fueron los desarrollos tecnológicos de los últimos 100-150 años los que verdaderamente han contribuido a un cambio en las tendencias de consumo de las grasas y a un cambio radical en la relación de consumo n-6/n-3.

La dieta actual de los países occidentales se caracteriza por una elevada relación n-6/n-3, que puede llegar a ser 15-20/1, debido al consumo elevado de n-6 y la disminución en la dieta de n-3. Esta desproporción afecta más a los países occidentales que a los orientales (relación n-6/n-3 en torno a 12/1) ya que en estos el consumo de pescado y productos del mar ricos en EPA y DHA es mayor[59].

El cociente n6/n3 idóneo está todavía por definir. En los pacientes con asma un cociente 10/1 se asoció a una mayor inflamación, mientras que un cociente 5/1 tuvo efectos beneficiosos. En la prevención secundaria de enfermedad cardiovascular, un cociente de 4/1 se asoció a un descenso del 70% en la mortalidad total. Este mismo cociente no fue suficiente para reducir la proliferación celular en el cáncer colorrectal y se necesitó un cociente 2.5/1. En pacientes con artritis reumatoide un cociente de 2-3/1 redujo el componente inflamatorio[60]. Todas estas discrepancias indican que el cociente óptimo varía según la enfermedad a la que nos refiramos ya que son enfermedades crónicas, multigénicas y multifactoriales. Además, es posible que la dosis terapéutica de AG n-3 dependa de la gravedad de la enfermedad y de la predisposición genética del individuo[61].

En los últimos 70 años se han desarrollado procesos como la hidrogenización de los aceites vegetales para conservar y manejar mejor los aceites vegetales y animales. Esto implica sin embargo una disminución del aporte de los AG esenciales y un aumento de la producción de AG trans, con efectos muy perjudiciales sobre la salud. Además, cada vez se consumen más cereales con AG n-6 y se dispone de más aceites vegetales (maíz, girasol, soja) ricos en LA y de productos hidrogenados, mientras que el consumo de productos marinos cada vez es menor[7].

No debemos olvidar las reflexiones del consenso publicado en 2009 por la American Heart Association (AHA)[62]. Reconoce que en muchas ocasiones, se recomienda disminuir la ingesta de n-6 en la dieta como estrategia para mejorar la relación n-6/n-3 y, en consecuencia, disminuir el riesgo cardiovascular. Sin embargo, según la revisión de la literatura científica realizada por la AHA, dicha estrategia no sólo podría ser poco efectiva, sino que además podría tener efectos contrarios a los esperados en la salud cardiovascular, ya que la ingesta de n-6 (5-10% de la energía total de la dieta) ha demostrado tener un efecto cardiovascular protector.

En conclusión, podríamos decir, que aumentar el consumo de n-3 parece ser la mejor estrategia a seguir para obtener una relación n-6/n-3 adecuadas[63,52]. Para conseguirlo habría que aumentar la ingesta de pescado a 2-3 raciones a la semana, o en ciertos casos valorar el uso de suplementos.

Por otra parte, ingestas elevadas de AG n-3 pueden causar un sangrado excesivo en ciertos individuos. La Sociedad Americana de Dietistas recomienda que aquellos pacientes que tomen más de 3 g/día de AG n-3 de cadena larga debieran ser seguidos por un médico[64]. La FDA[65] ha establecido como *"generalmente considerado como seguro"* niveles de 3 g/día de AGPI de cadena larga. Se han establecido las mismas recomendaciones por otras organizaciones como la Australia and New Zealand National Health and Medical Research Council[66].

También existe una gran preocupación en relación con la presencia de ciertos contaminantes en el pescado como son dioxinas, mercurio y otras sustancias, aunque diferentes estudios[67] han mostrado que los beneficios de la ingesta habitual de pescado exceden los riesgos potenciales. Para poblaciones especiales como niños, mujeres embarazadas o que planeen un embarazo, los beneficios de una ingesta moderada de pescado, salvo ciertas especies como pez espada, tiburón, caballa gigante y lofolátilo siguen siendo mayores que los riesgos.

Respecto a las recomendaciones de EPA, hasta hace pocos años, las recomendaciones diarias de ingesta (DRI) se habían centrado en el ALA, con menciones indirectas al aporte de AGPI de cadena larga, el EPA y DHA. En el año 2002 el Food and Nutrition Board of the American Institute of Medicine (FNB-IOM)[68] emitió un informe en el que se comunicaba que no existían datos científicos suficientes para establecer ingestas adecuadas ni ingestas de referencia para EPA o DHA. Posteriormente han surgido nuevas evidencias que justifican la reevaluación de las recomendaciones de EPA y DHA y sus repercusiones sobre la salud. La FAO/WHO establece que hay una evidencia insuficiente para establecer una ingesta mínima de EPA o DHA, por lo que recomiendan que ambos sean consumidos[69].

Otro problema es definir el cociente más beneficioso de EPA/DHA. Ambos metabolitos son químicamente diferentes y podrían tener efectos diferentes sobre el riesgo cardiovascular[70]. La naturaleza nos muestra que el cociente en el pescado se inclina a favor de DHA. Sin embargo, en el Gruppo Italiano per lo Studio della Sopravivenza nell'Infarto miocardio (GISSI) la dieta utilizada era más rica en EPA y sus efectos cardioprotectores fueron evidentes[56,58]. Ratios de EPA/DHA de 1/2 a 2/1 parecen ser beneficiosos. Además, tenemos experiencia con otros nutrientes en que el efecto terapéutico no lo conseguimos con un nutriente aislado, por lo que la mayoría de las recomendaciones internacionales no separan estos dos nutrientes.

En la tabla III[71-109] presentamos cronológicamente las recomendaciones de ingesta de AGPI para la población general de las diferentes sociedades científicas. Este orden nos parece importante porque estas recomendaciones van variando con los años a la luz de nuevos estudios y múltiples revisiones. Un gran número de

Tabla III
Recomendaciones de ingesta de AG poliinsaturados (AGP1) según diferentes sociedades científicas y consensos

	% total grasa	AG N-3		ALA		EPA + DHA		AG N-6 (LA sobre todo)	
		% energía	g/día	% energía	g/día	% energía	mg/día	% energía	g/día
National Nutrition Council of Norway (1989)[71]	–	–	1-2 (AG N-3 cadena larga)	–	–	0,5	–	–	–
North Atlantic Treaty Organization (NATO) Workshop on dietary ω3 and ω6 fatty acids (1989)[72]	–	–	–	–	0,8-1,1	0,27	300-400	–	–
Scientific Review Committee of Canada (1990)[73]	–	Mínimo 0,5	1,1-1,6	0,5	–	–	–	–	–
United Kingdom (UK) Committee on Medical Aspects of Food Policy (COMA) (1991)[74]	35	–	–	0,2	–	–	450 (dos raciones pescado/ semana)	1	–
British Nutrition Foundation Task Force (1992)[75]	–	–	–	–	–	EPA 0,2-0,5 DHA 0,5	–	6	12
National Health and Medical Research Council (Australia) 1992[76]	30	–	–	1	2	–	–	6	12
UK Committee on Medical Aspects of Food Policy (COMA) (1994)[77]	35	–	0,2	0,2	–	–	Mínimo 2 raciones pescado, una de pescado graso	–	–
Government Agencie of Japón (1996)[78]	30	0,8 (AG n-3 cadena larga)	1,6 (AG n-3 cadena larga)	–	–	–	–	5-6	10-12
Expert Workshop of the European Academy of Nutritional Sciences (1998)[79]	–	–	–	1	2	–	(10-40 g pescado graso)	–	–
British Nutrition Foundation (1999)[80]	–	–	–	–	–	–	1.500 la semana	–	–
National Heart Foundation of Australia, 1999[81]	–	–	–	1	≥ 2	0,08-0,22	160-430	8-10	16-20
International Society for the Study of Fatty Acids and Lipids (ISSFAL) Expert Workshop (1999)[82]	–	–	–	1	2,22	0,3 (0,1 de EPA y 0,1 DHA)	650/2.000 kcal/día DHA y EPA mínimo cada uno 220/2.000 kcal	2-3	4,4/6,67/ 2.000 cal
Nutrition Subcommittee of the Food Safety Authority of Ireland (1999)[83]	–	0,5	–	–	–	–	–	2	–
EURODIET conference (2000)[84]	20-30	–	–	–	2	–	200	–	4-8
Austrian, German and Swiss Society Society for Nutrition (2000)[85]	30	0,5	–	–	–	–	–	–	< 0,3
Health Council of the Netherlands (2001)[86]	20-40	–	0,2	1	–	–	200	2	–
Agence Française Sécurité Sanitaire des Aliments (AFFSA) France(2001)[87]	30-35	–		0,8	–		DHA 0,05% 120 mg/d		
Varones adultos			2			0,2	500	4	–
Mujeres adultas			1,6			0,2	400	4	–
Sociedad Española de Nutrición Comunitaria 2001 (SENC)[88]	30-35	–	–	–	–	–	> 200 (DHA)	–	–

Tabla III *(cont.)*
Recomendaciones de ingesta de AG poliinsaturados (AGP1) según diferentes sociedades científicas y consensos

	% total grasa	AG N-3		ALA		EPA + DHA		AG N-6 (LA sobre todo)	
		% energía	g/día	% energía	g/día	% energía	mg/día	% energía	g/día
USA IOM(2002/2005)[89] Varones adultos Mujeres adultas	20-35	0,6-1,2	–	0,6-1,2	1,6 1,1	–	496	5-10	14-17 11-12
World Health Organization (WHO)/FAO (2003)[90]	15-30	1,2	–	–	0,8-1,1	–	400-1.000	5-8	–
AFFSA (2003)[91]	33	–	–	–	–	–	–	4- 4,4	–
UK Scientific Advisory Committee on Nutrition SACN (2004)[92]	33	–	–	–	–	–	450	–	–
Conseil Superieur d'Hygiene, Service Public Federal Santé Publique, Belgium (2004)[93]	–	–	–	–	–	> 0,3	Dos raciones de pescado, mejor graso	–	–
ISSFAL (2004)[94]	–	–	–	0,7	–	–	≥ 500	2	–
Nordic Nutrition Recommendations 2004[95]	30	1	–	5-9	–	–	450	> 4	–
Ingestas referencia para población japonesa (2004)[96] Varones adultos Mujeres adultas	20-30	–	2,2-2,9 2-2,2	–	–	–	–	< 10	8-12 7-10
Deutsche Gesellschaft für Ernährung,(DGE) German Nutrition society (2004)[97]	–	–	–	–	–	–	250	–	–
Dietary guidelines for Americans (USA)2005[98]	25-35	0,6-1,2	–	–	–	–	500	5-10	–
Council for Responsible Nutrition (USA) 2005[99]	–	–	–	–	–	–	500	–	–
Health Council of Netherlands 2006[100]	20-40	1	0,45	1	–	–	450 150-200 de DHA	2	–
American Heart Association Nutrition Committee 2006 (AHA)[101]	25-35	–	–	–	–	–	Prevención 1ª 500 2ª 1.000	–	–
National Health and Medical Research Council for Australia and New Zealand (NHRC) 2006[102] Varones adultos Mujeres adultas	30	–	–	0,4-1	1,3 0,8	–	DHA + EPA + DPA/día 160 90	4-10	13 8
American Dietetic Association and Dietitians of Canada 2007[53]	20-35	–	–	0,6-1,2	1,3-2,7	–	500	3-10	7-22 Dieta de 2.000 cal
WHO/FAO(2008)[103]	20-35	0,5-2	–	–	–	–	250-2.000	2,5-9	–
National Heart Foundation of Australia 2008[104]	33	–	–	–	2	–	500	–	–
Austrian, German and Swiss Society for Nutrition (2008)[105]	30	0,5	–	0,5	–	–	250	2,5	–
Conseil Supérieur de la Santé, Belgium (2009)[106]	30-35	1,3-2	–	> 1	–	> 0,3	≈ 667	2	–
AFFSA (France) 2010[107]	35-40	–	–	1	–	–	500 250 DHA 250 EPA	4	–
Autoridad Europea de Seguridad Alimentaria (EFSA) 2010[108]	20-35	–	–	0,5	2	–	250	4	–
Sociedad Española de Nutrición Comunitaria 2011 (SENC)[109]	≤ 35	1-2	–	1-2	–	–	500-1.000 (DHA 200)	5	–

Tabla IV
Recomendaciones aporte EPA + DHA en embarazo y lactancia

Organización	*Año*	*Recomendación*
Conseil Superieur d'Hygiene, Service Public Federal de la Santé Publique, Belgium[93]	2004	250 mg/día
International Society for the Study of Fats and Lipids (ISSFAL)[94]	2004	DHA 300 mg/día
World Association of Perinatal Medicine[110]	2007	DHA 200 mg/día
The PeriLip and EARNEST projects of the European Commission[111]	2007	DHA 200 mg/día
Austrian, German and Swiss Society for Nutrition[105]	2008	Al menos DHA 200 mg/día
March of Dimes (USA)[112]	2009	200 mg/día DHA
AFFSA (France)[107]	2010	250 mg/día DHA 500 mg EPA + DHA/día
Autoridad Europea de Seguridad Alimentaria (EFSA) 2010[108]	2010	250 mg de EPA+DHA y adicionalmente 100-200 mg/día DHA

países han publicado sus Recomendaciones de Ingesta y Guías o han adoptado aquellas sugeridas por organismos internacionales o por otros países. Existe una gran disparidad entre los diferentes países y en las ingestas recomendadas para el total de la grasa y los AG. Además, no existe una metodología estandarizada para definir estos valores. Recientemente se ha publicado una revisión sistemática de las ingestas dietéticas recomendadas para la grasa y los AG[54].

En las últimas recomendaciones internacionales, en la población general, parece haber un cierto consenso con 400-500 mg/día, que serían los niveles mínimos de aporte de EPA + DHA. Esto equivale aproximadamente a dos raciones a la semana de pescado, preferiblemente azul. Respecto al aporte de AG n-6 y n-3 no hay tanto consenso y las recomendaciones son muy dispares. Se podría decir que en general la mayoría coinciden con las de la FAO/WHO de 2008[104] en recomendar el 2,5-10% del aporte calórico total en forma de AG n-6 y un 1-2% de n-3, lo que haría un cociente de 5/1. El límite inferior del 2,5% se establece para prevenir el déficit de ácidos grasos esenciales, mientras que el rango superior estaría indicado para reducir los niveles plasmáticos de LDL y triglicéridos. Este cociente está lejos del 12/1 o mayor de las dietas típicas de la dieta en la sociedad occidental industrializada. Debemos recordar que el cociente n-6/n-3 eficaz en patologías ha sido desde 5/1 en asma hasta 2,5/1 en cáncer colorrectal[60].

En mujeres embarazadas y lactantes, para un optimo desarrollo fetal la ingesta mínima de EPA + DHA sería de 300 mg/día, de los cuales al menos 200 mg deben ser de DHA (tabla IV). El DHA tiene un papel esencial en el desarrollo del cerebro y la retina durante la etapa fetal y los dos primeros años de vida. Estos hallazgos apoyan la necesidad de recomendaciones para una adecuada ingesta en embarazadas, lactancia y niños hasta dos años. El DHA debería considerarse condicionalmente esencial durante las etapas iniciales del desarrollo, dado que la formación de DHA a partir de ALA es muy limitada y muy variable (1-5%)[54].

Respecto a los pacientes con enfermedades cardiovasculares, en los últimos años hay cada vez más conocimiento acerca de la relación entre la ingesta de AG n-3 y la reducción del riesgo cardiovascular (tabla V). Las recomendaciones de las diferentes sociedades coinciden en que las personas adultas han de consumir pescado al menos dos veces por semana. En el caso de pacientes con enfermedad coronaria, las recomendaciones de consumo son de 1 gramo diario de EPA +

Tabla V
Recomendaciones de aporte EPA + DHA como prevención secundaria en diferentes patologías

Organización	*Patología cardiovascular*	*HTA*	*Hipertrigliceridemia*
American Heart Association, AHA (2002, 2006, 2009)[113,101,114]	1.000 mg/día	–	2.000-4.000 mg/día
Conseil Superieur d'Hygiene Service Public Federal de la Sante Publique, Belgium (2004)[93]	1.000 mg/día	–	–
National Heart Foundation of Australia (2008)[104]	1.000 mg/día	–	1.200 mg/día que se puede aumentar hasta 4.000 mg si necesario
AFFSA (France) 2010[38]	500-750 mg	–	–
European Food and Safety Authority (EFSA) 2009[108]	–	3 g/día	2.000-4.000 mg/día

Tabla VI
Fuentes dietéticas de los principales AG n-3 y n-6 con interés nutricional

Familia	*Principales AG*	*Fuentes dietéticas*
n-3	Ácido α linolenico (18:3 n-3)	Verduras de hoja verde, algunos aceites vegetales : soja o semillas de colza, aceite de linaza o algunos frutos secos.
	EPA (20:5 n-3) Y DHA (22:6 n-3)	pescados grasos (atún salmón, sardina, arenque, anchoa) o aceite de pescado.
n-6	Ácido linoleico (18:2 n-6)	Aceites vegetales: maíz girasol o soja, o en las margarinas.
	Acido gammalinoleico (18:3 n-6)	Aceite de onagra o prímula, borraja y grosella negra.
	Acido araquidónico (20:4 n-6)	Carne (grasas animales), hígado, huevos o pescado.

DHA procedente de aceites de pescado o suplementos. En el caso de pacientes con hipertrigliceridemia se recomienda el suplemento de 2 a 4 gramos diarios de EPA + DHA a fin de disminuir en un 20-40% los niveles de triglicéridos del plasma.

Fuentes alimentarias de AG n-3 y n-6

Sabemos que los AG esenciales deben ser obligatoriamente ingeridos a través de los alimentos para la producción de AGPI de cadena larga de la serie n-6 y n-3. Los AG n-6 derivan del LA, ampliamente distribuido en las plantas, salvo en el coco, cacao y la palma. Se encuentran sobre todo en los aceites de semillas vegetales como el maíz, girasol, cártamo, onagra, calabaza, cacahuete germen de trigo y soja. Es precursor del AA sintetizado en los mamíferos, y por lo tanto, presente en los alimentos de origen animal. Los AG n-3 derivan del ALA, que predomina en nueces, cloroplastos de las plantas de hoja verde oscuro y en los aceites vegetales de semillas de soja, lino, colza, linaza, grosella y otras frutas rojas. A partir de este último se sintetizan EPA y DHA, que también pueden ser ingeridos a través de la dieta con el consumo de pescados azules. En la tabla VI se reseñan los alimentos más ricos de estos AG[115].

Menos de un 0,2% del ALA se convierte en el organismo en EPA y sólo el 0,05% en DHA. Por ello para que estos dos AG alcancen concentraciones adecuadas deben ser aportados al organismo de forma regular y en cantidades suficientes con una dieta rica en productos marinos. La procedencia fundamental de estos ácidos es de algas microscópicas, plancton y crustáceos planctónicos, que están en la base de la cadena alimentaria.

Existen importantes diferencias en el contenido de EPA y DHA no sólo entre las distintas especies (máximo en el salmón y la caballa), sino dentro de una misma especie. La diferente composición lipídica va a depender de su hábitat, según varíen factores como la temperatura, la profundidad y la salinidad del agua, del momento de la captura y de si son animales salvajes o proceden de piscifactoría. El contenido de grasa total y AG n-3 es mayor en pescados de agua fría. También hay diferencias en las concentraciones de AG n-3 según la forma de preparación del pescado. En los pescados fritos (de restaurantes o de comida rápida) disminuye el contenido de AG n-3 y aumenta el cociente n-6/n-3 y el contenido en AG trans. Por todo esto, en la mayoría de las recomendaciones internacionales insisten en la ingesta de pescado más que en unas dosis precisas de AG n-3[1].

Nuevas fuentes de AG n-3

Un estudio epidemiológico reciente sitúa la baja ingesta de AG n-3 en el octavo puesto de causas prevenibles de mortalidad en Estados Unidos[116]. Por esto, cada vez hay más interés en buscar nuevas fuentes de n-3, especialmente los de cadena larga. Esto se debe al el problema de suministro de pescado, aparición de contaminantes, pérdida de la biodiversidad de especies que en un futuro afectará a toda la población mundial, etc... [117].

La biotecnología está desarrollando nuevos aceites enriquecidos en AG n-3 que pueden usarse en las comidas o como suplementos. A partir de algunas cepas bacterianas y microalgas que están en la microbiota intestinal de los peces de agua salada se obtienen aceites ricos en EPA y especialmente en DHA[117].

Se han alimentado también gallinas, pollos y cerdos con aceites marinos para incrementar así el contenido en DHA de la carne y de los huevos. La manipulación genética también ha contribuido a aumentar el aporte de n-3 en diferentes alimentos, como es el caso de nuevas cepas de semillas que pueden sintetizar DHA a partir de ALA[118].

Otra opción para aumentar el consumo de AG n-3 en la dieta es incorporarlos en alimentos de consumo habitual, desarrollando *alimentos funcionales* ricos en n-3. Estos productos enriquecidos en n-3 hacen que sea más fácil alcanzar las recomendaciones de estos AG. La tecnología moderna de alimentos hace posible hoy en día que una gran cantidad de alimentos puedan enriquecerse en AG n-3 y, de hecho, existe en todo el mundo una gran variedad de productos alimenticios enriquecidos. Algunos ejemplos de estos alimentos que se comercializan en la casi totalidad de los países de Europa son el pan y los productos de panadería, margarinas, grasas untables, huevos y derivados, pastas, salsas, zumos y bebidas no alcohólicas, carnes, productos lácteos y leche[119].

Tabla VII
Fórmulas de nutrición enteral estándar ordenadas por su composición en EPA + DHA por 1.500 cc

Nombre	*% Prot*	*% Grasa*	*Sat g/100*	*MUFA g/100*	*AGPI g/100*	*n-3 g/1.500*	*n-6 g/1.500*	*n-6/ n-3*	*EPA + DHA mg/1.500*	*EPA/ DHA*
Composición "recomendada"	15-16	20-40	0,7-1	2,2	0,6-1,1	0,5-2	4-17	2-5	500-1.000	2
Frebini original easybag	10,2	40	1,2	2,1	1,16	5,85	10,5	1,8	1.350	1,25
Nutrini	9,8	40	0,5	2,6	1,3	3,9	14,9	3,83	1.800	2,33
Nutrini Energy	11	40	0,8	3,9	2	5,85	22,05	3,76	990	0,26
Nutrini Energy Multi Fibre	11	40	0,8	3,9	2	5,85	22,05	3,76	990	0,26
Dienat G	16	35	1	2	0,87	1,65	10,8	4,89	511	2
Nutrison Multi Fibre	15,6	34	1	2,2	0,7	2,55	7,35	2,87	510	1,39
Nutrison	16	35,1	1	2,2	0,7	2,55	7,35	2,87	510	1,39
Fresubin original botella 500	15	30	0,3	2,2	0,9	4,05	9,45	2,6	450	2
Fresubin original easybag	15	30	0,3	2,1	1	3,75	8,85	2,3	450	2
Fresubin original fibre botella 500	15	30	0,3	2,1	1	3,75	8,85	2,3	450	2
Fresubin original fibre easybag	15	30	0,3	2,1	1	3,75	8,85	2,3	450	2
T-DIET plus standard	16	35	1	2	0,87	1,7	10,8	4,89	507	2
Vegenat- Med NP	15	30	2,9	7,8	3,6	15,45	31,95	2,07		
Edanec	16	30	0,84	1,92	0,5	1,5	6	4		
Osmolite HN	16	30	0,84	1,92	0,5	1,5	6	4		
Nutrison Soya	16	35,2	0,4	2,3	1,2	2,7	14,1	5,25		
Ensure Plus Fiber	16,7	29,5	0,46	2,91	1,32	2,7	16,5	6,11		
Jevity	16	30	1,03	1,59	0,73	1,35	9,3	6,89		
Isosource fibra	15	30	0,9	1,4	1,1			7		
Novasource GI Control	15	29	0,95	1,36	1,2	2,25	15,3	7		
Isosource standard	16	30	0,95	1,37	1,18			7		
Isosource fibra	15	30	0,9	1,4	1,1			7		
Novasource GI Control	15	29	0,95	1,36	1,2	2,25	15,3	7		
Ensure HN	15,9	30	0,31	1,99	0,91	0	26,7	44,5		
Ensure con fibra	14,7	30,9	0,49	0,97	1,93	0,6	28,2	47		

Sin embargo, este aporte puede ser de tan solo un 30%, existiendo grandes diferencias entre productos. Estos AG son muy susceptibles a la oxidación y reaccionan muy rápidamente cuando se exponen a condiciones o agentes oxidantes como el oxígeno del aire. Por esta razón, los aceites de pescado se adicionan a los alimentos con vitamina E y otros antioxidantes para prevenir la oxidación que, de lo contrario, produciría enranciamientos, malos olores e inestabilidad. Además, la producción de alimentos enriquecidos con AG n-3 es técnicamente difícil y requiere de métodos especiales para producir un aceite de pescado adecuado, apropiado para la adición a alimentos, sin olor ni sabor a pescado[115].

Debido a las dificultades para cubrir las ingestas recomendadas de AG n-3 han aparecido *suplementos alimenticios* que tratan de satisfacer los requerimientos nutritivos de estos AG. Al igual que ocurre con ciertos alimentos, en la suplementación existe gran variación en cuanto a su composición y concentración de EPA y DHA. En los últimos años se ha aprobado la administración de AG n-3 como fármaco de administración vía oral. En España existe una formulación galénica que proporciona 840 mg de AG n-3 (465 mg de EPA y 375 mg de DHA). Está autorizado para su utilización en prevención secundaria tras infarto de miocardio en combinación con tratamientos de referencia y en hipertrigliceridemia endógena como suplemento a dieta cuando hay una respuesta inadecuada a medidas dietéticas[4].

Los AG n-3 pueden entonces considerarse tanto como nutrientes esenciales, suplementos dietéticos o principios activos de fármacos, dependiendo de su nivel de ingesta y el motivo por el que se administren[120].

Composición en AG n-3 de las fórmulas de nutrición enteral comercializadas en España

La composición de estos AG n-3, así como su ratio n-6/n-3 es muy variable de unas fórmulas de nutrición enteral a otras. La clasificación de estas fórmulas se basa en si son completas o no, si son poliméricas, peptídicas o elementales, su riqueza y calidad de las proteínas, su concentración calórica y su contenido en fibra, pero no en la cantidad y calidad de las grasas que contienen[121].

Las fórmulas estándar aportan un 15-16% del valor calórico total en forma de proteínas, un 48-55% en carbohidratos y un 30-35% en grasas. La composición de estas grasas es muy heterogénea, siendo aún más irregular el contenido en n-3, n-6, EPA y DHA mucho más. En la tabla VII mostramos algunos productos de

nutrición estándar ordenados por su contenido en EPA+DHA. Los productos que no aportan EPA ni DHA los hemos ordenado por el cociente n-6/n-3. En la primera fila destacamos la composición recomendada, según las guías internacionales para la dieta oral.

En la mayoría de estas guías[54] se recomienda la ingesta de un 20-35% de la energía total en forma de grasas, aunque algunas lo aumentan al 40% en personas con peso adecuado. El aporte de grasas saturadas, suele estar reducido al 10% o incluso al 7% de la energía total por la American Heart Association[101]. En 100 cc de nutrición estándar obtenemos 100 kcal, por lo que el 7-10% de estas calorías corresponderían a 0,77-1,1 g de grasas saturadas. Respecto a las grasas monoinsaturadas (AGMI) en España su consumo se ha cifrado en torno al 20% del aporte energético total[109]. En 100 cc de fórmula estándar serían 20 kcal, que corresponden a 2,2 g de AGMI. Por último, la ingesta recomendada de grasas AGPI es de 6-10% (0,66 a 1,1 g de AGPI en 100 cc de fórmula estándar). En la tabla VII podemos observar que la mayoría de las fórmulas de nutrición estándar cumplen estos criterios.

El objetivo principal de nuestro estudio es analizar el contenido de AG n-3, n-6, así como de EPA y DHA de las fórmulas de nutrición enteral, así como establecer unas posibles recomendaciones. Para ello hemos calculado para un consumo medio de 1.500 cc/día, dado que es la dosis más habitual.

El aporte de AG n-3 recomendado para la población general es de 0,5-2 g/día[87,100] o bien 0,5-2% de la ingesta calórica total, con un límite superior de 3 g/día por el riesgo de hemorragias[64], disminución en la producción de citoquinas y aumento de la peroxidación lipídica[122]. Para un aporte de 1.500 cc de nutrición enteral estándar, con 1.500 kcal, la cantidad recomendada de 0.5-2% de la ingesta calórica procedente de AG n-3, corresponde a 7,5-30 kcal, esto es 0,83-3,3 g/día. En la tabla VII podemos observar que algunos de los productos que contienen EPA y DHA exceden el límite de los 3 g/día, excepto Dienat G, Nutrison y T Diet Plus Standard.

Respecto al aporte recomendable de AG n-6, la mayoría coinciden con las guías de la FAO/WHO de 2008[104] que recomiendan el 2,5-10% del aporte calórico total en forma de AG n-6. Para un aporte de 1.500 kcal/día, esto corresponde a 37,5-150 kcal en forma de AG n-6, o lo que es lo mismo, 4,16-16,6 g/día. En el caso de este nutriente, todos los productos están dentro de los márgenes recomendados.

El cociente n-6/n-3 no está bien definido pero la mayoría coinciden con las guías de la FAO/WHO de 2008[104] que recomiendan un cociente de 5/1. El cociente n-6/n-3 de las fórmulas de nutrición enteral varía mucho, pero la mayoría están en el entorno del 2/1 al 5/1 recomendado, excepto en los que el aporte de AG n-3 es muy escaso.

De la revisión sobre el metabolismo de los AG n-3 que hemos realizado al principio de este trabajo se deduce que es más importante el aporte de EPA y DHA de forma directa que el de sus precursores por varias razones:

1) La ingesta aumentada de ALA disminuye los niveles de DHA y además el EPA producido como metabolito de ALA se convierte a DHA y no tiene los efectos conocidos del EPA dietético.
2) Las bajas cifras de eficacia en la conversión enzimática de ALA a sus metabolitos (de ALA a EPA es 0,2%, a DPA n-3 del 0,13% y a DHA del 0,05%).
3) La formación de DHA a partir de ALA es muy limitada y variable (1-5%) por eso se recomienda la ingesta directa de DHA procedente de los alimentos, principalmente con la ingesta de pescado azules.
4) La conversión de AG n-3 a EPA y DHA es limitada y depende de factores genéticos y ambientales, por lo que su aporte directo es muy importante en determinadas situaciones.

Por todo lo anterior, cada vez hay más fórmulas estándar que contiene estos metabolitos. Para un consumo de 1.500 cc de fórmula de nutrición al día, los que contienen EPA y DHA, todos aportan al menos los 500 mg diarios mínimos recomendados, pero un número no desdeñable de nutriciones enterales estándar no los contienen. Dentro de los que contienen más cantidad de EPA + DHA (los primeros en la tabla VII), es de destacar que los cuatro primeros son fórmulas pediátricas, y es el recientemente aparecido Dienat G es la fórmula para adultos que mas aporta EPA + DHA siendo una dieta estándar.

Por último, la ratio EPA/DHA en la mayoría es de 2/1, como se recomienda en la dieta basada en alimentos, pero en algunos el aporte de DHA es muy escaso o inexistente. Este déficit de DHA es muy importante, por su función antiinflamatoria que deriva de las resolvinas D1 o neuroprotectinas explicadas anteriormente y por el papel que desempeña este AG en el desarrollo del cerebro y retina fetales hasta los dos años de vida y posteriormente en el mantenimiento de una correcta función neurológica, visual y reproductora. Este es el motivo por el que debería considerarse condicionalmente esencial durante el embarazo, lactancia y dos años después del nacimiento del recién nacido. Por otra parte, al EPA se le atribuyen propiedades antitrombóticas, vasodilatadoras, de descenso del colesterol plasmático y de participación en el desarrollo de una óptima función neurológica entre otras. Aunque no es seguro que estas funciones de los AG n-3 que se atribuyen a los AG EPA o a DHA sea tan específicas o que se deriven de la sinergia de ambas.

Los *productos hiperproteicos por sonda* aportan desde el 20 al 25% del valor calórico total en forma de proteínas. En la tabla VIII mostramos los principales productos ordenados por su aporte en EPA y DHA. El aporte de grasas es muy heterogéneo, pudiendo corresponder del 23 al 40% del valor calórico total. Para un consumo mínimo de 1.500 cc/día el aporte de AG n-3 puede variar de 4,35 g a otros que no declaran contenerlos, aunque en general están muy cerca del rango recomendado. El aporte de AG

Tabla VIII
Fórmulas de nutrición enteral hiperproteicas para sonda, ordenadas por su contenido en EPA + DHA

Nombre	*% Prot*	*% Grasa*	*Sat g/100*	*MUFA g/100*	*AGPI g/100*	*n-3 g/1.500*	*n-6 g/1.500*	*n-6/ n-3*	*EPA + DHA mg/1.500 cc*	*EPA/ DHA*
Composición "recomendada"	20-25	20-40	0,7-1	2,2	0,6-1,1	0,5-2	4-17	2-5	500-1.000	2
Fresubin HP energy botella 500	20	35	3,7	0,5	1,5	4,35	17,7	4	750	1,5
Fresubin HP energy easybag	20	35	3,7	0,5	1,5	4,35	17,7	4	750	1,5
T-DIET plus High protein	20	35	1,2	2,5	1,1	2	13,7	5,2	507	2
Novasource GI Protein	22	25	1,1	1,4	0,6	3,876	10,692	2,76		
Jevity Plus HP	25	31	1,04	2,44	0,55	1,8	6,6	3,67		
Promote	25	23	0,63	1,45	0,37	1,2	4,5	3,75		
Edanec HN	24,9	23,3	0,64	1,46	0,37	1,2	4,5	3,75		
Perative	20,5	25,4	1,56	1,06	0,82	2,1	9,9	4,71		
Nutrison Protein Plus Multi Fibre	20	35	0,5	2,9	1,5	3,315	17,006	5,13		
Nutrison Protein Plus	20	35	0,5	2,9	1,5	3,33	17,25	5,18		
Ensure Hiperproteico	25,3	23,8	0,33	1,78	0,97	2,25	12,3	5,47		
Nutrison MCT	20	30	2,3	0,6	0,4	0,77	4,233	5,48		
Isosource protein fibra	20	34	1,4	2	1,92			5,7		
Isosource protein	22	29	1,09	1,53	1,36			7		

n-6 también es muy variable de unos a otros, pero dentro de los límites recomendables. El cociente n 6/n 3 entre 2/1 y 5/1 aparece en la mayoría, excepto en el último que está mas alejado. El problema viene por el contenido en EPA y DHA, que es inexistente en la mayoría de los productos. Esta composición tan deficitaria en algunos productos de nutrición enteral es preocupante porque en ocasiones se utilizan estas fórmulas en pacientes con altos requerimientos de proteínas, como el paciente crítico, en el que están indicados los aportes de EPA y DHA.

Los *productos hiperproteicos y/o concentrados por vía oral* aportan entre un 18 y un 30% de su valor calórico total en forma de proteínas, por lo que se suelen usar en pacientes con muy escasa ingesta proteica. Este prototipo de paciente no suele ser capaz de comer la parte proteica de las comidas, por lo que es de suponer que ingerirá poco pescado. Con este planteamiento clínico llama la atención que sólo un producto con esta presentación contenga EPA y DHA.

En la tabla IX ordenamos las fórmulas de nutrición enteral primero por su contenido en EPA + DHA y luego de manera decreciente según su aporte proteico. Las cantidades de AG n-3, n-6, EPA y DHA las expresamos por 100 cc porque el consumo diario de estos productos es muy variable, ya que se toma para complementar la ingesta de alimentos deficitaria. En este contexto es ya muy difícil valorar si el paciente que toma estos productos sigue una dieta deficitaria o no y sólo podemos compararlos entre sí pero no respecto a la ingesta diaria recomendable.

El único producto de esta familia que contiene EPA y DHA es T-Diet plus High Protein. El resto no los contienen, por lo que existe poca posibilidad de discusión. Solo se puede agregar que el cociente n-6/n-3 está dentro de los límites recomendados en la mayoría.

En los últimos años se han comercializado un grupo de fórmulas de nutrición enteral especialmente indicadas para el *paciente anciano frágil.* En la tabla X presentamos estas fórmulas ordenadas por su contenido en EPA y DHA. Estos productos están especialmente enriquecidos con vitamina D, calcio, zinc, selenio, ácido fólico y vitamina B1, pero no todos aportan EPA y DHA.

De los que aportan EPA y DHA, alguno los contienen en dosis muy altas y con un cociente EPA/DHA muy reducido en DHA. No debemos olvidar que el uso de este tipo de cocientes es muy teórico y de dudosa utilidad clínica porque desconocemos las acciones individuales de uno y otro así como sus interacciones.

Conclusión

Las fórmulas de nutrición estándar presentan un contenido en grasas adecuado, pero en la mayoría de los productos que contienen EPA y DHA exceden el límite de los 3 g/día, excepto Dienat G, Nutrison y T Diet Plus Standard. En cambio, el contenido de AG n-6 está dentro de los márgenes recomendados. El cociente n-6/n-3 de las fórmulas de nutrición enteral varía mucho, pero la mayoría están en el entorno del 2/1 a 5/1 recomendado, excepto en los que el aporte de AG n-3 es muy escaso. De los que contienen EPA y DHA, todos aportan al menos los 500 mg diarios mínimos recomendados, pero un número no desdeñable de nutriciones enterales estándar no los contienen. Por último, la ratio EPA/DHA en la mayoría es de 2/1, como se recomienda en la dieta basada en alimentos, pero en algunos el aporte de DHA es muy escaso o inexistente.

En la mayoría de las *fórmulas hiperproteicas por sonda* el contenido en EPA y DHA es inexistente. Muchos de los pacientes que reciben este tipo de fórmulas se encuentran en una situación crítica, con patología con un importante componente inflamatorio que

Tabla IX
Fórmulas de nutrición enteral hiperproteicas y/o concentradas por vía oral

Nombre	*% Prot*	*% Grasa*	*Sat g/100*	*MUFA g/100*	*AGPI g/100*	*n-3 g/100*	*n-6 g/100*	*n-6/ n-3*	*EPA + DHA mg/100 cc*
Composición recomendada	20-50	20-40	0,7-1	2,2	0,6-1,1	0,03-0,13	0,26-1,13	2-5	33,3-66-6
T-DIET plus High protein	20	35	1,2	2,5	1,1	0,13	0,91	5,2	33,8
Resource protein	30	25	0,3	2,15	1,05	0,2	0,35	1,8	
Resource protein fibra	30	25	0,7	1,63	0,85	0,27	0,58	2,1	
Fresubin protein energy drink	27	40	0,6	4,9	1,2	0,22	0,96	4,5	
Resource HP/HC	25	35	1	2,2	2,6			7	
Fortimel Extra	24,9	36,2	0,8	3,8	1,9	0,29	1,5	5,1	
Fortimel Creme	23,8	28,2	0,7	3	1,3	0,22	1,1	5,09	
Resource Crema	23	39	7,35	0,54	1,9	0,55	1,25	2,3	
Fresubin crème	22	36	0,5	5,4	1,3	0,23	1	4,1	
Meritene complet	22	29	1,08	1,56	1,36			7	
Vegenat- Med HP	20	30	3,1	7,6	3,75	1,03	1,97	1,91	
Fortimel Complete	20	29,8	0,5	2,6	1,3	0,19	0,99	5,1	
Fortimel Compact	20	36	0,8	4,8	2,4	0,34	1,7	5,11	
T- DIET 20/2	20	35	0,79	4,9	2,2	1,4	3	2,1	
Fresubin 2 kcal drink	20	35	0,59	5,78	1,43	0,27	1,11	4,2	
Fresubin 2 kcal fibre drink	20	35	0,59	5,78	1,43	0,27	1,11	4,2	
Resource 2,0	18	39	0,7	5,7	2,3	0,67	1,44	2,13	
Ensure twocal	16,84	40,15	0,89	5,5	2,16	0,25	1,91	7,64	
Fortisip Compact	16	34,8	0,9	5,6	2,8	0,42	2,2	5,14	
Vegenat- Med NP	15	30	2,9	7,8	3,6	1,03	2,13	2,07	

Tabla X
Fórmulas de nutrición enteral diseñadas para el anciano frágil

Nombre	*% Prot*	*% Grasa*	*Sat g/100*	*MUFA g/100*	*AGPI g/100*	*n-3 g/100*	*n-6 g/100*	*n-6/ n-3*	*EPA + DHA mg/100*	*EPA/ DHA*
Composición recomendada	20- 50	20-40	0,7-1	2,2	0,6 -1,1	0,03 -0,13	0,26 -1,13	2-5	33,3 -66,6	2
Resource Senior Active	27	39	1	3,4	1,2	0,35	1	2,86	141	1,6
Supressi	20	35	1,5	2,3	1,1	0,12	0,84	4,12	67,5	0,5
Supressi NP	16	35	1,5	2,3	1,1	0,12	0,84	4,12	67,5	0,5
Cubitan	29,7	25,2	0,4	2,1	1	0,154	0,7885	5,12		
Nutrison Advanced Cubison	20,4	30	1,2	1,4	0,7	0,111	0,5828	5,25		
Ensure Plus Advance	22	29	0,47	2,28	1,81	0,28	1,53	5,46		

podrían beneficiarse del aporte de EPA y DHA en la nutrición enteral recibida.

Los *productos hiperproteicos y/o concentrados por vía oral* se suelen usar en pacientes con muy escasa ingesta proteica, por lo que es de suponer que ingerirá poco pescado, pero solo un producto de este grupo (T-Diet plus High Protein) contiene EPA y DHA.

Por último, las nuevas fórmulas para el *anciano frágil* no todas aportan EPA y DHA. Además, las que los contienen, su concentración puede ser incluso excesiva y en una relación poco parecida a la del aceite de pescado.

Agradecimientos

Querríamos expresar nuestro más sincero agradecimiento a todas las casas comerciales que nos han facilitado la composición de sus productos de nutrición enteral. En especial a Dña. Pilar Sanchez Vera por su ayuda técnica en la coordinación del grupo.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1803-1809
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Antropometría en el diagnóstico de pacientes obesos; una revisión

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Resumen

Objetivo: **Actualizar los conocimientos existentes sobre la antropometría utilizada en el diagnóstico de la obesidad en Cuba y el mundo.**

Material y métodos: **Revisión documental y bibliográfica durante marzo de 2010 y enero de 2012. Las bases de datos consultadas fueron Medline y Cochrane mediante PubMed. Se usaron las siguientes palabras claves: indicadores antropométricos, obesidad, adultos.**

Resultados y discusión: **Las evidencias muestran que los indicadores antropométricos existentes no son del todo eficaces para diagnosticar obesidad en la atención primaria de salud, unos por su difícil aplicabilidad y otros por no respetar el último concepto de obesidad emitido por la Organización Mundial de la Salud o por su inexactitud evaluativa.**

Conclusiones: **A pesar de la gran variedad de indicadores antropométricos existentes para diagnosticar obesidad en adultos todos tiene sus dificultades para su aplicación y generalización. Además de que la mayoría de estos no están adaptados y validados para poblaciones específicas.**

(*Nutr Hosp.* 2012;27:1803-1809)

DOI:10.3305/nh.2012.27.6.6044

Palabras clave: *Indicadores antropométricos. Obesidad. Adultos. Diagnóstico.*

ANTHROPOMETRY IN THE DIAGNOSIS OF OBESE PATIENTS; A REVIEW

Abstract

Objective: **To update existing knowledge of anthropometry used in the diagnosis of obesity in Cuba and the world.**

Material and methods: **Literature and document review during March 2010 and January 2012. The databases searched were Medline and Cochrane through PubMed. We used the following key words: anthropometry, obesity, adults.**

Results and discussion: **The evidence shows that existing anthropometric indicators are not entirely effective in diagnosing obesity in primary health care, some of their applicability and other hard not to respect the latter concept of obesity issued by the World Health Organization inaccuracy or evaluative.**

Conclusions: **Despite the wide variety of existing anthropometric indicators to diagnose obesity in adults all have their difficulties in application and generalization. Besides that most of these are not adapted and validated for specific populations.**

(*Nutr Hosp.* 2012;27:1803-1809)

DOI:10.3305/nh.2012.27.6.6044

Key words: *Anthropometry. Obesity. Adult. Diagnosis.*

Introducción

Según la organización mundial de la salud (OMS) la obesidad es la enfermedad crónica no transmisible mas frecuente, siendo el sobrepeso su antesala. En su reporte de marzo de 2011 la define como una "acumulación anormal o excesiva de grasa corporal que puede ser perjudicial para la salud"[1].

Existen a nivel global más de 1.000 millones de adultos con sobrepeso y según esta fuente en el 2015 la cifra alcanzara los 3.000 millones. Cuba no esta libre de este peligro y según encuestas realizadas por el Instituto Nacional de Higiene y Epidemiología son obesos el 7,95 por ciento de los hombres y el 15,44 de las mujeres y el sobrepeso se presenta en el 29,7 de los hombres y el 31,5 de las mujeres[2].

Esta patología se ha asociado con un alto riesgo de padecer enfermedades crónicas como hipertensión, insuficiencia cardiaca, diabetes mellitus tipo 2 entre otras, pero es impredecible calcular los costos sociales y las perdidas de bienestar psicosocial causando estrés y depresión[2,3].

Según el lugar donde se acumula el exceso de grasa corporal la obesidad puede ser androide o ginecoide:

- Obesidad androide: mayor concentración de grasa en la zona abdominal y menor en las otras partes del cuerpo. Es más frecuente en los hombres y es la de mayor riesgo para las enfermedades del corazón, por estar la grasa más cerca de órganos importantes (corazón, hígado, riñones, etc.).

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Recibido: 3-V-2012.
1.ª Revisión: 5-VII-2012.
Aceptado: 7-VIII-2012.

- Obesidad ginecoide: menor concentración de grasa en la zona abdominal y mayor en la cadera, los glúteos y los muslos. Es más frecuente en las mujeres y tiene menos riesgo para las enfermedades cardiovasculares.

Pero para realizar un correcto tratamiento de esta patología que tanto nos afecta es necesario partir de un correcto y eficaz diagnóstico, que debe de realizarse por médicos, nutricionistas y otros especialistas en la atención primaria de salud.

Las preguntas que buscamos responder con la revisión fueron las siguientes: ¿Cuáles son los indicadores antropométricos más utilizados actualmente en el diagnóstico de la obesidad en la atención primaria de salud en Cuba y el mundo? ¿Cuáles son sus ventajas y desventajas?

Actualizar los conocimientos existentes sobre los indicadores antropométricos utilizados en el diagnóstico de la obesidad en Cuba y el mundo es, por tanto, el objetivo que persigue este trabajo, para encontrar las respuestas acertadas.

Material y métodos

Por tal motivo se realizó una revisión documental y bibliográfica entre marzo de 2010 y enero de 2012. Las bases de datos consultadas fueron Medline y Cochrane mediante PubMed. Las búsquedas que se han realizado mediante PubMed y clasificadas por dos objetivos de búsqueda. Se usaron las siguientes palabras clave: indicadores antropométricos, obesidad, adultos, diagnóstico de la obesidad.

Para seleccionar los estudios fue adoptado como criterio de inclusión los artículos de indicadores antropométricos para el diagnóstico de la obesidad en adultos, publicados en inglés, portugués o español, en el período comprendido entre 2000 y 2012.

Se seleccionaron aquellos estudios que permitieran determinar los indicadores antropométricos que más se utilizan actualmente en el diagnóstico de la obesidad en la atención primaria de salud en Cuba y el mundo. Específicamente 44 estudios, 4 de ellos meta análisis y 44 de caso-control.

Resultados y discusión

Técnicas más exactas

Existen varias técnicas de laboratorio bastante exactas para valorar el porcentaje de grasa como parte de la composición corporal como la resonancia magnética nuclear, la tomografía axial computarizada (TAC), la densitometría, de impedancia eléctrica, medición de potasio 40, absorciometría dual (DEXA) entre otros. Estos métodos más avanzados exigen de un material altamente especializado y caro, imposibles de aplicar en la atención primaria de salud.

Antropometría en el diagnostico de la obesidad

Un cierto número de investigaciones han desarrollado técnicas de campo para predecir el porcentaje de grasa corporal y el grado de obesidad de poblaciones en la comunidad. Estas técnicas, conocidas como antropométricas, tienen muchas ventajas pues se necesita menos tiempo para su utilización, materiales relativamente baratos. Ellas utilizan cálipers, balanzas y cintas métricas que producen estimaciones bastante validas y fiables del grado de obesidad.

La antropometría ha devenido como una de las técnicas fundamentales para diagnosticar obesidad en poblaciones adultas mal nutridas por exceso por la relativa facilidad de su aplicación, su generalización y su aceptable rango de exactitud[4,5].

Los indicadores antropométricos más utilizados para este diagnóstico en la comunidad por médicos, enfermeras, nutricionistas y licenciados en cultura física son: el Peso Corporal (PC), el Peso para la Talla (PT) y el Índice de Masa Corporal (IMC), a pesar de que estos indicadores no miden adiposidad, ni siquiera de forma indirecta[6,7].

Análisis de algunos de los indicadores antropométricos existentes

El índice de Masa Corporal (IMC) mide el estado nutricional calculando el peso dividido por la estatura al cuadrado.

Fue diseñado por Quetelet, en el siglo XIX y aún es el más utilizado en la atención primaria de salud en Cuba y el mundo.

Es en estos momentos el índice mas validado por la Organización Mundial de la Salud en la evaluación del estado nutricional de adultos y a partir de ahí el diagnostico de la obesidad.

Los valores del IMC son un reflejo de las reservas corporales de energía. Esta afirmación se evidencia por su alta correlación con la grasa corporal estimada por métodos válidos como la densitometría, y por su alta correlación con los pliegues cutáneos que son predictores de la grasa corporal. Por este motivo en un inicio el IMC fue utilizado para describir la presencia de obesidad. Garrow en 1981 introduce un sistema de curvas que, a partir de un conjunto de puntos de corte, permite caracterizar la presencia de adiposidad, clasificando además al individuo según el grado de esta[8].

Ferro-Luzzi y otros en el Comité de Expertos de la FAO/OMS[11] completaron el sistema de puntos de corte de Garrow para evaluar tanto la presencia de obesidad como la de DEC. De esta forma queda definido un sistema de puntos de corte que permiten clasificar al individuo como normal, sobrepeso según cuatro categorías o DEC.

La tabla evaluativa es la siguiente:

Grado	Clasificación	IMC	Riesgo comorbilidad
	Normo peso	18,5-24,9	Normal
I	Sobrepeso o pre obeso	25-29,9	Incrementado
II	Obesidad leve	30-34,9	Moderado
III	Obesidad moderada	35-39,9	Alto
IV	Obesidad severa	Mas de 40	Muy alto

Los puntos de corte presentados en la tabla para caracterizar el estado nutricional de un individuo son válidos para adultos (mayores de 18 años) independientemente de su sexo. El hecho de que los valores sean válidos para uno y otro sexo tiene una alta importancia desde el punto de vista metodológico y práctico, pero merece algún comentario. Las reservas de grasa corporal en las mujeres son mayores que en los hombres, es por ello que los puntos de corte comunes para los 2 sexos son válidos para las mujeres en términos de que ellos son conservadores; pues se confeccionan básicamente con las características de los hombres, este punto les da valor a reserva de que las mujeres pueden tolerar puntajes más bajos del IMC que los presentados en la tabla. Los valores presentados no son aplicables a embarazadas[9-10].

En un estudio el IMC fue uno de los indicadores los más idóneos para el cribado de la obesidad en las etapas prepuberales y puberales puesto que presento un equilibrio mejor entre la sensibilidad y la especificidad y un menor fallo de clasificación[11].

La importancia del IMC para la epidemiología nutricional puede resumirse en los aspectos siguientes[12-14]:

- Por su simplicidad de cálculo e interpretación es muy útil para caracterizar el estado nutricional de grandes grupos de población.
- Como la malnutrición, medida según el IMC, es el reflejo de las condiciones de la alimentación de los individuos en el pasado, este índice es un trazador de los ingresos familiares, las condiciones socioeconómicas y el consumo de alimentos de una familia.
- Por el riesgo para la salud asociado con valores extremos (bajos o altos) del IMC.

Pero este índice ha sido criticado porque no permite distinguir entre masa magra y masa grasa, además tampoco determina la distribución de la adiposidad. Esto es importante porque la grasa abdominal, o sea, la que se ubica en la zona superior del cuerpo, está relacionada con los factores de riesgo (hipertensión arterial, diabetes y dislipidemia).

Mientras que aún cuando el IMC del individuo no supere el valor considerado como normal, estudios brindan evidencias tangibles que demuestran que el almacenamiento excesivo de grasa alrededor de la cintura expone un riesgo significativo para la salud, hasta en aquellas personas que no son consideradas obesas o pre-obesas por el IMC[15].

En un importante estudio realizado en una universidad privada de España la exactitud del IMC para estimar la composición corporal fue discutible estando afectada por sexo, raza y edad, lo cual condujo a una mala clasificación de la condición de obesidad. Es así como individuos diagnosticados con peso adecuado según el IMC, tuvieron un porcentaje de masa grasa elevado y otros diagnosticados como obesos con un IMC > 30 kg/m^2 tuvieron un porcentaje de grasa dentro de límites normales. Parece que el IMC no fue capaz de detectar un alto porcentaje de casos con exceso de grasa corporal, por lo que en este grupo, este índice pudo no reflejar adecuadamente la composición corporal como ya han puesto de manifiesto otros autores. Ante estos resultados se pudo concluir que a partir del IMC se ha encontrado un alto porcentaje de personas con sobrepeso aunque las cifras son más favorables a las de estudios realizados en población de edad similar, con un menor porcentaje de obesidad especialmente entre las mujeres. Las cifras también son alentadoras en cuanto al riesgo definido por la circunferencia de la cintura y el cociente cintura/cadera. Sin embargo, la utilización del porcentaje de grasa corporal como criterio para cuantificar la obesidad supone un importante incremento en el número de personas clasificadas como obesas. Estas diferencias en los resultados al utilizar distintos criterios para definir la situación de riesgo sugieren que habría que revisar los puntos de corte utilizados según se emplee uno u otro método[16].

El Índice Cintura Cadera (ICC) también ha sido cuestionado porque la grasa que se acumula en la región de las caderas varía mucho y eso puede inducir a error. Además, si en forma simultánea aumentan la obesidad en cintura y cadera, la razón se mantendrá constante sin que se considere el incremento del riesgo absoluto[17].

Estudios demuestran un coeficiente de correlación significativamente más bajo del ICC que de la Circunferencia de Cintura en correspondencia con los por cientos de grasa corporal (0,50 por 0,84)[18-20].

En tanto la Circunferencia de Cintura (CC), validada por el eminente investigador escoses Lean en 1995, es uno de los más aceptados a nivel mundial. Desde un inicio Lean demostró en sus estudios que la CC puede usarse en programas de promoción de salud para identificar individuos obesos que necesitan reducir su peso corporal Hombres con una CC >/= 94 cm y mujeres con una CC >/= 80 cm tienen pre obesidad abdominal y riesgo incrementado de comorbilidad; hombres con una CC >/= 102 cm y mujeres con una CC >/= 88 cm tienen obesidad abdominal y alto riesgo de comorbilidad[21].

La circunferencia de cintura (CC) es mundialmente utilizado como parámetro para cuantificar la obesidad central. Ha sido ampliamente utilizada como parámetro fundamental en la definición de síndrome metabólico (SM). Por sí sola puede ser utilizada para indicar la adiposidad o para reflejar factores de riesgo metabólicos[22].

Aún cuando el índice de masa corporal del individuo no supere el valor considerado normal, dicho estudio

brinda evidencias tangibles que demuestran que el almacenamiento excesivo de grasa alrededor de la cintura supone un riesgo significativo para la salud, hasta en aquellas personas que no son consideradas obesas o con sobrepeso[23-25].

Los estudios epidemiológicos han demostrado claramente que la adiposidad central está altamente correlacionada con la presencia de hipertensión, enfermedad coronaria, diabetes tipo 2, y mayor riesgo de mortalidad. La obesidad abdominal se asocia con un aumento del tejido adiposo visceral (IVA) de masa, y el IVA se asoció independientemente con la glucosa y las concentraciones de insulina en los hombres y las mujeres[26-29].

Varios estudios encontraron que la circunferencia de la cintura (CC) está más estrechamente asociado con el IVA y la adiposidad central que es o bien la cintura y la cadera, o índice de masa corporal (IMC, en kg/m^2). Magra et al., estudió 1.918 adultos de una población general en el norte de Glasgow y se encontró que la CC podría ser utilizada en programas de promoción de la salud para identificar a los adultos que necesitan el control de peso para evitar las enfermedades relacionadas con la obesidad. Booth et al., encontró que incluso auto-reporte de las estimaciones de mediciones de la CC son útiles para controlar el sobrepeso y la obesidad en estudios epidemiológicos[25-30].

En una guía sobre el tratamiento de la obesidad publicado recientemente por el National Institutes of Health (NIH), CC y el IMC fueron sugeridos como el medio más disponibles y fiables de identificación de la obesidad, el establecimiento de los riesgos relacionados con ella, y el seguimiento de su tratamiento. La guía del NIH sugiere que la medición CC tomarse justo por encima de la cresta ilíaca. Sin embargo, en una revisión de la literatura, se identificaron 14 diferentes descripciones del sitio para las mediciones de CC, incluyendo uno elaborado por el Grupo de Normalización de consenso antropométrico que difiere de la definición del NIH del sitio WC. Algunos métodos son ligeramente diferentes de los otros. En general, estos sitios pueden ser organizados en 4 grupos definidos por determinados puntos de referencia anatómicos: 1) inmediatamente por debajo de las costillas inferiores, 2) en la parte más estrecha de cintura, 3) el punto medio entre la última costilla y la cresta ilíaca, y 4), inmediatamente por encima de la ilíaca cresta[30].

De acuerdo con los investigadores del Imperial College de Londres, del Instituto Alemán de Nutrición Humana, y de otras instituciones de investigación europeas, los doctores deberían medir la cintura y de los pacientes, como parte de los chequeos estándares de salud[31].

Al comparar personas con el mismo índice de masa corporal, se comprobó que el riesgo de muerte prematura crecía de manera lineal según aumentaba la circunferencia de la cintura.

El riesgo de muerte prematura era mucho más elevado para las personas con cintura grande en comparación con las personas con una cintura más pequeña.

Según lo observado en el estudio, cada 5 centímetros de aumento en la circunferencia de la cintura se eleva el riesgo de muerte en un 17 por ciento para los hombres y en un 13 por ciento para las mujeres. El incremento en el riesgo de muerte puede estar particularmente relacionado con el almacenamiento de grasa alrededor de la cintura, porque el tejido adiposo en esta área segrega compuestos metabólicamente activos que pueden contribuir al desarrollo de enfermedades crónicas, sobre todo trastornos cardiovasculares y cáncer.

Estudios combinados de antropometría y tomografía axial computadorizada han demostrado una fuerte asociación entre la circunferencia de la cintura (CC) y la grasa intraabdominal. Es por ello que el valor de esta circunferencia ha comenzado a utilizarse en sustitución del índice cintura/cadera, al simplificar el pesquisaje antropométrico de aquellos en riesgo de morbilidad[32].

El aumento de la edad va asociado con el de la grasa corporal, que se manifiesta no solo en los valores de los pliegues grasos sino también en el incremento de la CC como reflejo de la grasa abdominal.

La variabilidad de la correspondencia entre los valores críticos de CC utilizados con carácter "universal" y la detección efectiva de morbilidad hace necesario el establecimiento de valores críticos poblacionales de la CC. Mientras no se cuente con esta información es aconsejable la utilización de los valores críticos actualmente en uso, dadas su utilidad, simplicidad y los beneficios que reporta en la detección de procesos morbosos. La posibilidad futura de mejorar el método con la obtención de valores críticos más idóneos a nuestra realidad, no debe limitar ni excluir el empleo de los valores críticos actualmente recomendados.

Estudios posteriores confirman que la obesidad abdominal medida por la CC es un fuerte y mejor predictor del riesgo de enfermedades cardiovasculares que el IMC. Sus puntos de corte más coincidentes, según diversos estudios, son los siguientes[30-33]:

Medición (cm)	Estado nutricional	Riesgo de comorbilidad
Hasta 80	Normal	sin riesgo
De 80 a 88	Pre obesidad abdominal	riesgo incrementado
Más de 88	Obesidad abdominal	alto riesgo

Aunque tiene el inconveniente de que sus valores y puntos de corte no han sido especificados para poblaciones latinoamericanas. Actualmente, se están utilizando aquellos que se aplican en los asiáticos. Además, este indicador no contempla la altura de los individuos y, como es de suponer, no es lo mismo tener 90 centímetros de cintura si uno mide 1,55 o 1,90 metros y por supuesto es imposible diagnosticas obesos ginecoides con este indicador.

Estudios revelan que la talla y la edad tienen una limitada influencia a diferencia de la cintura en individuos caucásicos de diferentes estaturas[31-34].

Otros destacan que si se utiliza la CC la prevalencia de obesidad en adultos pudiera ser significativamente

superior que si se utilizara sólo el IMC. Pudiendo ser la CC mejor indicador en estudios epidemiológicos de obesidad.

El cuarto de los indicadores es el Índice Cintura-Estatura, (ICE), diseñado por un colectivo de investigadores japoneses en el 2003 es muy sencillo de calcular porque sólo se deben dividir ambos valores en centímetros[35].

El ICE puede ser un óptimo predictor de factores de riesgo del síndrome metabólico y a obesidad abdominal específicamente, hasta el momento se han utilizado puntos de corte en adultos de de China de 0.50 en ambos sexos[36].

Ha demostrado una muy buena correlación con los por cientos de grasa corporal (0,85)[35,36].

La obesidad, especialmente central, está asociada con enfermedades crónicas no transmisibles y la asociación es independiente de la hipertensión, diabetes y síndrome metabólico. En los índices de obesidad de uso común, el ICE se asocia particularmente con estas Enfermedades[37].

El ICE en estudios asiáticos (en adultos de China) ha demostrado ser un mejor indicador de factores de riesgo coronarios, dislipidemias y diabetes tipo 2 que otros indicadores antropométricos como el IMC, la CC y el ICC en algunos estudios epidemiológicos realizados[37,38].

Este índice pudiera ser un método valioso para determinar obesidad abdominal en estudios de diagnóstico de la obesidad, mucho mejor en diversos estudios que el ICC[37-39].

Se sugiere que una herramienta-la simple, la detección rápida relación cintura-estatura podría ayudar a superar los debates sobre el uso de diferentes índices de masa corporal (IMC) los valores límite para la evaluación de riesgos para la salud en diferentes poblaciones. Hay seis razones de nuestra propuesta: el ICE es más sensible que el IMC como una alerta temprana de riesgos para la salud. El ICE es más barato y más fácil de medir y calcular que el IMC. Un valor límite de ICE = 0,5 indica un riesgo mayor para los hombres y las mujeres. Un valor límite de ICE = 0,5 indica un mayor riesgo para las personas de diferentes grupos étnicos. Los valores límite del ICE se puede convertir en un gráfico para el consumidor. EL ICE puede permitir que los valores límite mismo para niños y adultos. Mensajes sobre la comunicación de riesgo para la salud podrían ser mucho más simples si el mismo índice antropométrico y el mismo mensaje de salud pública se pueden utilizar durante toda la infancia, en la vida adulta, y en todo el mundo[40].

ICE ha sido validado como una alternativa mejor a la CC en la definición de síndrome metabólico (SM) entre los diabéticos, así como la población no diabética. Además de ser aplicable a través de las razas y sexos se ha demostrado ser más sensible y específica en la identificación de las personas con EM y personas con alto riesgo de enfermedad cardiovascular. Otros investigadores y lo han respaldado como un mejor predictor de riesgo cardiovascular, la obesidad y los Estados miembros, aunque no había una preocupación expresada con respecto a la terminología diversa que se utiliza. Un documento que propone el uso del ICE en la definición del Síndrome Metabólico ha sido aceptado recientemente y está en prensa. Sería de interés académico agradable a la vista los puntos de corte sugerido para el ICE en diferentes estudios, algunos de ellos ya publicados y en curso otros. Además de la ICE valor académico es muy útil en la difusión de un mensaje de concienciación sobre la salud de la comunidad.

A nivel internacional se han realizado algunos estudios sobre este último índice, obteniendo puntos de corte para poblaciones norteamericanas, asiáticas, brasileñas y chilenas; pero en todos los casos o se han descrito un solo valor para ambos sexos sin importar la edad, o en el mejor de los casos, puntos de corte para ambos sexos sin tener en cuenta la posible variación de estos por los años, además no especifican el grado nutricional, se dice que hay o no malnutrición por exceso y no se definen los individuos por aparentemente saludables, pre obesos u obesos[37-41].

El problema fundamental de este nuevo indicador es que no sirve para el diagnóstico de la obesidad ginecoide, pues esta es la acumulación excesiva de la grasa en glúteos, caderas y muslos. Esta obesidad se caracteriza por una acumulación de grasa en la región glúteo femoral: caderas, glúteos y muslos. Se la conoce como obesidad de la parte inferior del cuerpo y como obesidad en forma de pera.

Los adipocitos de la obesidad tipo ginecoide almacenan grasa con más facilidad y después no le es tan fácil perderla. El riesgo para la salud no es tan grande como el que se supone para la obesidad tipo androide, pero sí los tiene también. Se asocia con más frecuencia a osteoartritis en las articulaciones de carga, insuficiencia venosa, litiasis biliar, paniculopatía edemato fibroesclerótica y dificultades de locomoción.

Es por tanto también importante poder tener un indicador específico, eficaz y sencillo para diagnosticar obesidad ginecoide a nivel comunitario.

El último indicador diseñado es el Índice de Adiposidad Corporal (IAC). Este indicador en el estudio realizado da muy buena correlación con la grasa corporal, pero se requieren de otros estudios que lo validen pues las variables antropométricas que utiliza son la circunferencia de cadera y la talla, estas, según criterio del autor no son las indicadas para el diagnóstico correcto de la obesidad abdominal pues un individuo que concentre la mayor parte de su grasa en exceso en la zona media abdominal no necesariamente tiene que también acumularla en sus caderas y puede no dar obeso por este índice[42].

También se considera un poco complejo de aplicar en la Atención Primaria de Salud pues la resolución de la ecuación propuesta conlleva un cálculo no sencillo.

Estudios realizados en Cuba

En Cuba, los estudios de análisis de indicadores antropométricos se han enfocado en la validación del

IMC y la CC en nuestro país según los puntos de corte estandarizados internacionalmente, sin llegar a obtener los propios de nuestra población[43].

En nuestro país, en una búsqueda que lleva alrededor de dos año, hasta el momento no se ha encontrado ningún trabajo que trate al ICE, lo aplique, proponga o siquiera lo refiera en adultos en edad laboral de 20 a 59 años.

Los estudios más cercanos en este sentido se han enfocado en la determinación del estado nutricional de la población cubana adulta (Díaz Sánchez et al., 2005) en el marco de la Segunda Encuesta Nacional sobre Factores de Riesgo y Afecciones Crónicas no Transmisibles de la Población Cubana (2002) donde se realizaron las mediciones del peso, estatura, circunferencias de cintura y cadera y se calculó el índice de masa corporal y el índice cintura/cadera, la circunferencia de la cintura se utilizó para evaluar el riesgo de obesidad asociado con complicaciones metabólicas y como resultados tuvo que el 29,7% de los hombres y el 31,5% de las mujeres presentan sobrepeso mientras que el 7,95% de los hombres y el 15,4% de las mujeres presentan obesidad. En relación con la distribución de la grasa corporal, aproximadamente la cuarta parte de la población presenta un patrón de adiposidad superior lo que indica un riesgo de asociación con algunas enfermedades crónicas[44].

Y en la validación del IMC y la CC en nuestro país según los puntos de corte estandarizados internacionalmente (Berdasco, 2002), sin llegar a obtener los propios de nuestra población.

La utilización a nivel internacional de la CC y el ICE sólo se utilizan para conocer el riesgo de comorbilidad de poblaciones más que para el diagnóstico de la obesidad androide o abdominal, pues entendemos que esta última es su principal función evaluativa por su especificidad.

Por tanto, se considera que es necesario determinar mediante estudios experimentales y/o cuasi experimentales el indicador más eficaz y de mayor correlación con los por cientos de grasa corporal y luego de determinado este, conocer los puntos de corte que más se ajustan por sexo y grupos etáreos a la población adulta cubana, proponiendo indicadores más específicos y funcionales para el mejor diagnóstico de la obesidad androide o abdominal y ginecoide, para así mejorar la calidad de los servicios de salud en este sentido en nuestro país, de una patología que tanto nos afecta, pues de un correcto diagnóstico parte un mejor tratamiento.

Es indudable que los indicadores antropométricos existentes no son del todo eficaces para diagnosticar obesidad en la atención primaria de salud, unos por su difícil aplicabilidad y otros por no respetar el último concepto de obesidad emitido por la Organización Mundial de la Salud.

Es importante encontrar indicadores antropométricos mas específicos y funcionales para un mejor diagnóstico de la obesidad androide y ginecoide.

Conclusiones

Los resultados de la actual revisión indican que a pesar de la gran variedad de indicadores antropométricos existentes para diagnosticar obesidad en adultos todos tiene sus dificultades para su aplicación y generalización. Además de que la mayoría de estos no están adaptados y validados para poblaciones específicas por sexo, rango de edades, entre otras variables que harían mucho más eficaz su aplicación.

Se hace necesario entonces el desarrollo de investigaciones que validen nuevos indicadores ajustados a las características de la población a la cual evalúan.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1810-1816
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Hacia una integración comprensiva de la obesidad desde una perspectiva multidisciplinar

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Resumen

El presente artículo resume la situación actual de una de las epidemias del siglo XXI más importantes, la obesidad. Las altas tasas de obesidad de todos los países y especialmente en edades tempranas en nuestro país son preocupantes. Tradicionalmente, las investigaciones se han centrado en los aspectos más nutricionales, como factores dietéticos, metabolismo, aporte calórico y gasto energético. Sin embargo, otra disciplina como la psicología halla nuevos factores que influyen, como la adicción a la comida, la depresión, el estrés y la ansiedad, entre otros. En este trabajo, se analizan más de 80 artículos de todas las disciplinas relacionadas con la obesidad, obtenidos en diferentes bases de datos y, así mismo también se plantea un nuevo enfoque de carácter teórico para una mayor comprensión. Los estudios de la búsqueda bibliográfica realizada demuestran las evidencias necesarias para introducir un nuevo concepto de obesidad denominado edorexia y plantear cuestiones que deberán ser resueltas en futuras investigaciones centradas en una perspectiva multidisciplinar.

(*Nutr Hosp.* 2012;27:1810-1816)

DOI:10.3305/nh.2012.27.6.5882

Palabras clave: *Obesidad. Edorexia. Adicción a la comida. Depresión. Ansiedad. Perspectiva multidisciplinar. Nutrición. Psicología.*

TOWARDS A COMPRHENSIVE INTEGRATION OF OBESITY FROM AN INTERDISCIPLINAR PERSPECTIVE

Abstract

This article summarizes the current situation of one of the most important XXI century epidemics. The high rates of obesity in all countries and specially in our country at early ages are worrying. Traditionally, investigations have focused on the most nutritional aspects, such us dietary factors, metabolism, calory intake and energy expenditure. However, other sciences —such as Psychology— point out new influencing factors, such as food addiction, depression, stress and anxiety. In this piece of work, more than 80 articles from all disciplines and different databases and related to obesity are analyzed, as well as a new theoretical approach is proposed to ensure a more accurate comprehension. The literature review shows the necessary evidence to introduce a new model of obesity named edorexia, and raise issues to be resolved in future research oriented from a multidisciplinary perspective.

(*Nutr Hosp.* 2012;27:1810-1816)

DOI:10.3305/nh.2012.27.6.5882

Key words: *Obesity. Edorexia. Craving food. Depression. Anxiety. Multidisciplinary perspective. Nutrition. Psychology.*

Abreviaturas

IMC: Índice de masa corporal.

Introducción

En diferentes estudios se ha observado el aumento de la prevalencia en todos los países y especialmente en España Gelpi-Méndez et al.[1], la cual ha alcanzado unas cifras de obesidad infantil superior a la estadunidense. Esta situación ha provocado un gran interés y el aumento de la investigación de la obesidad en diferentes áreas del conocimiento. Destaca el interés por las disciplinas clásicas relacionadas con ella, como es el caso de la Nutrición, en la cual se publicó a finales del año pasado el último consenso entre la Federación Española de Sociedades de Nutrición, Alimentación y Dietética (FESNAD) con la Sociedad Española para el Estudio de la Obesidad (SEEDO); se trata de una reflexión sobre las hábitos alimenticios y otros aspectos nutricionales relevantes para la prevención y el tratamiento de la obesidad y que resalta el acercamiento desde las perspectiva nutricional a las variables psicológicas otorgándolas relevancia, como por ejemplo en el caso del ambiente. Además este documento actualiza

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Recibido: 2-IV-2012.
Aceptado: 7-VIII-2012.

los objetivos y tratamientos nutricionales asociados al exceso de peso (Consenso FESNAD–SEEDO[2]). Sin embargo, existe otra disciplina como la Psicología que aporta nuevos conocimientos asociados a la obesidad, en los cuales se establece una relación positiva y significativa entre la obesidad y los diversos factores psicológicos, como son la adicción a la comida, la depresión, la ansiedad y el estrés o sobre variables más especificas, como la motivación o la percepción de los alimentos, entre otros (Michaelides[3]; Pelchat[4]; Ziaudden, Subramaniam, Gaillard, Burke, Farooqi y Feltcher[5]). Además, destaca los avances neurológicos y sus investigaciones sobre sistemas como los dopaminergicos, así como las alteraciones neuronales provocadas por el abuso de los hidratos de carbono (Avena, Rada y Hoebel[6]; Michaelides[3]). Por consiguiente, se requiere de una perspectiva multidisciplinar para redefinir la obesidad, teniendo en cuenta todos los aspectos que se hacen referencia y así alcanzar un conocimiento completo sobre ella; de este modo se debe integrar todos los conocimientos científicos que han hallado, en vez de realizar estudios independientes y sin interactuar con otras áreas. Con esta perspectiva, se realiza un análisis retrospectivo de lo que se ha publicado hasta la actualidad y con el objetivo de establecer la situación vigente, como también las nuevas líneas de investigación que comienzan desde este enfoque.

Desde la anterior premisa, hemos realizado un análisis detenido de los contenidos que en los últimos años se han publicado en las principales revistas y bases de datos, tal como se citan en los siguientes apartados. Se ha tenido presente los estudios principales de todas las áreas que investigan el exceso de peso, las cuales son: la nutrición y la psicología. Además de los temas generales, se han analizado los subtemas más característicos de los aspectos psicológicos, los principales son: la adicción a la comida, la depresión, el estrés y la ansiedad. Se han considerado la mayoría de las publicaciones y aportaciones de los últimos treinta años en revistas, sobretodo extranjeras de lengua inglesa, por ser mayoría en este tipo de estudios. Por último, se ha dirigido la búsqueda de lo general a lo particular y más práctico (como la adicción a la comida en deportistas o en individuos que poseen un estado de normopeso, los factores genéticos de la obesidad, etc.). En concreto, destacan la publicación coordinada por Vaquero[7] en la que se muestra, entre otros temas, la influencia del genoma o la resistencia de la insulina para desarrollar un exceso de peso; y los estudios sobre el abuso de cafeína en deportistas (Sigmon[8]; Pauliska[9]; Sinclair y Geiger[10]).

Algunos datos sobre los estudios encontrados

De acuerdo a lo descrito en el epígrafe anterior, a partir de las bases de datos Academic Search Premier, PsycINFO, Medline, Pubmed, entre otras; se han analizado las publicaciones desarrolladas en los últimos treinta años, a continuación se muestran los principales datos en cuanto a contenidos estudiados e investigaciones de acuerdo a los artículos públicos y recogidos por las anteriores bases de datos. La mayoría de las publicaciones que tienen relación con la obesidad son el resultado de investigaciones en departamentos de medicina, tecnología de alimentos y nutrición, cuyos temas son similares: factores genéticos, hormonales, comorbilidad con otras enfermedades, programas de prevención de obesidad infantil y adolescente, se destacan trabajos como: Chen y Wang[11]; Manios[12]; Simarro Rueda et al[13]. A modo de ejemplo, se muestra en la tabla I los artículos publicados en los primeros meses del 2012, que denota la importancia de esta disciplina sobre esta patología en cuanto a producción. Entre los resultados destaca la importante investigación en programas de prevención para la obesidad infantil.

Tabla I
Áreas de investigación en los trabajos publicados sobre nutrición y obesidad en el año 2012

Tema	*Números artículos*	*Porcentaje*
Contaminación	1	4,76%
Alimentos y tipo de dieta	2	9,52%
Comorbilidad	1	4,76%
Prevención obesidad infantil	11	52,38%
Metabolismo	4	19,05%
Imagen corporal	1	4,76%
Calidad de vida	1	4,76%

No obstante, uno de los últimos avances de la nutrición es la nutrigenómica y nutrigenética. La nutrigenética engloba el análisis retrospectivo de las variantes genéticas de los nutrientes, y la nutrigenómica pretende proporcionar un conocimiento molecular (genético) sobre los componentes de la dieta, los cuales contribuyen a la salud mediante la alteración de la expresión y/o estructuras según la constitución genética individual (Martí del Moral, Moreno-Aliaga, Zulet y Martínez[14]). En esta especialidad se presta especial atención al metabolismo, los factores genéticos de la obesidad y factores hormonales, como por ejemplo la leptina, grelina e insulina (Palou, Bonet, Picó y Rodríguez[15]). Bostom et al.[16] identificaron una nueva hormona, la irisina que permite la conversión de los adipocitos denominados blancos a los adipocitos marrones, los primeros permiten almacenar las calorías y los segundos quemarlas; esta modificación se traduce en un incremento del gasto calórico sin la necesidad de aumentar la actividad física, es decir, con la misma actividad física el organismo gasta más energía facilitando el proceso de perdida de peso corporal.

De acuerdo con los datos obtenidos en la búsqueda, a continuación se describe brevemente autores, revistas y centros más representativos teniendo en cuenta el número de publicaciones, mientras las siguientes (2 a 4) se abordan los parámetros más característicos para com-

pletar una visión multidisciplinar de la obesidad. Entre los autores más reiterados en investigaciones relacionadas con aspectos psicológicos de la obesidad destacan Avena N. M., Caseli G, Meule A., Pelchat M. L. y Peters A. Las revistas con mayores publicaciones en dichas investigaciones son Apetite, International Journal of obesity, Journal of affective disorders, Journal of Nutrition y Obesity Reviews; y los centros de investigación más destacados: London South Bank University, Princeton University, University of Lübeck, University of Pennsylvania.

Con la finalidad de desarrollar una visión integradora de la obesidad, le concedemos a los componentes psicológicos una gran importancia en la misma. Aunque en las siguientes tres tablas se recogen aspectos de las diversas publicaciones, es necesario destacar aquellos autores y publicaciones que han reiterado especialmente los conceptos básicos para el desarrollo de este enfoque integral (Avena, Rada y Hoebel[17]; Croker[18]; Davis, Curtis, Levitan, Carter, Kaplan y Kennedy[19]; Meule[20]), además se muestran en ellas los principales datos sobre los factores psicológicos teniendo en cuenta las publicaciones de los últimos treinta años y a su vez se clasifican en tres grandes categorías: la adicción a la comida, la depresión y por último, la ansiedad y el estrés. Se analiza en primer lugar la adicción a la comida que es el subtema más estudiado en comparación con el resto y se observa una amplia diversidad de objetivos e hipótesis en cada uno de los estudios; también se observa como todos ellos se dirigen hacía un mismo objetivo, mediante la adicción a la comida se quiere encontrar la solución a la epidemia de la obesidad y como consecuencia ha despertado un interesante debate: algunos expertos de la psicología consideran que la comida puede considerarse una sustancia tóxica cuya adicción y abuso provocaría un exceso de peso. A lo largo de la mayoría de los artículos del periodo analizado, se asocia la adicción a la comida con un exceso de peso. Sin embargo, Pelchat[4] resalta el resultado del diagnostico de adicción a la comida en personas que no sufren exceso de peso, sino también en individuos que se encuentran en un estado de normopeso e incluso de peso insuficiente. Peters[21] concluye que no existen evidencias que relacione la adicción de carbohidratos con la obesidad, y que en realidad la causa de la obesidad está condicionada con el mal funcionamiento cerebral como consecuencia de factores estresantes (como la restricción calórica). Los expertos de la psicología sí coinciden en la posibilidad de atribuir el desencadenamiento de la adicción a cualquier alimento en condiciones específicas, por ejemplo la experiencia y el consumo repetitivo (Corwin y Grigson[22]).

En la tabla II, se observa la amplia área de investigación de la adicción a la comida; las variables psicológicas y aspectos cognitivos, como el tipo de pensamiento, actitud o percepción y propiedades de los alimentos. Destaca también el interés en aspectos fisiológicos que se han empleado como un argumento para establecer similitudes con otras adicciones. Sin embargo, en los resultados de la búsqueda bibliográfica se encuentra una ausencia significativa, la referencia a una posible adicción a la comida en un colectivo de individuos no obesos como los deportistas; al realiza una búsqueda más detallada se haya evidencias indirectas en diversas investigaciones como: (1) Estudios con cafeína en deportistas (Sigmon[8]; Pauliska[9]; Sinclair y Geiger[10]), concluyendo la aparición una dependencia a esa sustancia; (2) Conociendo la dieta habitual de un atleta (rica en hidratos de carbono) y la relación del abuso de esta sustancia con modificaciones neuronales similares a las encontradas en otras adicciones, facilita la aparición de una dependencia física a la sustancia causante (Avena, Rada y Hoebel[6]). Y por último, (3) los hallazgos de Dingemans y Van Furth[23] encuentran más similitudes que diferencias entre la población obesa y no obesa con relación al trastorno por atracón. En la misma situación puede encontrarse la adicción a la comida, ambas patologías se originaron de forma similar: se estudia la población obesa evitando la concepción de ingerir más alimentos sin repercutir en el peso corporal.

Tabla II
Áreas de investigación en los trabajos publicados sobre adicción a la comida en los últimos treinta años

Tema	*Números artículos*	*Porcentaje*
Variables psicológicas y aspectos cognitivo	10	24,39%
Aspectos fisiológicos	9	21%
Identificación y diagnostico de similitudes y diferencias con otras adicciones	7	17,07%
Estudios epidemiológico	6	14,63%
Desarrollo de cuestionarios, técnicas de tratamiento y programas de prevención	5	12,20%
Estudios centrados en la importancia del contexto	4	9,76%

En la tabla III, se muestran los resultados obtenidos en la búsqueda de la relación entre la depresión y la obesidad; los datos no concluyen con exactitud si la depresión es una causa o una consecuencia de la obesi-

Tabla III
Áreas de investigación en los trabajos publicados sobre la depresión y la obesidad en los últimos treinta años

Tema	*Números artículos*	*Porcentaje*
Evaluación de relación entre depresión y obesidad	5	38,46%
Aspectos fisiológicos	2	15,38%
Comparación cultural. Occidente *vs* oriente	2	15,38%
Estudios de calidad de vida	2	15,38%
Estudios estadísticos de comorbilidad	2	15,38%

Tabla IV
Áreas de investigación en los trabajos publicados sobre el estrés, la ansiedad y la obesidad en los últimos treinta años

Tema	*Números artículos*	*Porcentaje*
Deficiencia cognitiva y emocional en obesos	7	87,5%
Evaluación de los procesos cognitivos básicos y complejos	1	12,5%

dad. Shomaker et al[24] concluye que la sintomatología depresiva empeora la resistencia a la insulina, factor relacionado con la obesidad, pero la modificación del índice de masa corporal (IMC) no esta asociado. Grillo et al. [25] haya una correlación positiva entre la obesidad y la depresión, otorgando la causa a la alteración del hipocampo y la amígdala. Desai[26] destaca el aumento del IMC con la aparición de depresión. Sin embargo, también se encuentra el resultado inverso en las investigaciones orientales en comparación con los estudios de occidente (Apostolopoulou et al. [27]; Chang y Yen[28]). Por último destaca los hallazgos de Rivera et al. [28], en el que se identifica la depresión como predictor de la influencia del gen FTO, que permite el control en la conducta alimentaria y el gasto energético; lo que repercuta en un incremento del IMC (Fawcett y Barroso[30]).

Por último, se analizan las relaciones entre el estrés, la ansiedad y la obesidad (tabla IV), estos estudios se encuentran englobados en estudios sobre el déficit de aspectos cognitivos y emocionales (como la depresión, estrés y ansiedad). Las últimas investigaciones confirman la relación entre el estrés y la motivación para comer, aunque no está relacionado con el incremento del IMC (Groesz[31]). Elder et al. [32] relaciona el sueño, la depresión y el estrés con el cambio del peso. Entre sus resultados destaca la relación bidireccional entre la obesidad con la depresión y la relación negativa de la línea base de estrés con la perdida de peso. Villaseñor Bayardo, Onnteveros Esqueda y Cárdenas Cibrián[33] otorga a la depresión, al estrés y a la ansiedad la categoría de causa y consecuencia de la obesidad. Cserjési, Vermeulen, Lénárd y Luminet[34] asocian a la población con obesidad una reducción de la capacidad expresiva, presentando dificultades para buscar o mantener la atención en expresiones faciales negativas independientemente de la depresión o la ansiedad presentada. Por último, Michaelides[3] resalta la importancia de la regulación cognitiva y emocional: la motivación, la recompensa, la memoria, la emoción, la toma de decisiones, la representación sensorial y los estímulos interoceptivos durante la alimentación y la exposición al contexto alimentario; además mediante técnicas de neuroimagen se demuestra en estos factores diferencias entre la población con exceso de peso y normopeso; también se halla la comorbilidad con otros trastornos como depresión y ansiedad. Por tanto, el autor concluye que la alteración de uno o más de estos factores puede causar la aparición de la obesidad o el sobrepeso.

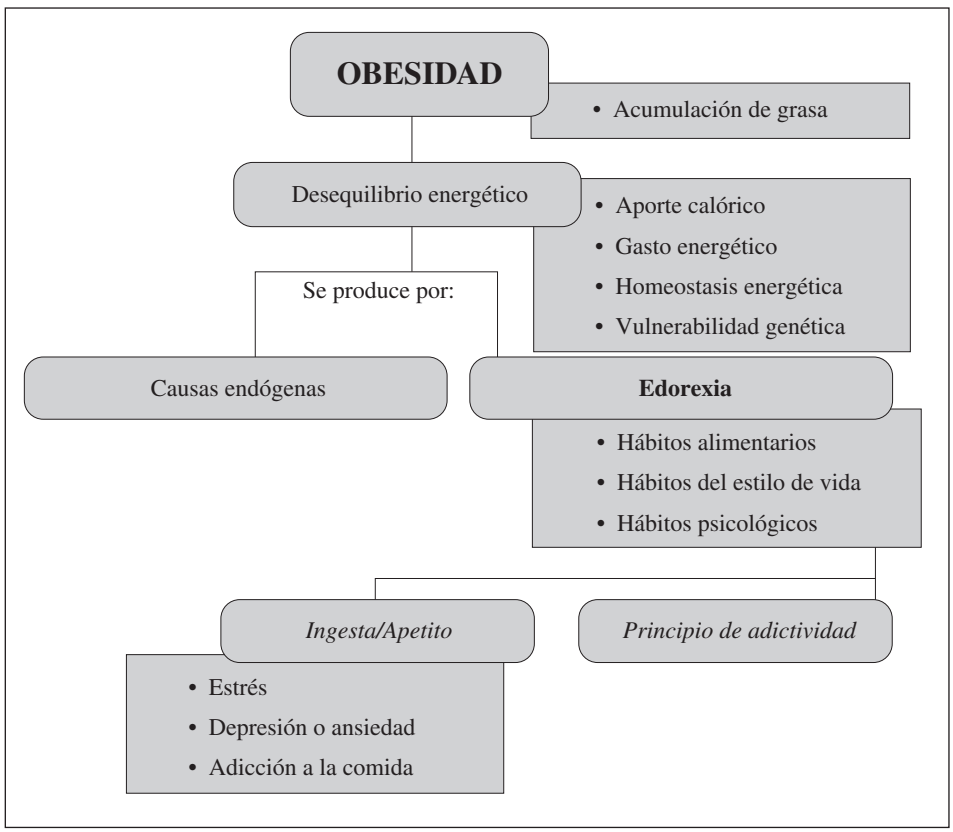


Fig. 1.—Modelo integrador comprensivo de la perspectiva multidisciplinar sobre la obesidad.

Discusión

Una vez revisado y analizado los resultados de la búsqueda bibliográfica realizada en los diversos temas relacionados con la obesidad, focalizando la atención en los aspectos psicológicos y especialmente en la adicción a la comida; y siempre desde la perspectiva de llegar a ofrecer una propuesta teórica que integre los distintos conocimientos que se conocen acerca de los procesos asociados a la obesidad, a continuación proponemos una serie de parámetros que en sintonía con Elder et al.[32], Meule[20], Michaelides[3], Peters[21], Wise[35] entre otros, nos permiten orientar el camino y seguir en la construcción de dicho planteamiento teórico. En el cuadro 1 se muestra simplificadamente los fundamentos del modelo integrador, comprensivo y multidisciplinar de la obesidad. En el cual, se considera la obesidad como un estado corporal cuya característica principal es la acumulación de grasa, ocasionada por un desequilibrio energético entre diversos factores, como el aporte calórico y gasto energético, mediante la influencia de la homeostasis energética y la vulnerabilidad genética. Aunque este desequilibrio energético en raras ocasiones es debido a causas endógenas, puede desencadenar una serie de consecuencias provocando una obesidad. Sin embargo, la mayoría de las ocasiones la obesidad es el resultado de los hábitos adquiridos y serán éstos la clave principal para mantener o romper el equilibrio antes mencionado (principio de adictividad). De este modo, además del riesgo añadido de padecer un síndrome metabólico entre otras complicaciones, destaca el apetito como el principal problema; así surgen pautas de comportamientos asociadas a la ingesta a pesar de no necesitar un aporte calórico, como es el caso del estrés, la depresión, la ansiedad y la adicción a la comida. Englobando este concepto surge el término edorexia, producto de la combinación de dos palabras latinas *(Edo* y *orexis* que significan comer y apetito respectivamente, es decir *"comer por apetito")*.

- Contexto multidisciplinar. A lo largo de los trabajos se ha comprobado la existencia de diferentes aspectos que interactúan entre sí provocando una obesidad: *Hábitos alimentarios*, como la ingesta calórica; *Hábitos del estilo de vida*, como el deporte, el sueño y la vida sedentaria; *Hábitos psicológicos* adquiridos por condicionamiento, aprendizaje vicario o transmisión de la información, como los aspectos cognitivos (pensamientos, creencias, esquemas), afectivos (motivaciones), fisiológicos, experiencias, etc. Clásicamente los factores más relevantes y estudiados se encuentran en los dos primeros hábitos (aspectos dietéticos y el deporte). Sin embargo, conforme avanzan las investigaciones se añaden nuevos factores asociados, como la depresión y el estrés.
- Desequilibrio energético y principio de adictividad. Un aporte calórico superior al gasto energético puede desencadenar una acumulación de grasa; sin embargo, esta situación no se repite en todas las circunstancias. Hemos comprobado cómo ingerir más alimentos no se encuentra asociado siempre con el incremento del peso corporal y el IMC, sino que influyen nuevos factores como la homeostasis energética y la vulnerabilidad genética. Sin embargo, la presencia de uno o más de estos factores no implica necesariamente el desarrollo de la obesidad, por lo que la suma de éstos (aporte calórico excesivo, gasto energético mínimo, alteración del mecanismo de homeostasis energética y vulnerabilidad genética) y sus conductas de riesgo asociadas (hábitos alimentarios, hábitos del estilo de vida y hábitos psicológicos) son los desencadenantes de la obesidad; así se establece el principio de adictividad del modelo teórico, distinguiendo entre las conductas favorables para lograr un buen estado de salud con las conductas de riesgo, las desencadenantes de la obesidad.
- Vulnerabilidad genética y homeostasis energética. Se ha comprobado la importancia de los factores genéticos, los individuos desarrollan una determinada vulnerabilidad en la cual, los agentes estresores provocan la acumulación de grasa. Por lo que los hábitos del individuo representan el último eslabón y son los responsables de desencadenar la obesidad. Sin embargo, el organismo está capacitado para establecer estrategias que permitan mantener el equilibrio; se desarrollan modificaciones metabólicas y conductuales para alcanzarlo en el caso del exceso en la ingesta. Además se conoce la amplia etiología de la alteración en la homeostasis energética en la cual, el estrés, el aprendizaje y otros factores psicológicos constituyen parte de la misma.
- Áreas cerebrales y procesos cognitivos. Es necesario resaltar los hallazgos neuropsicológicos, las alteraciones en los procesos cognitivos y su influencia en la obesidad; este contexto permite la conversión del concepto de una acumulación de grasa a un trastorno con áreas cerebrales afectadas como el hipotálamo, la amígdala y algunos autores incluyen el hipocampo, entre otras. Así se proporciona una visión multidisciplinar de la obesidad con aspectos generales como la adicción a la comida, la depresión, el estrés o la ansiedad y algunos más específicos como la percepción interoceptiva durante la alimentación o la expresión de emociones, entre otros.
- Edorexia y comer por apetito. La obesidad entendida como la acumulación de grasa por consecuencia de una ingesta superior al gasto energético, es una definición correcta pero también incompleta. Siguiendo con la conclusión de los epígrafes anteriores, la definición de la obesidad debería reflejar un estado corporal provocado por diversas causas, algunas endógenas y otras exógenas (como los hábitos). Surge así la necesidad de

definir el término denominado edorexia para englobar los factores y conductas descritas anteriormente y que provocan por si mismas un malestar clínicamente significativo o deterioro social, laboral o de otras áreas importantes de la actividad del individuo. Además se enfatiza el apetito como estimulante de las conductas de riesgo y establece los distintos aspectos o componentes que predominan e integran la obesidad, se distinguen los siguientes: apetito por estrés, apetito por depresión o ansiedad y apetito por adicción a la comida.

- Diagnostico multifactorial. En la misma línea de los epígrafes anteriores, la edorexia debe ser diagnosticada con un análisis multifactorial e identificada con un análisis funcional de la conducta. Se debe destacar especialmente el eje IV, los factores estresantes. De esta forma, se observa la edorexia como una enfermedad multidisciplinar en la que el aprendizaje es fundamental y desencadenante de la obesidad, se requiere de una intervención completa: compuesta por uno o varios módulos psicológicos y uno o varios módulos nutricionales.

Por otra parte, proponemos potenciales líneas de investigación de futuros estudios:

- Factores sociales y culturales. En comparación con la relación entre adicción a la comida y la obesidad, el estrés, la ansiedad y la depresión son unas áreas menos investigadas provocando resultados contradictorios. Aunque hay evidencias que afirman estas relaciones, también se ha comprobado como los factores sociales y culturales influyen en la aparición o no de la obesidad. Por ese motivo, las futuras investigaciones tendrán que considerar la percepción de la ansiedad, el estrés y la depresión, así como los repertorios de respuesta del individuo para afrontar las distintas situaciones que se plantean.
- Refuerzos positivos y negativos. Desde esta nueva perspectiva se procura evitar considerar la obesidad como la consecuencia de un desajuste entre el aporte calórico y el gasto energético. Se busca el origen de las respuestas problema (antecedentes) y sus consecuentes (refuerzos), ya que identificar los refuerzos en los que se recompensa la respuesta problema y los antecedentes es fundamental para definir y comprender la enfermedad y para desarrollar un planteamiento terapéutico. Entre los refuerzos positivos el más estudiado es el asociado con la adicción a la comida y entre los refuerzos negativos cabe destacar el escape o evitación de la obesidad cuando se realiza un régimen hipocalórico. Futuras investigaciones deberían considerar y demostrar estos datos.
- Programa de prevención y tratamiento de la obesidad. Diversos estudios nutricionales y alguno psicológico proporcionan información sobre los programas de prevención actuales. Aunque no se ha encontrado un programa de prevención ni de tratamiento multidisciplinar, en el cual los módulos de intervención serían tanto nutricionales como psicológicos, por el contrario sí se ha empleado un enfoque paliativo. Este programa se caracterizaría por: (a) tener en consideración los factores, las conductas de riesgo, antecedentes y consecuentes identificados; (b) adaptar el programa a las características personales del individuo como también al tipo y componentes que predominan en la edorexia que sufre y provocan una obesidad; (c) promocionar un estado de bienestar utilizando la definición multidisciplinar.
- Comprobación nutricional. En futuras investigaciones atendiendo a los aspectos psicológicos descritos anteriormente así como a los factores y conductas de riesgos, se analizará la determinación y el nivel de influencia que posee tanto los aspectos clásicos (nutricionales) como los psicológicos en el desarrollo de la obesidad.
- Clasificación de la obesidad. No se ha encontrado ninguna clasificación según su etiología, como tampoco se han observado evidencias que demuestre la obesidad como una patología única y por tanto que sea la misma en todos los individuos que la sufren. Por el contrario, existen escalas de diferentes grados de obesidad como el IMC, que por otro lado no es recomendable emplear para el diagnostico. Futuras investigaciones tendrán que desarrollar un instrumento para evaluar los diferentes tipos y facilitar el diagnostico de la edorexia y la obesidad.
- Adicción a la comida en individuos no obesos. Las investigaciones actuales sobre la adicción a la comida tiene como finalidad encontrar la solución a la obesidad, evitando los demás aspectos psicológicos y nutricionales. Esta situación provoca sesgos como los siguientes: ignorar la posibilidad de encontrar individuos que sufren adicción a la comida estando dentro de los parámetros normales de peso corporal y en algunas ocasiones definir la comida como una circunstancia similar a la que constituyen cualquier sustancia toxica. En las futuras investigaciones se tendrá que realizar estudios prestando atención a los datos mencionados como también a los factores y conductas de riesgo; asumiendo la posibilidad de encontrar aspectos, factores y conductas de riesgo (edorexia) sin presentar una obesidad.

En conclusión, al definir la obesidad en dos conductas principales, como son la ingesta excesiva de alimentos y los hábitos sedentarios, se estudia la obesidad superficialmente, evitando los aspectos más complejos. Las últimas investigaciones observan diversos aspectos psicológicos y factores que interactúan facilitando y dificultando las conductas principales anteriores. Además, existen suficientes evidencias para otorgar a los aspectos psicológicos relacionados con la obesidad (como son la adicción a la comida, la depre-

sión, el estrés y la ansiedad) la importancia para introducirlos como desencadenantes de la obesidad, integrarlos en la definición de edorexia y en las intervenciones de diversos ámbitos (promoción de la salud, prevención o tratamiento de la obesidad). Por ese motivo, las futuras investigaciones deberán tener en consideración los diversos estudios de todas las disciplinas que estudian la obesidad e integrarlos en sus conclusiones, si bien nosotros tenemos ya un modelo teórico tentativo de carácter integrador, que intenta comprender los factores que conducen a la obesidad.

Agradecimientos

Los autores desean agradecer al Ministerio de Educación, Cultura y Deporte por la concesión de la beca de colaboración para José Luis López Morales (Proceso n° 300056).

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(5):1817-1836
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Perioperative intravenous iron; an upfront therapy for treating anaemia and reducing transfusion requirements

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Abstract

Perioperative anaemia, with iron deficiency being its leading cause, is a frequent condition among surgical patients, and has been linked to increased postoperative morbidity and mortality, and decreased quality of life. Postoperative anaemia is even more frequent and is mainly caused by perioperative blood loss, aggravated by inflammation-induced blunting of erythropoiesis. Allogenic transfusion is commonly used for treating acute perioperative anaemia, but it also increases the rate of morbidity and mortality in surgical and critically ill patients. Thus, overall concerns about adverse effects of both preoperative anaemia and allogeneic transfusion have prompted the review of transfusion practice and the search for safer and more biologically rational treatment options. In this paper, the role of intravenous iron therapy (mostly with iron sucrose and ferric carboxymaltose), as a safe and efficacious tool for treating anaemia and reducing transfusion requirements in surgical patients, as well as in other medical areas, has been reviewed. From the analysis of published data and despite the lack of high quality evidence in some areas, it seems fair to conclude that perioperative intravenous iron administration, with or without erythropoiesis stimulating agents, is safe, results in lower transfusion requirements and hastens recovery from postoperative anaemia. In addition, some studies have reported decreased rates of postoperative infection and mortality, and shorter length of hospital stay in surgical patients receiving intravenous iron.

(*Nutr Hosp.* 2012;27:1817-1836)

DOI:10.3305/nh.2012.27.6.6087

Key words: *Perioperative anaemia. Allogenic transfusion. Intravenous iron. Safety. Efficacy.*

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Recibido: 27-VII-2012.
Aceptado: 7-VIII-2012.

HIERRO INTRAVENOSO PERIOPERATORIO; UNA OPCIÓN TERAPÉUTICA PARA EL TRATAMIENTO DE LA ANEMIA Y LA REDUCCIÓN DE LOS REQUERIMIENTOS DE TRANSFUSIÓN

Resumen

La anemia perioperatoria, cuya principal causa es la deficiencia de hierro, es frecuente entre pacientes quirúrgicos y se asocia a un aumento de la morbimortalidad postoperatoria y a una disminución de la calidad de vida. La anemia postoperatoria es aún más frecuente y está causada principalmente por la pérdida perioperatoria de sangre, agravada por la reducción de la actividad eritropóyetica inducida por la inflamación. La transfusión alogénica es el tratamiento habitual de la anemia aguda perioperatoria, pero también aumenta la tasas de morbimortalidad en pacientes quirúrgicos y críticos. La preocupación por los efectos adversos de la anemia preoperatoria y la transfusión alogénica han impulsado la revisión de la práctica transfusional y la búsqueda de opciones de tratamiento más seguras y biológicamente más racionales. En este artículo se revisa el papel de la terapia con hierro intravenoso (mayoritariamente hierro sacarosa y carboxymaltosa de hierro), como herramienta segura y eficaz para el tratamiento de la anemia y la reducción de los requerimientos transfusionales en el paciente quirúrgico, así como en otras áreas médicas. Del análisis de los datos publicados y a pesar de la falta de evidencia de alta calidad en algunas áreas, parece razonable concluir que la administración perioperatoria de hierro intravenoso, con o sin agentes estimuladores de la eritropoyesis, es segura, reduce las necesidades de transfusión y acelera la recuperación de la anemia postoperatoria. Además, algunos estudios han encontrado una reducción de las tasas de infección postoperatoria y de mortalidad, así como de la duración de la estancia hospitalaria, en pacientes quirúrgicos tratados con hierro intravenoso.

(*Nutr Hosp.* 2012;27:1817-1836)

DOI:10.3305/nh.2012.27.6.6087

Palabras clave: *Anemia perioperatoria. Transfusión alogénica. Hierro intravenoso. Seguridad. Eficacia.*

Abbreviations

ABT: Allogeneic blood transfusion.
ADEs: Adverse drugs events.
BS: Bariatric surgery.
CRC: colorectal cancer.
CHF: Chronic heart failure.
CKD: Chronic kidney disease.
ESAs: Erythropoiesis-stimulating agents.
FCM: Ferric carboxymaltose.
FID: Functional iron deficiency.
Hb: Haemoglobin.
HMWID: High molecular weight iron dextran.
IBD: Inflammatory bowel disease.
ICU: Intensive care unit.
ID: Iron deficiency.
IDA: Iron deficiency anaemia.
IS: Iron sucrose.
IV: Intravenous.
LMWID: Low molecular weight iron dextran.
NATA: Network for the Advancement of Transfusion Alternatives.
NSQIP: National Surgical Quality Improvement Program.
PHF: Pertrochanteric hip fracture.
RCT: Randomised controlled trial.
RES: Reticulo-endothelial system.
rHuEPO: Recombinant human erythropoietin.
SHF: Subcapital hip fracture.
THR: Total hip replacement.
TKR: Total knee replacement.

Introduction

Perioperative anaemia has been linked to increased postoperative morbidity and mortality, and decreased quality of life. Depending on the procedures and the definitions of anaemia, from 11% to 76% of surgical patients may present with preoperative anaemia.[1] Iron deficiency (ID) is the leading cause of anaemia in surgical patients, and results from the interplay of three distinct risk factors: increased iron requirements (e.g., associated with treatment with erythropoiesis-stimulating agents), limited external supply (e.g., *Helicobacter pylori* infection, autoimmune atrophic gastritis, chronic and acute inflammatory diseases, etc) and increased blood loss (e.g., due to phlebotomy or haemorrhage).[2]

Postoperative anaemia, which may be present in up to 90% of patients undergoing major surgery[1] is mainly caused by perioperative blood loss and may be aggravated by blunting of erythropoiesis by inflammatory responses, especially through decreased iron availability due to hepcidin-induced down-regulation of intestinal absorption and impaired mobilization of iron from body stores.[3]

Thus, iron deficiency can be either absolute or functional. In absolute ID, the iron stores are depleted; in functional iron deficiency (FID), iron stores, although replete, cannot be mobilized from the macrophages of the reticulo-endothelial system (RES). FID occurs in anaemia of inflammatory diseases because iron is trapped in the RES as a result of increased secretion of hepcidin, a hormone that controls iron release from cells.[3] FID may also occur in response to the therapeutic use of erythropoiesis-stimulating agents (ESAs), such as epoetin or darbopoetin, which place a significant demand on iron stores that may surpass the iron-release capacity of the RES.[3]

Iron deficiency can be investigated using different laboratory tests which fall into two categories: measurements providing evidence of iron depletion in the body (serum iron, transferrin, transferrin saturation, ferritin, soluble transferrin receptors, ferritin index, etc), and measurements reflecting iron deficient red cell production (haemoglobin [Hb], mean corpuscular volume, variability in red cell size, mean corpuscular Hb, percentage of hypochromic red cells, reticulocyte Hb content, etc.). The appropriate combination of these laboratory tests allow for differential diagnosis of anaemia and ID status.[3]

Anaemia, allogeneic blood transfusion and patient's outcome

Preoperative anaemia is one of the major predictive factors for allogeneic blood transfusion (ABT) related to surgery with moderate to high blood loss.[4,5] ABT is commonly used to rapidly and effectively restore the Hb levels, avoiding the deleterious effects of severe anaemia, especially when acutely developed or in elderly patients whose compensatory mechanisms have a limited capacity of response. However, though increasingly safer, ABT can never be a risk-free therapy and likely increases the rate of morbidity and mortality in surgical and critically ill patients.[6]

Wu et al.[7] retrospectively analyzed the National Surgical Quality Improvement Program (NSQIP) database for 239,286 patients older than 65 years of who underwent major non-cardiac surgery in 1997 to 2004 at veteran hospitals nationwide. Intraoperative ABT was associated with a lower 30-day postoperative mortality if there was substantial operative blood loss or low preoperative haematocrit levels (< 24%), whereas ABT was associated with increased mortality risks for those with preoperative haematocrit levels between 30% and 35.9% and < 500 mL of blood loss. In contrast, in another retrospective review of 10,100 patients undergoing general, vascular, or orthopaedic surgery, intraoperative ABT was associated with a higher risk of 30-day mortality and morbidity in patients with severe anaemia (haematocrit < 30%). It is unknown whether this association is due to the adverse effects of ABT or is the result of increased blood loss in the patients receiving blood.[8]

The analysis of a population-based follow-up study in Denmark identified 28,087 primary total hip

replacement (THR) procedures performed from 1999 to 2007. Using a propensity score matching, the authors compared postoperative outcomes of 2,254 transfused and 2,254 non-transfused THR patients, and found that ABT was associated with increased odds of death and pneumonia. Although the odds estimates may partly reflect unmeasured bias due to blood loss, they indicate the need for careful assessment of the risk versus benefit of ABT even in relation to routine THR procedures.[9]

Moreover, in colorectal cancer (CRC) surgery, ABT is also associated with increased rates of cancer recurrence.[10-12] In a meta-analysis, 23 out of 36 studies on 12,127 patients showed a detrimental effect of ABT. Patients randomized to ABT had a higher rate of tumour recurrence than those not transfused with a clustered odds ratio (OR): 1.42 (95% Confidence Interval [CI]:1.20-1.67). However, the authors considered that an effect of other variables, such as the surgical technique, cannot be excluded and that, therefore, a cause and effect relationship between ABT and tumour recurrence cannot be established. Nevertheless, they strongly recommend that is essential to minimize the use of ABT in surgery.[12]

On the other hand, perioperative anaemia in itself has been associated with harmful effects over and above the increased risk imparted by the increased need for ABT. A variety of studies in cardiac[13-16] and non-cardiac surgery[17-19] have linked anaemia with increased mortality. As for cardiac surgery, in a multicenter cohort study of 3,500 cardiac surgery patients, those with a Hb level of less than 12.5 g/dL (26%) fared worse in regard to cardiovascular outcomes after controlling for confounding variables and propensity score matching.[14] In other studies, preoperative anaemia was associated, not only with an increased risk of ABT,[15] but also with a greater risk for lower survival after coronary artery bypass grafting.[16] Disease severity and co-morbidity have the greatest effect on mortality in anaemic cardiac surgical patients, which may be aggravated by transfusion of stored blood, anaemia being just a consequence of some other disorders such as acute or chronic blood loss, nutritional ID, renal failure, malignancy, or chronic inflammatory disease.

As for patients undergoing non-cardiac surgery, Wu et al.[17] in a cohort of 310,311 elderly patients from the Department of Veterans Affairs hospitals, found a prevalence of preoperative anaemia of 42.9% (haematocrit < 39%), and data analysis demonstrated an increase in postoperative death and cardiac events associated with decreasing haematocrit levels. Musallam et al.[18] also analysed data from a prospective validated outcomes registry for 227,425 patients undergoing major non-cardiac surgery, of whom 69,229 (30.4%) had preoperative anaemia. They found that preoperative anaemia, even to a mild degree, was independently associated with an increased risk of 30-day morbidity and mortality. Finally, Leichtle et al.[19] analysed the NSQIP database for 23,348 patients undergoing elective open and laparoscopic colectomies, using multivariable models, controlling for potential confounders and stratifying on propensity scores. The results of this analysis suggested that the presence of severe, moderate and even mild preoperative anaemia is an independent risk factor for complications and a longer hospital stay.

Thus, overall concerns about adverse effects of both preoperative anaemia and ABT have prompted the review of transfusion practice and the search for a safer and more biologically rational treatment option, such as stimulation of erythropoiesis with intravenous iron, with or without ESAs. Consequently, the first step to be taken in the setting of elective surgery will be the preoperative identification and evaluation of anaemia early enough to implement the appropriate treatment.[20]

As for iron deficiency anaemia (IDA) caused by poor intake, chronic blood loss, etc, iron absorption is increased and, provided there is no pathology of the gastrointestinal tract, oral iron administration usually leads to correction of the anaemia.[3] However, for a person weighing 70 kg with a Hb 8.5 g/dL a body iron deficit of about 1,700 mg could be estimated. Even at the maximum daily iron absorption in the presence of ID (10 mg), nearly 6 months of oral iron replacement regimen would be required to correct the iron deficit in this patient. Such a time frame is unacceptable for most patients who require prompt surgery and preoperative IV iron administration might be considered, as it can allow up to a five-fold erytropoietic response to significant blood-loss anaemia in normal individuals.[3]

On the other hand, in anaemia of chronic inflammation (e.g., rheumatoid arthritis, Crohn's disease, chronic renal or heart failure, cancer, etc), as well as in that associated with acute inflammation (e.g., trauma, surgery, etc), the utility of oral iron administration is rather limited, since absorption is down-regulated, and the small amount of iron absorbed is directed to the RES, where it is sequestered. Hepdicin, a hepatic acute-phase protein, plays a major role in both processes.[2] Again, IV iron would be a more effective mode of administration in these situations, although some patients will most probably benefit from addition of ESAs to intravenous iron, as ESAs therapy increases iron mobilization from the RES into the erythroid precursors.[2,3]

Perioperative intravenous iron therapy

Most IV iron agents are colloids with spheroidal iron-carbohydrate nanoparticles. Each particle consists of and iron-oxyhydroxide core (Fe [III]) and a carbohydrate shell that stabilizes the iron-oxyhydroxide core. However, the structure of iron isomaltoside 1000 is somehow different as the linear oligosaccharide isomaltoside 1,000 allows for the formation of a matrix with interchanging iron and carbohydrate.[21] Differences in

core size and carbohydrate chemistry determine pharmacological and biologic differences between the different agents, including clearance after injection, iron release *in vitro*, early evidence of iron bioactivity *in vivo*, and maximum tolerated dose and rate of infusion. Among the existing preparations (table I), six different products are available in Europe: iron gluconate (Ferrlecit®), iron sucrose (Venofer®), low molecular weight iron dextran (LMWID, Cosmofer®), ferric carboxymaltose (FCM, Ferinject®), iron isomaltoside 1000 (Monofer®), and ferumoxytol (Rinso®, FeraHeme®), whereas high molecular weight iron dextran (HMWID, Dexferrum®) is only available in USA (See references 21-23 for further details). We will review the role of perioperative IV iron therapy (mostly with iron sucrose and FCM), as a safe and efficacious tool for reducing transfusion requirements.

Anaemia in obstetric and gynaecological surgery

Anaemia due to ID or iron loss is a common condition both during pregnancy and postpartum. During pregnancy, oral iron is the first option for treatment of IDA. However, iron sucrose with or without adjuvant ESAs might be considered for the treatment of gestational IDA resistant to therapy with orally administered iron alone.[24]

Similarly, oral or IV iron with or without ESAs have shown to be equally useful for the treatment of postpartum anaemia.[25] However, Broche et al.[26] showed that administration of IV iron sucrose (200-600 mg) was superior to oral iron for treating anaemic puerperae (Hb < 8 g/dL with 48 h of delivery), as it resulted in higher elevation of Hb levels at postpartum day 7 (1.9 g/dL *vs.* 0.9 g/dL, respectively; $p < 0.01$). Wagström et al.[27] reported a mean increment in Hb of 1.8 g/dL after 1 week, and 2.8 g/dL after 2 weeks in patients with Hb values < 8 g/dL within 72 h after who were given a total dose of 450 mg IV iron sucrose. In comparison to IV iron alone, the addition of ESAs did not further increase Hb.[27] Similar positive results have been reported for postpartum administration of iron sucrose[28-31] or FCM alone,[32,33] especially in women undergoing Caesarean section. In contrast, one study showed that IV FCM was just as effective as oral ferrous sulphate in correcting postpartum anaemia.[34] Thus, IV iron improves postpartum anaemia and iron status and reduces ABT frequency, whereas additional treatment with ESAs should be reserved for patients with profound postpartum inflammation.[24]

In gynaecological practice the greatest number of ABT occur at the time of abdominal radical hysterectomy. In the usual circumstance, ABT is prompted by surgical blood loss in a patient. Since many of these patients presented with IDA or ID, due to chronic blood loss, preoperative correction of anaemia emerges as a possible alternative to ABT. In two randomized controlled trials (RCT) including 81 mildly anaemic women who underwent total hysterectomy, patients who received ESAs once weekly for 3-4 weeks, plus oral iron supplementation had a significantly higher preoperative Hb levels and lower requirements for ABT than those who received only oral iron supplementation.[35,36] However, as ESAs administration in gynaecological surgery is an *off-label* indication, Díez-Lobo et al.[37] investigated the utility of preoperative IV iron in a series of 31 patients with IDA or ID undergoing abdominal hysterectomy who received a mean of 800 mg iron sucrose (500-1,600 mg) over 2-4 weeks preoperatively. A parallel series of 54 matched patients receiving no IV iron serves as control group. Compared to those from the control group, patients from the iron sucrose group presented with higher Hb levels both immediately before surgery (13.3 *vs.*11.7 g/dL, for IV iron and control, respectively; $p < 0.05$) and at discharge (12.5 *vs.*11.8 g/dL, respectively; $p < 0.05$), despite fewer patients received ABT (0% *vs.* 29%, respectively; $p < 0.05$). Only minor side effect to iron sucrose were observed (2 phlebitis, 10 pain at the injection site), but they did not result in treatment discontinuation. In addition, data from a phase III RCT in women with heavy uterine bleeding, clearly showed that IV FCM was more efficacious in correcting anaemia and replenishing iron stores at 6 weeks than oral ferrous sulphate.[38]

On the other hand, the efficacy and safety of treatment with IV iron for postoperative anaemia was prospectively assessed in 52 gynaecological surgery patients (46% abdominal hysterectomy; 21% myomectomy) with Hb levels of less than 10 g/dL, who received 3 x 200 mg doses of IV iron sucrose administered on consecutive days. Fifteen days after the last dose, patients came for a follow-up test and were asked about side effects. After treatment, Hb increased by 2.7 g/dL (95% CI 2.2-3.1; $p < 0.001$), one patient had side effects (pain at the injection site), and no patient received ABT.[30]

Therefore, the low incidence of serious side effects and the rapid recovery of Hb levels make IV iron a safe, effective option for treating perioperative anaemia in this patient population, and probably to correct persistent fatigue which is the most common complaint of patients following hysterectomy.[39]

Anaemia in inflammatory bowel disease

Approximately, one third of inflammatory bowel disease (IBD) patients suffer from recurrent anaemia (ranging from 6% to 73%, depending on Hb cut-off for the definition of anaemia; patient selection, IBD phenotype, and year of publication), and the prevalence of ID is even higher (mean prevalence: 45%).[40] Anaemia is also frequent in patients with ulcerative colitis requiring elective (22%) or urgent (67%) colectomy.[41] Both ID due to blood loss in the intestine, that cannot be matched by duodenal iron absorption,

Table I
Some characteristics of the different intravenous iron formulations

	Iron gluconate	*Iron sucrose*	*Low molecular weight iron dextran (LMWD)*	*Ferric carboxymaltose*	*Iron isomaltoside 1000*	*High molecular weight iron dextran (HMWID)*	*Ferumoxytol*
Brand name	Ferrlecit®	Venofer®	Cosmofer® INFeD®	Ferinject® Injectafer®	Monofer®	Dexferrum®	FeraHeme® Rinso®
Carbohydrate shell	Gluconate (monosaccharide)	Sucrose (disaccharide)	Dextran (branched polysaccharide)	Carboxymaltose (branched polysaccharide)	Isomaltoside (linear oligosaccharide)	Dextran (branched polysaccharide)	Polyglucose sorbitol carboxy-methy-lether
Complex type	Type III Labile and weak	Type II Semi-robust and moderately strong	Type I Robust and strong	Type I Robust and strong	Type I Robust and strong	Type I Robust and strong	Type I Robust and strong
Molecular weight (kD)	289-440	30-60	165	150	150	265	750
Initial distribution volume (L)	6	3.4	3.5	3.5	3.4	3.5	3.16
Plasma half-life (h)	1	6	20	16	20	60	15
Direct iron donation to transferrin (% injected dose)	5-6	4-5	1-2	1-2	<1	1-2	< 1
Test dose required	No	Yes/No*	Yes	No	No	Yes	No
Iron content (mg/mL)	12.5	20	50	50	100	50	30
Maximal single dose (mg)	125	200	20 mg/kg	20 mg/kg (max 1,000 mg in one infusion)	20 mg/kg	20 mg/kg	510
Premedication	No	No	No	No	No	TDI only	No
Life-threatening ADE (x 106 doses)	0.9	0.6	3.3	??	??	11.3	??

ADE: Adverse drug event; TDI:Total dose infusion. * Only in some European countries.

creating a negative iron balance, and the inflammatory nature of the disease contribute most to the development of anaemia in IBD, whereas cobalamin or folate deficiency and various other causes of anaemia occur infrequently. Finally, various pharmacologic drugs that are used for the treatment of IBD (e.g., sulfasalazine, azathioprine and 6-mercaptopurine) may interfere with erythropoiesis. Chronic fatigue, a frequent IBD symptom, is commonly caused by anaemia and may debilitate patient as much as abdominal pain or diarrhoea. However, in despite of being a condition having a significant impact on the quality of life of affected patients, anaemia treatment in IBD has been given scant attention.[40,42]

The efficacy of oral iron therapy in patients with IBD may be hindered by more pronounced gastrointestinal side effects of oral ferrous iron,[43] including an increase in clinical disease activity and reduced absorption due to chronic inflammation.[44] These limitations of oral iron therapy in IBD patients mean that parenteral routes of iron administration must be considered, especially in patients presenting with moderate to severe anaemia (Hb <10 g/dL), severe intestinal disease activity, or using ESAs, and in those scheduled for surgery in less than one month. After the initial resolution of anemia and the repletion of iron stores, patient's haematological and iron parameters should be carefully and periodically monitored, and maintenance iron treatment should be provided as required.[45]

A summary of the main published studies assessing the efficacy of IV iron in anaemic IBD patients is depicted in table II.[46-52] Overall, for patients who completed iron treatment, the mean response to the treatment of IBD-associated anaemia (Hb ≥ 2 g/dL or normal Hb) was 73.6% with IV iron and 65.1% with oral iron (OR = 1.49; 95% CI 1.02-2.17; p = 0.02). However, when the analysis was performed for data extracted from RCT only, the percentage of responses were 72.5% *vs.* 58.2%, respectively (OR = 1.87; 95% CI 1.13-3.09; p = 0.0097). In addition, reviewed data strongly suggest that for patients with IBD, treatment with IV iron is effective, safe, well tolerated (lower rates of treatment discontinuation due to adverse events with IV iron than with oral iron: 1.3% *vs.* 11.4%; p = 0.001), provides a fast Hb increase and a sufficient refill of iron stores, and presents a lower rate of treatment discontinuation than oral iron. The main disadvantage of IV iron sucrose is the need for multiple infusions as the maximum weekly dose should not exceed 600 mg. The availability of stable parenteral iron compounds allowing for higher dose infusion (table I) may greatly facilitate iron replacement therapy in IBD patients (table II). In this regard, an open-label phase III RCT by Evstatiev et al.[53] compared the efficacy and safety of a novel fixed-dose FCM regimen with that of individually calculated iron sucrose doses in 485 patients with IBD and IDA. Patients received either FCM in a maximum of 3 infusions of 1,000 or 500 mg iron, or Ganzoni-calculated iron sucrose dosages in up to 11 infusions of 200 mg. By week 12, both treatments improved quality of life scores, but more patients with FCM than with iron sucrose showed full adherence to treatment, achieved a Hb response of 2 g/dL or more (66% *vs.* 54%, p = 0.004), or Hb normalization (73% *vs.* 62, p = 0.015). Repeated measures analysis showed significantly stronger increases in Hb (from week 2 onwards), transferrin saturation, and ferritin (at all time points) in the FCM group. Nevertheless, repletion of iron stores (ferritin > 100 mg/L) at the end of treatment was achieved only for 31% of patients, indicating that iron needs in IBD patients were underestimated.[53] In this regard, a retrospective analysis of 88 patients showed that insufficient iron repletion relates to rapid recurrence of IDA within 4 months and consequent re-initiation of iron treatment,[54] highlighting the need for complete iron repletion and close follow-up in these patients. Data from an ongoing phase III, multi-centre, RCT (NCT00810004) on the efficacy and safety of a standardised maintenance dosage regimen of IV FCM versus placebo in 200 patients with IDA caused by IBD will probably further clarify this issue.

As for children, the safety and efficacy IV iron therapy was retrospectively evaluated in 70 paediatric patients with IBD who received 119 HMWID infusions to replenish total iron deficiency. The average increase in Hb concentration was 2.9 g/dL. The authors concluded that total dose infusion of HMWID, when appropriately used, is a safe and potentially efficacious treatment for children with IBD and IDA who are unresponsive to or noncompliant with oral iron therapy.[55] However, cited estimated adverse event rates of > 25% should urge clinicians not to use HMWID. Thus, it must be borne in mind that iron dextran has the disadvantage of potentially life-threatening dextran-associated anaphylactic reactions, especially when HMWID is used.[21-23] Studies on the use of newer IV iron formulation in children with IBD are urgently needed.

Anaemia in hip fracture surgery

As stated above, anaemia is common among patients needing surgery for hip fracture repair, and is the major predictive risk factor for receiving ABT.[4] Among this elderly population with hip fracture, ABT was not associated with changes in mortality, but was associated with an increased rate of postoperative infection.[56] As ID is the leading cause of preoperative anaemia in patients sustaining hip fractures, the efficacy of iron therapy for improving Hb and reducing ABT has been tested in several studies. When administered in the postoperative period, the results of several RCTs suggested that the administration of oral iron was no effective in correcting anaemia in patients presenting with hip fracture.[57-59] In contrast, Cuenca et al.[60,61] observed that preoperative administration of 200-300

Table II

Characteristics of the clinical trials involving IBD patients that compared non-dextran IV iron administration with oral iron or no intervention included in the review

Study year (ref.)	*n*	*Study design*	*Compound*	*Baseline Hb (g/dL)*	*Total dose, mg (Schedule)*	*Duration (weeks)*	*Response*	*DCT*
Gasche et al. 2001[43]	103	Multicentre, open-label	Iron sucrose	≤ 10.5	1,200 mg (6 x 200 mg)	4	65%	0%
Bodemar et al. 2004[45]	59	Retrospective	Iron sucrose	< 12	Mean 1,400 mg (1-2 x 200 mg/week)	8 12	60% 91%	0%
Schröeder et al. 2005[46]	46	Multicentre randomized open-label	Iron sucrose (22) Ferrous sulfate (24)	< 10.5♀ < 11♂	Mean 1,418 mg (7 mg/kg + 5 x 200 mg) Mean 5,600 mg (100-200 mg/day)	6	55% 53%	4.5% 20.8%
García-López et al. 2006[47]	70	Single centre prospective observational	Iron sucrose	< 10.5*	Mean 920 mg (200-1,800 mg) (200 mg/1-3 times a week)	Mean 5 (1-9)	67%	0%
Kulnigg et al. 2008[48]	200	Multicentre randomized open-label	Ferric carboxymaltose (137) Ferrous sulfate (63)	≤ 10	1.000-1.500 mg (1-2 infusion of 500-1,000 mg) 16,800 mg (200 mg/day)	12	77% 68%	1.5% 7.9%
Lindgren et al. 2009[49]	91	Multicentre randomized investigator-blinded	Iron sucrose (45) Ferrous sulfate (46)	< 11.5	Mean 1,700 mg (200 mg/1-2 weeks) Mean 38,400 mg (200-400 mg/day)	20	66%	7%
Gisbert et al. 2009[50]	100	Multicentre, open-label	Iron sucrose (22) Ferrous sulfate (78)	< 10 > 10	Not reported (2 x 200 mg/week if Hb < 10) (106 mg/day)	26 19,000 mg	77% 89%	0% 5.1%

Response: Hb ≥ 2 g/dL or normal Hb; DCT: discontinuation due to serious adverse events.
*Also those patients with no response or intolerance to oral iron, or with clinical need of quick recovery of anaemia.

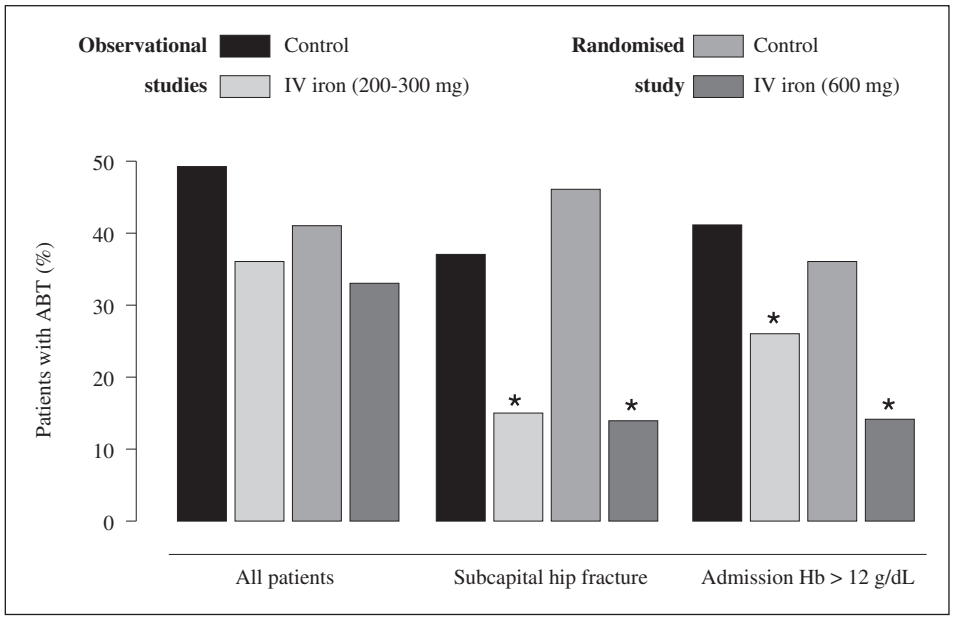


*Fig. 1.—Effect of preoperative IV iron sucrose administration on transfusion requirements in patients undergoing surgery for hip fracture repair included in observational[60,61] and randomised studies[62]. *p < 0.05, IV iron vs. control.*

mg IV iron sucrose to patients with pertrochanteric (PHF) or subcapital hip fracture (SHF) reduced the percentage of transfused patients, compared to a control group (especially in patients sustaining SFH or with admission Hb > 12 g/dL). These results have been recently confirmed by a RCT of patients sustaining PHF or SHF who received 600 mg iron sucrose preoperatively[62] (fig. 1). No adverse reactions were observed in patients receiving iron sucrose, but there were lower postoperative infection rate and lower 30-day mortality, plus a trend towards shorter hospital stay.[60,61] On the other hand, data from patients with admission Hb ≤ 12 g/dL suggest that a benefit could be obtained if IV iron sucrose and ESAs (e.g., recombinant human erythropoietin [rHuEPO]) were administered jointly.[60-62]

The effects of this combined therapy was explored in a study including patients with PHF or SHF who received 600 mg iron sucrose (plus 40.000 IU rHuEPO, if Hb < 130 g/L) and were managed with a restrictive transfusion protocol (transfusion trigger: Hb < 8 g/dL and/or symptoms of acute anaemia).[63] Once again, the treatment resulted in a reduction of both the percentage of transfused patients (70 *vs.* 24%), the number of transfused units (1.7 ± 1.3 *vs.* 0.6 ± 1.1), and the postoperative infection rate (31 *vs.* 13%), when compared with a control group. In addition, there was a trend to lower 30-day mortality, and no adverse reactions to iron sucrose administration were witnessed. However, a subsequent prospective audit at the authors' institution showed a low adhesion to this protocol, as only 81 out of 196 anaemic patients presenting with hip fracture in 2008 received IV iron plus rHuEPO (41%), whereas the remaining 59% received IV iron only.[64] A detailed data analysis revealed that there were significant differences in perioperative ABT rates between groups (42% *vs.* 60%, for those with or without rHuEPO, respectively; p = 0.013). However, the differences in ABT rates between groups were significant for PHF (64% *vs.* 43.5%, respectively; p = 0.027), but not for SHF (52.5% *vs.* 40%, respectively; p = 0.279). In addition, Hb levels on postoperative days 7 and 30 were higher among those receiving rHuEPO, who also presented higher Hb levels on postoperative day 30 than on admission (12.7 g/dL *vs.* 11.9 g/dL, respectively; p = 0.030). Administration of rHuEPO did not increase postoperative complications or 30-day mortality rate, and only three mild adverse events due to IV iron administration were witnessed.[64] Therefore, in anaemic PHF patients managed with perioperative IV iron and restrictive transfusion protocol, preoperative administration of rHuEPO is associated with reduced ABT requirements. However, appropriate training, education and awareness are needed to avoid protocol violations and to limit further exposure to ABT and ABT-related risks.

Elective orthopaedic surgery

Unilateral total knee replacement (TKR) or THR results in a substantial blood loss and 30-50% of these patients receive ABT; this transfusion rate may be even higher among anaemic patients.[65] Again, ID is one of the most prevalent causes of preoperative anaemia among these patients populations.[66,67] We assessed the requirements for ABT in 156 consecutive patients undergoing surgery for primary TKR, who received iron ferrous sulphate (256 mg/day; 80 mg of Fe^{2+}), vitamin C (1,000 mg/day) and folic acid (5 mg/day) during the 30-45 days preceding surgery, and who were transfused if Hb < 8 g/dL and/or clinical signs/symptoms of acute anaemia/hypoxemia (Group 2). A previous series of 156 TKR patients served as a control group (Group 1).[68] Compared to those in Group

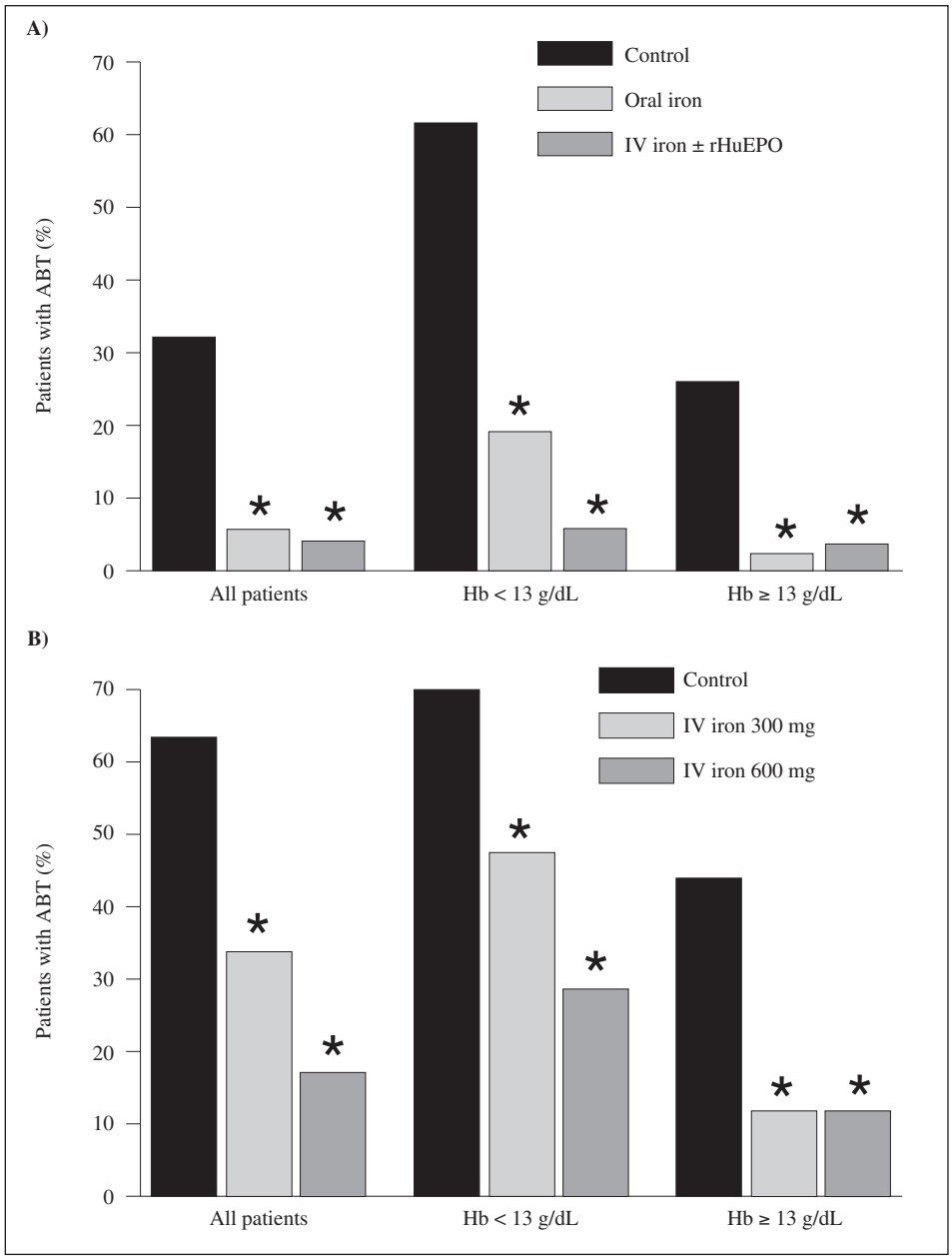


*Fig. 2.—Effect of perioperative IV iron administration on transfusion requirements in patients undergoing major orthopaedic surgery. A) Patients undergoing total knee replament received 200 mg IV iron 48 h before and after surgery or not treatment (control)[68,76]; patients presenting with Hb < 13 g/dL also received a single 40.000 IU rHuEPO preoperatively. B) Patients undergoing total knee or hip arthroplasty or hip fracture repair received 300 or 600 mg IV iron or no treatment (control) (Unpublished data). *p < 0.05, oral iron or IV iron vs. Control.*

1, patients in Group 2 presented a lower transfusion rate (5.8% *vs.* 32%; $p < 0.01$) (fig. 2A), and a lower transfusion index (1.8 *vs.* 2.2 units per transfused patient; $p < 0.05$). After patient's stratification according to a preoperative Hb above or below 13 g/dL, the differences in transfusion rate remained significant, although 19% of patients from Group 2 still needed ABT if their preoperative Hb < 13 g/dL (fig. 2A). Therefore, this protocol seems to be effective for avoiding ABT in non-anaemic TKR patients, suggesting a widespread underlying depletion of iron stores in this patient population despite a normal Hb,[69] although in another observational study of patients undergoing TKR or THR, preoperative oral ferrous sulphate therapy administered to non-anemic patients had no significant benefit on improving preoperative Hb and was associated with a high risk of adverse drug reactions.[70] In contrast, our data suggests that for anaemic patients another blood saving strategies, such as the administration of IV iron, should be implemented.

Following the recommendations of NATA (Network for the Advancement of Transfusion Alternatives) consensus statement on the role of IV iron for perioperative anaemia management,[71] we evaluated the efficacy of IV iron administration (approx. 1,000 mg; 3-5 weeks prior to surgery) for correction of preoperative anaemia in 160 patients scheduled for major elective surgery (45 colon cancer resections, 52 abdominal hysterectomies, 63 lower limb arthroplasties).[72] As for

orthopaedic patients, administration of IV iron caused a significant increase of Hb levels (+1.8 g/dL; p < 0.001), anaemia was resolved in 83% of patients, overall transfusion rate was only 19%, and no serious adverse effect was witnessed. Similar, although more modest results have been reported for patients with ID or IDA by Theusinger et al.[73] and González-Porras et al.[74] This strategy is also recommended in more recent NATA guidelines on detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient.[75]

However, quite often we do no have such a time frame to investigate anaemia and implement the appropriate treatment. In this regard, were evaluated the effects of perioperative administration of IV iron sucrose (2 x 200 mg , 24 hours before surgery and 24 hours after surgery) plus folic acid and vitamin C until discharge, on transfusion requirements in patients undergoing surgery for TKR and managed with a restrictive transfusion protocol. In addition, patients with preoperative Hb < 13 g/dL received one dose of rHuEPO (40,000 UI, 24 hours before surgery). No adverse effects of iron sucrose or rHuEPO administration were witnessed, and only 4% of patients received ABT overall[76] (fig. 2A). Interestingly, ABT rate in patients with preoperative Hb < 13 g/dL (9%) was no different from that previously reported for TKR receiving 4 x 40,000 UI rHuEPO plus oral iron (10.8%) .[77] Additionally, at postoperative day 30, only 15% were anaemic, 71% of Hb loss and 92% of preoperative Hb was recovered, and iron stores were increased.[78] Interestingly, ABT rate in patients with preoperative Hb < 13 g/dL (9%) was no different from that reported with the preoperative administration of rHuEPO at the dosage of 4 x 40,000 IU plus oral iron (10.8%)[79] or 4 x 10 000 IU plus 4 x 200 mg of iron sucrose (0%).[74]

More recently, Na et al.[80] randomised 108 iron deficient patients scheduled for bilateral TRK to receive 200 mg of iron sucrose IV and 3000 IU of rHuEPO during the operation and during the postoperative period if the Hb level was aoround 7-8 g/dL (Group IE) or no treatment (Group C, control). Haemoglobin, ferritin and transferrin saturation levels at 1, 2, and 3 days and at 2 and 6 weeks post-operation were significantly higher in Group IE. Furthermore, the transfusion rate (20.4% *vs.* 53.7%, p = 0.011) and transfusion index (0.2 *vs.* 0.8 units/patient; p = 0.005) were significantly lower in Group IE. Therefore, treatment with IV iron and low-dose rHuEPO- in bilateral TKR effectively attenuated anaemia and decreased transfusion requirements in iron-deficient patients. Hence, these short-term protocols seem to reduce ABT and may hasten the recovery from postoperative anaemia in TKR patients, although further studies are needed to ascertain which patients may benefit of extended IV iron and/or rHuEPO administration.

In the postoperative period, the results of several RCTs suggested that the administration of oral iron was no effective in correcting anaemia after orthopaedic surgery.[81-83] However, iron sucrose (3 mg/kg/day) was shown to be a more effective oral iron to restore postoperative Hb levels after spinal surgery in children,[84] although this positive effect was not seen in adult patients receiving IV iron with or without rHuEPO.[85] In lower limb arthroplasty surgery, we evaluated the effect of postoperative administration of 300-600 mg of IV iron sucrose or FCM on ABT requirements in 315 patients. Compared to no treatment, postoperative administration of either 600 mg iron sucrose or FCM seems to be safe, and more effective than that of 300 mg iron sucrose to reduce ABT requirements in THR, TKR and HF patients, although the intervention seems to be more efficacious for patients with preoperative Hb ≥ 13 g/dL (fig. 2B) (Unpublished observations). In addition, patients with postoperative Hb < 10 g/dL receiving 300 or 600 mg IV iron showed shorter length of hospital stay, and lower postoperative infection rate.[86] No adverse reactions to iron administration were witnessed, and FCM had the additional advantage of being given in a rapid single infusion. A RCT to confirm the efficacy of postoperative FCM in TKR patients is currently ongoing (EudraCT 2010-023038-22).

Anaemia in cardiac surgery

Up to 40% of patients scheduled for cardiac surgery presented with preoperative anaemia,[13,14,87-89] which is associated with and increased risk of perioperative transfusion and postoperative adverse outcome.[14-16,87-89] A recent study, 210 out of 576 patients (36.5%) undergoing elective cardiac surgery at one institution presented with anaemia, and logistic regression analysis revealed that age, chronic kidney disease (decreased EPO production), and consumption of proton pump inhibitors or histamine H_2 receptor antagonists (reduced iron absorption), and diuretics were independent risk factors for the presence of preoperative anaemia.[87] A small cohort study of 60 patients found that 45% of them were anaemic preoperatively, 22% had serum iron < 50 g/dL, 42% ferritin < 100 μg/L, 28% transferrin saturation < 20%, 22% C-reactive protein > 1 mg/dL, and 17% IL-6 > 10 pg/mL (Unpublished observations). Finally, a prospective observational study found that 37 out 100 patients were diagnosed with ID, which was associated with lower preoperative Hb levels, higher ABT rates and higher score of postoperative physical fatigue.[89] These data suggest that anaemic patients scheduled for cardiac surgery might benefit from treatment with iron and/or rHuEPO.[90]

In adult patients scheduled for cardiac surgery, preoperative treatment with rHuEPO reduced the risk of exposure to ABT (31% *vs.* 54%; RR, 0.57; 95% CI, 0.43-0.75; p < 0.001), but there were a great variability in total rHuEPO dose and iron supplementation, as well as in outcomes.[91,92] In valvular cardiac surgery, data for 59 consecutive anaemic patients who was

given rHuEPO 5 x 500 IU/kg/day (4 weekly doses and a fifth dose 48 hours before surgery) plus IV iron sucrose supplementation were compared to those from a control group. Multivariable logistic regression analysis showed that administration of combined therapy was independently associated not only with lower ABT rate, but also with decreased postoperative morbidity and in-hospital mortality, and shorter length of hospital stay.[93] Using a similar approach to that described for elective and non-elective orthopaedic surgery,[63,64,76] two studies have shown that very short term rHuEPO plus IV iron administration (1-4 days before surgery) improved postoperative Hb levels and iron parameters and reducig the requirements for ABT in off-pump coronary revascularization[94] and valvular heart surgery.[95] Unfortunately, there are no studies on preoperative IV iron as monotherapy.

In the postoperative period, the administration of oral iron after uncomplicated coronary artery bypass surgery did not help to restore red blood cell mass nor to maintain total body iron stores.[96] In contrast, postoperative IV iron alone preserved iron stores during recovery from anaemia.[97,98] Moreover, in one study, the increase in Hb level from postoperative day 4 (nadir) to postoperative day 30 was 1 g/dL higher in patients who received IV iron supplements, with or without rHuEPO, when compared to those who received placebo.[97]

On the other hand, a RCT in patients undergoing cardiac (42%) or orthopaedic surgery concluded that treatment with IV iron alone or in combination with rHuEPO does not appear to accelerate early recovery from postoperative anaemia, although reticulocyte counts and ferritin levels at postoperative day 7 were higher in the combination group and there was a trend towards lower transfusion requirements and better Hb recovery at postoperative day 42.[85] However, the study was prematurely stopped and the authors did not exclude the possibility that higher doses or different timing of postoperative intravenous iron and rHuEPO may be effective in accelerating correction of postoperative anaemia. Finally, a restrospective study of 863 cardiac surgery patients showed no differences in infection rates between patients receiving IV iron gluconate plus rHuEPO (n = 302) or standard care (i.e., ABT as indicated; n = 561), for correction of postoperative anaemia (OR = 1.03; 95% CI 0.908-1.170)[99]

Anaemia in colorectal cancer

Anaemia is one of the signs of CRC, which may be present in up to 75% of patients, depending of the Hb cut-off and tumour stage.[100-105] A study on 358 patients with CRC showed that one quarter of them had severe anaemia (Hb < 10 g/dL). The multivariate analysis showed that patient's age, tumor site (right colon), and tumor size (large size), but not clinical stage or histological type, were significant factors related to anaemia.[101] Similar results were obtained in more recent study 1,189 Norwegian patients.[102] As for other major surgical procedures, a hematocrit less than 30% has been shown to be an independent risk factor for requiring perioperative ABT in CRC patients.[103] However, the incidence of a low serum iron level was about twice the frequency of a Hb level < 10 g/dL,[101,104,105] and the multivariate analysis showed that none of the above mentioned factors were significantly related to ID.[101,104] Thus, both IDA and ID may be corrected pre-operatively by either oral iron, if time allows, or by the use of IV iron in CRC patients.

Okuyama et al.[106] studied 32 anaemic patients (Hb ≤ 10 g/dL) who received oral iron supplementation (sodium ferrous citrate, 200 mg/day) for at least 2 weeks preoperatively and 84 anaemic patients who did not. Iron supplementation resulted in higher Hb levels immediately before surgery (+1.2 g/dL; $p < 0.05$), and fewer patients receiving intraoperative ABT (9.4% *vs.* 27.4%, $p < 0.05$). However, there were no significant differences in postoperative Hb levels or ABT volumes between the two groups. Lidder et al.[107] conducted a small RCT of oral ferrous sulphate (200 mg/12 h) for a mean of 14 days pre-operatively (12-56 days) *versus* no iron therapy in patients with IDA or ID scheduled for CRC surgery. Oral iron was found to prevent Hb decrease from recruitment to admission, and to reduce ABT rate (25% *vs.* 59%, for iron and control, respectively; $p = 0.031$), although these differences were not significant for patients with IDA. More recently, in a series of 103 patients receiving oral ferrous sulphate (200 mg/12 h) for a median of 39 days pre-operatively (interquartile range = 7-63 days) and no preoperative ABT, Quinn et al.[108] observed that: 1) Fifty-eight (56.3%) patients were anaemic at presentation gaining a mean of 1.7 g/dL ($p < 0.001$); 2) Right-sided tumours (lower mean Hb at presentation) responded more to oral iron when compared to left-sided tumours ($p < 0.017$); 3) Increase in Hb was unrelated to pathological stage, but was greater in patients receiving iron for more than 14 days; and 4) The ABT rate for all curative resections was 0.69 units/patient (compared to 1.69 units/patient for an historical cohort).

Edwards et al.[109] conducted a pilot RTC to ascertain whether iron sucrose reduces the likelihood of postoperative ABT in patients undergoing elective CRC resection. Iron sucrose (600 mg; n = 34) or placebo (n = 26) was given IV in two divided doses, at least 24 h apart, 14 days before surgery, and no difference was demonstrated between groups regarding perioperative Hb levels or ABT rates. Therefore, the author concluded that patients undergoing resectional surgery for CRC do not benefit from preoperative administration of IV iron sucrose. However, this study has important limitations that preclude for drawing meaningful conclusions.[110,111] First, the primary endpoint (on which the sample size was also based) was a change in Hb of 0.5 g/dL, and such a small change is clinically insignificant and unlikely to have an impact on perioperative transfusion requirements. Second, recommendation for

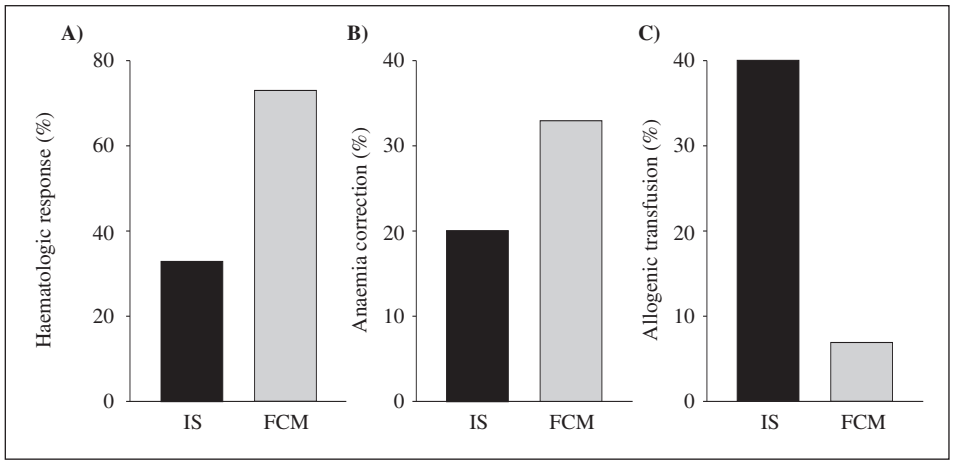


*Fig. 3.—Effect of preoperative IV iron sucrose (IS) or ferricarboxymaltose (FCM) administration in patients undergoing colorectal cancer surgery. A. Haematologic response, defined as a Hb increment ≥ 1.5 g/dL or a final Hb ≥ 13 g/dL. B. Anaemia correction, according to WHO definition. C. Transfusion rate[72]. *p < 0.05, IV IS vs. IV FCM.*

dosing IV iron sucrose is based on the individual patient's body weight and the differential between actual and target Hb values, rather than administration of a fixed dose as used in this study. Third, by recruiting all patients undergoing surgery for CRC, they included non-anaemic patients with no biochemical evidence of iron deficiency. In fact, in this study only nine patients in each group had a Hb level below normal. Therefore, the authors should have restricted the study to anaemic patients and had reduction in perioperative ABT as the primary outcome.

In a comparative study, clinical and laboratory data of 15 anaemic CRC patients receiving preoperative FCM (500-1,000 mg/session) to replenish total iron deficiency were compared with those from previous series of 30 patients receiving preoperative iron sucrose (100-200 mg/session).[72] In despite of similar total iron deficiency (1,125 mg *vs.* 1,025 mg) and lower baseline Hb level (9.2 g/dL *vs.* 10.1 g/dL; $p < 0.05$), patients in the FCM received more iron than those in the iron sucrose group (1,550 mg *vs.* 1,140 mg; $p < 0.05$), and showed a higher post-treatment Hb increment (+2.5 g/dL *vs.* +0.9 g/dL; $p < 0.05$). Thus, patients receiving FCM showed better haematologic response, more correction of anaemia and lower perioperative ABT (fig. 3). The "extra" amount of iron administered to the FCM group, which compensated for the ongoing blood loss from recruitment to surgery, might have account for the observed differences.

In another study, 43 CRC patients received preoperative treatment with oral iron if Hb > 14 g/dL and iron deficiency; iron sucrose (200 mg/week) if Hb 10-14 g/dL; or iron sucrose (200 mg twice a week) if Hb < 10 g/dL, during 2-3 weeks. Seventeen of these patients also received postoperative iron sucrose (200 mg on days 0, 2, and 4). A retrospective series of patients not receiving iron was used as a control group (n = 66). Despite a lower baseline Hb (12.3 g/dL *vs.* 11.5 g/dL; $p < 0.05$), iron therapy reduced the transfusion index (4.0 *vs.* 1.3 unit/patient; $p < 0.05$) and the percentage of patients who received preoperative ABT (33% *vs.* 9%; $p < 0.05$), but not the percentage of patients administered perioperative ABT (48% *vs.* 35%; p = 0.161). However, the treatment was ineffective in patients with a high transfusion index (> 5 units/patient).[112]

Diaz-Espallardo et al.[113] analysed data from 437 patients undergoing CRC surgery in the period 2005-2009. Patients presenting with Hb <13 g/dl and/or abnormal Fe metabolism (Group A, n = 242) received preoperative iron supplementation (178 patients received a mean of 867 mg IV iron sucrose, and 64 oral iron), whereas patients presenting with Hb ≥ 13 g/dl and/or normal Fe metabolism, received no treatment (Group B, n = 195). From diagnosis to the day of surgery, Hb increased by 0.6 g/dL in Group A, while it decreased by 0.8 g/dL in Group B ($p < 0.05$). Moreover, from diagnosis to hospital discharge, Hb decreased by 0.4 g/dL in Group A, and by 2.5 g/dL in Group B ($p < 0.05$). This tendency to progressive anaemia observed in both groups, may be secondary to the neoplastic disorder, chemo-radiotherapy treatment, the blood loss due to the tumour and later surgery. However, the differences between groups strongly suggest that iron therapy prevented patients from group A for reaching undesirably low Hb levels. In this regard, it is worth noting that the overall ABT rate was 8.6% (32/244, 13.1% *vs.* 6/195, 3.1%, for group A and B, respectively; p = NS) and no differences in complications were observed. Regarding postoperative complications after abdominal surgery, it must be borne in mind that infections were reported to be significantly more common in patients with low preoperative serum ferritin compared with patients with normal ferritin; confounders including Hb level were taken into account in the analysis.[114] In addition, Zago et al.[115] evaluated the usefulness of vitamin and mineral indicators as nutritional markers of general and surgical wound complications in 100 adult patients from programmed surgical procedures of hernia (n = 41) or gallbladder lithiasis (n = 59), and found lower plasma retinol (a marker of low vitamin A intake) and higher erythrocyte protoporphyrin (an early marker of ID) in patients with complication compared to those without complications. Thus, the authors considered

that these two markers would provide useful tools in evaluating surgical risk since they had been allowed to identify patients who were at risk of suffering postoperative complications.

In contrast, in a retrospective paired case-control study, Titos-Arcos et al.[116] observed that postoperative administration of IV iron sucrose (592 ± 445 mg) did not decrease ABT rates (28.8% *vs.* 30.8%, for case and control, respectively). In addition, for patients no receiving ABT, there were also no differences in Hb concentration decrease between the first postoperative day and hospital discharge (0.88 g/dL *vs.* 0.82 g/dL, for case and control, respectively).

Therefore, early treatment of anaemic CRC patients enables optimization of preoperative Hb, thus swichting them from a high transfusion risk to a low transfusion risk. It is possible that the effectiveness of perioperative iron treatment could be enhanced by concomitant rHuEPO administration. Thus, perioperative treatment with rHuEPO reduced the risk of exposure to ABT (38% *vs.* 47%; RR, 0.81; 95% CI, 0.61-1.00; p = 0.054), in patients with moderate anaemia scheduled for gastrointestinal cancer surgery (mostly colorectal), although a reduction of both the percentage of transfused patients and the number of transfused units was only observed for those receiving rHuEPO plus IV iron. Additionally, the use of IV iron allowed for a significant reduction in the total dose of EPO.[117] A recent systematic review and meta-analysis of 4 RCTs found there is insufficient evidence to support the use of rHuEPO in the preoperative and post-operative period for improving anaemia and decreasing ABT, although there was no evidence that rHuEPO increased complications or deaths.[118] Therefore, in line with our comments regarding the management of anaemia in IBD patients, future studies of IV iron and/or rHuEPO in CRC surgery should increase the doses and/or the duration of treatment.

Anaemia after kidney transplantation

A European survey of 4,263 adult patients found anaemia in almost 40% of renal transplant recipients.[119] In one study the prevalence of anaemia at 6 and 12 months after transplantation was 35% and 25%, respectively, and 60% of patients received at least one ABT.[120] Post-transplatation anaemia was particularly associated with impaired renal function, although only one third of patients received rHuEPO during the first few months post-transplantation.[120] The prevalence is even higher in children. As reported in a study of 162 paediatric renal transplantation recipients, almost 85% were anaemic in the first month after transplantation, and almost 65% were anaemic or present ID between 1-6 month and 6 years from transplantation.[121]

As for adults, the administration of rHuEPO (100 IU/kg, three times per week) in the immediate post-transplantation period (3 months) seems to have no relevant clinical impact on the correction of anaemia or reduction of blood transfusion rate, with respect to patients receiving no rHuEPO.[122] This might be related to the high prevalence of ID or FID during the early weeks after transplantation, as well as among long-term renal transplant recipients. However, iron treatment must be carefully administered and monitored because of the risk of post-transplant erytrocytosis.[123]

In this regard, Mudge et al.[124] conducted a RCT of IV iron polymaltose (500 mg single dose) versus oral ferrous sulphate (210 mg elemental iron daily, continuously) in 104 patients with post-transplant anaemia. The median time to resolution of anaemia (Hb > 11 g/dL) was 12 days in the IV group *versus* 21 days in the oral iron group (p = 0.32). There were also no differences in infections (20% *vs.* 24%, p = 0.62), acute rejection (8% *vs.* 6%, p = 0.68), blood transfusions (10% *vs.* 18%, p = 0.24), and severe gastrointestinal side-effects (6% *vs.* 12%, p = 0.29) between the IV iron and the oral iron groups. Therefore, both IV and oral iron were safe and effective in the management of post-transplant anaemia.

Gillespie & Symmons[125] treated 14 paediatric and young adults ID renal transplant recipients with iron gluconate (100-1,000 mg; 1-50 days), with or without rHuEPO. Data analysis revealed an overall increase in Hb levels (10.1 ± 1.6 g/dL vs. 11.4 ± 2.1 g/dL; p < 0.01), but only a weak trend towards an increase in transferrin saturation. In addition there was a trend to higher increase in Hb (2.1 ± 2.0 g/dL *vs.* 0.6 ± 0.8 g/dL, respectively; p = 0.087), but no differences in the number of responders (Hb increase ≥1 g/dL; 5 *vs.* 3, respectively; p = 0.592), in patients receiving rHuEPO plus iron when compared to those receiving iron alone. There were 4 incidents in 3 patients receiving iron gluconate 3.4, 5.1 and 6.4 mg/kg (infusion stopped in the later due to hypertension). Thus, IV iron appears to have potential to improve anaemia in young renal transplant recipients, but the paucity of published information on this topic highlights the need for stronger data. Meanwhile, it seems prudent to caution against the use of high dose of iron gluconate (> 3 mg/kg) or total iron repletion treatments in children.

Anaemia in other medical or surgical scenarios

– *Chronic heart failure (CHF).* There is increasing evidence that anaemia is one of the most relevant comorbid conditions associated with CHF, not only because it is common but also because it is a marker of greater impairment in functional capacity and an independent predictor of mortality and hospitalization among CHF patients.[126] Correction of anaemia with rHuEPO and oral iron leads to improvement in New York Heart Association status, measured exercise endurance, oxygen use during exercise, renal function and plasma B-type natriuretic peptide levels and reduces the need for hospitalization.[127-131] However,

both ID and FID may also play a role in the cardio-renal-anaemia syndrome. In this regard, the combined results from 5 RCTs indicate that IV iron therapy is associated with improved quality of life parameters, such as New York Heart Association class and the Minnesota Living With Heart Failure Questionnaire, mean ejection fraction, 6 min walk distance, and iron indices, and with lower rates of hospitalizations due to any cause and lower C-reactive protein levels, whereas no increase in the rate of adverse events was found.[132-136]

– *Chronic kidney disease (CKD).* Nowadays the administration of ESAs with iron supplements, but not ABT, is the standard therapy for the anaemia of CKD, although some patients are still being transfused. On the other hand, the effects of IV iron alone in partially correcting this anaemia were long ago reported. In anaemic non-dialyzed CKD patients, the haematocrit response was more rapid in patients receiving IV iron in combination with low-dose rHuEPO, but 50% of patients with iron alone showed an increase in haematocrit greater than 3%. In addition, 29% of these patients reached the target haematocrit (35%) compared with 40% of those receiving the combination therapy.[137] Another five studies show that administration of IV iron to CKD patients significantly increased the haematocrit, with 35-40% reaching target haematocrit, in absence of rHuEPO administration.[138-142] Thus, it is clear that IV iron alone can achieve some correction of anaemia in CKD, possibly sufficient to avoid ABT, but many patients will also require ESAs supplementation to attained target Hb level.

– *Anaemia of cancer.* Patients with cancer may have anaemia with ID or FID as a result of their disease or its treatment. These conditions can lead to an insufficient supply of iron for incorporation into erythrocytes during supportive care with ESAs for chemotherapy. A meta-analysis of 5 studies of cancer patients receiving chemotherapy have shown that intravenous IV iron increases the haematopoietic response to rHuEPO and may reduce ABT requirements with respect to those receiving oral iron or no iron. In addition, the effects on Hb levels and measures of iron metabolism were notably greater with IV iron formulations than with oral iron formulations.[143] The use of IV iron in this clinical setting seems to be cost-effective as it allows for a reduction of ESA dosage.[144] Morevover, data from 2 studies of patients with gynaecologic cancer receiving chemotherapy and/or radiotherapy showed that the administration of IV iron alone improves Hb levels and reduces ABT rate.[145,146]

– *Bariatric surgery (BS).* Obesity-induced chronic inflammation leads to activation of the immune system that causes alterations of iron homeostasis including hypoferraemia, iron-restricted erythropoiesis, and finally mild-to-moderate anaemia.[147,148] Thus, preoperative anaemia and ID are common among obese patients scheduled for BS.[148] On the other hand, BS is a long-lasting inflammatory stimulus in itself and entails a reduction of the gastric capacity and/or exclusion of part of the small bowel which impair nutrients absorption, including dietary iron. Chronic gastrointestinal blood loss and iron-losing enteropathy may also contribute to iron deficiency after BS. Iron supplements should be administered to patients after BS, but compliance with oral iron is no good. In addition, once iron deficiency has developed, it may prove refractory to oral treatment. In these situations, IV iron has emerged as a safe and effective alternative for perioperative anaemia management. Monitoring should continue indefinitely even after the initial iron repletion and anaemia resolution, and maintenance IV iron treatment should be provided as required (see ref. 148 for a detailed review).

– *Critically ill patients.* Anaemia is highly frequent among medical and surgical patients admitted to the intensive care unit (ICU) and generally has a multifactorial origin.[149] In order to avoid the deleterious effects of anaemia, 40% of ICU patients receive ABT, and this figure increases up to 70% if the ICU stay is longer than 7 days.[150,151] However, ABT is associated with a dose-dependent increase in morbidity and mortality.[150,151] Thus, pharmacological treatment for anaemia in ICU has been assayed.

A large proportion of critically ill patients presented with FID which correlates with the inflammatory status and the length of stay, and some 20% may have absolute ID (SAT < 20; ferritin < 100 and sTfR > 2.3).[152] Since oral supplementation of iron seems to be ineffective in surgical critically ill patients, except for those previously transfused,[153] these patients might benefit of IV iron therapy for correction of ID or FID, which in turn might help to ameliorate their inflammatory status, although available data are rather scant and inconclusive.[154] In contrast, the administration of rHuEPO plus iron supplements, especially IV iron, improves anaemia and modestly reduces ABT requirements (when there is not a predefined transfusion protocol), although it does not reduce mortality (except for younger patients and those with an admitting diagnose of trauma).[155] To ascertain whether treatment of anaemia in the critically ill with rHuEPO and IV iron might improve outcomes and to optimize drug administration schedules and dosage, further studies with sufficient statistical power and adequate follow-up are needed.

Safety of intravenous iron administration

Although no serious life-threatening adverse drug events (ADEs) has been reported in the different studies reviewed above, both the numbers of patients included in these studies and the follow-up time were not large enough to draw definitive conclusions regarding the safety of IV iron agents in different clinical settings reviewed.

However, according to the analysis of data from Food and Drug Administration US (2001-2003; $30x10^6$ doses), the incidence of life-threatening ADES, mostly

hypersensitivity reactions (2.2 per million doses), and deaths (0.4 per million doses), associated to the use of four IV iron preparations (iron gluconate, iron sucrose, HMWID, and LMWID), is much lower than that associated to the use of ABT (10 and 4 per million units, respectively).[156,157] An analysis of reported adverse events among patients using IV iron products from October 2009 through June 2010, concluded that iron sucrose and sodium ferric gluconate were associated with much lower rates of serious adverse events and deaths per million units sold than iron dextran or ferumoxytol, which were associated with the highest rates of all reported adverse event classifications.[158] The immunologic basis of allergic hypersensitivity to IV iron agents is not known. Both antibody-mediated and non-antibody-mediated, concentration-dependent mechanisms have been identified in patients after anaphylaxis to iron dextran.[159] HMWID is not commercially available in Europe, the National Comprehensive Cancer Network recommends against the use of Dexferrum, and the Food and Drug Administration US has altered HMWID (Dexferrum®) labelling to warn that it is not clinically interchangeable with LMWID (INFeD®).[160,161] On the other hand, most ADEs due acute iron toxicity might be linked to labile, biologically active iron. The risk of inducing the release of labile iron appears to depend on the dose of IV iron, the molecular weight of iron complex, the rate of iron infusion, and the available apotransferrin/transferrin to bind the iron. Many of the ADEs attributed to iron gluconate including flushing, hypotension, nausea, vomiting and diarrhea have been linked with the release of labile iron.[162,163]

Regarding the newer iron formulations, overall assessment of the benefits and risks of FCM demonstrates a favorable benefit-risk profile. There are, however, some safety concerns (e.g., hypophosphatemia) as well as important missing information (e.g., use in children and pregnant women, or use in hepatic diseases). Should the manufacturer appropriately address these concerns and FCM finally be approved by the Food and Drug Administration US, a widespread use of this IV iron preparation should be expected in the next years.[22] The iron isomaltoside 1000 (Monofer®) regulatory application includes references to general IV iron documentation, including evidence with iron dextran. The regulatory authorities have therefore placed Monofer® in the B03A C06 ATC code, but they recognise the unique properties of Monofer®, the unique generic name iron isomaltoside 1000 (a non-anaphylactic carbohydrate), and no requirement for a test dose application which is always the case with iron dextran.[21] Overall, with the exception of HMWID (increased rates of severe side effects and deaths), it seems that the acute safety differences among IV iron products are small when given at the recommended doses, though comparator trials are needed to be certain.

It has long been suggested that patients with iron overload are at increased risk of infection,[164] but no increased rates of postoperative infection have been observed in the reviewed studies. In addition, a meta-analysis of 6 observational studies (807 patients) revealed that the administration of IV iron to patients undergoing major orthopaedic surgery led to a significant decrease in both transfusion (RR: 0.60; 95% CI: 0.50-0.72; $p < 0.001$) and infection rates (RR: 0.45; 95%CI: 0.32-0.63; $p < 0.001$).[165] As stated above, orthopaedic surgical patients with postoperative Hb < 10 g/dL receiving 300 or 600 mg IV iron showed shorter length of hospital stay, and lower postoperative infection rate.[86] In contrast, studies of patients undergoing surgical hip fracture repair or abdominal surgery have found an association between low preoperative ferritin levels and increase rates of nosocomial infections.[115,166] Nevertheless, in despite of the absence of definitive clinical data, it seems sensible to avoid IV iron administration in the setting of acute infection, and to withhold IV iron in patients with pre-treatment ferritin values > 500 ng/mL.[20] Nevertheless, the evidence argues for caution, not complacency, in prescribing IV iron.[167]

Conclusions

In a recent, rather incomplete review of the topic, the authors concluded that *"in gastrointestinal or trauma surgery there is no evidence to support the routine preoperative treatment with intravenous iron, although it may be beneficial when it is used with erythropoietin. Intravenous iron alone or in combination with EPO in the postoperative period has not been proved useful for rapid correction of anemia, reduction of hospital stay or mortality"*.[168] However, from data reviewed in this article and despite the lack of high quality evidence in some areas, we believe that if fair to conclude that:

- Perioperative anaemia is a common condition among the patients admitted to the hospital for elective or non-elective surgery.
- Preoperative anaemia is more frequently due to iron deficiency or chronic inflammatory disease, and is one of the major predictive factors for perioperative blood transfusion.
- Postoperative anaemia is mainly caused by perioperative blood loss, and it might be aggravated by inflammation-induced inhibition of erythropoietin secretion and action, and functional iron deficiency that cannot be corrected by the administration of oral iron.
- Perioperative IV iron administration, with or without rHuEPO, to surgical patients is safe, as no treatment side-effects were observed, and resulted in lower transfusion requirements and hastened recovery of postoperative anaemia. In addition, some studies have reported decreased postoperative infection and mortality rates and shorter length of hospital stay in surgical patients receiving IV iron.

Conflict of interest

MM, JC and JAGE have received honoraria for lectures and/or consultancy and travel support from Vifor Pharma (Switzerland), Vifor-Uriach (Spain), and/or PharmaCosmos (Denmark), but not for this review. SGR, EMM and JP have nothing to declare.

Acknowledgement

The authors gratefully acknowledge the fruitful discussions with Dr. Michael Auebarch, Dr. Christian Breymann, Dr. Fernando Gomollón and Dr. Ángel F. Remacha on intravenous iron therapy, and the invaluable collaboration from Prof. Antonio Herrera, Dr. E. Bisbe and Dr. Enrique Naveira in conducting some of the studies reviewed in this paper.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(5):1837-1849
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Recommendations of the GARIN group for managing non-critically ill patients with diabetes or stress hyperglycaemia and artificial nutrition

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Abstract

Background & aims: **By means of this update, the GARIN working group aims to define its position regarding the treatment of patients with diabetes or stress hyperglycaemia and artificial nutrition. In this area there are many aspects of uncertainty, especially in non-critically ill patients.**

Methods: **Bibliographical review, and specific questions in advance were discussed and answered at a meeting in the form of conclusions.**

Results: **We propose a definition of stress hyperglycaemia. The indications and access routes for artificial nutrition are no different in patients with diabetes/stress hyperglycaemia than in non-diabetics. The objective must be to keep pre-prandial blood glucose levels between 100 and 140 mg/dl and post-prandial levels between 140 and 180 mg/dl. Hyperglycemia can be prevented through systematic monitoring of capillary glycaemias and adequately calculate energy-protein needs. We recommend using enteral formulas designed for patients with diabetes (high monounsaturated fat) to facilitate metabolic control. The best drug treatment for treating hyperglycaemia/diabetes in hospitalised patients is insulin and we make recommendations for adapt the theoretical insulin action to the nutrition infusion regimen. We also addressed recommendations for future investigation.**

Conclusions: **This recommendations about artificial nutrition in patients with diabetes or stress hyperglycaemia can add value to clinical work.**

(*Nutr Hosp.* 2012;27:1837-1849)

DOI:10.3305/nh.2012.27.6.6076

Key words: *Diabetes. Stress hyperglycaemia. Enteral nutrition. Parenteral nutrition. Non-critically ill patients.*

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Recibido: 23-VII-2012.
Aceptado: 7-VIII-2012.

RECOMENDACIONES DEL GRUPO GARIN PARA EL MANEJO DE PACIENTES NO CRÍTICOS CON DIABETES O HIPERGLUCEMIA DE ESTRÉS Y NUTRICIÓN ARTIFICIAL

Resumen

Introducción y objetivos: **En el tratamiento de los pacientes con diabetes o hiperglucemia de estrés y la nutrición artificial existen muchas áreas de incertidumbre, sobre todo en pacientes no críticos. El grupo de trabajo GARIN tiene como objetivo definir su posición en este campo.**

Material y métodos: **Revisión bibliográfica previa y reunión presencial en la que se discutieron y contestaron preguntas específicas sobre el tema.**

Resultados: **Proponemos una definición de hiperglucemia de estrés. Las indicaciones y las rutas de acceso a la nutrición artificial no difieren en los pacientes con hiperglucemia de estrés o diabetes respecto a los no diabéticos. El objetivo debe ser mantener los niveles de glucemia preprandial entre 100 y 140 mg/dl y postprandial entre 140 y 180 mg/dl. La hiperglucemia puede prevenirse a través de una monitorización sistemática de las glucemias capilares y un cálculo adecuado de las necesidades energético-proteicas.**

Recomendamos el uso de fórmulas enterales diseñadas para pacientes con diabetes (alto contenido en grasas monoinsaturadas) para facilitar el control metabólico. El mejor tratamiento farmacológico para tratar la hiperglucemia/diabetes en pacientes hospitalizados es la insulina, aconsejando adaptar la acción teórica de la insulina al régimen de infusión de la nutrición. También realizamos recomendaciones para investigaciones futuras.

Conclusiones: **Estas recomendaciones aportan respuestas concretas sobre cuestiones comunes en la asistencia a pacientes con diabetes o hiperglucemia de estrés y nutrición artificial.**

(*Nutr Hosp.* 2012;27:1837-1849)

DOI:10.3305/nh.2012.27.6.6076

Palabras clave: *Diabetes. Hiperglucemia de estrés. Nutrición enteral. Nutrición parenteral. Pacientes no críticos.*

Introduction

Although dietary recommendations have formed part of medicine for many centuries, nutrition has only been considered a scientific discipline for about 200 years, initially starting alongside advances in chemistry when early experiments into nutrient oxidation were conducted.[1] However, the "clinical nutrition" discipline did not emerge until the end of the 1960s when it was proven to be possible to maintain the growth and life of a child by exclusively administering nutrients parenterally.[2] Today, clinical nutrition is a multi-disciplinary area that supports most medical specialties and has come of age by incorporating scientific methodology and evidence-based medicine to establish clinical practice guidelines.[3,4]

Nevertheless, there are still many areas of uncertainty due to it being a relatively young specialty and it being difficult to conduct well-designed studies (observational and/or randomised, prospective clinical trials with a sufficient number of patients) allowing conclusions based on the best available evidence to be reached.

One of these areas is artificial nutrition in patients with diabetes or stress hyperglycaemia in which there are many aspects still requiring clarification, especially in non-critically ill patients. In fact, the latest clinical practice guidelines on the management of hyperglycaemia in non-critical hospitalised patients, published by the U.S. Endocrine Society[5] and the American Society for Parenteral and Enteral Nutrition (ASPEN),[6] only make three evidence-based recommendations on general aspects of care for patients receiving artificial nutrition (enteral or parenteral), which shows the high degree of uncertainty faced by clinicians; the first one[5] also only makes one strong recommendation based in high quality evidence and two weak recommendations based on very low quality evidence and the second one[6] two strong recommendations and it cannot make a recommendation about the third question because of lack of evidence. Also the recent clinical practice guidelines published by the American College of Physicians about use of Intensive Insulin Therapy for the Management of Glycemic Control in Hospitalized Patients only makes three recommendations focused on critical patients; the two strong recommendations are about not using intensive insulin therapy and the weaker recommends a target blood glucose level if insulin therapy is used.[7] Also the recent consensus of SEMICYUC-SENPE makes recommendations only centered in critically ill patients.[8]

Therefore, in fields with high levels of uncertainty and low quality evidence, expert consensus or recommendations can add value to clinical work.

By means of this revision and update, the GARIN (Grupo Andaluz de Reflexión e Investigación en Nutrición) working group aims to define its position regarding the treatment of patients with diabetes and artificial nutrition based on the critical reading of literature and also the experience of group members.

Material and methods

The main objectives of the GARIN group include reflecting on various aspects of clinical nutrition and generating recommendations agreed by consensus. Its members meet once a year in Osuna (Andalusia, Spain) after first systematically reviewing the best available evidence on a pre-agreed specific topic. Initially, a bibliographical review is carried out of the papers published on PubMed regarding enteral nutrition, parenteral nutrition and hyperglycaemia or diabetes: all members review this literature prior to the meeting (two months in advance). The topic was formally presented by the coordinator at the meeting for 45 minutes and then a series of specific questions that were written by the coordinator (GO) in advance (of which all were pre-informed) were discussed for the next four hours. These were answered at the meeting in the form of conclusions. The review of the literature and the answers to these questions are reflected in this article, which has been prepared by the coordinator and then discussed and adopted by all participants.

Review of the literature

Prevalence of diabetes mellitus and hyperglycemia in hospitalised patients receiving artificial nutrition

It is estimated that there are currently 246 million people with diabetes in the world and that this figure will increase over the next few years, reaching 380 million by the year 2025 according to the latest predictions.[9] An ageing population and lifestyle-related factors (changes in diet and increased sedentary lifestyle with consequent weight gain and obesity) are the main factors behind this epidemic.[10,11]

It is estimated that around 14% of the adult population in Spain has diabetes.[12,13] The prevalence of diabetes in the hospital setting is also very high, at about 11%, if data are taken from the administrative databases generated from hospital discharge reports,[13-15] exceeding 21% in the subgroup of patients over the age of 75 years.[14] However, if data are taken from hospital medical charts or prospective studies, the prevalence is higher still, at around 20-30%, while in patients over the age of 65 years or patients admitted to certain departments such as cardiology or cardiovascular surgery, the prevalence is even higher than 30%.[16-18]

The presence of diabetes in hospitalised patients is associated with an increased risk of death during hospitalisation, an increased length of hospital stay (3-4 days on average) and increased costs.[14,15,19]

Stress hyperglycaemia (in patients without diabetes) associated with acute diseases also seems to increase the morbidity and mortality of hospitalised patients [20]. Nevertheless, there are no reliable data regarding the

prevalence of this disorder as different definitions are given in the literature and none are accepted internationally.[21-23]

It is estimated that 8% of hospitalised patients receive some type of artificial enteral feeding support to treat or prevent malnutrition, whether as supplements or complete diets.[24,25] Approximately 2-3% more receives total parenteral nutritional support (TPN) for the same purpose.

Hyperglycaemia is a common complication in hospitalised patients receiving enteral nutrition.[26,27] Nevertheless, the prevalence of diabetes in patients receiving enteral nutrition is unknown. In one study involving an internal medicine department, 34% of patients receiving TEN had blood glucose levels over 200 mg/dl.[28] In another study assessing dependent geriatric patients (with severe cognitive impairment) admitted to long-term care units and receiving enteral nutrition, 50% had diabetes (defined as an HbA1C above 7%) with 44% of them being undiagnosed.[29] In a randomised study comparing two insulin therapy regimens in patients with enteral nutrition and diabetes (defined as two blood glucose levels above 130 mg/dl), half of the 50 randomised patients did not know they had diabetes.[30]

Between 16 and 30% of the subjects randomised to intervention trials comparing intensive and conventional insulin treatment in critically ill patients had diabetes mellitus prior to randomisation.[31-36] Nevertheless, the prevalence of hyperglycaemia or previously diagnosed diabetes in patients receiving TPN treatment, especially in patients from non-critically ill units, has not been well studied. In a series of 50 retrospective cases, Pleva et al. describe rates of hyperglycaemia above 150 mg/dl in more than 90% of patients receiving TPN.[37] Among hospitalised patients receiving TPN in Spain from general wards (not intensive care units), prevalences of hyperglycaemia above 200 mg/dl have been described in 12-27% of patients.[38,39] In a recent study conducted by the Group for the Study of Hyperglycaemia during Parenteral Nutrition of the Area of Nutrition of the Sociedad Española de Endocrinología y Nutrición (Spanish Society of Endocrinology and Nutrition),[40] 51% of patients (non-critically ill) prescribed TPN had some type of glucose metabolism alteration prior to starting TPN (based on blood glucose and glycated haemoglobin values): known diabetes 18%, undiagnosed diabetes 3.8%, stress hyperglycaemia 12.4%, being at risk for the development of diabetes 15%. During the TPN infusion, 80% of patients had at least one capillary blood glucose measurement above 140mg/dl with 51% above 180 mg/dl.

Effects of hyperglycaemia on the outcome of hospitalised patients

Short-term hyperglycaemia in hospitalised patients has been related to an increased susceptibility to infections and other alterations, such as increased oxidative stress, increased hypercoagulability, dyslipidemia, etc., resulting in a secondary increase in morbidity, mortality and generated costs.[25] This increase in complications and mortality has been observed with different clinical conditions (myocardial infarction, strokes, trauma, coronary bypass, COPD, elderly patients, etc.).[41]

Experimental data are currently available on potential mechanisms from observational and intervention clinical studies that support the fact that hyperglycaemia per se, in addition to being a marker of illness severity, causes major adverse effects that affect the prognosis of hospitalised patients, including increased mortality, rates of infection and length of hospital stay. Some studies also suggest that stricter control of blood glucose levels in critically ill patients with and without diabetes could improve their prognosis.[5,18,26,42]

In the case of patients receiving TPN (both in critically ill and non-critically ill patients), it seems that hyperglycaemia per se, possibly independently of the previous presence of diabetes, could worsen the prognosis of patients by increasing morbidity and mortality (increased cardiac, infectious and septic complications, renal failure, etc.), especially if not associated with insulin therapy.[26,43-49]

Objectives of hyperglycaemia treatment in non-critically ill patients

Until the beginning of the 21st century, it was generally accepted that blood glucose levels of hospitalised patients should be kept within safe limits between 150 and 250 mg/dl. However, following the first papers published by the Van den Berghe group in ICU patients,[36] this concept was rethought and substituted by another concept supporting a more active approach in order to achieve better glycaemic control. Therefore, over recent years, the management of hyperglycaemia during hospitalisation has become particularly relevant with recommendations being established that suggest that the objective of glycaemic control during hospitalisation should be to normalise blood glucose levels.[18,26,42]

Nevertheless, the treatment of hyperglycaemia with the objective of normalising blood glucose levels has had contradictory results in the literature, especially in critically ill patients, the area where most randomised and controlled trials have been conducted. Therefore, studies by Van den Berghe in critically ill patients showed a reduction in mortality in surgical patients assigned to intensive IV insulin treatment (objective 80-110 mg/dl) compared to conventional treatment (starting infusion with blood glucose levels above 220 mg/dl with the objective of 180-200 mg/dl).[36] The same group managed to replicate results (lower mortality) in critically ill patients in ICUs, but only in those patients receiving treatment for more than 3 days.[35] However, other randomised, multi-centre studies in critically ill

patients comparing intensive and conventional treatment (generally with stricter control in the conventional group than in studies conducted by Van den Berghe) have not been able to replicate the same results (no reduction in mortality has been observed and in some cases an increase in mortality has even been noted, possibly related to hypoglycaemia).[31-34]

Although there is a huge debate in the literature[41,48,50-52] regarding the disparity between results in the different papers on intensive treatment, part of the effects could be due to the nutritional therapy used in the different studies (higher parenteral infusion rate of glucose and nutrients in the Van den Berghe studies compared to the others).

In a recent systematic review and meta-analysis on the use of intensive insulin therapy (with an approximate treatment objective of 140-180 mg/dl) in non-critically ill patients, a reduced risk of infections and a tendency towards a higher incidence of hypoglycaemia compared to patients treated with conventional insulin therapy was observed.[53]

After initially adopting the objective of normoglycaemia, clinical practice guidelines and consensus currently recommend maintaining a pre-prandial glucose level of less than 140 mg/dl and a glucose level of 180 mg/dl at all other times in most "non-critically ill" patients.[5,18] Objectives may vary based on the clinical situation (with objectives being less strict, for example, in patients with a short vital prognosis or a high risk of hypoglycaemia).

Indications for artificial nutrition in patients with diabetes

Indications for artificial nutritional support in patients with diabetes are no different from those for patients without diabetes. Enteral nutrition is indicated in those patients that cannot, should not or do not want to meet adequate nutritional requirements by oral intake and who have a functioning, accessible gastrointestinal tract.

Between 5 and 8% of hospitalised patients receive some type of artificial enteral feeding support, either as supplements or complete diets.[25] If we apply the actual hospital diabetes prevalence rates, we can estimate that 1-2% of hospitalised patients are diabetic and receive some type of enteral artificial nutritional support.

The prescription of home enteral nutrition (HEN) is also gradually increasing.[54] The main indications for the use of HEN[54,55] are neurological alterations preventing swallowing and neoplasms, which are more common conditions in adults of advanced age. This means that the prevalence of diabetes in patients prescribed home enteral nutrition is potentially very high.

TPN is prescribed to approximately 1-3% of hospitalised patients (based on their complexity) and has proven to be effective and safe for restoring or maintaining the nutritional status of patients who cannot ingest or tolerate food via the digestive tract.[56]

However, as mentioned above, both parenteral and enteral nutrition increase the risk of hyperglycaemia regardless of the previously diagnosed presence of diabetes[28,40,44,49,57] and therefore strategies should be implemented to prevent deleterious effects on the outcome of patients, including the prevention and adequate treatment of this complication.

Treatment of hyperglycaemia/diabetes and enteral nutrition

Selection of enteral formulas in diabetes/hyperglycaemia

"Standard" commercial formulas used in enteral nutrition have a high carbohydrate content (about 50%), a low-moderate lipid content (about 30%) and contain no dietary fibre. These liquid formulations seem to increase the glycaemic and insulin response more in healthy people or patients with diabetes mellitus when compared with a similar intake of nutrients from a mixed meal. Although any formula can be used in patients with diabetes, adjusting the insulin therapy as required, enteral formulas designed specifically for patients with diabetes and stress hyperglycaemia have been marketed over recent years to reduce glycaemic response and also improve lipid profile and other cardiovascular risk factors.[25]

All formulas "for diabetes" contain sources of carbohydrates with a low glycaemic index, such as non-hydrolysed starch or modified maltodextrin. Although the addition of fructose is currently a matter of debate, most add this nutrient in moderate-low amounts. Likewise, all diabetic formulas add fibre, almost always with a high proportion or exclusive content of fermentable ("soluble") fibre, which is associated with an improved glucose and lipid profile.[58-62]

Also, most diabetes-specific enteral formulas have increased the percentage of fat (preferably monounsaturated) compared to carbohydrates. In general, post-prandial glycaemic response with a high intake of a formula with a high monounsaturated fat content is lower compared to formulas with a high carbohydrate content as response depends fundamentally on the total carbohydrate content. As the carbohydrate content of the formulas increases, other factors also affect glycaemic response, such as the carbohydrate source or content and the type of fibre.[58,60,62-64]

Diabetes and stress diabetes-specific diets (especially those high in fats) in hospitalised patients (in intensive care or on general wards) reduce blood glucose levels and insulin requirements without modifying aspects such as hospital stay, infectious morbidity or mortality.[65,66] High-fat diets also do not worsen lipid control and even tend to improve it[67] compared to high-carbohydrate diets. The use of a diabetes-specific supplement in outpatients, high in fat when compared to a hyperprotein supplement, reduced medium-term glycaemic

control (HbA1C).[68] Short and medium-term (up to three months) high-fat diabetes-specific diets in tube-fed outpatients also improve metabolic control (blood glucose levels, HbA1C and insulin requirements in some cases) compared to standard formulas (generally with fibre), although they do not modify morbidity.[69-73] These formulas may also reduce glycaemic variability and hypoglycaemia compared to standard formulas, at least in the short term.[71,73-75]

To summarise, it must be highlighted that diets designed for people with diabetes and stress hyperglycaemia (especially those high in monounsaturated fats) are safe and clearly reduce post-prandial blood glucose levels, insulin requirements and, according to some papers, glycaemic variability and medium-term HbA1C without worsening or maybe even improving the lipid profile.

Nevertheless, more randomised and preferably double-blind studies must be conducted that involve more patients, lower rates of withdrawal from the protocol and a longer duration in different clinical situations to assess the efficacy and efficiency (cost/effectiveness) of such diets on metabolic effect and morbidity and mortality in order to be able to give better evidence-based recommendations.

In fact, although there are meta-analysis supporting its use,[62] the recent ASPEN guidelines conclude that there aren't sufficient data to recommend the use of these formulas in hospitalized adult patients with hyperglycemia.[6]

Treatment of hyperglycaemia in patients with diabetes/stress hyperglycaemia and enteral nutrition

To date, only one prospective randomised study has been published that evaluates different insulin therapy regimens in this type of patient.[30] Korytkoswski et al. studied 50 patients, 25 randomised to receive treatment with insulin glargine and regular insulin compared to 25 randomised to sliding-scale insulin with added NPH insulin if poor control persisted. Both strategies showed a similar efficacy and safety in non-critically ill patients receiving enteral nutrition. Half of the patients in the sliding-scale group required added NPH insulin.

Other retrospective studies with a small number of patients have shown the efficacy of the injection of basal-bolus insulin regimens (insulin glargine + rapid-acting insulin), 70% NPH and 30% rapid-acting insulin biphasic insulin mixes (divided into 2 or 3 doses) and NPH insulin sliding-scale regimens (divided into 4-6 doses) in patients receiving continuous enteral nutrition with diabetes.[76,77,78] Although conclusions cannot easily be generalised (due to being retrospective studies with few patients), it seems that the biphasic insulin regimen in three doses or the NPH insulin sliding-scale regimen (four daily injections) could be advantageous for achieving better therapeutic objectives, thus reducing hypoglycaemia. The use of insulin glargine + insulin lispro in patients receiving enteral nutrition in boluses also seems to be effective at controlling hyperglycaemia.[79]

The percentage of hypoglycaemia in most studies conducted with enteral nutrition and insulin therapy varies between 3 and 5%, which is slightly higher than the percentage achieved in other studies in non-critically ill hospitalised patients not receiving enteral nutrition.[80] It must be considered that it is not uncommon for enteral nutrition to be unexpectedly suspended (due to gastrointestinal complications, diagnostic test requirements, accidental feeding tube removal, drug administration, etc.).

The lack of prospective randomised studies involving an adequate number of patients encourages guidelines, reviews and consensuses to make recommendations based not on evidence but on the experience of the different groups.[5,17,75,81]

Therefore, some authors suggest that the administration of lower but more frequent doses of intermediate-acting insulins (NPH, NPL or similar) or regular insulin could reduce the risk of hypoglycaemia and insulin-associated risks and, moreover, reduce the number of injections and controls. Furthermore, intermediate-acting insulins could be more useful when adjusting the dose of enteral nutrition received (since its half-life is shorter), adding regular insulin or rapid-acting insulin analogs as needed.[5,75,77] They could also be used in patients receiving night-time EN infusions in one or two doses. Long-acting insulins (insulin glargine or two doses of insulin detemir) would be reserved for patients with more stable requirements or receiving EN infusion as boluses combined with ultra-fast-acting insulin.[5,17,75] Nevertheless, all imaginable options are possible, especially if the theoretical insulin action is adapted to the enteral nutrition infusion regimen (continuous, bolus, cyclic, nocturnal, etc.).[5]

Treatment of hyperglycaemia in non-critically ill patients receiving TPN

The current discussion in literature regarding intensive treatment with insulin therapy in critically ill patients has been mentioned above. In most of these studies, parenteral nutrition and/or glucose solution infusions are combined with enteral nutrition administering insulin by way of perfusion pumps that are separate from the TPN. However, outside the intensive care units (where the health professional-to-patient ratio is high) or outside the context of clinical trials, the use of protocols for intravenous insulin therapy with separate nutrition infusion is less common, except in cases with very poor metabolic control.

In 2006, a group of hospital pharmacists in Spain reported that up to 18% of patients with TPN and hyperglycaemia with blood sugar levels above 200 mg/dl were not receiving any insulin treatment and

almost 57% were only receiving such treatment via subcutaneous injection.[39]

However, more recently, in 605 non-critically ill patients receiving TPN under the care of endocrinologists in the Nutrition Units, 71.1% of the cases evaluated were prescribed insulin, with 58.1% of the patients with no glucose metabolism alteration also receiving insulin. In this study, of all the cases treated with insulin (n = 433), intravenous insulin was used in 55% of the cases, added to the TPN bag (36%) or by intravenous perfusion (8.8%). Subcutaneous administration alone was used in 55.1 % of cases.[82]

The use of insulin added to the TPN bag, with adjustments of subcutaneous regular insulin every 6-8 hours (or rapid-acting insulin analogs every 4 to 6 hours), is a common practice in Spain and other countries that often allows reasonable metabolic control to be achieved in patients.[5,38,75,81,83] Nevertheless, there are no randomised studies comparing the efficacy and effectiveness of different insulin therapy regimens in TPN.[83] Although adsorption to the bags is a controversial subject,[84,85] the percentage lost seems to be minimal in ternary mixtures using the new bags. To adjust the insulin therapy, one-half to two-thirds of the subcutaneous units administered the previous day are added to the bag. The mean doses used in patients with known diabetes generally reach 0.7-0.8 IU/kg of bodyweight or 0.3 IU/gram of infused carbohydrate.[38,82] In patients with stress hyperglycaemia, the usual doses range between 0.1 and 0.15 IU per gram of carbohydrate infused via TPN. With this regimen, the risk of hypoglycaemia is low since the insulin perfusion is discontinued with TPN withdrawal.

There are other specific protocols for managing insulin in TPN that have been recently proposed, such as adding regular insulin (2/3 of the calculated dose) to the bag with NPH insulin every 6-8 hours (a total of 1 unit every 5 to 20 grams of carbohydrate based on whether diabetes was previously diagnosed or not and the blood glucose levels at the start) and "basal" insulin in diabetics or corticosteroids at doses of 0.15 to 0.25 IU/kg administered as NPH insulin every 6 to 8 hours. This regimen could be more effective than ad hoc regimens in which insulin was added on demand.[86] Satisfactory results have also been published in short studies or isolated clinical cases with other slow-acting insulins such as insulin glargine or NPL[78,87]. When it is not possible to control hyperglycaemia, the infusion of IV insulin separately from TPN may be necessary.[5]

On the other hand, as was mentioned earlier on, it is fundamental to adequately calculate requirements, not to administer high doses of glucose and to take into account all nutrients supplied (not just from TPN but also including dextrose/glucosaline solutions) in order to prevent and treat TPN-associated hyperglycaemia[83,88-90] as hyperglycaemia and complications would be affected by the total amount of glucose and calories infused.[49,91]

In the case of type 1 diabetes, some authors suggest administering low doses of insulin detemir or glargine to prevent ketoacidosis if TPN is suddenly discontinued.[17]

Although the use of special amino acid (e.g. enriched with glutamine)[92-94] or lipid formulas (based on olive oil or supplemented with omega-3 fatty acids)[83] may be beneficial to prevent or treat hyperglycaemia, there is not sufficient data in the literature to make recommendations.

Conclusions of the Garin Group

After systematically reading the literature and in view of the lack of studies allowing recommendations based upon high-level evidence to be reached regarding the best strategy for preventing and treating patients with diabetes and hyperglycaemia and artificial nutrition, we hereby make the following recommendations based on data from the literature and the group's clinical experience.

Question 1: Is hyperglycaemia and the presence of diabetes a major problem in patients receiving artificial nutrition?

1. Hyperglycaemia in patients receiving enteral or parenteral nutrition is a major problem in both hospitalised patients and outpatients due to its high prevalence and possible consequences in terms of morbidity and mortality, regardless of the pre-existence of glucose metabolism disorders.

2. It is recommended that these patients be monitored by nutritional support teams with specific training in clinical nutrition and diabetology given that it is common that specific hypoglycaemic treatments which can determine the effectiveness of parenteral and enteral artificial nutrition are used.

Question 2: Are the indications for artificial nutrition different in patients with diabetes or hyperglycaemia vs. non-diabetics?

3. The indications and access routes for artificial nutrition are no different in patients with diabetes or stress hyperglycaemia than in non-diabetics. As an exception, in the case of diabetic gastroparesis requiring EN, post-pyloric (non-gastric) enteral access placement is recommended.

Question 3: What is the definition of stress hyperglycaemia and "at risk for the development of diabetes"?

4. In hospitalised patients with unknown diabetes and in the context of an acute disease, stress hyperglycaemia is defined as plasma glucose levels above 126

Table I
Definition proposed for stress hyperglycaemia and "at risk for the development of diabetes" prior to admission

Stress hyperglycaemia	*"At risk for the development of diabetes" prior to admission*
Blood glucose levels ≥ = 126 mg/dl in fasting conditions or ≥ 200 mg/dl at any time	
No known diabetes, in context of hospital admission for acute disease	
HbA1C < 5.7%	HbA1C ≥ 5.7 and < 6.5%
Reassess after 3 months with blood glucose and HbA1C tests	

mg/dl in fasting conditions or above 200 mg/dl at any time with glycated haemoglobin levels below 5.7%. By definition, this increase would be transient (it disappears once the disease causing admission is resolved) then we recommend reassessing metabolic state three months after reaching clinical stability by doing blood glucose and HbA1C tests.

5. We propose defining hospitalised patients as being "at risk for the development of diabetes" prior to admission when said patients have unknown diabetes and, in the context of an acute disease, have plasma glucose levels above 126 mg/dl in fasting conditions or above 200 mg/dl at any time with glycated haemoglobin levels between 5.7% and 6.5% as having pre-admission glucose metabolism alteration. We recommend reassessing metabolic state three months after reaching clinical stability by performing blood glucose and HbA1C tests.

6. To define both stress hyperglycaemia and being pre-admission "at risk for the development of diabetes", it would be necessary to measure HbA1C in all hospitalised patients with hyperglycaemia (above 126 mg/dl) in order to correctly classify the condition and determine the best possible hypoglycaemic treatment during admission and upon discharge (table I).

Question 4: Are there any proven benefits from strictly controlling blood glucose levels in patients receiving artificial nutrition and what would be the objectives of such controls in non-critically ill patients?

7. Strict blood glucose level control (80-110 mg/dl) is not recommended for ICU patients or non-critically ill patients receiving artificial nutrition. The objectives of metabolic control (during admission), if receiving continuous nutrient infusion, must be to keep blood glucose levels between 140 and 180 mg/dl. In patients receiving discontinuous artificial feeding infusion, the objective must be to keep pre-prandial blood glucose levels between 100 and 140 mg/dl and post-prandial levels between 140 and 180 mg/dl. It is necessary to inform the patient of the importance of taking a series of blood glucose measurements and of starting drug treatment if these limits are exceeded. Insulin therapy must be started in patients with blood glucose levels above 180 mg/dl. We also recommend starting insulin therapy at levels above 140 mg/dl, although therapy can be personalised based on the patient's individual characteristics (risk of hypoglycaemia).

Question 5: Can hyperglycaemia be prevented in patients receiving artificial nutrition?

8. It is recommended that all patients starting artificial nutrition (enteral and/or parenteral), with or without a history of diabetes, have their blood glucose levels monitored initially every 6-8 hours and for at least 24 hours after reaching the total estimated requirements. After this, if blood glucose levels are below 140 mg/dl, the number of controls may be decreased based on the patient's clinical condition (table II).

9. Hyperglycaemia can be prevented in patients receiving artificial nutrition by implementing local protocols that adequately calculate energy-protein needs. It is vital to provide individualised nutritional requirements based on the patient's clinical condition, body composition, age and gender. This implies not giving excess calories to a population that often suffers from obesity. We therefore recommend calculating baseline requirements by applying the Harris-Benedict formula as this includes age as a variable. To calculate the total requirements, we recommend multiplying the baseline energy expenditure (Harris-Benedict) by a stress factor of between 1.1 and 1.3, depending on the condition indicating the use of artificial nutrition (greater requirements are only needed in exceptional cases). We recommend using the real weight in malnourished and normally nourished patients (up to a BMI of 25 kg/m^2) for calculations. Above this limit we recommend using the adjusted weight, taking the weight that would give a BMI of 24 kg/m^2.

10. In all patients receiving artificial nutrition, especially those receiving parenteral nutrition, it is necessary to take into account all glucose administered (including glucose drips) to prevent the deleterious effects of hyperglycaemia.

Table II
Strategies to prevent to hyperglycaemia during artificial nutrition

Monitor capillary blood glucose levels every 6-8 hours when starting artificial nutrition
Strict calculation of energy needs – Hospitalised patients. Harris-Benedict formula * Stress factor (1.1-1.3). Use adjusted bodyweight in patients with BMI > 25 kg/m^2 – Outpatients. Harris-Benedict formula * Physical activity factor, or equations proposed by US National Academy of Sciences.
Take into account all glucose supplies

11. In the case of outpatients, to calculate total energy expenditure we recommend applying the Harris-Benedict formula and multiplying by a coefficient that takes into account physical activity or using the equations proposed by the US National Academy of Sciences (which already include physical activity).[95,96]

12. The estimated protein requirement, in the absence of limiting renal or hepatic disease, will depend on the degree of metabolic stress shown by the patient. General estimates are 1 g/kg/day (in patients with no or minimum stress) and 1.5 g/kg/day (in patients with severe stress), which may be increased in exceptional cases with large additional losses (e.g. large burn areas).

Question 6: In the field of enteral nutrition and hyperglycaemia and diabetes, should diets designed for patients with diabetes be used in the presence of stress hyperglycaemia/ diabetes? What would be the recommended macronutrient composition?

13. In patients with enteral nutrition and stress diabetes, we recommend using diets designed for patients with diabetes and stress hyperglycaemia with a high or moderate monounsaturated fat content to facilitate metabolic control and achieve therapeutic objectives as these formulas have proven to reduce post-prandial blood glucose levels, insulin requirements and, in some papers, glycaemic variability and medium-term HbA1C without worsening or maybe even improving the lipid profile. However, there is no evidence of improvement in morbidity and mortality. We recommend initially avoiding these diets in patients with gastroparesis if enteral nutrition is given via the gastric route. We recommend high-monounsaturated fat formulas that give between 38 and 52% of lipids plus fibre (high proportion of fermentable/soluble fibre) and low glycaemic index/load carbohydrates.

14. In the presence of other underlying concomitant conditions requiring treatment with enteral nutrition and specific formulas (e.g. renal failure, liver failure), treatment according to the main condition will prevail. Choosing between the different preparations will therefore also depend on the clinical situation of the patient in question (presence of malabsorption, severe renal, liver or lung failure, presence of diabetic gastroparesis, site of formula infusion, special requirements, restriction of certain nutrients or volume, etc.). In these cases, compliance with therapeutic objectives will basically depend on the insulin therapy prescribed.

Question 7: What is the best drug treatment for treating hyperglycaemia/diabetes in hospitalised patients and outpatients?

15. In hospitalised patients with stress hyperglycaemia or diabetes, the best treatment is insulin therapy.

16. For outpatients, drug treatment will follow the same recommendations and clinical practice guidelines as all other general patients (with both insulin and oral anti-diabetic drugs being used).

Question 8: What is the best insulin therapy regimen in hospitalised patients and outpatients receiving enteral nutrition?

17. It is not known which is the best insulin therapy regimen in hospitalised patients or outpatients receiving artificial nutrition. We recommend (table III):

a) Basal-bolus regimens in patients receiving enteral nutrition by bolus feeding or gravity. Total initial requirements will depend on previous treatments.
   a) If treated previously with oral anti-diabetic drugs, we recommend estimating the total initial insulin dose between 0.3 and 0.5 U/kg of adjusted bodyweight/day (based on BMI, home treatment, intercurrent processes, admission blood glucose levels and/or corticosteroid prescription).
   b) If treated previously with insulin therapy, the dose will be personalised based on previous doses and clinical condition.
   c) In general, doses with 40% of total insulin as basal insulin and 60% as prandial insulin will be applied (to prevent hypoglycaemia if enteral nutrition is suddenly discontinued). Prandial insulin injections will preferably be ultra-rapid-acting insulin (aspart, lispro or glulisine) injected just before starting the infusion or after completing infusion (if there is a risk of intolerance to prevent hypoglycaemia). The prandial dose will depend on the amount of carbohydrates infused and adjustment based on blood glucose levels prior to infusion.
   d) When starting enteral nutrition or in unstable patients (requiring frequent dose adjustments), we recommend covering baseline requirements with NPH, NPL or detemir. In stable patients or patients receiving enteral nutrition at final doses, insulin glargine may also be used.
b) In patients receiving continuous enteral nutrition, we recommend a baseline insulin regimen of 40% basal insulin and 60% prandial insulin preferably every 8 hours with rapid-acting insulin (regular) as nutritional insulin in three equal parts (every 8 hours) + adjustment regimen (based on pre-injection blood glucose levels). Basal insulin may be insulin glargine once a day, detemir twice a day, NPH or NPL 2-3 times a day or NPH or NPL insulin mix two or three times a day. Dose calculation will be similar to that described above.
c) In patients receiving cyclic (e.g. night-time) feeding, we recommend using a medium-acting basal insulin (NPH, NPL or Detemir) injected a

Table III
Approach to insulin therapy in control nutrition (EN)

	Basal	*Prandial*	*Adjustment regimen*
Continous EN	40% Glargine (one a day) Detemir (twice a day) NPH, NPL (2-3 times a day)	60% Every 8 hours In 3 equal parts 1st option: Regular insulin	Based on capillary blood glucose levels Same insulin as prandial
Bolus or gravity EN	40% When starting EN or stable patients ➔ NPH, NPL or detemir Stable patients or patients receiving EN at final dose ➔ can also use glargine	60% Rapid-acting insulin analogs (lispro, aspart, glulisine) according to amount of carbohydrates infused	Same insulin as prandial (base on capillary blood glucose levels prior to infusion)
Cyclic EN	Medium-acting insulin (NPH, NPL or detemir) 30-60 minutes before infusion		At the start and every 4-8 hours according to capillary blood glucose levels Regular or rapid-acting insulin analogs

Calculation of total initial insulin requirements. According to previous treatment:
With oral anti-diabetic drugs: 0.3-0.5 U/kg adjusted bodyweight/day (based on BMN, home treatment, admission blood glucose levels, intercurrent processes, corticosteroids).

half hour to an hour before starting infusion + adjustments, if required, with regular or ultra-rapid-acting insulin on starting the infusion and every 4-8 hours according to controls.

Question 9: In the field of parenteral nutrition and hyperglycaemia and diabetes, what proportion of macronutrients would be best?

18. There are no specific studies regarding the best proportion of macronutrients to prevent hyperglycaemia in patients with diabetes or stress hyperglycaemia. However, if total requirements are estimated according to the recommendations given above, the proportion of carbohydrates and lipids for infusion will be adequate. After estimating total calories, we recommend calculating amino acid requirements and subtracting the resulting calories from the total. The remaining calories (non-protein) will then be divided between carbohydrates and lipids in percentages that may range between 60% carbohydrates and 40% lipids to a maximum of 60% lipids and 40% carbohydrates (if there is a greater risk of hyperglycaemia or hyperglycaemia cannot be controlled). Either way, this calculation procedure entails infusing 2-4 grams/kg of bodyweight/day of carbohydrates and 1-1.3 g/kg of bodyweight/day of lipids (we recommend not exceeding 1.5 grams of lipids per kg/day, especially in severely ill patients).

Question 10: In the field of parenteral nutrition and hyperglycaemia and diabetes, what type of macro- and micronutrients would be best?

19. There are no data in the literature specifically evaluating these aspects. However, based on physiopathological studies, the use of glutamine or lipids based on olive oil or supplemented with omega-3 fatty acids in patients with increasing metabolic stress could be a reasonable option.

Question 11: What is the best insulin therapy regimen in non-critically ill hospitalised patients with diabetes/hyperglycaemia receiving TPN?

20. We recommend adding regular insulin to TPN bags with a subcutaneous regular (not rapid-acting insulin analogs) insulin regimen every 6-8 hours based on capillary blood glucose levels, with adjustments above 140 mg/dl. In all cases, if the therapeutic objectives are not achieved, the equivalent of 2/3 of the subcutaneous rescue insulin dose required the previous day will be added daily to the bag (table IV). We have applied the following assumptions:

a) No known diabetes and blood glucose levels prior to starting the TPN infusion above 140 mg/dl or no clinical condition commonly associated with hyperglycaemia (severe acute pancreatitis, concomitant use of corticosteroids): start with 1 IU/10 g of glucose in the TPN. Alternative: start with 0.25 IU/kg of adjusted bodyweight.
b) Known diabetes without insulin therapy: start with 1 IU (low stress) to 2 IU (high stress or corticosteroids) for every 10 g of glucose in the TPN.
c) Known diabetes undergoing home treatment with insulin: start with 2 IU per 10 g of glucose or 0.5 IU/kg of bodyweight. As an alternative, start with half (if low stress) to 2/3 (if high stress) of previous outpatient requirements in the bag.

Table IV
Approach to insulin therapy in parenteral nutrition

Parenteral nutrition in hospitalised patients:
– Add regular insulin to TPN bags in combination with subcutaneous regular (not rapid-acting insulin analogs) insulin regimen every 6-8 hours based on capillary blood glucose levels, with adjustments above 140 mg/dl.
– Add the equivalent of 2/3 of subcutaneous rescue insulin dose required the previous day every day
– In cases of uncontrolled hyperglycaemia, separate intravenous insulin infusions from TPN may be required.
Recommended initial insulin dose:
– Unknown diabetes and prior blood glucose levels > 140 mg/dl or no clinical condition commonly associated with hyperglycaemia (severe acute pancreatitis, corticosteroids): start with 1 IU/10 g glucose in TPN, or start with 0.25 IU/ kg adjusted bodyweight.
– Known diabetes without insulin therapy: start with 1 IU (low stress) to 2 IU (high stress or corticosteroids) for every 10 g glucose in TPN.
– Known diabetes receiving home insulin therapy: start with 2 IU/10 g glucose or 0.5 IU/kg of bodyweight, or start with 50-66% of previous outpatient requirements in bag.
In patients with type 1 diabetes, in addition to insulin placed in bag and adjustment regimen, inject 0.05-0.1 IU/kg bodyweight of subcutaneous basal insulin.
Home parenteral nutrition and cyclic infusion: Medium-acting basal insulin (detemir or similar) prior to infusion. Add adjustment regimen if required.

21. In patients with type 1 diabetes, in addition to the insulin placed in the bag and the adjustment regimen, we recommend injecting between 0.05 and 0.1 IU/kg of subcutaneous basal insulin (to prevent ketoacidosis if the TPN infusion is suddenly discontinued). We recommend a preferable use of insulin glargine (once a day) or detemir (once or twice a day) in these cases.

22. In patients receiving home parenteral nutrition and cyclic infusion, subcutaneous insulin may achieve reasonable control of TPN-associated hyperglycaemia in non-diabetic patients. We recommend a dose of detemir prior to infusion.

23. If metabolic objectives are not achieved with the usual regimen, continuous insulin infusion using separate infusion pumps from TPN would be proposed.

Question 12: What would your future investigation recommendations be in the field of diabetes/ hyperglycaemia and artificial nutrition?

24. It is necessary to expand on studies assessing the prevalence of glucose metabolism alterations (diabetes and stress hyperglycaemia) in patients receiving both parenteral and enteral artificial nutrition (in different clinical situations, both hospitalised and as outpatients).

25. It is necessary to assess the physiopathological determining factors of stress hyperglycaemia and, at a clinical level, the natural history of this condition, with it being necessary to reassess the persistence of long-term glucose metabolism alterations after acute processes in order to reclassify patients. Considering these data, a consensus should be reached regarding diagnostic criteria for stress hyperglycaemia and other glucose metabolism alterations.

26. More studies are required in non-critically ill hospitalised patients in order to define glycaemic control objectives by evaluating morbidity, mortality and efficiency criteria.

27. Prospective clinical studies must be conducted to compare the use of different enteral nutrition formulas in patients with diabetes and/or stress hyperglycaemia. These must include more patients, lower protocol withdrawal rates, longer duration (especially in outpatients), be randomised and preferably double-blind in different clinical situations and should assess the efficacy and efficiency (cost/effectiveness) of such formulas on metabolic effect and morbidity/mortality in order to be able to make evidence-based recommendations.

28. It is necessary to conduct clinical trials comparing different insulin therapy regimens in both enteral and parenteral nutrition and different clinical scenarios, assessing not only metabolic control parameters but also their effect on morbidity and mortality.

29. Studies assessing the role of other aspects of the treatment of patients receiving artificial nutrition with hyperglycaemia should be conducted (such as the addition of micronutrients, drug nutrients, glutamine, whey proteins, omega-3 fatty acids, etc.).

Statement of Authorship

All authors contributed to the conception and design of the study, drafting of the manuscript and critical revision thereof.

Conflicts of interest Statement

None of the authors has any conflict of interest to disclose.

Funding

Nestlé Health Nutrition covered all expenses for transportation and rental of the room where the meeting was held but did not take part in any way in the conception or design of the study, manuscript revision or group conclusions.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1850-1859
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Regulación de la ingesta alimentaria y del balance energético; factores y mecanismos implicados

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Resumen

La regulación de la ingesta energética representa un proceso de vital importancia en el organismo ya que posibilita el mantenimiento de un equilibrio entre la cantidad de energía almacenada en forma de grasa corporal y el catabolismo de la misma.

Objetivo: **El objetivo de este trabajo ha sido analizar los principales factores implicados en la regulación de la ingesta alimentaria, el balance energético y su fisiopatología.**

Metodología: **Se realizó una búsqueda en Medline y Ebsco de artículos publicados en inglés y español en el período comprendido entre enero de 2009 y enero de 2012. Los términos de búsqueda fueron "food intake", "energy balance", "regulation", "nutritional homeostasis".**

Resultados: **Se encontraron un total de 198 estudios científicos, de los cuales únicamente 70 cumplían los requisitos de la búsqueda. Todos los estudios consultados coinciden en la importancia de las hormonas gastrointestinales como principales agentes moduladores de la homeostasis energética. Dicho efecto modulador sobre el apetito y la saciedad tiene lugar mediante su acción directa sobre el hipotálamo o el núcleo del tracto solitario a nivel del tronco encefálico (sistema nervioso vegetativo). Únicamente la ghrelina, ha sido relacionada con el inicio de la ingesta considerándola una de las principales señales orexigénicas en los modelos animales estudiados y en humanos.**

Discusión: **La regulación de la ingesta alimentaria y el balance energético constituye un proceso extremadamente complejo cuyo funcionamiento y equilibrio es posible gracias a la acción de las distintas señales endocrinas del tracto gastrointestinal.**

(*Nutr Hosp.* 2012;27:1850-1859)

DOI:10.3305/nh.2012.27.6.6099

Palabras clave: *Ingesta alimentaria. Balance energético. Regulación. Homeóstasis nutricional.*

REGULATION OF DIETARY INTAKE AND ENERGY BALANCE; FACTORS AND MECHANISMS INVOLVED

Abstract

The regulation of energy intake is a vital process in the body as possible to maintain a balance between the amount of energy stored as body fat and the catabolism of the same.

Objective: **The objective of this study was to analyze the main factors involved in regulating food intake, energy balance and pathophysiology.**

Methods: **We searched Medline and Ebsco of articles published in English and Spanish in the period between January 2009 and January 2012. Search terms were "food intake", "energy balance", "regulation", "nutritional homeostasis."**

Results: **There were a total of 198 scientific studies, of which only 70 met the requirements of the search. All studies consulted agree on the importance of gastrointestinal hormones modulating agents as primary energy homeostasis. Such a modulatory effect on appetite and satiety is mediated by direct action on the hypothalamus or the nucleus of the solitary tract at the brainstem (autonomic nervous system). Only ghrelin has been linked to the start of the intake considering a major orexigénicas signals studied in animal models and humans.**

Discussion: **The regulation of food intake and energy balance is an extremely complex process whose operation and balance is made possible by the action of various endocrine signals of the gastrointestinal tract.**

(*Nutr Hosp.* 2012;27:1850-1859)

DOI:10.3305/nh.2012.27.6.6099

Key words: *Food intake. Energy balance. Regulation. Nutritional homeostasis.*

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Recibido: 6-VII-2012.
1.ª Revisión: 6-VIII-2012.
Aceptado: 7-VIII-2012.

Abreviaturas

SNC: Sistema Nervioso Central.
CCK: Colecistokinina.
CCK-1: Receptor 1 de Colecistokinina.
CCK-A: Receptor para la Alimentación de Colecistokinina.
CCK-2: Receptor 2 de Colecistokinina.
CCK-B: Receptor para Cerebro de Colecistokinina.
NPY: Neuropéptido Y.
Kb: Kilobase.
MCH: Hormona Concentradora de Melanina.
GH: Hormona del Crecimiento.
AgRP: Proteína Relacionada con Agoutí.
MC3: Receptor 3 de Melanocortina.
MC4: Receptor 4 de Melanocortina.
α-MSH: Hormona Estimulante de los Melanocitos.
POMC: Proopiomelanocortina.
CRH: Hormona Liberadora de Corticotropina.
TRH: Hormona Liberadora de Tirotropina.

Introducción

La regulación orgánica de la ingesta energética constituye un proceso esencial para el adecuado funcionamiento celular ya que posibilita un equilibrio necesario entre la cantidad de energía almacenada en forma de grasa corporal y el catabolismo de la misma[1]. Este equilibrio es posible gracias a la coordinación entre diferentes sistemas que van desde estructuras nerviosas centrales hasta la unidad funcional última del tejido adiposo, el adipocito[2]. Este complejo proceso de regulación es controlado a nivel del sistema nervioso central por el hipotálamo. Además, en esta regulación participan numerosos péptidos con acciones sinérgicas o antagónicas sintetizados en distintos tejidos los cuales interactúan entre sí y con diferentes señales neurales conduciendo la información hasta distintos núcleos quienes a su vez emitirán una respuesta en términos de comienzo o finalización de la ingesta y por ende de aumento o inhibición del gasto calórico[3]. La alteración del equilibrio de este complejo entramado de señales puede originar el desarrollo de procesos patológicos crónicos como la obesidad. Si bien, el mayor conocimiento de estos procesos así como de la naturaleza de las biomoléculas implicadas ha posibilitado en la actualidad, vislumbrar nuevas perspectivas terapéuticas en el control de enfermedades crónicas como la obesidad[4].

Material y métodos

Se realizó una búsqueda bibliográfica en Medline y Ebsco de los artículos publicados en inglés y español en el período de tiempo comprendido entre enero de 2009 y enero de 2012. Los términos de búsqueda fueron "food intake", "energy balance", "regulation", "nutritional homeostasis". Se encontraron un total de 198 estudios de los cuales únicamente 70 cumplían los requisitos de la búsqueda. Una vez seleccionados los 70 artículos se realizó un análisis minucioso sobre los contenidos de cada estudio, estableciendo puntos en común y controversias plateadas por los diferentes autores en torno a los principales mecanismos y biomoléculas implicadas en la regulación de la ingesta y balance energético.

Homeostasis nutricional

La homeostasis nutricional supone el conjunto de procesos fisiológicos implicados en los mecanismos de digestión, absorción de los nutrientes, almacenamiento de los mismos, así como su utilización y consiguiente gasto cuando proceda[5]. Todo ello con un único objetivo: permitir un crecimiento adecuado en talla y peso durante la infancia y la adolescencia, para en etapas posteriores, esto es, en la edad adulta, adquirir y mantener un peso apropiado[5]. El proceso de homeostasis nutricional tiene su inicio con la ingestión de los alimentos y su posterior digestión y absorción de las sustancias nutritivas, donde participan numerosas enzimas y hormonas gastrointestinales[6].

Secuencialmente a estos procesos, se lleva acabo una distribución y llenado de los depósitos de glucógeno hepático y muscular (depósitos de utilización inmediata), así como el depósito de triglicéridos en el interior de los adipocitos en la fase pospandrial[7]. Este ciclo tiene su continuación en la fase de ayuno en la que para obtener el aporte de nutrientes necesario se pondrán en marcha distintos procesos metabólicos (lipolisis, glucogenolisis y neoglucogénesis)[8]. Atendiendo al gasto energético, debemos establecer una diferenciación entre el gasto ligado a los procesos de mantenimiento del propio organismo (metabolismo basal), de aquel gasto derivado de la actividad física, crecimiento, acción dinámico-específica de los alimentos y la energía perdida a través de las secreciones y fluidos corporales (orina, heces y sudor). A continuación, en la figura 1, se muestran los principales aspectos implicados en el proceso de homeóstasis nutricional.

Todo este entramado de procesos queda a su vez interconectado y controlado por un amplio número de señales nerviosas periféricas, diferentes moléculas y mediadores de acción neuroendocrina, integrados a su vez en el sistema nervioso central (SNC)[10]. Localizados en el hipotálamo, residen las estructuras responsables del control de las sensaciones de saciedad y de hambre en el organismo sano[10]. Por un lado, el núcleo lateral, responsable de la sensación de hambre. En segundo lugar, el núcleo ventromedial, encargado del manejo y control de la saciedad durante el proceso de ingestión de alimentos. Desde estos centros tiene lugar una respuesta nerviosa eferente, desde la que se controla el volumen de energía almacenado o consumido a corto, medio y largo plazo[11]. Todo ello encaminado a mantener al sujeto en una situación de normopeso.

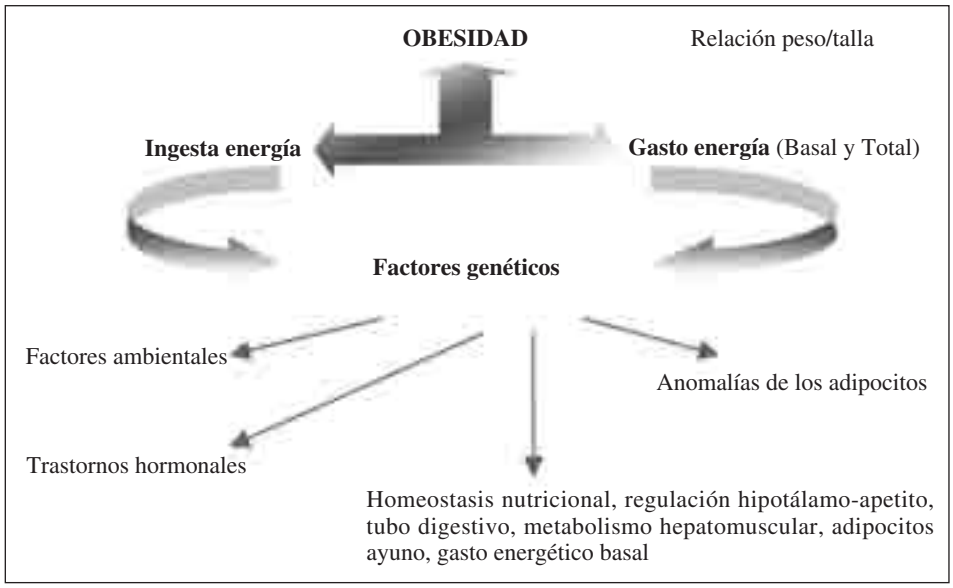


Fig. 1.—Homeostasis nutricional. Principales aspectos implicados. Adaptado de: Hermoso López, 2002[9].

Señales de regulación energética

Mecanismos de regulación de la ingesta a corto plazo

Desde un punto de vista conceptual, el hecho de tener apetito en un determinado momento, se ha venido relacionando con una ingesta inmediata de nutrientes. En esta misma línea conceptual, debemos hacer mención al ya arcaico concepto por el que se considera la bajada de los niveles de glucosa y lípidos en sangre como el principal elemento propiciador de la sensación de hambre y en consecuencia de una ingesta. Se ha podido comprobar cómo este proceso resulta ser de un orden de complejidad mucho mayor[12].

Desde que percibimos los alimentos hasta el inicio de su ingesta, van a tener lugar la intervención de toda una serie de señales sensitivas (olor de los alimentos, sabor de los mismos, textura, temperatura e incluso la apariencia o presentación de éstos), señales que a través de los pares craneales van a ser transmitidas hasta el sistema nervioso central (SNC)[13]. Por otra parte, el inicio de la secreción insulínica mediado a su vez también por dichas señales sensitivas parece ser otro de los factores que van a desencadenar la ingesta de nutrientes. A todo este conjunto de señales inductoras de la ingestión de alimentos se le conoce como fase cefálica de la alimentación. Como compensación a esta fase de inducción a la ingesta o *feed-back* positivo, destaca la existencia un mecanismo de disminución del apetito en el sujeto[13]. Dicho mecanismo se sustenta, en la existencia de unos receptores a nivel orofaríngeo, receptores que van a controlar el volumen calórico total ingerido en cada ingesta, generando así señales para la culminación de la toma. Ante situaciones de demora en una o varias de las tomas de alimento diarias, se va a producir un descenso de los niveles de glucosa en sangre. Consecuencia de ello, la sensación de hambre emergente será mayor con objeto de recobrar la reserva energética consumida durante el período de ayuno. A este proceso se le conoce como teoría glucostática[14].

Las reservas orgánicas de lípidos, por su parte, suponen otra de las fuentes de información que el organismo utiliza para controlar la ingesta de nutrientes en cada toma. Para ello y a nivel del sistema nervioso central, destaca la existencia de unos receptores encargados de regular las concentraciones de ciertas moléculas de composición grasa como ácidos grasos, glicerol o 3-hidroxibutirato, moléculas que a su vez ofrecen información acerca de las reservas grasas existentes en el organismo. A esta teoría se la conoce como teoría lipostática[15]. Sin embargo, y a pesar de lo elemental de ambas teorías, existe un amplio consenso en aceptar que una disminución en la oxidación de los nutrientes se correlaciona con sensación de hambre y su aumento con la saciedad. A esta teoría se la conoce como teoría energostática[16].

A nivel gastrointestinal, se han identificado varias moléculas peptídicas implicadas en la inducción a la saciedad y cuya síntesis y secreción irá en proporción a la cantidad de comida ingerida[17]. Sus mecanismos de actuación van a resultar variables, pudiendo actuar localmente o bien ser liberados al torrente sanguíneo, en cuyo caso su nivel de acción pasa a ser endocrino[18]. La información que dichos péptidos proporcionan llega hasta nuestro cerebro, concretamente al núcleo del tracto solitario (área ubicada en el tronco del encéfalo) a través de fibras vagales aferentes de nervios periféricos. Desde dicha región, la información será transmitida a su vez hacia el hipotálamo. A la actuación de dichos péptidos debemos añadir la distensión gástrica alcanzada durante la ingesta, efecto que potencia a su vez la acción peptídica ya comentada.

De los péptidos anteriormente comentados cabe destacar por su relevancia la colecistokinina (CCK), bom-

besina, glucagón, enterostatina, el polipéptido pancreático y amilina, entre otros. El efecto saciante de la colecistokinina (CCK), fue descrito por primera vez por Gibbs y cols. en 1973[19], quienes observaron cómo su administración vía peritoneal suprimía la ingesta alimentaria en la rata y posteriormente en el humano. Su liberación tiene lugar por las células enteroendocrinas de la mucosa duodeno-yeyunal como respuesta a la ingesta de grasas (ácidos grasos no saturados y de cadena larga principalmente) y proteínas[20]. Su actuación vendrá mediada por dos tipos de receptores. Receptores del tipo CCK-1, anteriormente denominados CCK-A (alimentary), dada su localización en el tracto alimentario, concretamente a nivel de las terminales aferentes vagales desde donde estimulan la transmisión nerviosa enviando un mensaje de saciedad al núcleo del tracto solitario[21]. Estos receptores se hallan igualmente presentes en páncreas, vesícula biliar, píloro y en múltiples localizaciones del sistema nervioso central (SNC) de entre las que destacan el núcleo del tracto solitario, área postrema e hipotálamo dorsomedial [21]. Los receptores de los tipos CCK-2, anteriormente denominados como CCK–B (Brain), sobre los cuáles actúa la colecistoquinina liberada cerebralmente para alcanzar así un efecto anorexígeno. Estos receptores se localizan en el nervio vago y en el sistema nervioso central (SNC)[22]. La bombesina, por su parte, actúa disminuyendo el volumen de alimentos ingerido en cada comida. El glucagón, con un mecanismo de actuación vagal suprime igualmente la ingesta de alimentos aunque actuando de forma particular sobre las proteínas[23]. La enterostatina, cuyo origen radica en la fragmentación de lipasa pancreática a nivel intestinal, provoca una disminución en la duración de las comidas [23]. El polipéptido pancreático y la amilina, ésta última por su interacción con el área postrema, inducen igualmente a una reducción en la ingesta de alimentos[23].

Mecanismos de regulación de la ingesta a medio plazo

La regulación del apetito a medio plazo viene mediada por el efecto de una hormona denominada péptido YY[24]. Atendiendo a su estructura química, se trata de una hormona compuesta por 36 aminoácidos, perteneciente al mismo grupo del polipéptido pancreático y neuropéptido Y (NPY)[24]. Se sintetiza en las células L del intestino, ubicadas en la región más distal del mismo, en el páncreas y cerebro. Actualmente se han identificado dos tipos de péptido Y con origen endógeno, el subtipo 1-36 y el 3-36, siendo el primero el más activo metabólicamente. Se ha comprobado que el péptido YY, concretamente el subtipo 3-36, tiene la capacidad de disminuir un 36% el volumen de alimento ingerido de forma inmediata y en un 33% el volumen total de 24 horas. Esta es la razón por la que es considerado como el principal regulador de la ingesta en períodos intermedios de tiempo[25].

Mecanismos de regulación de la ingesta a largo plazo

Este tipo de regulación a largo plazo tiene lugar a expensas de las llamadas señales periféricas de adiposidad y neurotransmisores centrales[26].

Señales periféricas de adiposidad con efecto anorexígeno (catabólico)

Las llamadas señales periféricas de adiposidad están integradas por dos moléculas de origen hormonal, la llamada leptina y la insulina. La secreción de ambas queda regulada en función del volumen graso orgánico total. Tanto una como la otra actúan inhibiendo los procesos anabólicos y estimulando los catabólicos[27].

Leptina

La leptina constituye el resultado o la síntesis final del *gen-ob*. Dicho gen, se encuentra localizado en el caso humano en el cromosoma 7q 31.3. Cuenta con 650 kb y está constituido por tres exones separados a su vez por dos intrones, siendo los exones dos y tres los portadores de la región que codifica la síntesis de leptina[28]. Por su estructura bioquímica, se trata de un péptido compuesto por 167 aminoácidos cuya secuencia resulta similar en diferentes especies. Tanto es así, que la leptina del ratón mantiene un 84% de homología con la leptina del humano, y un 83% de homología con la humana, en el caso de la rata[28]. A través de esta hormona, el hipotálamo ejerce un efecto controlador del estado nutricional del organismo, modulando la ingesta y contrarrestando un potencial balance energético positivo[29]. Para ello, la leptina provoca una activación de los sistemas efectores catabólicos. Éstos van a provocar una reducción de la adiposidad por medio de una inhibición del apetito (efecto anorexígeno), estimulando con ello el gasto energético e inhabilitando los sistemas efectores anabólicos cuyo objetivo es aumentar la adiposidad corporal (vía aumento de apetito), favoreciendo así el proceso de lipolisis del tejido adiposo[30].

Su síntesis es llevada a cabo principalmente por los adipocitos, aunque también se ha encontrado en determinados órganos y tejidos tales como la hipófisis, el hipotálamo, músculo esquelético, placenta, mucosa gástrica y epitelio mamario[31]. En cuanto a su concentración circulante variará en proporción directa al volumen de reserva grasa existente en el organismo, es decir, la cantidad de leptina producida por el adipocito y en consecuencia circulante, es proporcional al volumen de ácidos grasos acumulados en el interior del adipocito[31]. En relación a su secreción en el organismo, resulta conveniente resaltar que su liberación se produce siguiendo el ritmo circadiano, mediante pulsos con un intervalo de uno a otro de aproximadamente 45

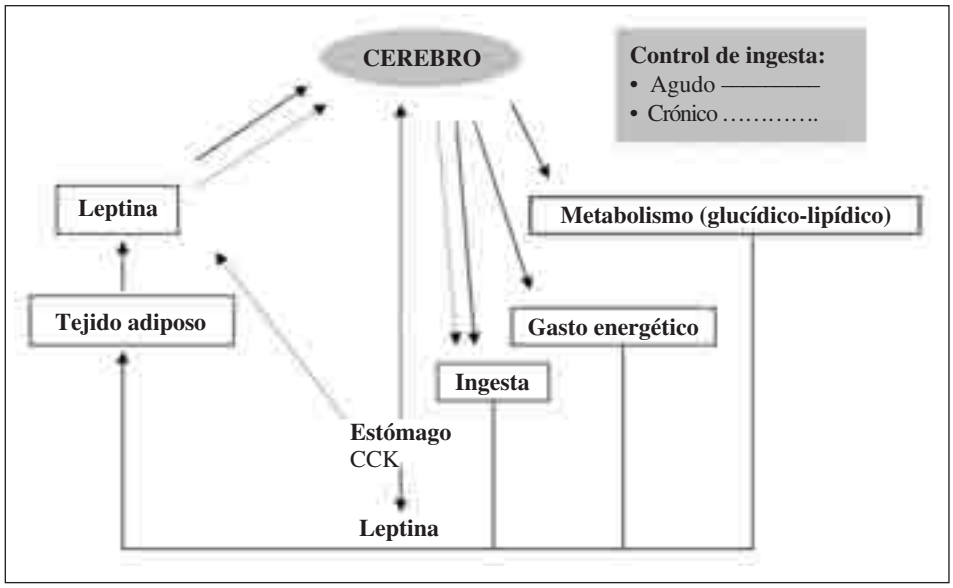


Fig. 2.—Mecanismo de control del comportamiento alimentario. Adaptado de Palou y cols., 2000[37].

minutos[32]. De este modo, la concentración de dicha hormona va aumentando a lo largo del día, para terminar alcanzando su máximo nivel a la media noche, y continuar decreciendo así de un modo gradual hasta un nuevo ciclo, que por lo general tendrá lugar con la llegada del amanecer[33].

Se ha verificado un cierto grado de diferencia sexual en la concentración de leptina en plasma sanguíneo, encontrándose niveles plasmáticos más elevados en mujeres[34]. Parecen ser los andrógenos los responsables de su menor concentración en el plasma del varón[34]. Atendiendo a su fisiología, la leptina circulante ejerce sus efectos anorexígenos mediante dos procesos de actuación. Un mecanismo de actuación periférica, para el que son requeridos de modo indispensable la existencia de receptores específicos para esta hormona, a nivel de tejidos periféricos así como también en órganos como pulmón, riñón, hígado, músculo esquelético, testículos, islotes pancreáticos, estómago, tejido adiposo (blanco y marrón) y células hematopoyéticas[35]. Para ejercer su acción a nivel central, la leptina circulante, deberá atravesar la barrera hemato-encefálica por medio de un mecanismo de transporte saturable, en donde se unirá a receptores específicos presentes en determinadas estructuras del hipotálamo tales como los núcleos arcuato, paraventricular y ventromedial[36]. En la figura 2 son representados los mecanismos de control del comportamiento alimentario (agudo y crónico), basándose para ello en la acción de la leptina en el caso del control crónico y de péptidos gastrointestinales para el control agudo.

La carencia de leptina en sujetos, bien sea por un déficit en su producción, bien por defectos en los receptores específicos de ésta, va a determinar el desarrollo de complicaciones precoces en los sujetos que la padecen tales como obesidad severa de aparición precoz, hiperfagia, diabetes, e infertilidad[38]. Así, se ha comprobado cómo aportaciones exógenas de leptina mejoran sustancialmente estos síntomas y su intensidad[38]. Sin embargo, y de un modo casi paradójico, la mayoría de sujetos con obesidad severa (excepto aquellos con una mutación en el gen *ob/ob* y el consiguiente déficit inducido de leptina), presentan unos niveles de leptina e insulina plasmáticos considerablemente elevados[39]. Esta situación, nos lleva a sospechar de un posible fenómeno de resistencia a la acción de estas hormonas, aspecto ya verificado en el caso de la insulina. Dicha resistencia a la leptina podría venir mediada por alteraciones en el proceso de transporte de la leptina a través de la célula endotelial de la barrera hemato-encefálica hacia el líquido cefalorraquídeo Disfunción de la trasducción de la señal del receptor de la leptina. Por defectos en el receptor de la leptina o bien por alteraciones en uno o varios de los sistemas neuronales que responden a la señalización de la leptina[40,41]. A pesar de desconocer aún en la actualidad múltiples de los procesos relacionados con la leptina y su implicación en la obesidad, son numerosos los aspectos que nos llevan a pensar más en una situación de resistencia orgánica a la leptina que a la carencia de ésta en aquellos sujetos con obesidad[42].

Insulina

La insulina comparte con la leptina numerosas propiedades referidas a la regulación del balance energético. En este sentido, las concentraciones en sangre de sendas hormonas, resultan ser directamente proporcionales al volumen graso corporal del sujeto[43]. La insulina circulante, al igual que la leptina, puede acceder al sistema nervioso central, mediante un proceso de transporte saturable basado en receptores presentes en las células endoteliales de capilares y vasos cerebrales. También los receptores de insulina se hallan ubicados en áreas cerebrales hipotalámicas[43]. A pesar de las semejanzas entre sendas moléculas, la liberación de insulina, a diferencia de la leptina, se hace en respuesta

al estímulo de una única comida. Se ha comprobado, cómo la administración de insulina a nivel del sistema nervioso central, provoca un considerable efecto anorexígeno y una consiguiente pérdida de peso corporal en el sujeto en cuestión. Bien es cierto que dichos efectos resultan ser dosis-dependientes[44]. Esta circunstancia se ha podido comprobar mediante la situación inversa, esto es, la disminución de los niveles de insulina a nivel cerebral (por inoculación central de anticuerpos antiinsulina), que genera un incremento de la ingesta y por consiguiente una ganancia de peso en el sujeto. Ante tales evidencias, no cabe duda sobre el papel de la insulina como agente anorexígeno. No obstante, no debemos olvidar otras funciones de esta hormona como el efecto que la insulina ejerce en el almacenamiento de los nutrientes ingeridos[45].

Señales periféricas y centrales de adiposidad con efecto orexígeno (anabólico) y anorexígeno (catabólico)

Dentro de este apartado, encontramos un amplio grupo de moléculas cuya implicación e intervención metabólica va a repercutir en la producción de un efecto anabólico respecto a la energía que el sujeto obtiene de la dieta. A nivel periférico destaca la grelina[46]. Por su parte, a nivel central, distinguimos moléculas como el neuropéptido Y (NPY), proteína relacionada con agoutí y la hormona concentradora de melanina (MCH). Además, y por su efecto orexígeno cabría añadir a este apartado ciertos aminoácidos como son el glutamato y el ácido aminobutírico[47].

Señales orexígenas periféricas

Ghrelina

El aislamiento a partir de extractos de estómago de rata de un ligando endógeno para un receptor huérfano previamente determinado cuya activación inducía una potente liberación de hormona de crecimiento (GH) se realizó con éxito en 1999 y recibió el sobrenombre de Ghrelina[48]. La grelina pertenece a la familia de los secretagogos de hormona del crecimiento (GH), cuyo grupo lo integran moléculas peptídicas y no peptídicas. Consta de 28 aminoácidos siendo su forma molecular más activa la acilada por el ácido octanoico en su tercer residuo serina[48]. Su estructura determina su capacidad para cruzar la barrera hematoencefálica permitiéndole actuar sobre receptores específicos localizados en el núcleo arcuato hipotalámico relacionados con la conducta alimentaria[49]. Su origen y producción está fuera del sistema nervioso central, concretamente a nivel de estómago, siendo la única y principal hormona de origen gastrointestinal con efecto orexígeno. Sin embargo, esta sustancia también es producida en otras localizaciones como hipotálamo, hipófisis, páncreas, riñón, intestino, linfocitos y corazón. También ha sido aislada en placenta y testículos[50]. En cuanto a su liberación, los niveles más elevados de la hormona corresponden con períodos de ayuno o estados de caquexia en los que se genera una sensación de hambre, siendo por el contrario baja su concentración en sujetos obesos y en individuos sanos tras una ingesta de nutrientes[50].

La importancia de esta molécula en la regulación de la ingesta alimentaria tiene lugar por varios mecanismos entre los que destaca su carácter competitivo con la leptina y su interacción con el nervio vago[51], desde donde puede inducir una activación neuronal en el núcleo del tracto solitario y dorsomotor causando con ello la motilidad, secreción gástrica y en definitiva una inducción al apetito y consumo de alimento[52]. Sin embargo, su principal vía de actuación y ejercicio orexígeno tiene lugar en con su interacción en el núcleo arcuato hipotalámico, lugar donde se expresan otros péptidos orexígenos como el neuropéptido Y (NPY) y la proteína relacionada con agoutí (AgRP), ejerciendo un estímulo para la síntesis de éstos[53].

Señales orexígenas centrales

Neuropéptido Y (NPY)

El neuropéptido Y (NPY), representa una molécula de gran potencial orexígeno. Es sintetizado en el hipotálamo, concretamente a nivel del núcleo arcuato. Su acción es ejercida a nivel central, en el núcleo paraventricular desde donde estimula y potencia la ingesta de alimentos y con ello la ganancia ponderal de peso. Sus niveles se elevan ante la depleción de los depósitos de grasa corporal lo cual se da en situaciones de ayuno o en cuadros de diabetes mellitus no controlada[54].

Por otra parte, la síntesis de este péptido resulta inhibida por la leptina y su efecto metabólico anorexígeno[55]. Se ha comprobado como el neuropéptido Y disminuye el estímulo ejercido por el sistema nervioso simpático al tejido adiposo pardo. Esta situación, se traduce en una disminución del gasto energético y un consiguiente aumento y desarrollo del tejido adiposo blanco[56]. Sin embargo, estudios experimentales en ratones, ponen de relieve cómo aquellos roedores que presentan un déficit del receptor específico para este péptido orexígeno, en contra de lo que por otra parte resultaría obvio, carecen de un fenotipo delgado, llegando en determinados casos a desarrollar una obesidad moderada[56]. Esta circunstancia pone de manifiesto que el neuropéptido Y (NPY) no representa el factor clave de la vía anabólica efectora por antonomasia sino más bien una más de entre otras posibles.

Proteína relacionada con agoutí (AGRP)

Se trata de una molécula de origen peptídico, cuyo descubrimiento en el cerebro humano supuso un

Tabla I

Biomoléculas reguladoras de la ingesta, peso corporal y gasto energético. Adaptado de: Solomon y cols., 2006[70]

Hormona/péptido	*Ingesta*	*Peso corporal*	*Gasto energético*	*Síntesis*
AGRP	Aumenta	Aumenta	Disminuye	Cerebro
Amilina	Disminuye	Disminuye?	Aumenta?	Páncreas
Bombesina	Disminuye	–	Aumenta	Estómago, intestino y cerebro
CART	Disminuye	Disminuye	Aumenta?	Cerebro
CCK	Disminuye	–	–	Intestino delgado
Citoquinas	Disminuye	Disminuye	–	Estómago e intestino
Corticosteroides	Aumenta	–	–	Intestino delgado
CRH	Disminuye	Disminuye	Aumenta	Cerebro
Endocanabinoides	Aumenta	–	–	Intestino delgado
Galanina	Aumenta	–	–	Intestino delgado
GALP	Disminuye	Disminuye	Aumenta	Cerebro
Gastrina	Disminuye	–	–	Estómago
Ghrelina	Aumenta	Aumenta	–	Estómago, intestino y cerebro
GIP	-?	Aumenta	Disminuye?	Intestino
GLP-1	Disminuye	Disminuye?	–	Estómago, intestino y cerebro
Glucagón	Disminuye	Disminuye	–	Páncreas
GRP	Disminuye	–	–	Estómago
Insulina*	Disminuye	Disminuye	Aumenta	Páncreas
Leptina	Disminuye	Disminuye	Aumenta	Tejido adiposo y estómago
MCH	Aumenta	–	Disminuye	Cerebro
Neurotensina	Disminuye	–	–	Cerebro y estómago
NPY	Aumenta	Aumenta	Disminuye	Cerebro
Obestatina	Disminuye	Disminuye	–	Estómago e intestino
Opioides	Aumenta	–	–	Cerebro
Orexinas	Aumenta	Aumenta	–	Cerebro
Oxintomodulina	Disminuye	–	–	Intestino y cerebro
Oxitocina	Disminuye	–	–	Cerebro
Péptido YY	Disminuye	–	–	Estómago
POMC	Disminuye	Disminuye	Aumenta	Cerebro
PP	Disminuye	–	–	Páncreas
TRH	Disminuye	–	Aumenta	Cerebro

hallazgo fortuito, en tanto que fue descubierta a partir de un estudio cuyo objetivo no era determinar dicha molécula sino más bien aislar posibles análogos de origen endógeno respecto de la proteína agoutí[57]. Su síntesis tiene lugar en el hipotálamo, específicamente a nivel del núcleo arcuato y se distribuye hacia el núcleo paraventricular entre otras regiones del sistema nervioso central[57]. Su relevancia en el campo nutricional deriva de su gran potencial como agente inductor del apetito y en consecuencia del aumento del peso corporal. Su mecanismo de acción se basa en su efecto antagonizante respecto de los receptores MC3 y MC4 de la α–MSH[58]. Su acción sobre el sistema nervioso, a diferencia de lo que ocurre con el neuropéptido Y, resulta ser más prolongada en el tiempo, pudiendo alcanzar sus efectos el transcurso de varios días[59].

Hormona concentradora de melanina (MCH)

La hormona concentradora de melanina (MCH, Melanin Concentrating Hormone), constituye otra de

las posibles vías o mecanismo de acción anabólica en lo que al balance energético corporal concierne. Esta hormona es un neuropéptido de 19 aminoácidos cuya síntesis es llevada a cabo en el hipotálamo lateral durante períodos de ayuno y en respuesta a un déficit de los niveles de leptina[60]. Asimismo, atendiendo a su efecto inhibidor del eje hipotálamo-hipófiso-tiroideo al igual que la proteína relacionada con agoutí (AgRP) y el neuropéptido Y (NPY), debemos considerar que al mismo tiempo que controla el grado de apetito también puede reducir el gasto energético del sujeto[61]. Mediante la realización de estudios con ratones, se ha podido evidenciar como la inactivación del gen que produce esta hormona va a generar cuadros de hipofagia y delgadez extrema en estos animales[62]. En la actualidad, son numerosas las iniciativas y perspectivas de terapia que contemplan esta vía como otra de las posibles piezas clave en el complejo rompecabezas que dicho cuadro representa en la actualidad.

Señales anorexígenas centrales

Hormona α-Melanocito Estimulante (α-MSH)

La hormona estimulante de los melanocitos (α-MSH), es un péptido derivado de la proteolisis de una prohormona denominada propiomelanocortina (POMC). Este proceso tiene lugar en las neuronas del núcleo arqueado activadas a su vez por la leptina. La acción anorexígena de esta hormona, se produce por su unión a los receptores MC4-R para los cuales representa su principal agonista[63]. En ratones, se ha verificado cómo la inactivación del gen que codifica para el receptor MC4-R genera cuadros de obesidad[64]. Estudios con sujetos obesos ponen de manifiesto la existencia de un gran número de pacientes con mutaciones en su receptor MC4, mutación en cierta medida responsable del incorrecto funcionamiento de esta hormona y subsiguiente disbalance energético en estos individuos[65]. De este modelo de alteración genética, surge un cuadro de obesidad generalmente temprana y que irá acompañado de hiperfagia, hiperinsulinemia e hiperglucemia[66]. Por tanto, la presencia de mutaciones en los receptores MC4-R se torna en la principal causa de obesidad monogénica en humanos[66].

Hormona liberadora de Corticotropina (CRH) y Hormona liberadora de Tirotropina (TRH)

A nivel del hipotálamo, y por las neuronas del núcleo paraventricular, son sintetizados dos neuropéptidos cuyo efecto central resulta ser la inhibición del apetito. Estas moléculas son la hormona liberadora de corticotropina (CRH) y la hormona liberadora de tirotropina (TRH)[67]. La primera, aumenta el gasto energético a expensas de la activación del sistema nervioso simpático. Además, ejerce un poder regulador del eje hipotálamo-pituitaria-tiroides[68]. La hormona liberadora de tirotropina (TRH), interviene de igual modo en la regulación de dicho eje[68]. Ambas hormonas han sido identificadas por su implicación o mediación en los efectos de la leptina dado que se ha verificado que la síntesis de dichas hormonas en el hipotálamo aumenta en respuesta a la leptina[69]. En la tabla I, se muestran representadas de forma sintética todas y cada una de las hormonas y péptidos anteriormente comentados, especificando su lugar de síntesis en el organismo humano junto con sus efectos sobre la ingesta, peso corporal y gasto energético.

Discusión

Los numerosos estudios realizados han puesto de manifiesto la complejidad fisiopatológica de la regulación de la ingesta alimentaria y balance energético. Las investigaciones realizadas, confirman que las señales endocrinas originadas en el tracto gastrointestinal son fundamentales en la regulación de la ingestión de alimentos y la homeostasis energética. Así, a excepción de la ghrelina, el resto de hormonas gastrointestinales poseen efectos inhibidores del apetito. En este sentido, el mejor conocimiento de los procesos fisiológicos por los que estas moléculas regulan la ingestión de alimentos resultará fundamental para el desarrollo de nuevas estrategias frente a trastornos alimentarios como la obesidad. No obstante, a pesar de los avances conseguidos, será necesario continuar realizando nuevos estudios para profundizar aún más en la implicación y actividad de muchas de las biomoléculas identificadas de cuyas funciones, en muchos casos tenemos un gran desconocimiento.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(5):1860-1865
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Antitumor effect of oleic acid; mechanisms of action. A review

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Abstract

Introduction: **The beneficial effects of oleic acid in cancer processes can no longer be doubted, but little is known about the mechanisms of action behind this phenomenon.**

Aim: **The aim of the present review is to clarify whether oleic acid has an effect on important mechanisms related to the carcinogenic processes.**

Methods: **We searched electronic databases and bibliographies of selected articles were inspected for further reference. We focused our research on two cellular transformations characterizing cancer development: proliferation and cell death or apoptosis.**

Results: **Numerous studies have reported an inhibition in cell proliferation induced by oleic acid in different tumor cell lines. Herein, oleic acid could suppress the over-expression of HER2 (erbB-2), a well-characterized oncogene which plays a key role in the etiology, invasive progression and metastasis in several human cancers. In addition, oleic acid could play a role in intracellular calcium signaling pathways linked to the proliferation event. Regarding cell death, oleic acid has been shown to induce apoptosis in carcinoma cells. The mechanisms behind the apoptotic event induced by oleic acid could be related to an increase in intracellular ROS production or caspase 3 activity. Several unsaturated fatty acids have been reported to induce apoptosis through a release of calcium from intracellular stores. However, evidence regarding such a role in oleic acid is lacking.**

Conclusions: **Oleic acid plays a role in the activation of different intracellular pathways involved in carcinoma cell development. Such a role could be the root of its antitumoral effects reported in clinical studies.**

(*Nutr Hosp.* 2012;27:1860-1865)

DOI:10.3305/nh.2012.27.6.6010

Key words: *Oleic acid. Apoptosis. Proliferation. Intracellular signaling.*

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Recibido: 17-VI-2012.
Aceptado: 7-VIII-2012.

EFECTO ANTITUMORAL DEL ÁCIDO OLEICO; MECANISMOS DE ACCIÓN; REVISIÓN CIENTÍFICA

Resumen

Introducción: **Los estudios epidemiológicos atribuyen un papel protector al ácido oleico frente a determinados tipos de cáncer. Sin embargo, el conocimiento relativo al mecanismo por el cual tal ácido graso ejerce sus efectos es escaso.**

Objetivo: **La presente revisión bibliográfica tiene como objetivo recopilar aquellos trabajos que centran su atención en los mecanismos intracelulares que podrían explicar los efectos clínicos atribuidos al ácido oleico.**

Métodos: **Se ha realizado una búsqueda bibliográfica a través de bases de datos electrónicas y las referencias de los artículos de interés han sido utilizadas como fuente de búsquedas más avanzadas. Nuestra revisión se ha centrado en la descripción de dos de las transformaciones celulares que caracterizan el desarrollo de cáncer: proliferación y muerte celular.**

Resultados: **Numerosos estudios atribuyen un papel inhibidor de la proliferación de células tumorales al ácido oleico. Entre los mecanismos de acción, se encuentran su capacidad para suprimir la expresión de HER2 (erbB-2), un oncogén bien conocido por su implicación en la etiología, progresión y metástasis de distintos tipos de cáncer. Además, el ácido oleico podría jugar un papel en la activación de la señalización de calcio intracelular, rutas igualmente ligadas a la proliferación celular. En cuanto a su papel en los fenómenos de muerte celular, el ácido oleico puede inducir apoptosis en células tumorales describiéndose como mecanismos implicados la producción de intracelular de especies reactivas o la activación de la actividad caspasa 3. Aunque muchos estudios relacionan la apoptosis inducida por los ácidos grasos insaturados con la liberación de calcio de los depósitos intracelulares, faltan estudios que aclaren el papel del ácido oleico a este respecto.**

Conclusión: **El ácido oleico juega un papel en la activación de diferentes rutas intracelulares implicadas en el desarrollo de células tumorales. Estos mecanismos podrían ser la base de los efectos protectores que le atribuyen los estudios clínicos.**

(*Nutr Hosp.* 2012;27:1860-1865)

DOI:10.3305/nh.2012.27.6.6010

Palabras clave: *Ácido oleico. Apoptosis. Proliferación celular. Señalización celular.*

Abbreviations

OA: Oleic acid.
PUFA: Polyunsaturated fatty acids.
MUFA: Monounsaturated fatty acids.
SOC: Store-operated channels.
SOCE: Store-operated Ca^{2+} entry.
ROS: Reactive oxygen species.
DHA: Docosahexaenoic acid.

Introduction

General evidence of the antitumor effect of oleic acid

Epidemiological studies have suggested a positive association between the total fat intake and the risk of cancer, particularly breast, colorectal and prostate cancers.[1] Carcinogenesis models have also provided evidence for a lipid specific action beyond their caloric supply, thus suggesting that the type of fat and its unique composition are of greater importance than overall fat intake.[2-7]

Whereas a high intake of n-6 polyunsaturated fatty acids (PUFA) has tumor-enhancing effects, n-3 PUFA have inhibitory effects. However, there are few experimental studies addressing the role of monounsaturated fatty acids (MUFA) of the n-9 family, such as oleic acid (OA), on cancer, if compared to the investigations about the role of other dietary lipids.

OA has attracted much attention, especially in the last few years, as the "Mediterranean diet", characterized by a high olive oil (rich in OA) consumption, has been traditionally linked to a protective effect against cancer.[8] A wide range of studies have been conducted into breast cancer, where a potential protective effect of olive oil and OA has been described.[9-11] In addition, epidemiological studies suggest that olive oil may have a protective effect on colorectal cancer development.[12-14] In this sense, some animal studies have also shown that dietary olive oil prevented the development of colon carcinomas in rats, corroborating that olive oil may have chemopreventive properties against colon carcinogenesis.[15-17]

Finally, a novel approach to chemotherapy has the potential to yield novel dietary-drug combinations that can provide additive or even synergistic protection against the progression of cancer and it is especially relevant when the etiology of disease development has varied mechanistic routes. With regard to this novel approach, OA has been reported to act synergistically with cytotoxic drugs, thus enhancing their antitumor effect.[17-19]

Thus, both epidemiological and animal studies have reported a protective role of oleic acid in several cancers. However, the mechanisms behind the antitumor effect of such a fatty acid are not well understood. The aim of the present review is to clarify where the knowledge concerning this topic is.

Materials and methods

Search strategy

We consulted studies published in electronic databases such as Pubmed or Medline. The bibliographies of selected articles were inspected for any further reference.

Firstly, we studied the title and abstract of all kind of papers (regular or review papers) with a potential interest to understand the role of oleic acid in cancer events. We mostly focused on those related to the mechanisms of action of such a fatty acid at the cellular level. Thus, the main key words used in the search were: "oleic acid", "apoptosis", "proliferation", "carcinoma cells", "intracellular signaling". Then, the text of the main trials that met the criteria previously mentioned was fully examined to extract the specific data included in the review.

Results and discussion

Cancer development is characterized by specific cellular transformations involving changes in proliferation rates, inactivation of tumor-suppressor genes and inhibition of apoptosis. Thus, we will describe the ability of oleic acid to induce apoptosis and/or inhibit cell proliferation in cancer cell lines.

Oleic acid-proliferation

It has been recently shown that OA promoted the growth of non-malignant cells but, in fact, it had the opposite effect, in malignant cells.[20] Several researchers have also demonstrated that both oleic and α-linolenic acid showed a proliferation inhibition effect on prostate carcinoma cells.[21,22] According to these results, numerous studies have also reported an inhibition in cell proliferation induced by OA in different tumor cell lines.[23,24] However, other inconsistent results have been also obtained, including non-promoting, weak-promoting, and even promoting effects on tumor growth.[25-29] Such contradictory observations may be in part the result of the different methods used in the determinations.

On the basis that OA and other fatty acids are good cellular fuels that can be degraded through β-oxidation when imported into the mitochondria, some researchers have designed a new synthetic OA analog, "minerval" with a modification that blocks the biological activity of fatty acids. Thus, enzymes involved in those processes may not recognize this modified fatty acid, so that its utilization as a source of energy would be decreased, and subsequently, its availability to modify cell signaling increased. Supporting the above-mention suggestion, they showed a markedly increase of the antiproliferative activity of minerval with respect to

Table I
Key studies evaluating the antitumor effect of OA

Reference	*Key findings*
General evidences of the protective effect of oleic acid and olive oil	
Chajes V et al.,[9] Escrich E et al.,[10] Martín-Moreno JM et al.[11]	OA has a protective effect in breast cancer
Macquart-Moulin et al.,[12] Stoneham M et al.,[13] Bautista D et al.[14]	Olive oil has a protective effect on colorrectal cancer development
Bartoli R et al.,[15] Reddy BS and Maeura Y,[16] Schwartz B et al.[17]	Olive oil prevents the development of colon carcinomas in rats
Mechanisms involved: OA-proliferation	
Zeng L et al.[20]	OA promoted the growth of non-malignant cells but has the opposite effect in malignant cells
Liu J et al.,[21] Hughes-Fulford M et al.,[22] Martíne J et al.,[23] Grao L et al.[24]	OA showed an inhibitory proliferation effect in different carcinoma cells
Hardy S et al.,[25] Soto-Guzmán A et al.,[26] Welsch CW,[27] Ip C,[28] Zusman I et al[29]	OA has a non-promoting, weak-promoting, and even promoting effect on tumor growth
Martínez J et al.[30]	Minerval inhibits the growth of cancers in both animal models and cultured cells
Menéndez JA and Lupu R,[36] Menéndez JA et al.,[37] Menéndez JA et al.,[38] Nelson R[39]	OA can suppress the over-expression of HER2 (erbB-2)
Gamberucci A et al.[51]	OA can inhibit SOCE in Ehrlich tumor cells
Carrillo C et al.[52]	OA can inhibit SOCE in a colon adenocarcinoma cell line
Mechanisms involved: OA-apoptosis	
Menéndez JA et al.[55]	OA induces apoptosis in breast cancer cells
Puertollano MA et al.[61]	ROS was substantially increased after YAC-1 tumor cell incubation with OA
Azevedo-Martins AK et al.[62]	OA reduced catalase activity in human leukaemia cell lines
Puertollano MA et al.,[61] Cury-Boaventura MF et al.[65]	OA increases caspase 3 activity in different carcinoma cell lines

OA in human adenocarcinoma cells, with no apparent toxic effects. They additionally showed that exposure to minerval inhibits the growth of cancers in both animal models and cultured cells.[30]

Several mechanisms have been proposed for the antiproliferative effect of unsaturated fatty acids. Among them, a reduction in the synthesis of eicosanoids derived from arachidonic acid could be considered to be involved in the growth inhibitory effect.[31-33] Specific changes in gene expression patterns have been also suggested.[34,35] In this sense, OA can suppress the over-expression of HER2 (erbB-2), a well-characterized oncogene which plays a key role in the etiology, invasive progression and metastasis in several human cancers.[36-39] Finally, different studies have reported that unsaturated fatty acids can modulate the activity of the components of intracellular signaling.[40-42] It is well established that Ca^{2+} is among the major intracellular factors involved in the signaling transduction pathways evoking cell growth and proliferation, and other key processes such as gene expression.[43,44] Within Ca^{2+} mechanisms contributing to the increases in intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$), particular attention has been paid to the role of Ca^{2+} entry through store-operated channels (SOC).[45] Thus, store-operated Ca^{2+} entry (SOCE) has been involved in cell signaling occurring in non-excitable cells to evoke different cell processes including gene regulation and cell growth.[46] Entry in cell cycle is preceded by SOC activation.[47] In addition, the growth factor stimulation of cell proliferation is accompanied by increased activity and/or expression of TRP channels that are related to SOCE.[48] Moreover, SOCE inhibition by different means abolishes tumor cell proliferation.[49,50] It has been recently observed that the addition of PUFA to cells cultured *in vitro*, modifies the extent of SOCE.[51] Thus, OA can inhibit SOCE in Ehrlich tumor cells, possibly because they intercalate into the plasma membrane and directly affect the activity of the channels involved.[51] In addition, it has been recently reported a SOCE-inhibitory effect induced by oleic acid in a colon adenocarcinoma cell line.[52]

Oleic acid-apoptosis

Unsaturated fatty acids have been widely reported to induce apoptosis in several cell lines.[53-55] The mechanisms behind cell death are numerous and involve a complex set of pathways.

In the apoptotic pathway, the collapse of the mitochondrial membrane potential is a common event that leads to mitochondrial dysfunction and the production of reactive oxygen species (ROS). In fact, increased ROS production has been associated with the induction of apoptotic cell death in different cells.[56] According to these findings, exposure of neonatal cardiomyocytes to hydrogen peroxide or superoxide anion ($O_2^{\cdot-}$) induces apoptosis.[57] Whether apoptosis induced by fatty acids is associated with an increased production of ROS

remains controversial and seems to depend on the type of fatty acid. Some researchers studied the role of ROS in palmitate-induced apoptosis in the neonatal rat cardiomyocyte and reported no evidence of ROS involvement.[58] By contrast, docosahexaenoic acid (DHA), a n-3 PUFA, is able to disrupt the mitochondrial membrane permeability and induce ROS production in tumor cells.[59,60] Regarding the effect of the MUFA, some researchers have reported that the production of ROS was substantially increased after YAC-1 tumor cell incubation with OA and other unsaturated fatty acids.[61]

Moreover, fatty acid may disturb the redox state of the cells not only owing to an increase in ROS generation as previously shown, but also due to a reduction in antioxidant enzyme activities. Thus, some researchers demonstrated that OA reduced catalase activity in human leukaemia cell lines.[62]

Apart from (and in line with) this increase in intracellular ROS production, unsaturated fatty acids-induced apoptosis has been reported to be mediated by an increase in caspase-3 activity in different carcinoma cell lines.[59,61,63-65]

In addition, alterations in intracellular Ca^{2+} homeostasis are commonly observed during apoptosis.[66,67] It has been demonstrated that the depletion of the endoplasmic reticulum Ca^{2+} stores can directly induce apoptosis.[68] Several reports have shown the ability of unsaturated fatty acids to induce Ca^{2+} release from the intracellular stores[59,69,70] and to induce ROS generation with a subsequent cell death.[59,71] This way, Aires et al. propose a model for the mechanism of action of DHA in which this fatty acid mobilizes Ca^{2+} from the intracellular pool and stimulates ROS production from the mitochondria, followed by downstream signaling, which will involve the activation of caspase-3, leading to chromatin fragmentation and apoptosis.[59] However, evidence regarding the role of OA in these pathways is lacking.

In summary, research has demonstrated the advantageous effects of olive oil and OA on health at both the epidemiologic and cellular level. However, as far as we are concerned, little is known about the mechanisms by which OA could affect cell proliferation and cell death of cancer cells. Thus, much research needs to be conducted especially at the cellular level, to more fully understand the pathways by which OA could reduce cancer risk.

Acknowledgements

We thank Gonzalo Moreno for his support.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(5):1866-1875
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Interactions between antihypertensive drugs and food

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Abstract

Objective: **A drug interaction is defined as any alteration, pharmacokinetics and/or pharmacodynamics, produced by different substances, other drug treatments, dietary factors and habits such as drinking and smoking. These interactions can affect the antihypertensive drugs, altering their therapeutic efficacy and causing toxic effects. The aim of this study was to conduct a review of available data about interactions between antihypertensive agents and food.**

Methods: **The purpose of this review was to report an update of main findings with respect to the interactions between food and antihypertensive drugs by way of a search conducted in PubMed, which yielded a total of 236 articles initially.**

Results: **After excluding different articles, which were not focusing on the specific objective, the main results refer to interactions between antihypertensive drugs and food (in general) as well as between antihypertensive agents and grapefruit juice.**

Discussion: **Food may affect the bioavailability of antihypertensive drugs and this should be carefully considered. Advising patients to remove the grapefruit juice from their diet when treatment with these drugs seems to be the best recommendation. Given these interactions and the associated potential adverse effects the anamnesis must include detailed information about the specific eating habits of the patients.**

(*Nutr Hosp.* 2012;27:1866-1875)

DOI:10.3305/nh.2012.27.6.6127

Key words: *Antihypertensive drugs. Food-drugs interactions. Grapefruit juice. Diet.*

INTERACCIONES ENTRE FÁRMACOS ANTIHIPERTENSIVOS Y ALIMENTOS

Resumen

Objetivo: **la interacción de medicamentos se define como cualquier alteración, farmacocinética y/o farmacodinámica, producida por diferentes sustancias, otros tratamientos, factores dietéticos y hábitos como beber y fumar. Estas interacciones pueden afectar a los fármacos antihipertensivos, alterando su eficacia terapéutica y causando efectos tóxicos. El objetivo de este estudio fue realizar una revisión de los datos disponibles acerca de las interacciones entre los fármacos antihipertensivos y los alimentos.**

Métodos: **El objetivo de esta revisión fue proporcionar una puesta al día sobre los principales resultados con respecto a las interacciones entre alimentos y fármacos antihipertensivos mediante una búsqueda realizada en PubMed, que dio lugar inicialmente a un total de 236 artículos.**

Resultados: **Tras la exclusión de diferentes artículos que no estaban centrados en el objetivo específico, los resultados principales se refieren a las interacciones entre los fármacos antiarrítmicos y alimentos en general y entre dichos fármacos y el zumo de pomelo.**

Discusión: **Los alimentos pueden afectar a la biodisponibilidad de los fármacos antihipertensivos y ello debe ser considerado cuidadosamente. Advertir a los pacientes que supriman el zumo de pomelo en su dieta cuando están en tratamiento con estos fármacos parece la mejor recomendación. Dadas estas interacciones y sus potenciales efectos adversos, la anamnesis debe incluir información detallada sobre los hábitos alimentarios de los pacientes.**

(*Nutr Hosp.* 2012;27:1866-1875)

DOI:10.3305/nh.2012.27.6.6127

Palabras clave: Fármacos antihipertensivos. Interacciones entre alimentos y medicamentos. Zumo de pomelo. Dieta.

Abbreviations

ACE: Angiotensin-converting enzyme.
ARBs: Angiotensin II receptor blockers.
AT1 receptor: Angiotensin 1 receptor.
AUC: Area under the curve (Area under the plasma concentration time curve).
BA: Bioavailability.
BP: Blood pressure.
C_{max}: Maximum plasma concentration.
cGMP: cyclic guanosine monophosphate.
CYP: Cytochrome P450 gene family.
DASH: Dietary Approach to Stop Hypertension.
DBP: Diastolic blood pressure.
HT: Hypertension.
IP3: Inositol triphosphate.

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Recibido: 21-VIII-2012.
Aceptado: 24-VIII-2012.

NaCl: Sodium chloride, common salt.
OAT: Organic anion transporter.
OCT: Organic cation transporter.
P-gp: P-glycoprotein.
SBP: Systolic blood pressure.
$t_{1/2}$: Drug elimination half-life.
t_{max}: Time after administration of a drug when the maximum plasma concentration is reached.

Introduction

Hypertension (HT), which is defined as a chronic elevation of systolic and/or diastolic blood pressure (BP), is in all probability the most common chronic disease today. The main clinical significance of HT, which is not a disease in the usual sense of the word, lies on the future risk of vascular disease. Apart from various causes of HT, the most frequent case is the essential HT (up to 95%).[1,2]

In the regulation of BP, there are different involving factors (sympathetic nervous system, kidney, hormonal systems), one of them being the composition of the diet. Thus, sodium, potassium, magnesium, lipids and total energy intake influence the control of BP.[3] In the largest international study on the relationship between sodium and BP (INTERSALT),[4] the analysis of more than 10,000 participants showed that a variation of 100 mmol sodium intake modified the systolic BP (SBP) 2.2 mmHg, being lower the effect on diastolic BP (DBP). As for diet, one of the most relevant studies (DASH: Dietary Approaches to Stop Hypertension)[5] showed that BP levels decreased with a diet low in saturated fat, cholesterol and total fat and high in fruits, vegetables and skimmed or semi-skimmed milk, that is a diet rich in magnesium, calcium, potassium, protein and fibre. In a later study (DASH-sodium),[6] it was observed that with any level of sodium, the greatest reduction in BP was achieved with the DASH diet and even better with a sodium intake of only 1,500 mg of sodium per day.

Regarding the treatment of HT, it is correct when its continued efficacy is proven and it has minimal side effects. The goal is to achieve and maintain a SBP below 140 mmHg and a DBP below 90 mmHg.[7] Apart from general measures of treatment (stress management, moderate salt restriction, regular exercise and moderate reduction of other risk factors) [8] there is a full arsenal of antihypertensive drugs: diuretics, alpha and beta-blockers, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs) and others such as sodium nitroprusside, monoxidine, hydralazine and minoxidil.

With regard to the bioavailability (BA) of antihypertensive drugs, it is noted the importance of the cytochrome P450, a family of enzymes (encoded by the gene CYP) located in the liver and gastrointestinal tract, which represents the major source of metabolic activity for the phase I reactions. Regarding the use of other drugs and food intake, it is remarkable the presence of inducers and inhibitors of the CYP system, so the association of antihypertensive drugs with other drugs and/or food which use the CYP for their metabolism may be toxic. Together with CYP, it should be noted, due to its metabolic importance, the P-glycoprotein (P-gp), a family of membrane transporters located in the brush border of the enterocytes' membranes. In addition to mobilizing endogenous substances, the P-gp mobilizes certain drugs including some antihypertensive drugs.[9-11]

Drug interactions are defined as any alteration, pharmacokinetics and/or pharmacodynamics, produced by different substances, other drug treatments, dietary factors and habits such as drinking and smoking.[12] These interactions may affect the antihypertensive drugs, modifying their therapeutic efficacy and the adverse effects.

The aim of this study was to conduct a review of available data about interactions between antihypertensive drugs and food.

Method

The review was conducted through a PubMed search. The initial search term was "Interactions between antihypertensive drugs and food," which resulted in a total of 337 articles. Later, other specific searches were performed, by entering " Interactions between loop diuretics and food", " Interactions between calcium channel blockers and food", "Interactions between ACE inhibitors and food", "Interactions between ARBs and food", "Interactions between hydralazine and food" and "Interactions between grapefruit juice and antihypertensive agents". Having excluded the repeated articles, a total of 236 articles were considered. Then those that did not make specific reference to the object of the review were rejected. Articles without an abstract were also excluded. With respect to case reports and letters, because of the scarcity of articles focusing specifically on a subject, some of them were considered. Apart from the articles included after the search, some other articles and/or chapters were considered due to its relevance.

Results

Interactions between food and diuretics

The simultaneous intake of food and some loop diuretics such as furosemide and bumetanide causes a decrease of the BA of these drugs, which in the case of furosemide seems to be very high (approximately 30%).[13] In a review, Bard et al. corroborated the existence of a decrease in the BA of loop diuretics when administered orally with food, although, only one study found a decrease in urinary excretion of these drugs after taken with food (such excretion is related to the threshold of the diuretic effectiveness) [14]. In rats with protein-calorie malnutrition, the BA of furosemide

significantly increased after oral administration, a fact attributable to a decrease in the metabolism of gastrointestinal and hepatic first step.[15] With respect to spironolactone and canrenone, its major active metabolite, food intake with simultaneous drug intake increases the BA of both drugs by increasing its absorption and possibly reducing the first pass metabolism.[16,17] This food intake also increases the BA of hydrochlorothiazide.[18] With respect to indapamide, a study has revealed that its administration in sustained release form is unaffected when taken with food.[19]

Interactions between food and alpha- and beta-blockers

Blockers of α1-adrenergic receptors causes a competitive and reversible blockage of those receptors, thus lessening or removing the actions of catecholamines mediated by way of the stimulation of those receptors. In regard to β-adrenergic blockers, these agents block competitively and reversibly the actions of catecholamines mediated by way of the stimulation of β-adrenergic receptors. Furthermore, some of these agents have vasodilator properties, which are associated with an increase in nitric oxide release or with the blocking of the α-adrenergic receptors.[20]

With respect to doxazosin, the BA of a single dose of 8 mg by means of a controlled release gastrointestinal form under fasting conditions and after ingestion, and a single standard dose of 2 mg under fasting conditions have been studied comparatively. Under fasting conditions, C_{max} was similar for both presentations, with a BA of 75% in the case of the sustained release form with respect to the standard one. In the case of the sustained release form, an administration with fat-rich food leads to a C_{max} and AUC 31% and 18% higher respectively.[21]

Regarding indoramin, there are not any published studies with respect to its use as antihypertensive and possible drug-nutrients interactions. The same applies to prazosin from a clinical point of view.

Regarding urapidil, a pioneer study showed that food intake did not influence the BA of the drug when administered in tablet form. However, after administration by a sustained release formulation, C_{max} and t_{max} increased, whereas $t_{1/2}$ decreased with food intake. Despite these differences, the AUC was not influenced by concomitant food intake in the case of sustained release form. In fasting, the AUC after administration of the sustained release form was 28% lower than after administration of the standard form, while food intake, with the sustained release capsule, eliminated such difference. Since the decreases of BP in hypertensive patients treated with urapidil are more pronounced in the inclined portion of the curve of serum concentration of the drug, maximizing that part of the curve, as is the case of administration of the sustained release capsule with breakfast, could be advantageous.[22]

In the case of prazosin, an animal experimental work has shown that its administration at the paraventricular nucleus of the hypothalamus is able to reduce the SBP only in undernourished animals.[23] However, no studies concerning potential interactions between the drug and food in humans are developed.

With respect to beta-blockers, the BA of bevantolol, metoprolol when administered as sustained release form, propranolol when administered as sustained release form and timolol is not affected by the simultaneous ingestion of food.[24-27] In the case of acebutolol and diacetolol there is a decrease of BA when administered with food but without relevant clinical effects.[28] The BA of propranolol may be increased with simultaneous food intake and specifically with a high-in-protein diet. Nevertheless no relevant clinical effects have been reported.[29] Other diets (high-in-carbohydrates diet and low-in-protein diet) do not modify the BA of propranolol.[29] In addition, the simultaneous intake of propranolol and garlic increases the BA without causing clinical effects.[30,31] With respect to metoprolol, a high-in-protein diet seems to increase the BA but without relevant clinical effects.[32]

Interactions between food and calcium-channel blockers

These antihypertensive agents are drugs that reduce the tone of vascular smooth muscle and produce peripheral and coronary vasodilation, improving the coronary flow and reducing vascular resistance. There are three groups: a) dihydropyridine derivatives (nifedipine, amlodipine, nicardipine, felodipine, nisoldipine, barnidipine and isradipine), b) derived from phenylalkylamines (verapamil) and c) derived from benzodiazepines (diltiazem).[20]

Felodipine has a delayed absorption when administered by sustained release forms along with food, which is attributed to increased drug retention in the stomach.[33]

With respect to verapamil, a more rapid absorption by using a generic drug compared with the reference drug has been found when taken with food and using sustained release forms. In addition, an absence of BA changes in verapamil has been reported by taking it with rich-in-protein foods.[34,35] The use of sustained release capsules compared with the dispersion of the content of the capsules in food has not shown significant differences on the pharmacokinetics neither of verapamil nor of norverapamil.[36]

With respect to nisoldipine, at the time of maximum plasma concentration the additional decrease in BP relative to baseline due to the food effect seems to be about 7-15% for DBP and 3-9% for DBP.[37] Considering nisoldipine coat-core, the concomitant use of other drugs, which may produce marked induction or inhibition of CYP3A4 is contraindicated. The concomitant intake of the coat-core tablet with high-fat, high-calorie foods results in an increase in the maximum plasma concentrations of nisoldipine. This "food-effect" can be avoided by administration of the coat-core tablet up to 30 minutes before the intake of food.[38]

The pharmacokinetic properties of barnidipine are unaffected by food.[9]

With regard to the salt, it is known that a high intake of common salt (NaCl) plays a fundamental role in the development and maintenance of HT.[40,41] Nevertheless, the antihypertensive effect of felodipine, a calcium channel blocker with natriuretic properties, is maintained during high salt intake, at least when given at the maximal antihypertensive dose.[42] Isradipine, another calcium channel blocker, decreases the sitting SBP and the sitting DBP during a high salt diet with a lowest effect during the salt restriction diets.[43] With respect to sodium restriction, it must be noted that calcium antagonists may have better efficacy when prescribed to salt-replete hypertensive persons.[44]

Interactions between food and angiotensin-converting enzyme (ACE) inhibitors

They are agents that act by blocking one of the steps in the formation of angiotensin II, a key effector of the renin-angiotensin-aldosterone system. ACE inhibitors are one of several groups of drugs capable of interfering with the renin-angiotensin-aldosterone system, others being inhibitors of renin and AT1 receptor blockers. ACE inhibitors inhibit competitively the angiotensin-converting enzyme.[20]

ACE inhibitors constitute a heterogeneous group of agents with pharmacologic, pharmacokinetic and therapeutic differences among them.[45] With respect to the classification, three groups are usually distinguished based on the existence of a sulfhydryl-, carboxyl- or phosphinyl-group.[46] In general, there are not any relevant food-drug interactions described for these agents.

Thus, food seems not to affect the BA of lisinopril.[47,48] With respect to captopril, the co-administration of food or antacids with this agent has been shown to diminish the BA of the latter and decrease its clearance, respectively. Nevertheless the decreased BA of captopril when taken with meals does not significantly alter clinical responses to the drug.[49,50]

Considering enalapril, its BA is not modified when taken with meals[51] and benazepril can be taken any time of day, with or without food, this not being relevant for its BA.[52]

Benazepril is rapidly converted to benazeprilat and despite foods delaying slightly the absorption of the first, the BA of the latter is not modified.[53] The absorption of quinapril is unaffected by food. Peak serum concentrations of quinapril and quinaprilat are achieved within one and two hours, respectively.[54]

Moexiprilat, the active metabolite of moexipril, has shown an extended duration of action owing to a long terminal pharmacokinetic half-life and produces a persistent ACE inhibition. Although the pharmacokinetic is partly influenced by food intake, ACE inhibition is not affected. This might be explained by a second compartment directly related to the ACE which is less prone to food effects and the reaching of a ceiling in the sigmoidal concentration-effect curve, even with the lower C_{max} concentrations associated with the postprandial state.[55]

In general the BA of ACE inhibitors may be reduced by concomitant food or antacids, which may slow gastric emptying and raise gastric pH.[56] In the case of nifedipine, a low-fat (high-carbohydrate) meal slows the rate but does not alter the extent of nifedipine absorption. Insofar as certain side effects may be related to the high peak plasma levels associated with rapid absorption, administration with meals might serve to reduce the incidence of such effects. For the majority of patients on routine maintenance therapeutic regimens, nifedipine capsules may be administered without regard to food intake.[57]

Interactions between food and angiotensin II receptor blockers (ARBs)

Angiotensin II receptor blockers (ARBs) represent a class of effective and well tolerated orally active antihypertensive agents. The ARBs specifically block the interaction of angiotensin II at the AT1 receptor, thereby relaxing smooth muscle, increasing salt and water excretion, reducing plasma volume, and decreasing cellular hypertrophy. After oral administration, the ARBs are rapidly absorbed (time for peak plasma levels = 0.5-4 h) but they have a wide range of BA (from a low of 13% for eprosartan to a high of 60-80% for irbesartan). In general, food does not influence the BA, except for valsartan (a reduction of 40-50%) and eprosartan (increase).[58] The fact that most ARBs do not interact with food makes it oral administration very straightforward for this class of agents. Several of the ARBs, irbesartan and losartan, are metabolized by cytochrome P450 (CYP), and are therefore subject to potential drug-drug interactions with other drugs that alter CYP activity.[59] Despite the absence of general relevant effects of food intake on ARBs BA, foods retard the absorption and decrease the C_{max} of losartan (5-10%) and telmisartan (10-20%). In addition, foods decrease the BA, $C_{máx}$ and AUC (3,5%) of valsartan, although plasmatic concentrations are similar to those reached without food within the next eight hours. On the contrary, high-fat foods increase $C_{máx}$ and AUC of eprosartan (80% and 55%, respectively).[60]

Irbesartan is a specific AT1 receptor antagonist with rapid oral BA (peak plasma concentrations occurring at 1.5-2 h after administration) and a long half-life (11-15 h) that provides 24-h BP control with a single daily dose. The maximal BP fall occurs between 3 and 6 h after the dose. This antihypertensive agent is relatively unaffected by food or drugs.[61,62]

Interactions between food and hydrazines

Hydralazine acts directly on arteriolar smooth muscle, where it activates the guanylyl-cyclase and increases the

levels of intracellular cyclic-guanosine 3'-5'-monophosphate (cGMP). It also inhibits the release of calcium from the sarcoplasmic reticulum induced by inositol-1,4,5-triphosphate (IP3). The result is a decrease in intravascular calcium concentration, which leads to a reduction of the peripheral vascular resistances and BP, whereas venous tone is nearly unmodified.[20]

Hydralazine has been widely used in combination with other antihypertensive agents, particularly beta-blockers and diuretics. One of the main reasons for this combination relates to the pharmacological effects of hydralazine, such as fluid retention and reflex tachycardia. The logic behind the inclusion of a diuretic is the elimination of fluid retention, while the beta-blocker would control the tachycardia.[63] In a former study about the pharmacokinetics of hydralazine, the AUC and C_{max} values were much higher under the fasted and enteral infusion conditions than under the standard breakfast or enteral bolus conditions, indicating that the absorption and/or disposition kinetics of hydralazine may be altered by food. In addition the rate of administration, but not necessarily the physical form, of the nutrients appeared to be a significant factor to determine the magnitude of the food effect.[64]

In a former study, the peak blood hydralazine levels were reduced by food after both hydralazine and slow-release hydralazine, by 69 and 66%, respectively. Time to peak blood hydralazine concentration was delayed significantly with the slow-release form and a statistically significant food-related reduction of area under blood hydralazine concentration versus time curves (AUC) only with hydralazine (by 44%) was observed. The AUC for slow-release hydralazine was decreased only 29% by food. Authors concluded that hydralazine should be taken at a consistent time with respect to meals,[65] thus confirming another previous study.[66]

With respect to endralazine, comparing a dose of 5 mg and 10 mg after a standard breakfast, in the case of 5 mg the peak endralazine concentration averaged 57.5% lower and the AUC decreased significantly by 49.9%, whereas after 10 mg the postprandial peak level and the AUC were 82.9% and 64.7%, lower. In the 5 mg study the mean arterial BP was decreased by 30 mmHg in the fasting subjects and by 21 mmHg in the postprandial group. For the 10 mg dose the corresponding values were 35 and 24 mmHg. The BP lowering effect was only weakly correlated with the food-related reduction in the plasma endralazine levels. The results suggested that endralazine has a similar kinetic interaction with food as that found for hydralazine.[67]

Interactions between antihypertensive agents and grapefruit juice

In 1998, Bailey et al., indicated that grapefruit juice acted by inhibiting the drug pre-systemic metabolism mediated by CYP, particularly the isoform CYP3A4 in the bowel. In addition, they reported that people with higher levels of CYP3A4 with liver failure and with clinical situations that predispose to increase the effects and toxicity of drugs would be more likely to suffer from the interaction of grapefruit juice with administered drugs.[68] Grapefruit juice acts on intestinal CYP3A4, which metabolizes more than 60% of commonly prescribed drugs, drug transporter proteins (such as P-gp) and transporter proteins of organic cations (OCT), all in the intestine. The hepatic CYP3A4 appears to not be inhibited and, on the other hand, the above-mentioned P-gp would be inhibited.[69] It must be noted that the intake of grapefruit juice with drugs effectively inhibits P-gp, but the habitual intake of grapefruit juice could increase the expression of P-gp.[70] On the other hand, flavonoids (some of them like naringin and quercetin are present in grapefruit juice) may interfere with the P-gp not only at the binding site but also inhibiting OCT and organic anion transporter (OAT), transport systems of the basal membrane of intestinal epithelium.[71,72] Grapefruit juice has different bioactive components such as flavonoids (flavanones, flavones, flavonols, anthocyanins), limonoid aglycones, glycosides, furanocoumarins (bergamottin, dihydroxybergamottin), ascorbic acid, folic acid, glucaric or saccharic acid, carotenoids, pectin and potassium. Traditionally, drug interactions have been attributed to furanocoumarins.[69,73,74] Inactivation of CYP3A4 seems to be irreversible, it occurs when taking 200-300 ml, and the effect of increasing the BA of the drugs, that may occur even after 24 hours of the intake, are particularly relevant.[75]

After having described an increase in the levels of the dihydropyridine calcium channel antagonists felodipine and nifedipine when taken with grapefruit juice,[76] different drugs in this antihypertensive group have been seen to interact with grapefruit juice. Thus, amlodipine, azelnidipine, benidipine, cilnidipine, efonidipine, felodipine, manidipine, nicardipine, nifedipine, nimodipine, nisoldipine, nitrendipine and pranidipine. The result of the interaction is an enhancement of plasma concentration of these drugs.[77-88] With respect to barnidipine, minor increases in its availability may occur with concomitant use of alcohol or grapefruit juice, but these are unlikely to have clinical relevance.[39] Paine et al. have reported in an experimental design that furanocoumarins are the active ingredients of grapefruit juice responsible for enhancing the systemic exposure of felodipine and probably other CYP3A4 substrates that undergo extensive intestinal first-pass metabolism.[89] It has been suggested that felodipine-grapefruit juice interaction should be taken into account among elderly people[90] and that taking grapefruit juice should be separated by at least 2-3 days of the drug intake.[91] In addition, the existence of interindividual variability in the effect of that interaction has been noted[92] and also the fact that among calcium channel blockers felodipine is the one with the clearest interaction.[93] Finally, with respect to felodipine, one of the most recent studies concludes that previous research may have overestimated the effect of that interaction.[94]

In other cases, the interaction between grapefruit juice and some drugs causes a reduction of C_{max}, AUC and $t_{1/2}$. This is the case of aliskiren, a renin inhibitor.[95]

Amlodipine seems to not be affected by the concomitant intake of grapefruit juice.[96]

With respect to diltiazem, a single intake of grapefruit juice (250 ml) has been found to cause a slight but statistically significant increase in the systemic exposure of diltiazem. The inhibition of intestinal metabolism and/or P-gp efflux transport might be responsible for this effect.[97]

Considering verapamil, grapefruit juice significantly increases the AUC and the C_{max}. The increase in concentrations present for (R)- and (S)-enantiomers seems to be slightly greater for verapamil than for norverapamil.[98] In the study of Ho et al., it is demonstrated an interaction between verapamil and grapefruit juice, which is likely due to an inhibition of intestinal metabolism resulting in increased oral BA.[99] Nevertheless, certain controversy remains with respect to verapamil-grapefruit juice interaction due to the previous study of Zaidenstein et al., in which a single administration of grapefruit juice with short-acting verapamil had no significant effect on the pharmacokinetics of verapamil.[100]

With regard to angiotensin II receptor blockers, it must be noted that the AUC of losartan increased insignificantly when taken with grapefruit juice and the time to drug appearance in serum was prolonged. Grapefruit juice also caused a change in the pharmacokinetic properties of the pharmacologically active metabolite of losartan. The half-life of the metabolite as well as the mean retention time were significantly longer; however, the AUC was decreased. Losartan is thought to be primarily metabolized by CYP2C9, but the results of the study of Zaidenstein et al., show that grapefruit juice's effect on CYP3A4 in the gut is able to alter the pharmacokinetics of losartan.[101]

Among beta-blockers, talinolol absorption is modified by an inhibitory action of naringin on the P-gp and the OAT system.[102] The most potent inhibitor of talinolol among the components of grapefruit juice is 6'7'-epoxy-bergamottin, followed by 6'7'-dihydroxy-bergamottin and bergamottin. In regard to other components, naringenine causes a more potent inhibition than naringin.[103] After the intake of a glass of grapefruit juice a reduced BA of talinolol has been found as occurs with the repeated intake. The parameters affected are AUC, maximum plasmatic concentration and urinary excretion values.[104] However, the inhibitory action on the P-gp would result in an increased BA.[105] With respect to acebutolol and its major metabolite, diacetolol, the intake of grapefruit juice slightly decreases plasma concentrations by interfering with intestinal absorption, without significant clinical manifestations.[106] The reduced celiprolol concentrations when taken with grapefruit juice are probably caused by physicochemical factors that interfere with celiprolol absorption, although other mechanisms cannot be excluded. It must be noted that the grapefruit juice-celiprolol interaction is probably of clinical relevance.[107]

Other interactions

With respect to orange juice, hesperidin, one of its flavonoids, would be responsible for a lower intestinal absorption of celiprolol[108] and a moderate interference between the orange juice and the absorption of atenolol has also been reported.[109] Differently, the BA of celiprolol diminishes when taken along with orange juice by possible mechanisms related to pH variations and changes in the function of the transporters in the intestine.[110] The bitter Seville orange juice has an interaction with felodipine similar to grapefruit juice (inactivation of intestinal CYP3A4), but without any action at P-gp level.[111] In a comparative study with grapefruit juice, lime juice and red wine, it was concluded that interaction with felodipine is not caused by an inhibitory action on CYP3A4 bergamottin.[112] Bitter orange hesperidin increases the BA of verapamil by interference at the intestinal outflow level.[113]

Peppermint oil, menthol, menthyl acetate, and ascorbyl palmitate have found to be moderately potent reversible inhibitors of in vitro CYP3A4 activity. As well as grapefruit juice, peppermint oil may increase the oral BA of felodipine by inhibition of CYP3A4-mediated presystemic drug metabolism. In the case of ascorbyl palmitate, it did not inhibit CYP3A4 activity in vivo.[114]

With respect to ramipril, it has been found experimentally that in combination with felodipine and with a low salt diet (or potassium or magnesium alternative salts) a greater beneficial cardiovascular effect is achieved.[115]

Regarding nicardipine, an interaction with the use of ginkgo *(Ginkgo biloba)* by induction of CYP3A2 isoform has been experimentally proven[116] and the consumption of honey from the genus *Rhododendron*, with a toxin called grayanotoxin, has resulted in a reported case of complete atrioventricular block alongside taking verapamil.[117] In regard to vitamins, the administration of ascorbic acid seems to affect the absorption and first pass metabolism of propranolol, producing a decrease in C_{max}, and the time to reach it, as well as a decrease of AUC, although with no clinical significance.[118]

Conclusions

The response to antihypertensive agents may vary among patients as well as in each individual patient, with potentially serious consequences, this being influenced by some interactions, either drug-drug or drug-food. Taking various and very different drugs (antihypertensive and others) is common and food shall be accompanied by the taking thereof. Sometimes that

coincidence is required (for example, adherence could be improved) but occasionally may cause potentially dangerous interactions.[72]

The BA and effectiveness of the antihypertensive drugs is determined mainly by the metabolism of these agents, specifically by the enzymatic system known as cytochrome P450 (CYP). The CYP system has different isoforms, CYP3A4 contributing to the inactivation and removal of 50-60% of drugs.[119,120-122] This isoform is localized in the epithelial cells of the small intestine (70%) as well as in the liver (30%), so that the passage of the drugs will result in the corresponding enzymatic action or first pass oxidative metabolism.[123] An amount of unaltered drug will undergo into the systemic circulation, in relation to the dose administered orally, which will depend on how much this enzymatic action is avoided. In any situation where the usual BA is increased by a greater passage of drug into the systemic circulation, the chance of side effects and toxicity will be increased, especially for those drugs with a narrow therapeutic window. In other cases, it is not an increased blood flow which modifies the BA, but an action on the CYP3A4 by means of an irreversible and inhibitory interaction at the intestinal level. Inhibition of CYP3A4 by certain foods will interfere with the correct metabolism of the drug in question with a resulting increase in AUC. On the other hand, some changes in BA will depend on the food action inhibiting P-gp transporter that returns a certain amount of the drug into the intestinal lumen. The inhibition of this binding protein will cause an increase in the amount of drug absorbed. Finally, the action on the transport systems OAT and OCT have been involved in some interactions. If the P-gp returns part of the drugs into the intestinal lumen, the above-mentioned transport systems act contrary. Thus a food that selectively inhibits, for example, P-gp and OAT would cause the effect of increasing BA of a drug and, secondly, its decrease.[119]

In view of the results some conclusions such as the following should be taken into account:

- The simultaneous intake of food and diuretics such as furosemide may cause a decrease of the BA of the diuretic. In the case of spironolactone and hydrochlorothiazide the BA may be increased.
- The C_{max} and AUC of doxazosin may be increased when taken with fat-rich foods.
- The administration of sustained release forms of urapidil with breakfast seems to be advantageous to achieve a better decrease of BP.
- Despite increasing the BA of propranolol when taken with a high-in-protein diet, that has not relevant clinical effects. The same applies to the use of garlic.
- Felodipine has a delayed absorption when administered by sustained release forms along with food due to more prolonged drug retention in the stomach.
- The increase of plasma concentration of nisoldipine coat-core when taken with high-fat, high-calorie foods can be avoided by administration of the drug up to 30 minutes before the intake of food.
- In general the BA of ACE inhibitors may be reduced by concomitant food or antacids, which may slow gastric emptying and raise gastric pH.
- Despite de absence of general relevant effects of food intake on the BA of ARBs, pharmacokinetics of losartan, telmisartan, valsartan and eprosartan may be changed when taken with food.
- Different studies have reported that pharmacokinetic parameters of hydralazine may be altered with food intake, so hydralazine should be taken at a consistent time with respect to meals. Similar interactions have been reported in the case of endralazine.
- The concomitant use of grapefruit juice enhances the plasma concentration of the following agents: azelnidipine, benidipine, cilnidipine, efonidipine, felodipine, manidipine, nicardipine, nifedipine, nisoldipine, nimodipine, nitrendipine, and pranidipine. Amlodipine seems to not be affected by the simultaneous use of grapefruit juice.
- With respect to felodipine (one of the calcium channel blockers with the clearest interaction with grapefruit juice), taking grapefruit juice should be separated by at least 2-3 days of the drug intake. It must be noted that the bitter Sevilla orange juice has an interaction with felodipine similar to grapefruit juice.
- In the case of verapamil and the intake of grapefruit juice, certain controversy remains because despite increasing the AUC and the C_{max}, the study of Zaidenstein et al., had not reported significant effects on BA of verapamil when taken with grapefruit juice.
- With regard to talinolol, acebutolol and celiprolol, the simultaneous intake of grapefruit juice may reduce the BA but without relevant clinical effects.

Food may affect the BA of the antihypertensive agents and in some specific cases this should be carefully considered. Grapefruit juice is the food with the highest potentiality for interactions and toxicity associated with the intake of some antihypertensive agents as well as antiarrhythmic drugs.[124] Therefore, the best recommendation seems to advise patients to remove the grapefruit juice from their diet when cardiovascular treatments. With regard to grapefruit juice consumption in Spain, over 50% of consumers associate it with doing diets, especially women, and 16.4% use it frequently, especially between 56 and 65 years old. Half of those who take grapefruit do so at breakfast, usually without other foods, and almost 21% take it at mid-morning.[125] Given the effect of grapefruit juice, even 24 hours after ingestion, changes in the BA of antihypertensive agents affected by the interaction and the consequent possible toxic effects should be taken into account by studying in detail the eating habits of patients with HT before the prescription of these drugs. Particular care should be taken into account in the elderly, so a proper separation of antihypertensive drugs and grapefruit juice should be considered. Other juices, like orange juice, should be taken into account when prescribing antihypertensive drugs.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1876-1885
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Cuestionario de calidad de vida relacionado con el estado nutricional (CaVEN)

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Resumen

Objetivo: **Construir y validar un instrumento para medir la calidad de vida percibida en relación con el estado nutricional.**

Material y método: **Mediante grupos focales y entrevistas con expertos en nutrición se identificaron las dimensiones con mayor afectación. Tras la prueba de jueces se definió el cuestionario CaVEN. Para su validación se realizó un estudio multicéntrico, participando 7 hospitales españoles. La validez factorial del cuestionario se evaluó mediante análisis factorial exploratorio, solución en componentes principales y rotación varimax; la validez de criterio mediante correlaciones con los Gold standard nutricionales. La fiabilidad se estimó mediante el coeficiente α de Cronbach.**

Resultados: **Se construyó un cuestionario de 26 ítems con 6 dimensiones de salud. Se aplicó a 68 pacientes que fueron valorados en las Unidades de Nutrición. El valor del test KMO fue de 0,756, mostrando que se adecua al modelo de Análisis Factorial. Se comprobó la existencia de direcciones principales de inercia (Bartlett p < 0,01). Las 6 dimensiones presentaron una varianza acumulada del 77,670. Se observó una relación directa entre la Valoración Global Subjetiva y CaVEN (p < 0,01) y entre Mini Nutritional Assessment Short (p = 0,02) lo que se interpretó como a mayor afectación del estado nutricional, peor calidad de vida detectada por el CaVEN.**

Conclusiones: **El cuestionario CaVEN se ha revelado como un instrumento útil para evaluar la calidad de vida relacionada con el estado nutricional, incluso en colectivos con poca afectación del estado nutricional.**

(*Nutr Hosp.* 2012;27:1876-1885)

DOI:10.3305/nh.2012.27.6.6025

Palabras clave: *Calidad de vida. Estado nutricional. Cuestionarios. CaVEN.*

QUALITY OF LIFE QUESTIONNAIRE RELATED TO NUTRITIONAL STATUS

Abstract

Objective: **To build and validate an instrument to measure the perceived quality of life in the nutritional status.**

Material and methods: **By focal groups and interviews with nutrition experts, the dimensions with greater affectation were identified. After the judge test, the CaVEN questionnaire was defined. For its valuation a multicentric study was performed, participating 7 Spanish hospitals. The internal structure of the questionnaire was evaluated by explanatory factorial analysis. Reliability was tested using the Cronbach α coefficient and the validity of the criteria with the nutritional Gold Standards.**

Results: **A questionnaire of 26 items with 6 health dimensions was built. It was applied to 68 patients that were valued in the Nutrition Units. The test KMO was 0.756, showing a good accuracy in the Factorial Analysis. The existence of principal dimension of inertia was found (Bartlett p < 0.01). The 6 dimensions showed an accumulative variance of 77.670. It was observed a direct relationship in the Subjective Global Valuation and CaVEN (p < 0.01) and with the "Mini Nutritional Assessment Short" (p = 0.02), which was interpreted as the greater affectation of the nutritional status, the lower the quality of life detected by the CaVEN.**

Conclusions: **The CaVEN questionnaire has proved a useful tool for assessing the quality of life related to nutritional status, even in groups with little nutritional alterations.**

(*Nutr Hosp.* 2012;27:1876-1885)

DOI:10.3305/nh.2012.27.6.6025

Key words: *Quality of life. Nutritional status. Questionnaires. CaVEN.*

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Recibido: 26-VI-2012.
Aceptado: 15-VII-2012.

Introducción

La calidad de vida relacionada con la salud (CVRS) es un término que frecuentemente vemos referido como sinónimo de calidad de vida, estado de salud, bienestar etc., lo que contribuye a crear confusión entre los diferentes profesionales que toman parte en cuestiones relativas a ella. Es un concepto amplio que incluye no solo el estado de salud, sino también la economía, la educación, el medio ambiente, la legislación, el sistema de salud y las expectativas del propio sujeto. Reúne tres conceptos (salud, estado de salud y calidad de vida) agrupando los factores que forman parte del individuo, así como los que siendo externos interaccionan con él, pudiendo modificar su estado de salud[1]. La descripción de salud más aceptada y difundida, es la de la Organización Mundial de Salud, en la que se define salud como un estado completo de bienestar físico, mental y social, y no solamente la ausencia de enfermedad[2].

La CVRS se refiere a la forma en que la enfermedad como productora de dolor, disfunción física y malestar, provoca limitaciones o alteraciones en las conductas cotidianas, las actividades sociales, bienestar psicológico y en otros aspectos de la vida diaria de los individuos[3-4]. Es un constructo multidimensional, no observable directamente, que solo puede ser deducido de manera indirecta a través de indicadores o perfiles, generados en la mayoría de los casos a partir de cuestionarios.

Los avances tecnológicos y el aumento de la longevidad han producido un cambio en el escenario de la atención sanitaria, enfermedades rápidamente mortales se han convertido en enfermedades crónicas. También han aumentado las situaciones en las que la intervención sanitaria está dirigida a paliar los síntomas y a prevenir complicaciones para recuperar y/o mantener la calidad de vida.

El efecto sobre la CVRS de las intervenciones sanitarias es frecuente en las publicaciones científicas, sobre todo cuando tienen que ver con la valoración de los resultados de cualquier intervención terapéutica que no es por sí misma curativa. La afirmación de que una determinada intervención médica aumenta la calidad de vida del paciente está presente de forma amplia en la bibliografía científica, no obstante, en pocas ocasiones viene refrendada por una medición de la calidad de vida[5].

Los primeros cuestionarios que intentan valorar la calidad de vida relacionada con la salud, percibida por los individuos, de una manera estandarizada y multidimensional aparecen en la década de los sesenta, siendo los más destacados: el Sickness Impact Profile[6] y el Nottingham Health Profile[7], cuestionarios que por su extensión, complicaban su aplicación clínica rutinaria. Posteriormente se van reduciendo, lo que facilita su aplicación en la práctica clínica, es el caso del Dartmouth COOP Charts[8-10] y otros. Finalmente en la década de los noventa se empiezan a desarrollar instrumentos más específicos que intentan cuantificar el efecto sobre la calidad de vida de un grupo poblacional definido con determinadas patologías[11,12].

Las alteraciones del estado nutricional tienen efectos que condicionan de manera importante la calidad de vida del individuo, impidiendo o cuando menos dificultando su desarrollo físico, fisiológico, psicológico y social. Sin embargo, no es fácil encontrar en las publicaciones científicas ninguna aproximación a la medida del impacto que pueden tener estas alteraciones nutricionales sobre la calidad de vida, a no ser las realizadas a partir de cuestionarios generales o genéricos.

El uso de los cuestionarios genéricos para valorar el efecto de los tratamientos y los soportes nutricionales sobre la calidad de vida, tiene el inconveniente de estar midiendo otra cosa muy diferente a lo que se está intentando medir[13].

La carencia de instrumentos específicos junto a la necesidad de conocer el impacto de un problema concreto, como es el estado nutricional, obligan a la utilización de varios instrumentos concomitantemente, lo que conduce a una falta de operatividad y a una visión probablemente contaminada por otras variables modificadoras de efecto, presentes en el contexto patológico del paciente, que los cuestionarios genéricos recogen de forma predominante[14].

Conscientes de la dificultad que entraña el desarrollo de un instrumento de medida, el primer paso de este estudio fue considerar la existencia de cualquier instrumento que pudiera satisfacer la propuesta de medir la calidad de vida en los pacientes desnutridos y que proporcionara información de cómo su estado de nutrición la estaba afectando. Se comenzó por una revisión sistemática de los instrumentos utilizados que pudieran ser aplicables para el objetivo propuesto "medir el impacto del estado nutricional en la calidad de vida" para decidir si era apropiada la utilización de una o varias de estas escalas, concluyendo que sería más indicado el desarrollo de un nuevo instrumento[15]. Se tomó, por tanto, la decisión de diseñar un instrumento que respondiera a las necesidades del objetivo, pretendiendo construir un instrumento que midiera hipotéticamente el impacto de la desnutrición sobre la calidad de vida de los pacientes, independientemente de la patología de base. Disponer de este instrumento de medida, permitirá tener un indicador que, junto a otros parámetros clásicos, informe del momento adecuado para iniciar una intervención nutricional o para retirarla. También, reconocerá el verdadero efecto sobre la calidad de vida de aquellas intervenciones nutricionales indicadas y mantenidas con el propósito de mejorar o preservar la calidad de vida del paciente, informando si realmente están sirviendo a su objetivo.

En consecuencia, el objetivo de este trabajo ha sido construir y validar un instrumento para medir la calidad de vida percibida en relación con el estado nutricional.

Material y método

El proyecto se diseñó y desarrolló en tres fases:

Fase I: estudio cualitativo, mediante entrevistas semiestructuradas a profesionales de la nutrición clínica y grupos focales formados por pacientes con diferentes grados de desnutrición por diferentes causas. En esta fase se identificaron los ítems y definieron las dimensiones relacionadas con el estado nutricional. El número de expertos y de grupos focales entrevistados no se estableció a priori, concluyéndose al comprobar que el discurso se había saturado, es decir cuando los nuevos individuos entrevistados o los nuevos grupos focales realizados no aportaron datos nuevos ni discordantes con los obtenidos hasta el momento.

Fase II: diseño del cuestionario, basándose en los hallazgos de la primera fase, se incluyeron los ítems de las dimensiones que habían sido identificadas en el resultado del análisis cualitativo de las entrevistas y los grupos focales. La primera versión del cuestionario se sometió a la prueba de jueces, con el propósito de evaluar la estructura del cuestionario; evaluando una serie de aspectos del mismo; la validez de constructo, la validez de contenido y la claridad e inteligibilidad de los ítems formulados.

Se analizó si las preguntas formuladas en cada uno de los "bloques" o dimensiones, eran representativas del constructo, es decir, si estos aspectos así definidos y estructurados eran representativos y adecuados para poder evaluar correctamente la posible afectación de la calidad de vida a causa del estado nutricional del sujeto. Para ello se formularon a los jueces dos preguntas que debían calificar del 0 al 10 como mejor puntuación:

a) ¿Hasta qué punto cree que el cuestionario mide lo que realmente dice medir?
b) ¿En qué grado cree que los ítems recogen la posible afectación de la calidad de vida por un estado de desnutrición?
c) De la misma forma se evaluó la validez de contenido, para comprobar en qué medida los ítems propuestos eran representativos de las dimensiones establecidas en el cuestionario. Para ello los jueces calificaron la pregunta:
   a) ¿En qué medida cada uno de los ítems mide la afectación que dice medir?

También se evaluó la claridad e inteligibilidad en la formulación de los ítems, teniendo en cuenta que éstos van dirigidos a sujetos de diferentes niveles culturales.

En los tres casos, el criterio para reformular una pregunta fue encontrar en el análisis una media inferior a 6 y/o un cociente de variación superior al 25%.

Una vez concluida esta fase, con el cuestionario resultante, se procedió a la realización de una prueba piloto, aplicándola a 10 pacientes de diferentes edades, sexo, nivel cultural y origen con el fin de obtener un cuestionario de fácil interpretación, para lo que se aplicaron los criterios de Streiner & Norman[16].

Fase III: Se diseñó un estudio prospectivo multicéntrico con la participación de 7 hospitales, en el que se incluyeron pacientes mayores de 18 años, atendidos en consulta de forma secuencial y que presentasen cualquier grado de desnutrición a los que se les informó obteniendo su consentimiento. En esta fase se ha estudiado:

- Validez de criterio, mediante correlaciones entre las dimensiones exploradas y el resultado de los parámetros nutricionales conocidos como Gold Standard, definidos como el índice de masa corporal, nivel de albúmina, Valoración Global Subjetiva[17] (VGS) y el Mini Nutritional Assessment[18] (MNA).
- Validez de constructo, mediante análisis factorial exploratorio. Para la obtención de los factores se empleó el método de Análisis de Componentes Principales (ACP) con rotación Varimax, para evaluar la adecuación del análisis se utilizó la medida de Kaiser-Meyer-Olkin (KMO) y la prueba de esfericidad de Bartlett[19].
  La fiabilidad de los instrumentos de medida se estimó mediante el coeficiente α de Cronbach, teniendo en cuenta que cuanto más se aproxime a su valor máximo, 1, mayor será la consistencia interna del cuestionario.
- Validez concurrente-discriminante con otros cuestionarios, diseñados para valorar la calidad de vida relacionada con la salud, para ello se efectuaron correlaciones de Pearson entre los resultados en los componentes estandarizados físico y mental del SF-3620, y una Escala Analógico Visual (EVA) que evalúa subjetivamente 0 como peor CV imaginable y 100 como mejor CV imaginable.

Las variables recogidas en el estudio fueron: edad, sexo, grupo diagnóstico, Índice de Masa Corporal (IMC), pérdida de peso en el último mes, niveles de albúmina en sangre (mg/dl), valores de transferrina en sangre (mg/dl). Valoración de la calidad de vida mediante una EVA para disponer de un punto subjetivo de referencia que permita conocer cómo perciben los pacientes la afectación de su calidad de vida por su estado nutricional. Estado funcional, evaluado mediante el cuestionario de Barthel[21] que puntúa la capacidad funcional entre 0 = totalmente dependiente y 100 = totalmente independiente. Índice de comorbilidad de Charlson[22,23] que considera ausencia de comorbilidad entre 0 y 1 puntos, comorbilidad baja cuando el índice es 2 y comorbilidad alta cuando es igual o superior a 3 puntos. Evaluación del estado nutricional mediante el cuestionario Mini Nutritional Assessment (MNA) que contine 6 primeras preguntas conocidas como "MNA short o evaluación de cribaje" que tiene un punto de corte en ≤ 11 como posible desnutrición y obliga a con-

Tabla I
Grupos diagnósticos de la muestra estudiada

Diagnóstico	*Frecuencia*	*Porcentaje*
Enfermedades oncológicas	46	52,9%
Enfermedad inflamatoria intestinal	10	14,7%
Enfermedades neurológicas	5	7,3%
Intestino corto	5	7,3%
Síndromes congénitos	4	5,8%
Otras enfermedades	4	5,8%
Obstrucción del tracto gastrointestinal	2	2,9%

tinuar con el total del cuestionario que clasifica < 17 desnutrición; entre 17 a 23,5 riesgo de desnutrición; > 23,5 ausencia de riesgo. La Valoración Subjetiva Global (VSG) que clasifica a la población en A = normonutridos; B = desnutrición leve-moderada; C = desnutrición severa.

Resultados

Se entrevistaron a 14 expertos en nutrición y se realizaron 6 grupos focales hasta conseguir saturar el discurso.

En la evaluación de las diferentes versiones del cuestionario participaron 17 jueces (relacionados en agradecimientos), expertos en nutrición clínica, validación de cuestionarios y otras áreas de conocimiento. Después de eliminar y/o reformular los ítems ambiguos, incomprensibles, redundantes o inconsistentes desde el punto de vista teórico, resultó un cuestionario CaVEN de 26 ítems referidos a 6 dimensiones de salud: Percepción de Salud General (8 ítems), Actividad Física (4 ítems), Actividad Laboral (2 ítems), Estado de Ánimo (6 ítems), Relaciones Sociales y Familiares (3 ítems), Dolor y/o Malestar (3 ítems).

CaVEN se diseñó como cuestionario auto administrado y se redactó para que los sujetos pudieran expresar directamente sus sensaciones y percepciones sobre su CV, referidas al último mes, de acuerdo a una escala tipo Likert de 1-6 (tabla I). Todas las preguntas se expresan en escala politómica con seis categorías de respuesta: "Nada, Algo, Poco, Bastante, Mucho, Muchísimo" (fig. 1). La puntuación de los ítems considera como ausencia de afectación de la calidad de vida el valor 1, significando que el sujeto no se identifica con la afirmación propuesta, mientras que un valor de 2 al 3 estima que el sujeto percibe el impacto sobre su calidad de vida con moderada intensidad y a partir de 3 la afectación es percibida de forma intensa, tomando valor 6 la afirmación con la que el sujeto se siente totalmente identificado, significando una grave afectación de su calidad de vida. Para obtener la puntuación de cada dimensión deben sumarse las puntuaciones de sus respectivos ítems y la puntuación global del cuestionario se obtiene con la suma de las puntuaciones todas las dimensiones, presentando una puntuación que va desde 26 (la mejor percepción de la calidad de vida) hasta 156 (la peor percepción de la calidad de vida).

El ítem A1, primer ítem del cuestionario, no presenta la misma uniformidad y las categorías de respuesta van desde "excelente" correspondiendo a un grado de afectación "nada" a "muchísimo" correspondiendo a "muy malo" y conservando la misma dirección en la puntuación.

Descripción de las dimensiones del cuestionario CaVEN

Percepción de Salud General: esta subescala valora el impacto del estado nutricional en la calidad de vida percibida por el enfermo. Sus puntuaciones oscilan entre 8 y 48. En este caso, a mayor puntuación peor percepción de la calidad de vida en relación a su estado nutricional.

Actividad Física: esta subescala valora la incidencia del estado nutricional en la actividad física. Las puntuaciones oscilan entre 4 y 24. A mayor puntuación peor percepción de su calidad de vida.

Actividad Laboral: esta subescala valora la incidencia del estado nutricional en sus actividades laborales o profesionales. Las puntuaciones oscilan entre 2 y 12.

Estado de Ánimo/Estado Emocional: la subescala evalúa la relación entre el estado nutricional y el estado de ánimo del paciente. Las puntuaciones oscilan entre 6 y 36. A mayor puntuación peor es el estado de ánimo.

Relaciones Sociales y Familiares: esta subescala evalúa la incidencia del estado nutricional en las relaciones sociales y familiares. Las puntuaciones oscilan entre 3 y 18. A mayor puntuación mayor es el impacto del estado nutricional en las relaciones familiares.

Dolor y/o Malestar: esta subescala está dirigida a evaluar la influencia del estado nutricional en la percepción del dolor o malestar. Las puntuaciones oscilan

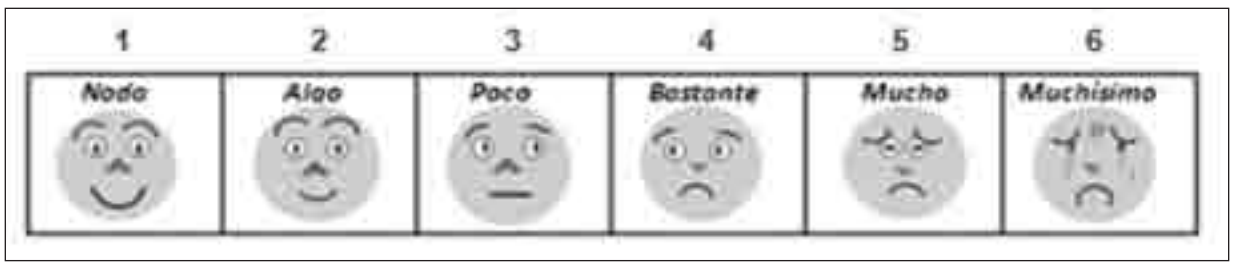


Fig. 1.—Puntuaciones de los ítems del CaVEN.

Tabla II
Distribución de las características nutricionales, funcionales y de calidad de vida de la muestra estudiada

	Percentiles		
	25	*50*	*75*
Índice de masa corporal	18,25	20	23,17
Pérdida de peso	0	0	0
Albúmina	3,57	4,10	4,25
Transferrina	204,50	244	266,50
Linfocitos	750	1.400	1.900
Colesterol total	138	160	180
MNA Short	8,50	11	11,50
MNA	17,50	22	24,25
Í. Barthel	100	100	100
Í. Charlson	0	1	2
EVA CV	50	65	75
CaVEN	45	69	81

entre 3 y 18. Por tanto, altas puntuaciones se corresponden con alto impacto del estado nutricional en la calidad de vida.

Características de la muestra

Se aplicó el cuestionario a una muestra de 68 sujetos atendidos en unidades de 7 hospitales españoles: la Fe de Valencia, General Universitario de Alicante, La Vall d'Hebrón de Barcelona, General Universitario de Albacete, San Pedro de Logroño, Virgen de las Nieves de Granada y Clínico Universitario de Santiago de Compostela.

El 100% de los pacientes respondieron a todas las preguntas del CaVEN.

La muestra estudiada presentó una edad media de 55,3 ± 16,10 años, sin diferencias entre sexos, siendo el 63,2% varones. Los diagnósticos de base se muestran en la tabla I.

El índice de masa corporal (IMC) presentó una media de 21,75 kg/m^2 ± 4,19 con un mínimo de 13,20 y máximo de 31,51. La media de pérdida reciente de peso registrada en el último mes fue de 1,43% de su peso habitual ± 2,92% con un mínimo de 0% y un máximo de 11%. La distribución percentual de las características nutricionales de la muestra se muestran en la tabla II.

Tabla III
Matriz factorial del CaVEN, tras rotación Varimax, para la muestra completa de pacientes

Factorial exploratorio	*Factor 1*	*Factor 2*	*Factor 3*	*Factor 4*	*Factor 5*	*Factor 6*
Percepción de Salud General						
A1	0,655					
A2	0,792					
A3	0,801					
A4	0,685					
A5	0,725					
A6	0,620					
A7	0,619					
A8	0,655					
Actividad Física						
B1			0,556			
B2			0,869			
B3			0,854			
B4			0,609			
Actividad Laboral						
C1						0,919
C2						0,925
Estado Emocional						
D1		0,755				
D2		0,822				
D3		0,852				
D4		0,681				
D5		0,756				
D6		0,466				
Relaciones Sociales/Familiares						
E1					0,708	
E2					0,681	
E3					0,799	
Dolor/Malestar						
F1				0,831		
F2				0,795		
F3				0,524		

Estructura Factorial del CaVEN

El valor del test KMO del CaVEN fue de 0,756, lo que indica que los datos se adecuan al modelo de Análisis Factorial. La prueba de esfericidad de Bartlett señala que la hipótesis nula de variables iniciales no correlacionadas se rechaza ($p < 0,01$).

En el análisis se han retenido 6 factores porque son el número de dimensiones teóricas de las que consta el instrumento de medida y son las que se quieren corroborar. Las seis primeras dimensiones recogen el 78% de la información. Tras la aplicación del Análisis Factorial con rotación Varimax (tabla III), y para facilitar la interpretación de las variables latentes subyacentes, se tomaron solo los factores con carga > 0,450. Se observó que el primer eje se caracterizó por saturaciones altas de los ítems de la subescala "Percepción de Salud General". El segundo eje tomó valores altos en los ítems relacionados con la subescala "Estado Emocional". El tercer eje mostró saturaciones altas de los ítems de la escala "Actividad Física". El factor cuatro tuvo saturaciones altas de los ítems correspondientes a la subescala «Dolor y/o Malestar». El Factor cinco presentó saturaciones altas de los ítems de la subescala «Relaciones Sociales y/o Familiares» y el eje seis saturaciones altas de la subescala «Actividad Laboral». Por tanto, el Análisis Factorial, con la rotación Varimax, permitió corroborar las dimensiones latentes hipotetizadas.

La fiabilidad total del CaVEN alcanza un valor de 0,939. Los valores obtenidos para la estimación de la consistencia interna mediante el coeficiente α de Cronbach, son: 0,925 en Percepción General de Salud; 0,855 en Actividad Física; 0,889 en Actividad Laboral;

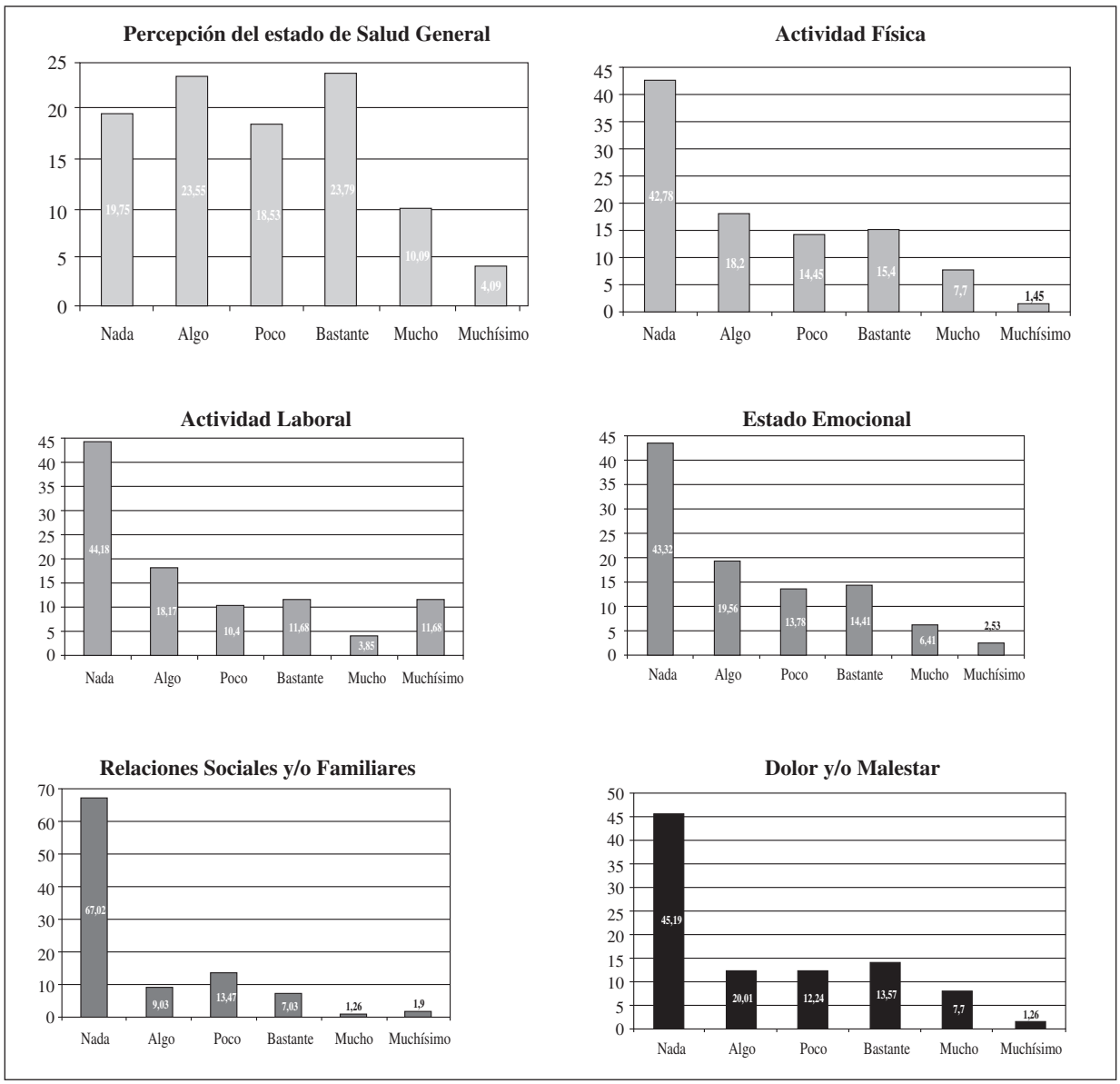


Fig. 2.—Distribución porcentual de las opciones de respuesta de las 6 dimensiones de CaVEN.

0,920 en Estado Emocional; 0,706 en Relaciones Sociales y Familiares y 0,863 en Dolor y/o Malestar.

Evaluación del impacto del estado nutricional en la calidad de vida

La valoración de la calidad de vida con la Escala Analógico Visual (EVA) puso de manifiesto que el 56,6% de los pacientes declararon tener una calidad de vida ≥ 50, el 7,5% evaluaron su calidad de vida por debajo de 25, mientras que el 24,5% afirmaba tener por encima de 75.

El 41,9% de los pacientes consideraron, evaluándolo mediante EVA que su estado nutricional es un factor importante, y que afecta a su calidad de vida con un peso ≥ 50.

La Distribución de la respuestas del CaVEN analizadas en cada una de las dimensiones se muestra en la figura 2.

En Percepción de Salud General se observó que un 23,7% de los sujetos escogieron la opción "Bastante", seguida por "Algo" con un 23,54%. Un 32,7% de los encuestados afirmó que su estado de nutrición hace que se encuentre cansado y un 48,1% percibió, de manera general, su estado de salud como bueno mientras que un 28,8% creía que su estado de nutrición influye "Bastante" en su estado de salud.

La escala Actividad Física varió en relación a la anterior. Las opciones "Nada" y "Algo" aunaron la parte más importante de las respuestas (60,98%), mientras que la última categoría tan sólo recogió un 1,45%. Un 67,3% de los encuestados indicó que su estado de nutrición no le impide "Nada" realizar las cosas básicas de la vida (ir al aseo, ducharse, vestirse, preparase el alimento, etc.). Un 21,2% afirmó que dependía "Bastante" de los demás para sus tareas cotidianas debido a su estado de nutrición y tan sólo un 5,8% afirmó que le costaba "Muchísimo" moverse como antes por culpa de su estado nutricional.

Las respuestas en la subescala de Actividad Laboral se concentran en las dos primeras categorías con un 62,35% de las respuestas. Un 34,6% afirma que no se siente "Nada" perjudicado en su trabajo o profesión por su estado de nutrición frente a un 9,6% que afirma que su estado de nutrición afecta Muchísimo su trabajo.

En la escala Estado Emocional la opción de respuesta más frecuente ha sido "Nada" con un 43,32% quedando la última categoría "Muchísimo" con un 2,53%. Como aspecto más destacable señalar que un 53,8% constata que su estado de nutrición en "Nada" ha hecho perder el interés por las cosas. Un 19,2% siente "Bastante" ansiedad por causa de su estado nutricional.

Las Relaciones Sociales y Familiares se ven escasamente afectadas por el estado nutricional. Así un 67,02% ha respondido que su estado nutricional no afecta "Nada" a sus relaciones sociales o familiares frente a un 1,90% que afirma que afecta "Muchísimo".

Tabla IV
Relación entre los índices de Barthel y de Charlson con el cuestionario CaVEN

		CaVEN
Índice de Barthel	Correlación de Pearson	0,022
	Sig. (bilateral)	0,876
Índice de Charlson	Correlación de Pearson	-0,316*
	Sig. (bilateral)	0,024

*La correlación es significativa al nivel 0,05 (bilateral).

A la pregunta de si su estado de nutrición hace que se siente diferente alos demás, un 84,6% ha afirmado que "Nada", frente a un 1,9% que sostiene que "Bastante".

En la dimensión Dolor y/o Malestar un 45,19% de las respuestas se concentran en la primera categoría "Nada", pese a este alto porcentaje un 15,7% de los pacientes afirmó que su estado nutricional hace que se sienta "bastante mal", incluso después de una comida ligera.

En relación al índice de comorbilidad de Charlson, el 3,8% de los pacientes presentó un índice de 4, el 35,8% tuvo un índice de 2 y el 35,8% de 0. La capacidad funcional, valorada mediante el cuestionario de Barthel, fue en la mayoría de los pacientes buena con una media de 99,66 puntos ± 10,50 (mínimo 37 y máximo 100). La relación entre la capacidad funcional y el CaVEN no mostró significación (tabla IV).

La evaluación del estado nutricional mediante la VGS clasificó a la muestra en 46,2% "normonutridos"; 30,8% como "desnutridos leves o moderados" y 23,1% como "desnutridos severos". Entre la VGS y el CaVEN se encontró una relación directa y significativa (tabla V), lo que se interpreta como a mayor afectación del estado nutricional peor calidad de vida percibida (mayor puntuación en el CaVEN). El MNA Short mostró que el 60,5% presentaban una posible desnutrición, siendo necesario continuar con la valoración completa del MNA, observándose una relación directa y significativa con el CaVEN (tabla V).

En la muestra, la percepción de la CV detectada por el CaVEN presentó un mínimo de 29 y un máximo de 121, la mediana fue de 69; la distribución percentual se muestra en la tabla II, no observándose diferencias

Tabla V
Relación entre la valoración nutricional y el cuestionario CaVEN

		CaVEN
VSG	Correlación de Pearson	0,356*
	Sig. (bilateral)	0,010
MNA Short	Correlación de Pearson	-0,344*
	Sig. (bilateral)	0,024
MNA	Correlación de Pearson	-0,323*
	Sig. (bilateral)	0,048

*La correlación es significativa al nivel 0,05 (bilateral).

Tabla VI
Porcentaje de la muestra que se sitúa en los percentiles para la población española de 55-64 años del SF 36

			Percentiles			
			< 25	*25-50*	*50-75*	*> 75*
SF 36	C. Físico	Mujeres	81,8%	9,1%	4,5%	4,5%
		Varones	86,7%	6,7%	3,3%	3,3%
	C. Mental	Mujeres	59,1%	31,8%	4,5%	4,5%
		Varones	76,7%	13,3%	3,3%	6,7%

estadísticamente significativas en función de la edad ni del sexo (p = 0,236 y p = 0,351 respectivamente). Con la EVA, el mínimo fue de 20 y el máximo de 100, la mediana de 65 y sin diferencias en función de la edad (p = 0,409) y el sexo (p = 0,07). Se observó una relación inversa y significativa entre el CaVEN y la EVA (Pearson -0,525; p < 0,001). El Componente Físico del SF-36 obtuvo un mínimo de 16,97 y un máximo de 58,29 con una mediana de 38,12 y sin encontrar diferencias en función de la edad (Pearson 0,094; p = 0,509) y el sexo (t de Student-0,509; p = 0,613). El Componente Mental del SF-36 detectó un mínimo de 18,59 y un máximo de 66,37, la mediana fue de 48,96 sin apreciarse diferencias por edad (Pearson 0,059; p = 0,675) y sexo (t de Student -0,489 p = 0,627) la distribución de la muestra en los percentiles de referencia de la población española[24] se muestra en la tabla VI. Los componentes físico y mental estandarizados del SF36 se relacionaron inversa y significativamente con el CaVEN (Pearson -0,665; p = 0,001 y Pearson -0,458; p = 0,001 respectivamente).

Discusión

El presente estudio ha permitido corroborar estadísticamente las 6 dimensiones de la calidad de vida subyacentes en el cuestionario CaVEN, las cuales se corresponden con las hipotetizadas por los expertos, tras el correspondiente análisis cualitativo.

Los valores obtenidos del coeficiente alfa de Cronbach han sido excelentes para la globalidad del CaVEN, y para cada una de las dimensiones fluctuaron entre muy buenos y excelentes, lo que indica una muy elevada consistencia interna[25].

CaVEN ha mostrado reunir las características psicométricas adecuadas para cumplir el cometido propuesto, medir la calidad de vida percibida por los pacientes con diferentes estados de desnutrición. Se puede usar para identificar no solo el nivel de afectación que provocan los diferentes grados de desnutrición sobre la calidad de vida, sino también para evaluar el impacto sobre la calidad de vida de las diferentes intervenciones dirigidas a modificar el estado de nutrición[26].

La validez factorial del instrumento se ha inspeccionado con un Análisis Factorial Exploratorio. La solución en Componentes Principales con rotación Varimax dio excelentes resultados ya que capturó completamente la estructura teórica subyacente. Este análisis es el más frecuentemente utilizado en la literatura por lo cual consideramos que facilitará los estudios comparativos posteriores.

Aunque, algunos autores[27] recomiendan un análisis factorial confirmatorio para corroborar la estructura subyacente, entendemos que, dada la claridad de la estructura factorial encontrada en este estudio, el uso del análisis factorial confirmatorio no está justificado pues solo corroboraría lo ya encontrado y añade, sin embargo, una complejidad en los análisis estadísticos no justificada.

CaVEN se ha mostrado como un instrumento de fácil interpretación ya que ningún paciente ha dejado de responder a ninguna de las preguntas presentes en el cuestionario, rápido de responder y de gran facilidad en el cálculo de las puntuaciones. Observándose mayor tasa de respuesta que en estudios de validación de otros cuestionarios[20]. Cabe resaltar que gran parte de la muestra eran jubilados, por lo que la dimensión "actividad laboral" del cuestionario probablemente se viera más afectada en otro tipo de población.

Es de destacar que el nivel de desnutrición de la muestra no ha sido elevado. Esto podría explicar el hecho de que con un instrumento genérico como el SF36 se hayan detectado niveles de calidad de vida bajos, debido probablemente al peso de algunas patologías, como la oncológica, predominante en la muestra y que altera de forma importante la percepción de salud general. Los valores de calidad de vida detectados con el CaVEN, cuestionario específico y por lo tanto centrado en la valoración de los aspectos del área del estado nutricional, también han resultado afectados.

A partir de ahora será necesario desarrollar estudios que apliquen el CaVEN en amplias muestras de pacientes y que permitan determinar el peso relativo de cada uno de los factores presentes en los mismos y que pueden estar afectando las dimensiones de calidad de vida recogida por el cuestionario, como el diagnóstico, el estado evolutivo del mismo o la presencia de otros síntomas[28].

Es indudable que éste es el primer trabajo con el CAVEN y que posteriores estudios irán definiendo más sus cualidades y sus posibles limitaciones. Se debe tener en cuenta que las puntuaciones obtenidas han de

seguir siendo estudiadas para mejorar la interpretación clínica de las mismas, la interpretación del significado y la proporcionalidad clínica.

Es importante destacar que no se dispone de estudios en población normonutrida y que serían deseables para situar los puntos de referencia de la población española[24].

El cuestionario CaVEN se encontrará a disposición de todos los interesados en su uso en www.caven.es

A modo de conclusión se puede decir que el estado nutricional y funcional de la muestra estudiada, a pesar de no estar muy afectado, permite que el cuestionario CaVEN muestre su capacidad de medir la afectación de la calidad de vida de los sujetos. De haber contado con una muestra nutricionalmente más alterada, probablemente el CaVEN hubiera arrojado resultados aún más significativos.

El CaVEN comparado con los otros cuestionarios utilizados como referentes o *Gold Standard* se ha comportado como un instrumento válido y fiable para medir la Calidad de Vida relacionada con el Estado Nutricional.

Agradecimientos y conflicto de interés

Los autores declaran que no existe ningún tipo de conflicto de interés.

Expresamos nuestro agradecimiento a los expertos que han participado como jueces en la validación del cuestionario: Jordi Alonso (IMIM Institut de Recerca Hospital del Mar), Andreu Nolasco (Universidad de Alicante), Rosa Ballester (Universidad Miguel Hernández, Alicante), Ángel Gil (Universidad de Granada), Miguel León (Hospital 12 Octubre, Madrid), Josep Bernabeu (Universidad de Alicante), Emilio Martínez de Victoria (Universidad de Granada), Pedro Pablo García Luna (Hospital Virgen Macarena, Sevilla), Alfonso Mesejo (Hospital General Universitario, Valencia), M.ª Dolores Ruiz (Universidad de Granada), Gabriel Oliveira Fuster (Hospital Carlos Haya, Málaga), José Antonio Irles (Hospital Ntra. Sra. de Valme, Sevilla), Lucia Laborda (Hospital de Cruces, Bilbao), Luis Miguel Luengo (Hospital Infanta Cristina, Badajoz), Alejandro Sanz Paris (Hospital Miguel Servet, Zaragoza), Antonio Pérez de la Cruz (Hospital Virgen de las Nieves, Granada).

Queremos agradecer la participación en las entrevistas de los expertos en nutrición: Pilar Gómez Enterría (Hospital Central de Asturias, Oviedo), Javier Ordóñez (Hospital Marqués de Valdecilla, Santander), Irene Bretón (Hospital Gregorio Marañón), Alejandro Sanz Paris (Hospital Miguel Servet, Zaragoza), Ana Ayucar (Hospital Juan Canalejo, La Coruña), Gabriel Oliveira Fuster (Hospital Carlos Haya, Málaga), Francisca Pereyra (Hospital Ntra. Sra. de la Candelaria, Tenerife), Emma Camarero (Hospital Clínico de Santiago de Compostela), Angela Martín Palmero (Hospital San Pedro y San Pablo de Logroño), Merce Planas (Hospital la Vall D'Hebrón, Barcelona). Cristina Velasco (Hospital Gregorio Marañón), María Dolores Carbonell (Hospital La Fe de Valencia), Pilar Riobó (Hospital Fundación Jimenez Díaz, Madrid), Antonio Perez de la Cruz (Hospital Virgen de las Nieves, Granada).

Nuestro agradecimiento a todos los pacientes que han participado en los grupos focales y a los que han prestado su consentimiento para su inclusión en el estudio.

Nuestro más sincero agradecimiento al apoyo y financiamiento recibido por la empresa Nutricia para hacer posible el desarrollo de este trabajo.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1886-1893
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Association between dietary antioxidant quality score (DAQs) and bone mineral density in Spanish women

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Abstract

Background: **Several lines of evidence suggest a tight association between oxidative stress and the pathogenesis of osteoporosis in humans. The intake of antioxidants may influence Bone Mineral Density by acting as free radical scavengers, preventing oxidation-induced damage to bone cells.**

Objective: **The aim of this study was to assess the association between the Dietary Antioxidant Quality Score and bone mineral density in a sample of healthy women.**

Methods: **A total of 280 women were grouped into three major groups: women aged ≤ 35 years; women aged 36-45, and finally women aged >45 years. Calcaneous Bone Mineral Density (g/cm²) was measured by dual energy X-ray absorptiometry. Data on the eating habits of each participant were collected with a structured 24-hour diet recall questionnaire. A Dietary Antioxidant Quality Score was used to calculate antioxidant-nutrient intake.**

Results: **A significant and positive association was observed among Bone Mineral Density and dietary intake of vitamin C and selenium. Zinc intake was significantly related to Bone Mineral Density in the youngest group. Low antioxidant consumers were considered individuals whose Dietary Antioxidant Quality Score was lower or equal than the median (3.5), and high antioxidant consumers were those whose Dietary Antioxidant Quality Score were higher than 3.5. Bone Mineral Density was higher in the participants defined as high antioxidant consumers in all aged groups.**

Conclusion: **The study showed that there is an association between Bone Mineral Density and the Dietary Antioxidant Quality Score in all the women studied. Therefore, new therapies for osteoporosis based on higher dietary antioxidant intakes might be developed basing on the results obtained in this study.**

(*Nutr Hosp.* 2012;27:1886-1893)

DOI:10.3305/nh.2012.27.6.6039

Key words: *Antioxidants. Nutrition. Bone mineral density.*

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Recibido: 4-VI-2012.
1.ª Revisión: 2-VII-2012.
Aceptado: 13-VII-2012.

ASOCIACIÓN ENTRE EL ÍNDICE DE CALIDAD ANTIOXIDANTE DE LA DIETA Y LA DENSIDAD MINERAL ÓSEA EN MUJERES ESPAÑOLAS

Resumen

Antecedentes: **Varias líneas de evidencia sugieren que existe una estrecha relación entre el estrés oxidativo y la patogénesis de la osteoporosis en humanos. La ingesta de nutrientes antioxidantes puede influenciar la densidad mineral ósea al neutralizar los radicales libres, previniendo el daño oxidativo a las células de hueso.**

Objetivo: **El objetivo del presente estudio es establecer la asociación entre un Índice de Calidad Antioxidante de la Dieta y la densidad mineral ósea en una muestra de mujeres sanas.**

Métodos: **Un total de 280 mujeres participaron en el estudio. Las participantes fueron agrupadas por edad en tres categorías: edad ≤ 35 años; edad entre 36 y 45 años y con edad superior a 45 años. Las medidas de la densidad mineral ósea (g/cm²) del calcáneo fueron realizadas por absorciometría dual de rayos X. Los datos sobre los hábitos alimentarios de cada participante fueron recogidos mediante recordatorios de 24 horas. El Índice de Calidad Antioxidante de la Dieta se utilizó para calcular la ingesta total de nutrientes antioxidantes.**

Resultados: **La ingesta de vitamina C y selenio está asociada significativamente a la densidad mineral ósea. En el grupo de mujeres de edad inferior, la ingesta de zinc está relacionada con la masa ósea. Los individuos cuyo Índice de Calidad Antioxidante de la Dieta es inferior o igual a la mediana (3,5) son considerados de bajo consumo antioxidante, y aquellos individuos cuyo Índice de Calidad Antioxidante de la Dieta es superior a 3,5 se consideran de alto consumo antioxidante. En todos los grupos estudiados, la densidad mineral ósea fue significativamente superior en los sujetos cuya dieta tiene un alto consumo de nutrientes antioxidantes.**

Conclusión: **El trabajo muestra que existe una asociación entre la densidad mineral ósea y el Índice de Calidad Antioxidante de la Dieta en todos los grupos de mujeres estudiadas. Por lo tanto, basándose en los resultados de este estudio, se pueden desarrollar nuevas terapias para la osteoporosis basadas en una ingesta elevada de nutrientes antioxidantes.**

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DOI:10.3305/nh.2012.27.6.6039

Palabras clave: *Antioxidantes. Nutrición. Densidad mineral ósea.*

Abbreviations

BMD: Bone mineral density.
DAQS: Dietary antioxidant score.
DEXA: Dual energy X-ray absorptiometry.
RDI: Recommended intake.
SD: Standard deviation.
BMI: Body mass index.

Introduction

Osteoporosis is a major growing public health problem worldwide.[1] The mechanisms involved in osteoporosis pathogenesis are not fully understood. Bone is a specialized connective tissue that functions as the load-bearing structure of the body. Free radicals may affect bone remodelling by regulating osteoclast activity in either the physiological or pathological condition.[2] Oxidative stress is a pivotal pathogenic factor for age-related bone loss in mice and rat, leading to an increase in osteoblast and osteocyte apoptosis, among other changes, and a decreased in osteoblast numbers and in the rate of bone formation via Wnt/β-catenin signalling.[3]

Several lines of evidence suggest a tight association between oxidative stress and the pathogenesis of osteoporosis in humans. It has been shown that osteoporotic women have lower serum antioxidants levels as compared with controls.[4] In addition, it has been demonstrated that postmenopausal women with osteoporosis had significantly lower serum antioxidant enzyme activity than non-osteoporotic healthy controls.[5]

The intake of antioxidants may influence Bone Mineral Density (BMD) by acting as free radical scavengers, preventing oxidation-induced damage to bone cells.[6] To date, studies on the relation between antioxidants and BMD have received little attention. It has been established that an inadequate dietary intake of antioxidants increases considerably the risk of hip fracture in current smokers, whereas current smokers with a more adequate intake of antioxidants seem to have a fracture risk similar to that observed among never smokers, thus supporting the theory that oxidative stress has important effects on human bone.[7] In addition, epidemiological studies have reported that there is an inverse association between antioxidant vitamins and carotenoid intake, and low BMD, the risk of fracture, and/or osteoporosis.[4,8,9]

To date, the most consistently followed approach to examine the potential relation between antioxidant dietary intake and skeletal health was based on particular nutrients.[10] However, people do not eat isolated nutrients but meals consisting of a variety of foods with complex combinations of antioxidant nutrients.[11] The traditional analysis considering the effect of a few isolated nutrients on bone health misses a lot of information regarding complex or cumulative correlations and interactions between these antioxidants contained in food. For this reason, there is an increasing interest in the study of diet quality indexes that could answer some questions and promote the development of appropriate recommendations for overall dietary habits.

It is necessary to conduct studies that clarify the effect of antioxidant intake on bone health, in order to establish the role of antioxidant-rich diet in the prevention of osteoporosis. The aim of this study was to assess the association between the Dietary Antioxidant Quality Score (DAQS) and bone mineral density in a sample of healthy women.

Materials and methods

Participants

In this survey, The original study participants (n = 328) were recruited from participants of an ongoing University of Granada project that is assessing the effect of aquatic activities on bone mineral density, in a sample of sedentary women.The study design was approved by the ethics committee of the University of Granada, and an individual written informed consent from the sample participants was obtained. We excluded individuals with known metabolic bone disease, osteoporosis defined as nontraumatic vertebral fractures, current estrogen or dietary supplement use, ever treatment with glucocorticoids for more than 6 months, current or past malignancy and chronic disease if newly diagnosed or out of control. In addition, we excluded participants with incomplete questionnaires, with missing bone mineral density measurements or those that did not meet the criteria of the study. Since age and menopausal status are some of the most important predictors of bone mass, the final participants (n = 280) were grouped into three major groups: women aged ≤ 35 years (n = 89), women aged 36-45 (n = 93), and women aged > 45 years (n = 98). These subgroups represented 31.79%, 33.21%, and 35% of the sample respectively. Women aged ≤ 35 years and 36-45 years were considered as women of reproductive age (premenopausal), and women aged > 45 were postmenopausal women that had ceased menstruating for at least 12 months.

Anthropometry

Body weight was measured to the nearest 0.1 kg by using a precision scale with the participants wearing light clothing and without shoes.[12] Height was measured without shoes and recorded to the nearest millimetre on a portable stand meter. The BMI was calculated as body weight (kg) divided by height squared (m^2). Waist circumference was measured at the midpoint between the lower rib margin and the iliac crest and hip circumference at the level of the trocanter.

Each value represented the mean of three consecutive measurements performed by the same nutritionist to minimize interobserver variation.

Measurement of Bone Mineral Density

Calcaneous BMD (g/cm^2) were measured by Dual Energy X-ray Absorptiometry (DEXA, LUNAR-DPX-L, Lunar Co., Madison, WI). The equipment was calibrated every day. The variation coefficient was 0.32%. The equipment provided automatic T-scores for the measurements, which were derived from the difference between the measured value and the best mean value of young adults of the same gender expressed as a deviation from the normal value. T-scores were generated using peak gender-matched reference data from females. In addition, Z-score was automatically calculated by the equipment, and it is derived from the number of standard deviations below an average person of the same age. Measurements were performed by the same assistant.

Questionnaires

Data on the eating habits of each participant were collected by trained nutritionists with face-to-face interviews based on a structured 24-hour diet recall questionnaire, previously validated with a food frequency questionnaire.[13] The 24-hour recall was carried out three times during the study period, to avoid the influence of seasonal variations. Conversion of food into energy and nutrients was performed using the computer program DIETSOURCE version 1.2.

The number of hours devoted to aquatic activities —two to five hours/week— and the frequency and duration of participation in occupational and leisure-time physical activities were recorded on the questionnaire. Time spent on each of the above activities was multiplied by the metabolic equivalent (MET) value of the activity,[14,15] and all MET-hour products were summed to produce an estimate of daily physical activity. In addition, the socio-demographic data of each participant, as well as their occupation, medical record and smoking habits were recorded.

Measurement of Diet Adequacy

A dietary antioxidant quality score (DAQS) was used to calculate antioxidant-nutrient intake.[16] The score refers to the intake of certain vitamins and minerals that have been proven to act as dietary antioxidants: selenium, zinc, vitamin A, vitamin C and vitamin E. Daily nutrient intake was compared to that of the daily recommended intake for Spanish people[17] (RDI). The intake of each of the five antioxidant nutrients evaluated was assessed separately by assigning a value of 0 or 1 to each nutrient. When the intake was below 2/3 of the RDI, it was assigned a value of 0. Similarly, when the intake was higher than 2/3 of the RDI, it was assigned a value of 1. Thus, the total dietary antioxidant quality score ranged from 0 (very poor quality) to 5 (high quality).

Statistical Analysis

SPSS version 15.0 was used for the statistical analyses. Continuous variables are presented as mean ± standard deviation (SD) and categorical variables are presented as absolute frequencies. Distribution of variables was tested with the Kolmogorov-Smirnov test, showing most of the examined variables were normally distributed. ANOVA tests were used to compare anthropometric and sociological variables and food intake among the three groups of women. A enter multiple regression analysis was used to assess the association between BMD, antioxidants intake and DAQs score after adjustment for other factors, known to affect BMD such as age, body weight and height, calcium intake, cigarette consuming and aquatic physical activity. Standardized β-coefficients, R, R^2, adjusted R^2, t and p values are reported. The specific effect of nutrients significantly associated to bone mineral density was explored by partial correlations. Covariate-adjusted means of the BMD among low and high antioxidants consumers was conducted by analysis of covariance (ANCOVA). The same covariates to the multiple regression analysis were used in ANCOVA. Low antioxidant consumers were considered individuals whose DAQS was lower or equal than the median (3.5), and high antioxidant consumers were those whose DAQS were higher than 3.5.

Results

Descriptive characteristics of the participants per age groups are as shown in table I. Besides age and menopausal status, the groups significantly differed in mean weight, BMI, waist/hip ratio, and educational level. Nutrient intakes expressed as the percentage of recommended dietary intake are presented in table II. The average caloric intakes were lower than the recommended dietary guidelines in the studied population. The percentage of energy from protein and lipids exceeded the dietary goals, and energy from carbohydrates was lower than the desirable levels, as compared with the Nutritional Objectives for the Spanish Population. The intake of nutrients known to be important for bone health (Ca, vitamin D) was lower than the recommended in all age groups.

Table III summarizes the intake of antioxidant nutrients and the percentage of population which intakes are below 2/3 of the RDI. In general terms, we can observe that the average intakes of vitamin E was lower than the

Table I
Anthropometric and sociological characteristics of the study population

	Mean (SD)	*Minimum*	*Macimum*	*p**
Weight (kg)				
18-35 y.	62.4 (8.45)	51.0	91.0	
36-45 y.	66.9 (9.61)	52.1	96.0	0.005
> 45 y.	71.4 (11.9)	53.1	98.0	
Height (cm)				
18-35 y.	161.2 (5.30)	149.0	173.0	
36-45 y.	159.1 (6.64)	147.0	175.5	0.007
> 45 y.	156.1 (6.33)	146.0	170.0	
BMI (kg/m²)				
18-35 y.	23.9 (3.20)	19.32	33.83	
36-45 y.	26.5 (4.11)	21.13	37.97	0.001
> 45 y.	29.31 (4.53)	21.73	42.86	
Waist/hip ratio				
18-35 y.	0.75 (0.06)	0.64	0.89	
36-45 y.	0.80 (0.09)	0.66	1.07	0.001
> 45 y.	0.84 (0.08)	0.71	1.13	
Cigarretes/day				
18-35 y.	1.65 (3.88)	0.0	15.0	
36-45 y.	3.73 (7.68)	0.0	25.0	0.232
> 45 y.	1.50 (4.28)	0.0	20.0	
Physical activity (MET-hour/day)				
18-35 y.	40.05 (2.50)	32.20	45.60	
36-45 y.	39.20 (1.40)	30.10	41.50	0.040
> 45 y.	38.60 (1.30)	30.60	40.50	
	Primary school	*Secundary school*	*University degree*	*P*
Educational level frequency (%)				
18-35 y.	5.63	25.84	68.53	
36-45 y.	29.03	34.41	36.56	0.037
> 45 y.	41.84	34.69	23.47	

y: years; BMI: Body mass index.
*Anova test.

recommended, whereas the intake of the rest of antioxidant nutrients reached the dietary goals. In addition, inadequate antioxidant nutrient intakes (defined as intakes below 2/3 of the RDI) were more prevalent for vitamin E.

The association between BMD and antioxidant nutrients was examined using multiple regression analysis models adjusted by age, body weight and height, calcium intake, smoking habits and aquatic physical activity (table IV). A significant and positive association was observed among BMD and dietary intake of vitamin C and selenium in all age groups. Zinc intake was significantly related to BMD in the youngest group. In addition, multiple linear regression models show that Dietary Antioxidant Quality Score was significantly associated to bone mineral density in the studied population.

Partial correlations were conducted to study the specific effects of vitamin C, zinc and selenium, after controlling the rest of variables. In the youngest group, vitamin C ($r = 0.435$, $p < 0.0001$), Zn ($r = 0.398$, $p < 0.0001$) and Se ($r = 0.398$, $p < 0.0001$) were significantly correlated with BMD. In the 36-45 age group, a significant positive association was observed among BMD and dietary intake of vitamin C ($r = 0.252$, $p = 0.031$) and Se ($r = 0.463$, $p < 0.0001$). In the older group, vitamin C ($r = 0.244$, $p = 0.032$) and Se ($r = 0.223$, $p = 0.035$) were related to BMD after controlling the rest of variables.

Covariate-adjusted means of the BMD among major categories of Dietary Antioxidant Quality Score were compared by analysis of covariance (ANCOVA) to assess differences in bone mineral density between low antioxidant consumers (Individuals who DAQS < 3.5) and high antioxidant consumers (Individuals who DAQS > 3.5). Factors that are known to affect BMD such as age, body weight and height, calcium and vitamin D intake, cigarette consuming and physical activity were used as covariates in ANCOVA analysis. After implementing the ANCOVA model in the studied participants, we found that a significant association exists between the DAQS and BMD. Figure 1 shows the adjusted means of BMD in the major categories of Dietary Antioxidant Quality Score. In the

Table II
Nutrient intake expressed as percentage of recommended dietary intake

	18-35 y.	*36-45 y.*	*> 45 y.*	*p**
Energy (kcal)	85.98 (28.42)	84.59 (19.67)	84.42 (28.72)	0.961
Carbohydrates (%)[1]	71.48 (19.02)	68.04(±15.02)	85.32 (91.97)	0.447
Protein (%)[1]	112.2 (33.94)	123.07(±35.69)	113.83 (30.01)	0.399
Fat (%)[1]	144.7 (31.98)	146.36(±27.60)	151.68 (31.93)	0.644
Thiamin (mg)	119.4 (53.81)	125.50 (47.90)	121.90 (55.53)	0.906
Riboflavin (mg)	125.4 (61.37)	137.47 (33.90)	146.14 (46.07)	0.249
Niacin (mg)	101.1 (43.81)	130.10 (60.70)	122.70 (61.17)	0.134
Vitamin B-6 (mg)	80.59 (29.07)	86.49 (34.38)	88.35 (31.57)	0.628
Folate (ug)	44.14 (32.92)	36.33 (11.30)	43.09 (23.75)	0.401
Vitamin D (ug)	80.95 (93.69)	96.32 (108.3)	83.75 (138.8)	0.863
Vitamin E (mg)	46.60 (22.93)	46.46 (24.83)	56.55 (29.15)	0.214
Vitamin A (ug)	140.22 (20.14)	160.36 (14.25)	110.23 (11.32)	0.418
Vitamin C (mg)	117.5 (69.30)	117.12 (70.18)	131.88 (84.61)	0.677
Zn (mg)	122.2 (51.11)	137.52 (49.37)	126.28 (71.32)	0.587
Se (ug)	109.4 (74.66)	126.47 (50.71)	123.42 (20.56)	0.411
Fe (mg)	101.2 (214.0)	68.39 (19.48)	108.0 (49.21)	0.405
Ca (mg)	87.56 (34.81)	90.73 (39.77)	92.27 (46.36)	0.463
Magnesium (mg)	63.40 (15.56)	71.10 (23.32)	80.77 (84.76)	0.450

y: years.
[1]Percentage of energy consumption.
*Anova test.

youngest group, 41.57% of the population was classified as low antioxidant consumers and 58.43% of the sample was defined as high antioxidant consumers, with covariate adjusted mean BMD values of 0.4970 (0.018) and 0.5540 (0.010), respectively. In the 36-45 age group, low antioxidant consumers (43% of participants) showed mean BMD value of 0.4963 (0.013), and high antioxidant consumers (57% of participants), with a mean BMD value of 0.5538 (0.002). In the older group, bone mineral density was 0.4294 (0.018) in low antioxidant consumers (54% of participants) and 0.5096 (0.010) in high antioxidant consumers (46%).

Discussion

The objective of this study was to investigate the association between dietary patterns of antioxidant nutrient intake and BMD in different age groups of Spanish women. The results indicate that the intake of vitamin C, selenium and zinc was associated with BMD. Furthermore, we found that the overall antioxidant intake was significantly associated with BMD in all age groups. To our knowledge, this is the first study that examines the relation between Dietary Antioxidant Quality Score and bone mineral density.

Several studies have supported an association between select dietary antioxidants and BMD. Most studies have focused on single antioxidants and examined the relationship between antioxidant intake and/or

Table III
Description of the antioxidant nutrient daily consumption in the study population

	Intake mean ± SD	*% sample < 2/3 RDI*
Vitamin C (mg)		
18-35 y.	88.14 (51.97)	14.60
36-45 y.	87.84 (4.08)	16.12
> 45 y.	98.91 (63.46)	15.30
Vitamin E (mg)		
18-35 y.	6.99 (3.44)	73.03
36-45 y.	6.96 (3.72)	68.81
> 45 y.	8.48 (4.37)	59.18
Vitamin A (ug)		
18-35 y.	859.4 (668.5)	11.23
36-45 y.	1,102.8 (729.2)	7.86
> 45 y.	944.4 (1634.8)	53.33
Zn (mg)		
18-35 y.	9.77 (4.08)	14.60
36-45 y.	11.0 (3.95)	18.27
> 45 y.	10.11 (5.70)	11.22
Se (ug)		
18-35 y.	60.21 (41.1)	16.12
36-45 y.	69.56 (427.8)	11.23
> 45 y.	75.81 (48.04)	10.20

y: years.
RDI: Recommended Dietary intake for the Spanish population.

Table IV
Multiple regression analysis models exploring the association of nutrient intake with BMD

Variables	*R*	*R2*	*Adjusted R2*	*SE*	*Coefficient*	*t*	*p*
Vitamin C (mg)							
18-35 y.	0.623	0.388	0.329	0.101	0.417	2.808	0.019
36-45 y.	0.687	0.472	0.424	0.092	0.344	2.130	0.041
> 45 y.	0.458	0.210	0.143	0.102	0.366	2.130	0.020
Vitamin E (mg)							
18-35 y.	0.580	0.337	0.273	0.106	0.331	1.571	0.191
36-45 y.	0.662	0.439	0.388	0.0957	-0.114	0.549	0.615
> 45 y.	0.402	0.162	0.091	0.1059	0.235	1.219	0.239
Vitamin A (ug)							
18-35 y.	0.559	0.313	0.246	0.107	0.008	0.437	0.969
36-45 y.	0.661	0.436	0.386	0.095	0.024	0.224	0.907
> 45 y.	0.394	0.155	0.084	0.106	0.255	0.962	0.189
Zn (mg)							
18-35 y.	0.598	0.358	0.295	0.104	0.452	2.130	0.050
36-45 y.	0.661	0.437	0.386	0.095	-0.083	-0.704	0.694
> 45 y.	0.388	0.150	0.078	0.106	0.134	0.704	0.532
Se (ug)							
18-35 y.	0.603	0.364	0.302	0.103	0.347	2.282	0.047
36-45 y.	0.733	0.538	0.496	0.086	0.554	3.841	0.0001
> 45 y.	0.451	0.203	0.136	0.103	0.366	2.290	0.041
DAQS							
18-35 y.	0.598	0.357	0.295	0.104	0.326	2.127	0.046
36-45 y.	0.686	0.471	0.423	0.092	0.395	2.092	0.045
> 45 y.	0.459	0.210	0.144	0.102	0.435	2.435	0.021

y: years.
DAQS: Dietary Antioxidant Quality Score.
*Adjusted by age, weight, height, smoking habits and physical activity.

serum level and the status of bone health.[8] Our findings support the hypothesis that high intakes of single antioxidants micronutrients may provide benefits to bone. In the present study, a positive association between vitamin C, selenium and zinc intakes and BMD was observed after adjustments for age, weight, height, smoking habits and physical activity.

This study shows evidence of a relation between vitamin C and BMD by itself. Numerous studies have assessed the relation between vitamin C intake and bone mineral density in the last two decades. Vitamin C has been proven to limit bone resorption, thus it might reduce the effects of free radicals and antioxidants, as it is a powerful antioxidant.[6] Similarly, vitamin C is essential for the synthesis of collagen —which represents 90% of the bone matrix—, and for the synthesis of hydroxyprolline and hydroxylysine required for the formation of stable triple helixes.[18] The association between vitamin C and bone mineral density has been analysed in different epidemiological studies.[19,20,21] However, only some of these studies proved that vitamin C intake has beneficial effects on bone mineral density.

Bone material and the structure of animal models have been confirmed to improve with vitamins E and A, so they help prevent osteoporosis.[2] The results obtained in the limited studies on the relation between vitamins E and A, and BMD have been combined.[21,22,23] Our results did not show any association between these vitamins and BMD in any of the age groups studied.

Besides vitamin C, Zinc also plays a role in collagen synthesis and bone mineralization, so it is likely to be important for bone health.[24] Patients with osteoporosis have been found to have lower levels of skeletal and serum zinc than controls.[25] A relationship between low bone mass and low zinc intake in women has been established in previous studies,[26] and the bone loss caused by certain bone disorders has been shown to improve with dietary zinc supplementation.[25] Thus, the results obtained in the present study are consistent with those of previous studies, as an association between dietary zinc intake and BMD in the youngest group has been found.

The present study reveals an association between dietary intake of selenium and BMD in all age groups of women. Different studies have found that selenium deficiency combined with iodine deficiency caused bone and cartilage growth disorders, and negatively affected bone tissues.[24,27] Conversely, other studies did not found any significant differences in hip fracture risk between high and low dietary selenium intake participants.[5]

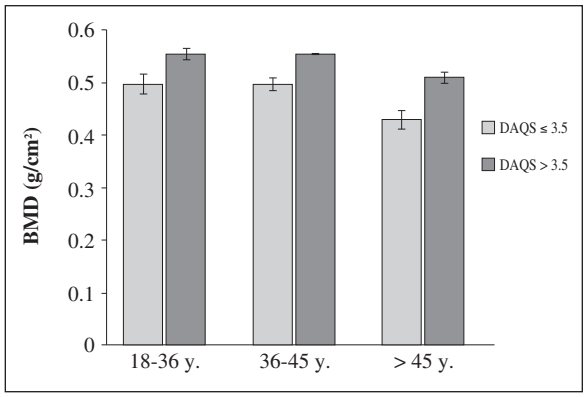


Fig. 1.—Bone mineral density in relation to Dietary Antioxidant Quality Score, DAQS, in studied women. Values are covariate adjusted means with their standard errors represented by vertical bars. Analysis of covariance (ANCOVA) in all studied women showed a p = 0.048 in Group 18-35 years; p = 0.045 in Group 36-45 years and p < 0.036 in Group > 45 years.

An important limitation of the studies that focused on the effects of the intake of particular nutrients on health is that the potential interactions between the different dietary intakes are overlooked. For this reason, recent studies are centring on diet quality indexes, which is a more realistic approach.[28] The same occurs in epidemiological studies on the relation between antioxidants and bone health, a limitation that should be overcome. In a recent study, the relation between BMD and dietary intake of antioxidant vitamins and carotenoids was proven.[8] In this study, its authors stress the importance of assessing dietary patterns rather than single antioxidant nutrient intakes, and the need for the development of recommendations for overall dietary habits.

In the present study, a positive association was found between bone mass and individual dietary intake of vitamin C, Zn and Se. On the contrary, vitamin E and vitamin A did not show any effect. However, this approach focused on single nutrients may not adequately account for the complicated interactions of these nutrients because people eat foods with combination of antioxidants. For this reason, we further considered to examine the association of an antioxidant diet quality index with BMD. The results indicate that Dietary Antioxidant Quality Score is significant associated to bone mineral density in all study participants. Our findings support the hypothesis that high intakes of antioxidants, may be beneficial to bone health.

This study has some limitations. A major limitation of this study is that dietary changes or lifetime dietary intake were not assessed, as this was a cross-sectional study that only analysed dietary intake partially. Another limitation is that the sample size was limited, and thus further large-scale studies are required. Lastly, the dietary intakes of other antioxidants such as flavonoids were not evaluated.

Further studies that examine dietary patterns, the interaction between different antioxidant nutrients and their effects on bone health would be useful to the population.[29] In fact, our study showed that there is an association between BMD and the Dietary Antioxidant Quality Score in all the women studied. Therefore, new therapies for osteoporosis based on higher dietary antioxidant intakes might be developed basing on the results obtained in this study.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1894-1899
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

High increments of overweight along with low length-for-age growth during the first 24 months of life

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Abstract

Background: **It has been reported that children nursed in orphanages loose one month of lineal growth for every three months they spend in the orphanage.**

Objective: **The purpose of this study was to evaluate the daily variation of weight- for- length and length-for-age among infants under 24 months of age, living in a temporary public orphanage in Mexico.**

Methods: **Ninety children from 0 to 24 months of age, who were institutionalized at an orphanage, were assessed during a three month period. Upon arrival their height and weight were measured daily, Monday through Friday. Daily growth velocity for weight and length was calculated. Length-for age (LAZ) and weight-for-length (WHZ) age z- scores were calculated based on WHO criteria. Risk of overweight (ROW) and overweight (OW) were classified using the WHO criteria.**

Results: **The increments of daily weight were lower than the normal range (9 g daily), but the ROW and OW increased from 10% and 3% at the beginning of the study to 14% and 11% at the end. At the end of the follow-up, WHZ was inversely associated to length (cm/day) velocity ($r = -302$, $p < 0.01$). Although a significant increase in ROW and OW was observed, at the end of the study, 31% of the children showed signs of stunting (-2 SD in length-age) and 5% remained emaciated (-2 SD in weight-length).**

Conclusions: **Children living in an orphanage showed reduced increments of weight and length-for-age, as well as a reduced length velocity and an increased ROW and OW.**

(*Nutr Hosp.* 2012;27:1894-1899)

DOI:10.3305/nh.2012.27.6.5991

Key words: *Obesity in lactancy. Catch-up growth. Delayed lineal growth. Mexican children. Orphanage.*

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Recibido: 6-VI-2012.
Aceptado: 15-VII-2012.

AUMENTO DE SOBREPESO CON BAJO CRECIMIENTO DE TALLA-PARA-EDAD DURANTE LOS PRIMEROS 24 MESES DE VIDA

Resumen

Antecedentes: **Se ha descrito que los niños de orfanatorios pierden un mes lineal por cada tres meses que residen en un orfanatorio.**

Objetivo: **El propósito de este estudio fue evaluar la variación diaria de peso-para-talla y talla-para edad, entre infantes de menos de 24 meses de edad, que residen en un orfanatorio público temporal de México**

Métodos: **Se valoraron durante un período de tres meses, noventa niños de 0 a 24 meses de edad, institucionalizados en un orfanatorio. Desde su ingreso se midieron diariamente la estatura y el peso de manera estandarizada, del lunes al viernes. Se calculó la velocidad de crecimiento diario del peso y la estatura. Las puntuaciones del z-score de la talla-para-edad y del peso-para-talla (zPT), se calcularon basados en los criterios de la OMS. El riesgo de sobrepeso (RSP) y el sobrepeso (SP) se clasificó de acuerdo a los criterios recomendados por la OMS.**

Resultados: **Los aumentos diarios de peso fueron menores que el rango normal para la edad (9 g diarios), pero el RSP y el SP aumentó de 10 a 3% al inicio del estudio, a 14 y 11% al final del estudio. Al final del seguimiento, el zPT estuvo inversamente asociado a la velocidad de crecimiento (cm/dia) lineal ($r = -302$, $p < 0,01$). Aunque se observó un aumento significativo de RSP y SP, al final del estudio 31% de los niños presentaban signos de retraso de crecimiento (-2 SD de talla-para-edad) y 5% seguían emaciados (-2 SD de peso-para-edad).**

Conclusiones: **Los niños que viven en orfanatos presentan aumentos reducidos de peso y talla para la edad, reducción de la velocidad de crecimiento lineal y un aumento de RSP y SP.**

(*Nutr Hosp.* 2012;27:1894-1899)

DOI:10.3305/nh.2012.27.6.5991

Palabras clave: *Obesidad en la lactancia. Período de crecimiento rápido. Retraso en el crecimiento lineal. Niños mexicanos. Orfanatorio.*

Introduction

Pre and postnatal factors have been shown to be associated with obesity and metabolic syndrome later in life.[1] Inappropriate nutrition during pregnancy, low and high birth weight, lack of breastfeeding, early weaning, and early adiposity rebound are associated with obesity and these features compound the metabolic syndrome in childhood and later in life.[2] There is enough evidence showing that fetal nutrition, as a result of deficient maternal and placenta nutrition, results in growth impairment in children.[3,4,5,6,7,8,9,10,11,12] Additionally, for the purpose of enhancing efficiency in catch-up fat, suppressed thermogenesis in certain tissues plays a role in the pathophysiological consequences of catch-up growth.[1] Catch-up growth is a fast recovery of weight after periods of deprivation, and catch-up fat is the recovery of weight at the expenses of fat deposition, this phenomenon of preferential fat accumulation has been described as post starvation obesity, and it has been related to abdominal obesity and metabolic syndrome.[1,13,14,15]

Ong et al.,[14] indicated that catch-up growth in infants posed a higher risk of type 2 diabetes, cardiovascular disease, obesity, and metabolic syndrome. Low birth weight has been associated to "catch-up growth" and especially catch-up fat, especially trunk fat, during the first year of life. It has been reported that there is an association between this catch- up growth and catch-up fat with a reduction in insulin sensitivity, HDL cholesterol, and an increase in waist circumference and triglycerides in adult life.[1,14,15,16] It has also been observed that a high weight birth is associated to higher body mass index (BMI). Ong[14] indicated that catch-up fat might be partially explained by the need of those with intrauterine deprivation for catching-up the weight to standard levels, which is usually done by catching-up fat in the trunk area.

A high percentage of children in orphanages might have undergone intrauterine deprivation, thus, these children are at high risk of becoming obese, having abdominal obesity and its later consequences.

Anemia and low levels of hemoglobin during pregnancy might be prolonged after birth and during the first months of life.[17] In Mexico it has been reported that more than half of women suffer of anemia and iron deficiency, these problems are higher among more vulnerable women groups, such as those in indigenous and rural populations and living under the poverty level of income.[18,19] Iron deficiency in children might also play an important role in length impairment.

Growth deficit is a problem affecting wide sectors of the infant population in Mexico and Latin America, especially those living in poverty.[20,21,22] In the Euro-Growth Study it was found that there is a positive correlation between weight and age when height is increased. It was suggested that age has a mediated effect on weight during early life as a result of intrauterine factors, mainly nutrition factors.[23] Thus, prenatal factors contribute to early life fetal programming which subsequently leads to a higher susceptibility for both higher rates and earlier onset of certain diseases later in life.[24] The last trimester of pregnancy is an essential period for fat mass programming, independently of the postnatal pattern of growth.[25]

Several studies have reported negative effects on growth as a result of living in an orphanage, poverty, undernutrition, and emotional and psychosocial deprivation.[26,27,28,29,30]

However, we have found no studies showing whether lineal growth delay is associated with the incidence of obesity in infants, nor the effect of living in an orphanage environment on the incidence of obesity.

The purpose of this study is to assess the daily weight and length increments of infants living in an orphanage in Mexico, and to evaluate whether there is an association between growth velocity and overweight.

Methods

Population

The state of Baja California shares a strong economic and cultural relationship with the United States due to its geographical location. In 2006, it had approximately 3,155 070 residents, of which, Tijuana, Baja California had approximately 1,559 683 residents.[31] Children at orphanages are mainly "mestizos" (half-blood). The orphanage can accommodate 250 to 300 children (60% boys). Ninety of these children (57% boys) participated in the study.

Study design

The study was conducted from June 15th to December 15th of 2009, in Tijuana, Mexico. This is a longitudinal study of infants 0-24 months old, living in a public orphanage, with a follow up of three months. Since the orphanage is a short term facility, children residing in the orphanage are usually relocated to a long term orphanage or are given back to their parents upon request and approval. Children with diseases other than obesity or under nutrition, which might affect growth development, were excluded from the study. More than half (56%) of the children were measured the same day they were admitted to the orphanage. Ninety children ranging from 0 to 24 months of age, who were temporarily institutionalized, were measured during 16 weeks on their weight and height. The average age was 8.5 months (3 days to 20 months) and 57% were boys. The range of stay in the orphanage for the rest of the children varied from 5 to 60 days.

Ethics Approval

The project was approved by the ethics committee of the nutrition academic body at Universidad Autonoma

de Baja California. The authorities of the orphanage authorized the study and followed the protocol to accept a research project on the children, and the physician and nutritionist in charge participated in the study.

Measurements

Age was calculated from the date of birth and the date of the first measurement. Children were measured at the same time each day before feeding, using a measuring mat SECA (model 210, Hamburg, Germany) or a portable stadiometer SECA (model 410, Hamburg, Germany), with precision of 1 mm. Upon arrival, and Monday through Friday, daily length/height and weight were measured until the end of the period. Children were weighed, without diapers and clothes, using a pediatric scale (Health o Meter, Kilo-Pound Beam, Model 1524 KL HON 1901). Weight was measured daily and the scale was also calibrated daily. WHZ was calculated based on WHO criteria. WHZ were compared by age and gender of each child with the corresponding tables of the WHO-2006.[26] The scores and percentiles of each child were calculated with SPSS v16, using the parameters provided by the WHO (2006). Weight and length velocity were calculated considering the difference in weight and height change each day.

Indices

Weight-for-length/height (WHZ) z-scores and length/height-for-age (HAZ) z-scores were calculated according to age and gender using the WHO (2006) criteria. Weekly variation of height-for-age and weight-for-height was computed during the six month period.

WHZ classification was used according to WHO: severely emaciated (≤ -3 SD), emaciated (-2.99 SD to ≤ -2 SD), normal weight (-1.99 SD to ≤ 1 SD), possible risk of OW (> 1 SD to ≤ 2 DE), OW (> 2 SD to ≤ 3 SD), and obesity (> 3 SD). HAZ classification was used according to WHO: Severely stunting (≤ -3 SD), stunting (-2.99 SD to ≤ -2 SD), normal height (-1.99 SD to ≤ 3 SD), and tall (> 3 DE).

Statistical Analysis

All variables were examined to see if a normal distribution was followed, using the Kolmogorov-Smirnov test. Mann Whitney Ranks non parametric test and student's t-test for independent samples were used to assess differences in z scores and growth velocity, and the days of living in the orphanage. Growth velocity differences by age group were analyzed using one way ANOVA. Spearman's correlation was conducted to analyze the association between growth velocity, weight and length increments and weight and weight for length status.

Results

The prevalence of severely stunted at the beginning of the study was 6.5%, stunted 8.5%, normal length 80%, and tall 5%. During the first three months at the orphanage a weekly decrease in length - for- age z-scores was observed in all age groups, but more significantly in younger than three months of age (fig. 1). At the end of the study the prevalence of severe stunting was 20%, stunted 11%, normal length 67%, and tall 2%.

On the other hand, at the beginning of the study the prevalence of severe emaciation was 5.6%, emaciated was 6.5%, normal weight was 75.5%, possible ROW was 10%, and OW was 3%. During the first three months in the orphanage, different slopes of weight -for-length z-scores were observed, but children younger than three months had a steady increase in weight for length (fig. 2). At the end of the study the prevalence of severe emaciation was 1.5%, emaciated was 3.5%, normal weight was 71%, possible ROW was 14% and OW was 11%.

A difference in z- scores and growth velocity in both genders was observed, and this was further seen among children who had lived one or more weeks at the orphanage. By the end of the study 31% of the children remained behind (< -2 DE) in length-for-age and 5% remained emaciated (< -2 DE in weight-for-length). There were no differences in growth velocity between genders. Children that had more than a week in the orphanage presented a lower growth velocity than the newly arrived [0.008± 0.003 and 0.013 ± 0.004 cm/day ($p = 0.0001$)]. This might be due to age differences or to long term effect of emotional deprivation. The average age of newcomers was 7 ± 6 months, while those with more than a week of stay were 10 ± 5 months ($p = 0.005$).

On average the 0-3 months group had the highest increment in g/d ($p = 0.0001$) and the 3-6 months group had the highest cm/d ($p = 0.02$) increment. Table I shows weight and length daily growth. There were no differences in weight increments between the new comers and those that were already at the orphanage. Initial z- scores of length-for-age were greater than the final z- scores in all age groups.

Also, it was observed that children with normal z-score of weight-for-length increased their weight from 40 to 60 g/week; children with more than 1SD from 10 to 90 g/week, and children with -2SD from 40 to 90 g/week. Those children who at the beginning of the study had z-scores of length-for-age at -2 SD presented greater increments in length.

Weekly increments of weight- for- length z-scores varies depending on the initial weight status, but most emaciated children (< -2SD) had higher increments on weight-for- length z-scores, while normal and those with > 1SD weight-for-length z-scores children had lower weight increments (fig. 3). At the end of the follow-up, the increment of weight was inversely associated to z-scores in length-for-age ($r = -0.398$, $p < 0.01$), BMI was also inversely associated to length (cm/day) velocity ($r = -0.302$, $p < 0.01$).

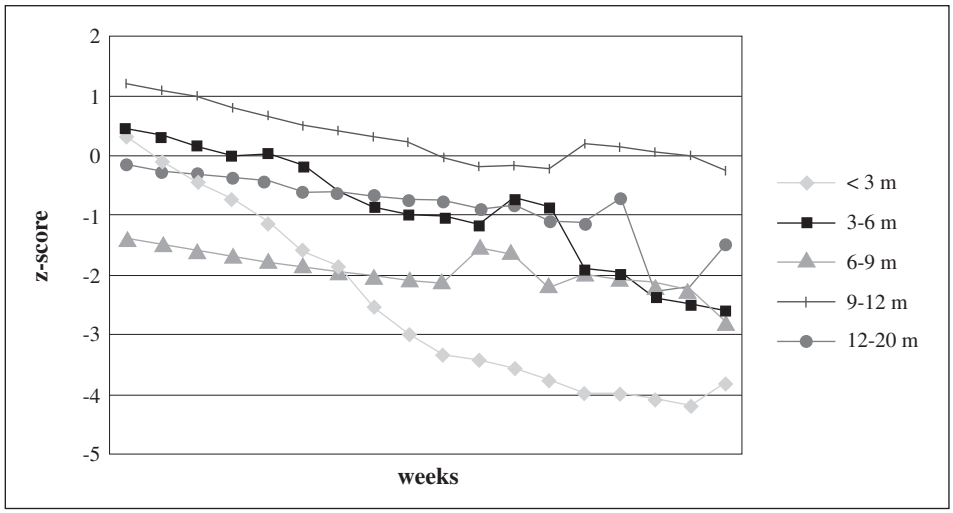


Fig. 1.—Weekly mean height-for-age z-scores by age groups.

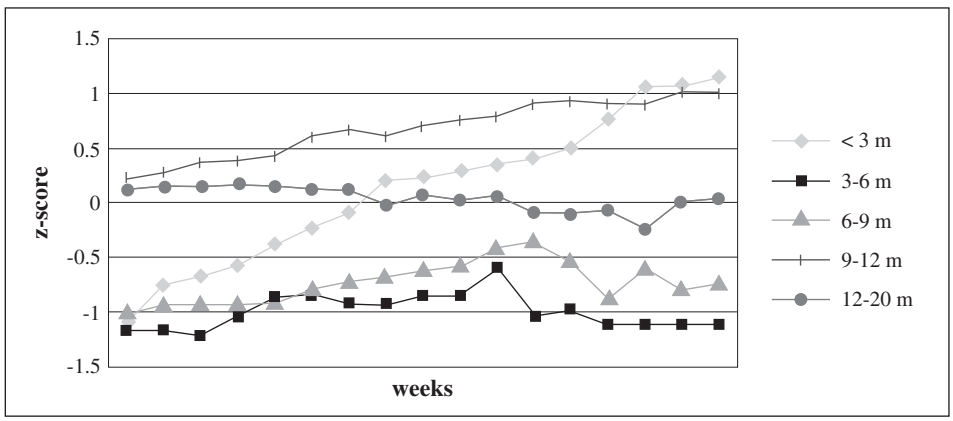


Fig. 2.—Weekly mean weight-for-height z-scores by group age.

Table I
Weight and length daily growth

Months	*Weight g/day*	*Length cm/day*
0-3	8.5 ± 3.4	0.013 ± 0.003
3-6	7.1 ± 3.0	0.013 ± 0.005
6-9	7.0 ± 3.5	0.013 ± 0.004
9-12	7.1 ± 2.7	0.010 ± 0.003
12-20	4.6 ± 2.1	0.009 ± 0.004

Weekly weight increments were higher in children with < -2SD of length-for-age z-score (fig. 4).

Discussion

At the end of three month follow-up of BMI, infants living in an orphanage were inversely associated to length (cm/day) velocity. A paradoxical trend of weight and length increments was observed. Infants having lower than the average weight increments for their age (9 g/day) had a 12 percentage points (pp) increase in prevalence of ROW and OW. At the same time, the prevalence of severe stunting and stunting also increased 16 pp. The high prevalence of ROW and OW observed at the end of the follow-up is consistent with the high prevalence reported among 6 to 24 months old, low-income children from three different cities in Mexico.[32] These results might indicate that even with a slight catch-up growth and catch-up fat, infants are prone towards ROW an OW, which may be at the expense of the reduced length velocity or an increase of metabolic efficiency toward fat deposition.

Dulloo[1] indicates that an increase in metabolic efficiency directed at fat deposition is a fundamental physiological process operating to accelerate fat recovery after growth retardation or weight loss. Through the catch-up fat, continues Dulloo, "a normal physiological process is expressed and characterized by an elevation in the efficiency of cellular energy utilization". Therefore, rather than a catch-up growth that would include growth velocity and a weight increase, catch-up fat seems to prevail even with small increments of weight, which results in ROW and OW. As Dulloo[1] states, "the process of catch-up growth per se is a state characterized by a proportionately greater rate of fat deposition relative to lean tissue deposition". This may occur even with as little increments of weight as 9

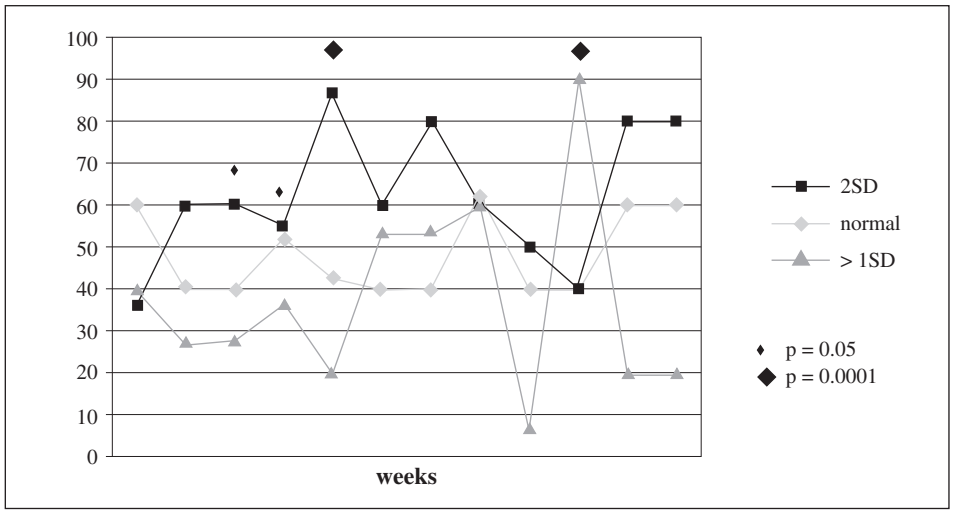


Fig. 3.—Mean weekly weight increments by baseline weight-for-length z-score.

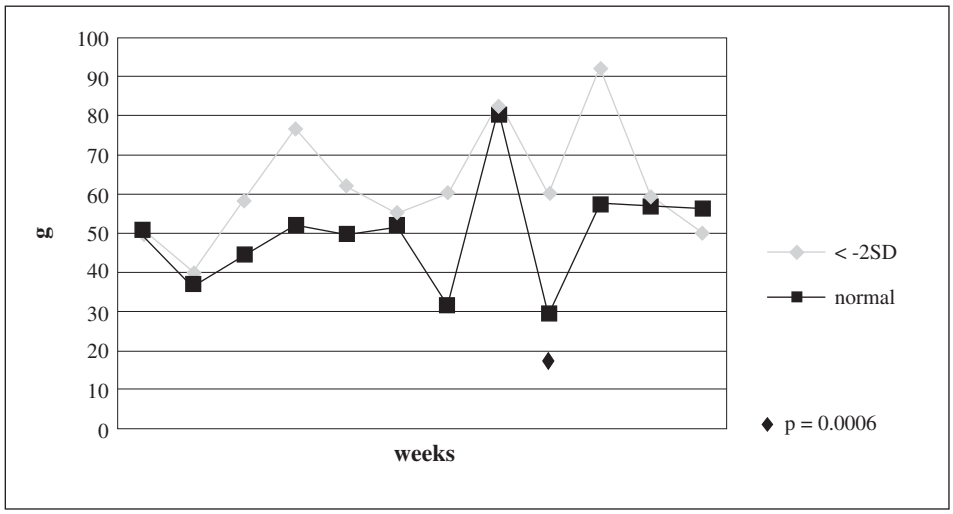


Fig. 4.—Mean weekly weight increments by baseline height-for-age z-score.

g/day in the first two months of age, as it occurred in these children. This state of preferential catch-up fat, says Dulloo,[1] "is brought about, at least in part, via the suppression of thermogenesis, which precedes the appearance of excess body fat and central fat distribution, and is a central event that predisposes individuals with catch-up fat to abdominal obesity, type 2 diabetes and cardiovascular disease".[1]

Some maternal diseases might affect the weight and height of children.[33,34,35] Unfortunately, we did not have maternal health history, but no children were HIV positive. Most children living in an orphanage come from an adverse pre and postnatal environment, including lack of pre natal control, maternal alcoholism, smoking or taking other drugs during pregnancy and inappropriate delivery settings when the child is born.[36,37]

The inverse association of the length velocity with the increase of obesity observed in this study might indicate that an objective to prevent childhood obesity should be focused to prevent the reduced length velocity in infants, as well as appropriate pre-natal care.

The strengths of this study include that it was conducted in a homogeneous environment, the same physician and personnel helped throughout the study, and the children's care was not interrupted. However, the limitations rest on the lack of records of maternal health prior, during, and after the birth and the birth weight of the children. All those data might indicate the neglecting care before the arrival of the child to the orphanage.

Several studies have reported negative effects on growth as a result of living in an orphanage, poverty, undernutrition, emotional and psychosocial deprivation.[24,25,26,27,28]

Inappropriate nutrition during pregnancy, low and high birth weight, lack of breastfeeding, and early weaning, not reported in most of these children, might also be associated with the high increments of obesity.[2]

Children living in an orphanage showed a process of reduced increments of weight and length for their age, as well as a reduced length velocity along with increase ROW and OW. These results suggest the urgent need of including a nutritionally aggressive care plan for children

growing up in adverse environments in order to treat undernutrition and prevent obesity. Additionally, the process should be further studied to find out how this might have an effect on long term consequences of abdominal obesity, to see if this physiologic process is leading to higher levels of obesity among low income populations, and to find out which might be the appropriate nutrient composition to prevent early abdominal fat deposition and length delay in children living in poverty, and in economical or emotional deprivation.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1900-1907
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Cholestasis induced by total parenteral nutrition; effects of the addition of Taurine (Tauramin®) on hepatic function parameters; possible synergistic action of structured lipids (SMOFlipid®)

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Abstract

Objective: Assess the hepatoprotective effect of Taurine (Tau) in cases of hepatic cholestasis induced by Total Parenteral Nutrition (TPN).

Methods: **We describe a retrospective series of 54 patients who received TPN, in which cholestasis was detected at an (Intermediate) point that separates the duration of TPN into 2 Phases. From this moment —Phase 2— on, and according to clinical criteria, some patients (Group A, n = 27) received amino acids with Tau (22.41 ± 3.57 mg/kg/day)(Tauramin®), while the rest (Group B, n = 27) received the standard solution without Tau. The mean TPN durations were 39.2 ± 17.1 and 36.4 ± 18.1 days respectively, with the Intermediate points on days 19.56 ± 10.51 and 17.89 ± 11.14. They all received diets that were homogeneous in terms of kcal and macronutrients. In Phase 2, 21 patients from Group A received structured lipids (SMOFlipid®); while 20 from Group B received soy MCT/LCT [Medium Chain Triglycerides/Long Chain Triglycerides] (physical or structured mixture). In a retrospective study, differences could not be avoided. The analytical parameters from three periods (Initial, Intermediate, and Final) were obtained from Nutridata® and Servolab®. We compared interperiod values using the Wilcoxon test SPSS® ($p < 0.05$).**

Results: **After introducing Taurine AST, ALT, and GGT were significantly reduced; Bilirubin was also reduced, but not significantly. The values obtained for GGT in Group A were (Mean(σ)/median): Initial 48.6 (23.1)/46; Intermediate 473.7 (276.2)/438, and Final 328.9 (190.4)/305. We stress that the mean GGT value is reduced by 30.56% after adding Taurine, while in its absence all parameters are elevated, and mean GGT increases 45.36%.**

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Recibido: 4-VI-2012.
1.ª Revisión: 6-VII-2012.
Aceptado: 15-VII-2012.

COLESTASIS INDUCIDA POR NUTRICIÓN PARENTERAL TOTAL; EFECTO DE LA ADICIÓN DE TAURINA (TAURAMIN®) SOBRE LOS PARÁMETROS DE FUNCIÓN HEPÁTICA; POSIBLE ACCIÓN SINÉRGICA DE LÍPIDOS ESTRUCTURADOS (SMOFLIPID®)

Resumen

Objetivo: **Evaluar el papel hepatoprotector de Taurina (Tau) en situación de colestasis hepática inducida por Nutrición Parenteral Total (NPT).**

Métodos: **Se describe una serie retrospectiva de 54 pacientes, que recibieron NPT, detectándose colestasis en un momento (Intermedio) que separa en 2 Fases la duración de la NPT. A partir de este momento —Fase 2— y según criterios clínicos, unos —grupo A, n = 27— recibieron aminoácidos con Tau -22,41 ± 3,57 mg/kg/día (Tauramin®), mientras otros —grupo B, n = 27— recibieron solución estándar sin Tau. La duración media de NPT fue de 39,2 ± 17,1 y 36,4 ± 18,1 días respectivamente; con el punto Intermedio en día 19,56 ± 10,51 y 17,89 ± 11,14. Todos recibieron dietas homogéneas en kcal y macronutrientes. En la Fase 2, 21 pacientes del grupo A recibieron lípidos estructurados (SMOFlipid®); mientras que 20 del grupo B recibieron MCT/LCT soja (mezcla física o estructurada). Las diferencias no se han podido obviar en un estudio retrospectivo. Se rescataron de Nutridata® y Servolab® los parámetros analíticos en tres momentos (Inicio, Intermedio y Final). Utilizando SPSS® se compararon según Test de Wilcoxon para valores intermomentos ($p < 0,05$).**

Resultados: **Hubo disminución significativa de AST, ALT y GGT tras la introducción de Taurina; Bilirrubina desciende sin significación. Los valores obtenidos para GGT en el Grupo A fueron (Media(σ)/mediana): Inicio 48,6 (23,1)/46; Intermedio 473,7 (276,2)/438 y Final 328,9 (190,4)/305. Destacamos que el valor medio de GGT disminuye un 30,56% tras adición de Taurina; mientras en su ausencia se elevan de todos los parámetros, aumentando un 45,36% la media de GGT.**

Conclusión: **Estos resultados abundan en el papel hepatoprotector de la Taurina, y apoyan su utilización en situación de colestasis inducida por NPT. Asumimos la posibilidad de que la diferencia de perfil entre SMOF y**

Conclusion: **These results show Taurine's hepatoprotective effect and support its use in cases of TPN-induced cholestasis. We acknowledge the possibility that the differences between SMOF and the MCT/LCT mixtures also may have influenced the results in a combined effect with taurine.**

(*Nutr Hosp.* 2012;27:1900-1907)

DOI:10.3305/nh.2012.27.6.6047

Key words: *Parenteral nutrition. Cholestasis. Taurine. Liver. Fat emulsions intravenous.*

Conclusión: Estos resultados muestran el efecto hepatoprotector de la taurina y apoyan su uso en casos de colestasis inducida por NPT. Reconocemos la posibilidad de que las diferencias entre SMOF y las mezclas MCT/LCT haya influido como efecto combinado utilizado junto a taurina.

(*Nutr Hosp.* 2012;27:1900-1907)

DOI:10.3305/nh.2012.27.6.6047

Palabras clave: *Nutrición parenteral. Colestasis. Taurina. Hígado. Emulsiones lipídicas intravenosas.*

Introduction

As early as 1971 Peden[1] described hepatic damage in a child that had received total parenteral nutrition (TPN) for 71 days. These pathological changes are brought about by TPN itself, the liver's attempt to compensate them, and their interaction over time.[2]

During TPN nutrients reach the liver through the hepatic artery instead of the portal vein; this causes a redirection of the hepatic blood flow which can lead to relative over-saturation or deficits in its metabolic functions. The changes in the nutritive mixture's composition, almost always different from the physiological one due to hyperosmolarity, affect the cholangioles.[3] Changes in the cholangioles' ionic resorption, especially of Ca and Na, are induced, and this increases water reabsorption and alters the bile's final composition. The reduction in the tauro/glyco conjugates and conjugated/not conjugated ratios is especially important, as is the intrahepatic increase of lithocholic acid, the most hepatotoxic of them. Different publications confirm these findings.[4]

Long-lasting TPN may give rise to progressive and potentially irreversible pathological phenomena (adaptive changes), in which the hepatic ultrastructure is affected, especially in the cell membrane and organelles, with an increase in lipid peroxidation and fibrogenesis.[5] We may speak of pathologies associated with parenteral nutrition (Parenteral Nutrition-Associated Liver Disease, PNALD).

In children, PNALD's more common manifestation is cholestasis[6] while in adults steatohepatitis is more frequent. This difference becomes less evident in prolonged TPN.[7] Alterations in hepatic function tests have been described in 20 to 90% of patients receiving TPN.[8] Cholestasis is the blocking of bile flow, both in the hepatocytes and the cholangioles and the rest of the intra- and extra-hepatic biliary tract.

PNALD pathogenesis is not known for certain, and probably has a multifactorial origin.[9] Some of the risk factors for developing the condition are the following: 1) Consequences of TPN: lack of enteral stimulation, bacterial overgrowth, activation of the inflammatory process; 2) factors related to TPN: excessive caloric supply, specific nutrients present in the mixture —amino acids, lipids—, deficiencies in certain nutrients —carnitine and others—; and 3) factors related to the underlying process: prematurity and low weight, sepsis, short bowel syndrome (SBS), medication.[10]

In certain situations, such as SBS, with cholangitis or sepsis, with multiple surgical procedures (for example, Crohn's Disease), hepatic changes are faster and progressive, progressing to irreversible damage, with fibrosis and cirrhosis.[11] Short Bowel Syndrome (SBS) and PNALD onset are correlated. The livers of 60% of infants and 40% of adults with long-term TPN due to bowel failure are affected.[12] Bacterial overgrowth may contribute to the liver being affected.[13]

Among the components of TPN, lipids are the ones that cause changes in liver structure and function with the highest frequency.[14] In addition, the composition of administered fats, as long or medium chain triglycerides (respectively, LCTs and MCTs), can also cause changes in liver composition, function, and ultrastructure.[15] Existing data suggest that an MCT/LCT mixture is less likely to cause liver complications than LCTs alone.[16] In addition, the onset of cholestasis has been associated with administration of more than 1 g/kg/day of lipids (adult patients).[12] Thus, TPN alters the composition of the liver's fat and its histomorphology.[17]

Phytosterols, soy derivatives present in many commercial lipid formulations, have been considered potentially toxic and may accumulate and alter bile flow. The amount of phytosterols present in 100% soy emulsions is three times greater than that in soy/coconut/olive/fish emulsions (143.6 mg/l *vs.* 47.6 mg/l).[18]

The protein content and amino acid mixture composition in TPN have also been suggested as possible liver dysfunction inducing factors. In fact, cholestasis develops earlier in patients receiving TPN with higher protein content.[19] Some associations, such as taurine or carnitine deficits and lipid supply in the form of LCTs, as well as glutamine and glutathione deficits have been shown experimentally.[20] All of these are essentially associated with nutrient solution formulations. Currently, it is recommended that a mixture of carbohydrates (70-85% of non-protein kcal) and fats (15-30%) be used. The excess in calories caused by glucose and the excess of lipids may be toxic to the liver and cause steatosis and cholestasis.[21]

The term cholestasis is associated with an increase in the serum concentrations of compounds that are normally excreted with bile, such as bile acids, bilirubin, cholesterol, and, among other enzymes, alka-

line phosphatase (ALP) and gamma glutamyl transpeptidase (GGT). In addition, and as a consequence of retaining potentially toxic compounds inside the hepatocytes, these cell may become necrotic, which in turn elevates the serum concentrations of alanine transaminase (ALT or SGPT) and aspartate transaminase (AST or SGOT), and trigger the processes of liver fibrosis that may lead to cirrhosis.[22]

GGT is characterized by its extreme sensitivity, and in cases of cholestasis it becomes elevated before ALP. However, given its lack of specificity, GGT determination has no clinical value unless its values are compared with those of other, more organospecific, enzymes such as ALP and ALT.[16] Both dissociated and intrahepatic cholestasis result in elevated ALP, with its value increasing twofold or threefold.[16]

In its initial phase, TPN-Induced Cholestasis (TPN-IC) manifests itself as a dissociated cholestasis, characterized by increases in AST, ALT, GGT, and ALP (two or three times its normal value), and normal serum bilirubin. When we speak of intrahepatic cholestasis proper, we see an increase of total bilirubin, above 1.5 mg/dl and up to 10 mg/dl, at the expense of direct bilirubin.[16] Elevated bilirubin values are seen after the first two weeks of TPN, although they may also appear several months later.[23]

Pharmacological hepatotoxicity is still a relatively unknown phenomenon. Its mechanism is probably double: direct hepatotoxicity and adverse immune reactions. The list of possible drugs is long, and among those more frequently associated with cholestatic liver damage we could mention chlorpromazine, phenothiazines, sulphamides, NSAIDs, ACEs, tricyclic antidepressants, carbamazepine, erythromycin, sulfonylureas, anabolic steroids, and oral contraceptives.[24]

Twenty years ago, Cooper et al. reported a marked taurine deficiency in children with TPN-IC.[25] Later studies showed that adding taurine increased taurine-conjugated bile acids in rats,[26] increased the flow and secretion of bile acids and protected from hepatotoxic bile acids in pigs.[25]

Taurine has been shown to promote bile flow,[27] increase the maximum bile acid secretion rate,[28] and prevent cholestasis induced by sulfated lithocholic acid, both in its free and glycine-conjugated forms.[27] Because taurine is involved in the formation of bile acid conjugates, its deficiency seems to play a role in the pathogenesis of TPN-induced cholestasis.[29] It is known that, in adults, the plasma concentration of taurine is reduced in cases of prolonged parenteral nutrition, starvation, surgery, and a variety of clinical conditions [such as] chronic liver pathology, chronic heart failure or kidney failure.[30] Taurine is essential in newborns and conditionally essential in some adults requiring long-term TPN.[30] Because most episodes of TPN-IC take place after 2 weeks of TPN,[31] longer study times are needed to demonstrate taurine's effect.

In healthy adults, the proportion of taurine and glucose conjugated bile acids is 3:1; this varies from one individual to another, and is influenced by the *pool* of hepatic taurine.[32] In addition, and differently form nonconjugated or glucose-conjugated bile acids, taurine-conjugated bile acids have a choleretic effect and prevent cholestasis.[33] Supplementing with taurine improves the hepatic activity of cholesterol 7-α-hydroxylase, the enzyme that limits the rate at which bile acids are synthesized.[34] Taurine stimulates bile flow, increases bile acid production, and protects against cholestasis.[35]

Adding taurine to newborns' TPN is well documented, but few studies have been performed regarding taurine use in adults receiving TPN. In his review, *Belli* suggests that taurine plays a key role in several biological actions, especially in the liver, and recommends that it be added to the amino acid solutions used in parenteral nutrition.[36] At present, the taurine content in TPN solution is highly variable. It is generally accepted that adults receiving long-term parenteral nutrition have a nutritional requirement for taurine.[37]

All this justifies performing a study on the effects of adding taurine on the hepatobiliary function of adult patients without a primary biliopancreatic pathology that are receiving long term TPN.

Objective

The objective of this study is to determine the effect on the hepatic function parameters of patients with long term TPN-IC of adding taurine to the amino acid solutions used in nutritional support .

Material and methods

This is a 3-year retrospective, observational, and analytical study of cohorts performed at the Virgen de la Victoria University Hospital (VVUH) that took place between January 2008 and December 2010. All patients without biliopancreatic pathologies that received TPN according to protocol, i.e., standard diets or diets for their specific clinical condition, during their hospitalization, and that developed cholestasis during nutritional support were selected. Patients were excluded if their hepatic parameters that denote cholestasis increased in the first five days of support or if TPN lasted less than five days after cholestasis onset.

Following clinical criteria, some of these patients received TPN supplemented with taurine (Tauramin® 1.2 or 1.5 g/l of Tau) while the rest did not receive the supplement. Thus the following two groups are defined as follows:

- *Group A:* After the apparition of parameters suggesting cholestasis, they received TPN supplemented with taurine.
- *Group B:* After the apparition of parameters suggesting cholestasis, they continued to receive unsupplemented TPN.

Table I
TPN macronutrient composition mean (σ)

	Initial	*Intermediate*	*Final*
Group A			
N g/kg/day	0.20 (0.05)	0.24 (0.05)	0.23 (0.06)
Lipid g/kg/day	0.97 (0.28)	0.81 (0.28)	0.79 (0.30)
Glucose g/kg/day	3.69 (1.06)	3.75 (0.87)	3.53 (0.93)
Kcal/kg/day	29.63 (7.89)	29.54 (6.86)	27.85 (7.20)
Group B			
N g/kg/day	0.19 (0.05)	0.20 (0.05)	0.18 (0.6)
Lipid g/kg/day	0.86 (0.20)	0.86 (0.29)	0.82 (0.32)
Glucose g/kg/day	3.34 (0.88)	3.48 (0.97)	3.27 (0.81)
Kcal/kg/day	26.83 (6.00)	27.79 (6.99)	25.87 (7.75)

With the aid of Pharmacy (Nutridata® and X-farma®) and laboratory (Servolab®) databases, and the patients' medical records we obtained the following parameters:

- Anthropometric (weight, height, Body Mass Index [BMI]).
- Demographic (age, sex).
- Clinical (parenteral nutrition indication, sepsis or septic shock, SBS).
- Analytical (serum levels of ALP, GGT, AST, ALT, total bilirubin).
- Nutritional (reason why TPN was discontinued, its duration, time to cholestasis onset, grams of nitrogen, glucose, lipids, total kcal, and mg of taurine per kilogram and day, type of lipid administered).
- Pharmacological (drugs that induce acute liver damage administered during nutritional support).
- Metabolic.

The presence of sepsis or septic shock of either bacterial or fungal origin during TPN support, before or during TPN-IC, was established through the Clinical Documentation computerized database, as stated in the ICD-9-CM code for the Hospital's MBDS.

Analytical, nutritional, and metabolic parameters were gathered at three points in time:

- *Initial:* the time at which nutritional support with TPN begins.
- *Intermediate:* the time at which the analytical data suggest cholestasis onset. In the group receiving taurine this point is the time at which it was decided to administer a solution enriched with taurine. The clinician in charge of the patient made the decision to administer taurine or not, with or without previous advice from the nutritional support team. Patients receiving taurine do so from this moment until the end.
- *Final:* the end of TPN support.

These points in time determine two phases in the study: Phase 1 (from initial to intermediate) and Phase 2 (from intermediate to final).

The serum levels of patients receiving TPN according to hospital protocol are measured before it begins and then weekly, as are the remaining analytical parameters of the nutritional profile. The reference ranges used are: GGT (9-69 IU/l), ALP (40-130 IU/l), AST (10-37 IU/l), ALT (12-78 IU/l), total bilirubin (0.2-1.10 mg/dl). AST, ALT, GGT, ALP and total bilirubin were determined using analytical spectrophotometry and the Dimension Vista® Auto Analyzer, Siemens Healthcare Diagnostic Inc., Newark (USA).

In Phase 1, both groups received a diet with a standard amino acid (Aa) source (Synthamin®, Aminoplasmal®, or Aminosteril KE®), and the sources of lipids were soy LCTs or soy MCTs/LCTs as a physical or structured mixture. In Phase 2, Group A received Aas enriched with taurine (Tauramin®, 1.2 or 1.5 g/l of Tau), and —preferably— soy-olive-fish MCT/LCT structured lipids (SMOF®). Group B continued to receive the standard source of Aas and -preferably- soy MCT/LCT lipids as a physical or structured mixture (Lipofundin® or Structolipid®). Table I summarizes the macronutrient and total kilocalories provided. The types of lipids administered to both groups in each phase of the study are shown in table II. During Phase 2 patients in Group A received an average of 22.41 ± 3.57 mg of taurine/kg/day.

In both groups the source of carbohydrates was glucose at different concentrations.

The drugs that induce acute liver damage administered to each patient were recorded in both phases, as were pharmacological treatment duration and the kind of associated acute liver damage (hepatocellular, cholestatic, or mixed).[38] According to the CIOMS scale,[39] for an initial treatment to be considered suggestive of liver damage it must be maintained between 5 and 90 days.

A data collection sheet was designed, and patients were identified and individualized. After data collection was complete, the data collection sheet was imported into the SPSS® statistical software for its posterior analysis. Hepatic parameters were compared with the Wilcoxon test for nonparametric quantitative

Table II
Types of administered lipids

Group / *Phase*	*Group A*				*Group B*			
	Phase 1		*Phase 2*		*Phase 1*		*Phase 2*	
Types of lipids	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*
Soy LCT	12	44.4	1	3.7	18	66.7	3	11.1
MCT/LCT*	13	48.1	5	18.5	9	33.3	20	74.1
SMOF	2	7.4	21	77.8	–	–	4	14.8

*Physical (Lipofundin®) or structured (Structolipid®) mixtures.

variables, and the significance level chosen was $p < 0.05$.

Results

Fifty-four patients were included. Twenty-seven of them received taurine-supplemented TPN from the Intermediate moment (Group A), while the remaining 27 continued to receive nutritional support without taurine supplementation (Group B).

The weight, height, and demographic data of patients from both groups were homogeneous. The data from Group A are: 66.7% males, 33.3% females, mean age: 59.41 (± 13.9) years old, weight: 67.02 (± 14.18) kg, height in meters: 1.68 (± 0.08). The data for Group B are: 59.3% males, 40.7% females, mean age: 59.37 (± 15.7) years old, weight: 70.21 (± 13.24) kg, height in meters: 1.65 (± 0.09).

Total TPN duration (Group A: 39.2 ± 17.1 days; Group B: 36.4 ± 18.1 days). Phase 1 duration (Group A: 19.56 ± 10.51 days; Group B: 17.89 ± 11.14 days), and Phase 2 (Group A: 16.07 ± 11.75 days; Group B: 18.96 ± 12.42 days). TPN at the VVUH lasted an average of 15.8 ± 15.3 days (n = 460 patients) in 2008, 15.4 ± 13.1 days (n = 450 patients) in 2009, and 14.2 ± 11.8 days (n = 411 patients) in 2010. TPN duration was determined by the conditions that made hospitalization necessary.

The most common reasons to begin TPN in Group A were: digestive tract obstruction with moderate to severe malnutrition and deferred intervention (26%), followed by post surgical peritonitis (13%), total gastrectomy (9%), hypoalbuminemia (9%), and other causes (43%). Only one patient had SBS.

In Group B they were: digestive tract obstruction with moderate to severe malnutrition and deferred intervention (22%), followed by inflammatory diseases (15%), total gastrectomy (11%), peritonitis (7%), and other causes (45%). Only one patient had SBS.

We found patients with sepsis or septic shock previous or simultaneous with TPN-IC onset in both groups. It was diagnosed in 9 patients from Group A and 8 patients from Group B.

During nutritional support patients in both groups received drugs that cause acute liver damage. Eleven of 12 patients in Group A received cholestatic drugs, as did all 13 patients in Group B. The mean number of acute liver damage-inducing drugs received per patient was 2 in Group A and 1.54 in Group B; and the mean number of cholestasis-inducing drugs per patient was 1.67 in Group A and 1.15 in Group B.

The hepatic profile analytical parameters were collected in the three moments that define the study, and the results are shown in table III.

Figure 1 is a box plot depicting how GGT changed in both groups. The mean ALT and AST values for each group at the three different study moments are shown in figure 2.

The number of patients with bilirubin > 1.5 mg/dl at the Intermediate and Final moments were 9 and 3 respectively in Group A and 8 and 6 respectively in Group B.

Discussion

It might seem surprising that patients in Group A have higher values of the cholestasis-suggesting studied parameters than patients in Group B in the intermediate point of the study, i.e., when the decision to introduce Taurine or not is made. However, this is reasonable given that, as explained above, during the study the clinician in charge was at liberty to modify the patients' diets. Although the nutritional support team could advise the clinician, the decision was never made automatically when certain predetermined analytical thresholds were reached. Thus, it is logical that the more significant increases are the ones that catch our eye.

In Phase 1, there is a significant elevation of all studied parameters in both groups. In Phase 2, patients in treated with Taurine experience a significant reduction in GGT, AST, and ALT, and their final values are lower than those not treated with Taurine, even though at the Intermediate point the values for this group were lower than those for the group treated with Taurine. The same is true for total bilirubin, although in this case the decrease in the Taurine group is not significant.

ALP behaves differently during the course of TPN. After the big increase in both groups during Phase I, it

Table III
Hepatic parametes by group mean (σ) median

Parameter	*Initial*	*Intermediate*	*Final*
Group A			
GGT (IU/L)	48.6 (23.1)/46	473.7 (276.2)*/438	328.9 (190.4)**/305
AST (U/L)	23.4 (12.5)/20	100.5 (120)*/67	36.2 (24.1)**/29
ALT (U/L)	34.7 (13.8)/31	119.7 (79.1)*/89	68 (55.5)**/52
Total bilirubin (mg/dl)	0.45 (0.24)/0.37	1.19 (1.16)*/0.65	0.79 (0.58)NS/0.6
ALP (U/l)	85.2 (26.9)/83	281.9 (196.2)*/183	309.9 (360.3)NS/203
Group B			
GGT (IU/L)	49.8 (29.5)/47	270.5 (124.1)*/237	393.2 (271.9)**/282
AST (U/L)	24.6 (18.6)/21	42.9 (27.3)*/35	77.1 (113) NS/41
ALT (U/L)	28.6 (15.2)/24	58.6 (60.7)*/41	94 (122.7) NS/56
Total bilirubin (mg/dl)	0.62 (0.36)/0.61	1.37 (1.42)*/0.82	1.31 (1.85) NS/0.67
ALP (U/l)	82.3 (29.1)/79	189.6 (98.4)*/140	293 (245.8)**/227

*p ≤ 0.05 when compared with initial; **p ≤ 0.05 when compared with intermediate; NS: Not significant.

continues to increase in Phase 2; although only in Group B does it reach significance, while in the taurine-treated group it tends to stabilize.

Moderate AST and ALT elevations take place in both groups, as is the case with GGT and ALP. This may reveal that cholestasis accompanies an incipient steatosis (a benign accumulation of hepatic fat). The significant reductions in AST and ALT that accompany the GGT reduction due to the effect of Taurine may be evidence of an improvement in liver fat mobilization. We do not have histological studies.

It is worth noting that at the Intermediate point total bilirubin reaches values above 1.5 mg/dl in only 9 of 27 patients (max. 5.3 mg/dl), and this number is reduced to 3 (max. 2.5 mg/dl) after taurine treatment. This means that in most cases the intrahepatic Cholestasis was Dissociated Cholestasis.[23] The number of patients in whom total bilirubin was above 1.5 mg/dl was greater in the non-taurine treated group than in the treated one, but even in the final moment it did not reach values above 10 mg/dl in any patient. Given TPN duration in Groups A and B (39.2 ± 17.1 and y 36.4 ± 18.1 days respectively) it doesn't seem strange, given that there are no patients with very long TPN, although it is enough (more than 2.5 times the mean overall duration) to have the aforementioned effects.

Among the results obtained we can highlight that the taurine-treated group's mean GGT value in the Final moment fell 30.56% when compared with the mean value before using a taurine-enriched Aa source in the TPN. On the other hand, in Phase 2 the group without taurine experiences a 50.9% increase.

Septic conditions and SBS, which can favor the onset of cholestasis, were equally distributed between the groups Also, by rejecting primary biliary, pancreatic, or hepatic pathologies, and patients in whom drugs caused any of the initial parameters to be higher than normal, we ensured that both groups did not differ in terms of factors other than TPN.

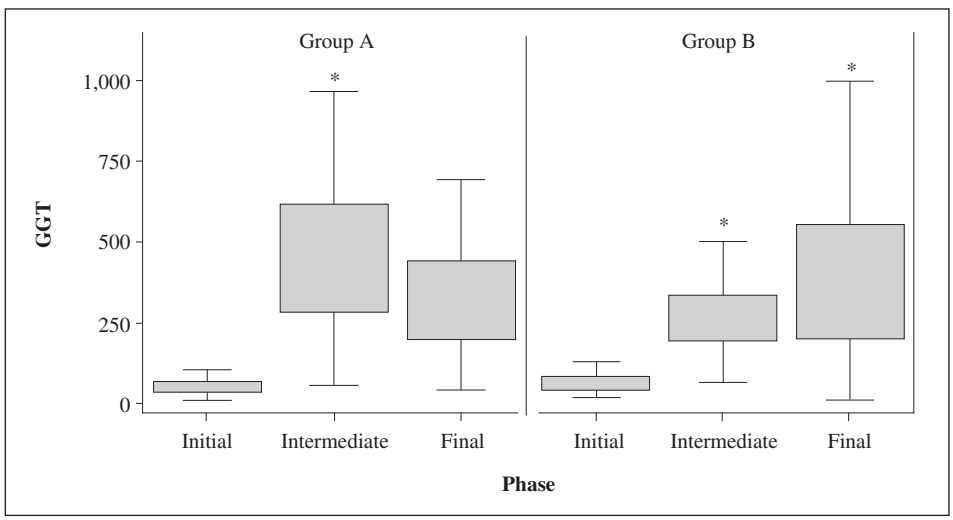


Fig. 1.—GGT Progress (IU/L).

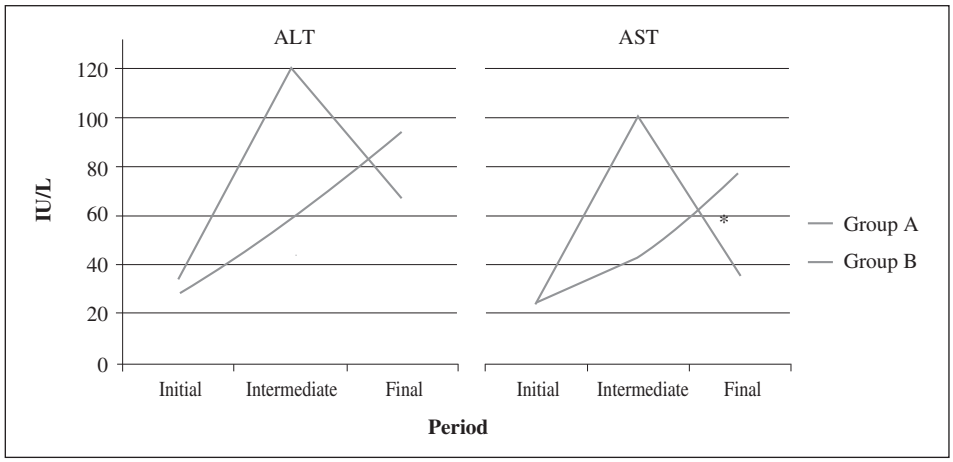


Fig. 2.—Mean ALT and AST values (IU/L) in the different study periods.

The variety in the lipid sources used in both Phases, depicted in table II, can be explained by the clinician in charge choosing between the different diets available in the TPN protocol, case by case recommendations made by the Nutritional Support Team, and even by the possibility of customizing the diets by choosing a certain type of fat. In addition, some standard diets begin with 100% soy LCT fats and after > 15 days of treatment switch, following protocol, to MCT/LCT to reduce cholestatic effects.[40] It may also be due to switching to prepared bags with mixed or structured MCT/LCT or to catered diets with those characteristics. Depending on the clinical condition, they could contain MCT/LCT from the start. During the time the study was being performed we did not have lipid emulsions based on olive oil (OOBE).

We will now raise some considerations about the possible influence of this variability in utilized fats on the results. In Phase 1, 44.4% of patients in the group that in Phase 2 was treated with Taurine received soy LCT, while in the other group this value was 66.7%. However, this difference was not correlated with a smaller increase in the analytical parameters in the group receiving less soy in Phase 1; in effect, the opposite was true. Regarding Phase 2, which measures the effect of Taurine, we see that the most important difference is that 74.1% of patients in Group B received MCT/LCT (mixture or structured), while those in Group A (treated with taurine) 77.8% received SMOF. We may ask ourselves if the lower Phytosterol[41] content of the olive LCT fraction that substituted the soy LCT, or the use of SMOF, could explain the observed effect. This question cannot be answered by this retrospective study, but we prefer to think that such a reduction in soy content (from 50 or 65%, depending on if the MCT/LCT is mixed or structured to 30% in SMOF) is not responsible for the results. This is supported by the observation that the modification in the lipids performed in Phase 2 was not enough to stop the enzymatic increases in Group B patients, and also by the total lipid doses administered, and, finally, patients whose lipid source in Phase 2 that they recieved different source from the mayority of the group, had the same trend in the overall results of each group. There may be a theoretical basis for the use of OOBE or SMOF from the start of TPNs that there is reason to believe will be long-lasting, or if there are other cholestasis risk factors present: it may reduce the incidence and severity of the negative effects due to fats. In any case, studies to determine up to what point OOBE and SMOF are better than the MCT/LCT sources in preventing and/or treating cholestasis or successive and more severe complications associated with TPN have to be designed. Clinical trials to determine what lipid composition is best at preventing or reverting TPN's hepatic toxicity are lacking.[40,41] The study by Puiggross et al.[42] did not show the superiority of any emulsion over the others, but this may be due to its the small number of patients and short duration.

For the reasons explained above, we believe that the administered Taurine dose (22.41 ± 3.57 mg/kg/day) is the main cause of the improvement in the hepatic profile parameters considered. This is so even if we admit the possibility of a synergistic or coadjutant effect between taurine and the change in lipid profile used: in the presence of taurine it was predominantly SMOF (78%) while in its absence it was the MCT/LCT (physical or structured) mixture (74.1%). We are planning a new study in which we will measure the effect of taurine when SMOF is the only source of fat. Our current local protocol for TPN-IC includes taurine and SMOF.

The possibility that standard use of an A.a solution enriched with taurine may reduce the incidence of cholestasis, as well as its cost/benefit ratio and the optimal taurine dose, could be studied.

Conclusions

The 22.41 ± 3.57 mg/kg/day dose of taurine in the TPN's source of amino acids significantly reduces the hepatic profile analytical parameters that define cholestasis. We acknowledge the possibility that the different profiles between SMOF and the MCT/LCT

mixtures may also have had an influence together with taurine.

These results show taurine's hepatoprotective effect and support its use in cases of cholestasis that arise during TPN.

It is worth considering a reduction in the incidence of cholestasis by including taurine from the start in the TPN of patients at risk, as well as in those that are anticipated to be long-lasting or, in any case, to reach 15 days of treatment without any enteral or oral elements.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1908-1915
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Effect of a mixture of inulin and fructo-oligosaccharide on *lactobacillus* and *bifidobacterium* intestinal microbiota of patients receiving radiotherapy; a randomised, double-blind, placebo-controlled trial

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Abstract

Background & aims: **The pathogenesis of enteritis after abdominal radiotherapy is unknown, although changes in faecal microbiota may be involved. In several studies, *Lactobacillus* and *Bifidobacterium* have proven beneficial for the host. Prebiotics stimulate the proliferation of *Lactobacillus* and *Bifidobacterium,* and this may have positive effects on the intestinal mucosa during abdominal radiotherapy.**

Methods: **We performed a randomised double-blind, placebo-controlled trial including 31 patients with gynaecological cancer who received radiotherapy (29 sessions, 52.2 Gy) after surgery. Patients were randomised to two groups: prebiotic and placebo. The first group received a mixture of fibre (50% inulin and 50% fructo-oligosaccharide) and the second received 6 g of maltodextrin twice daily from one week before to three weeks after radiotherapy. *Lactobacillus* and *Bifidobacterium* counts were determined in faeces samples (day –7 before radiotherapy, day 15 of radiotherapy, at the end of treatment, and three weeks after radiotherapy) by culture in selective media and fluorescent in situ hybridization (FISH) using genus-specific probes. Bacterial counts by FISH were significantly higher than by culture method.**

Results: **There were no differences in baseline microbiota between groups. At the end of radiotherapy, we observed a statistically significant decrease in *Lactobacillus* and *Bifidobacterium* counts in both groups. By cultural analysis, we observed higher numbers of *Lactobacillus* and *Bifidobacterium* three weeks after radiotherapy in the prebiotic group (5.6 *vs.* 6.3, p = 0.04 and 5.5 *vs.* 6 log cfu/g, p = 0.03).**

Conclusions: **Abdominal radiotherapy negatively affects Lactobacillus and Bifidobacterium counts. The prebiotic mixture of inulin and fructoligosaccharide can improve the recovery of both genera after radiotherapy.**

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Recibido: 9-VI-2012.
Aceptado: 15-VII-2012.

EFECTO DE UNA MEZCLA DE INULINA Y FRUCTO-OLIGOSACÁRIDO SOBRE LA MICROFLORA INTESTINAL DE LACTOBACILLUS Y BIFIDOBACTERIUM DE PACIENTES QUE RECIBEN RADIOTERAPIA; UN ENSAYO ALEATORIO, A DOBLE CIEGO Y CONTROLADO CON PLACEBO

Resumen

Antecedentes y objetivos: **Se desconoce la patogenia de la enteritis tras la radioterapia abdominal, si bien podrían estar implicados cambios en la microflora fecal. Diversos estudios han demostrado que los *Lactobacillus* y *Bifidobacterium* confieren beneficios al huésped. Los prebióticos estimulan la proliferación de *Lactobacillus* y *Bifidobacterium* y esto podría tener efectos positivos sobre la mucosa intestinal durante la radioterapia abdominal.**

Métodos: **Realizamos un estudio de distribución aleatoria, a doble ciego y controlado con placebo que incluyó a 31 pacientes con cáncer ginecológico que recibieron radioterapia (29 sesiones, 52,2 Gy) tras la cirugía. Se distribuyó al azar a las pacientes en dos grupos: prebiótico y placebo. El primer grupo recibió una mezcla de fibra (50% de inulina y 50% de fructo-oligosacárido) y el segundo 6 g de maltodextrina dos veces al día desde una semana antes hasta 3 semanas después de la radioterapia. Se determinaron los recuentos de *Lactobacillus* y *Bifidobacterium* en muestras fecales (día 7 antes de la radioterapia, día 15 de radioterapia, al final del tratamiento y tres semanas después de la radioterapia) mediante un cultivo en medios seleccionados y con hibridación in situ fluorescente (FISH) con sondas específicas de la especie. Los recuentos bacterianos con FISH fueron significativamente superiores que por el método de cultivo.**

Resultados: **No hubo diferencias en la microflora basal entre los grupos. Al final de la radioterapia, observamos un descenso estadísticamente significativo en los recuentos de *Lactobacillus* y *Bifidobacterium* en ambos grupos. Mediante el análisis de los cultivos, observamos un mayor recuento de *Lactobacillus* y *Bifidobacterium* a las tres semanas de finalizar la radioterapia en el grupo con prebiótico (5,6 frente a 6,3, p = 0,04 and 5,5 frente a 6 log ufc/g, p = 0,03).**

Conclusiones: **La radioterapia abdominal afecta de forma negativa los recuentos de *Lactobacillus* y *Bifidobac-***

Registered under ClinicalTrials.gov Identifier no. NCT01549782

(*Nutr Hosp.* 2012;27:1908-1915)

DOI:10.3305/nh.2012.27.6.5992

Key words: *Prebiotics. Microbiota. Radiotherapy. Gynecological cancer.*

***terium*. La mezcla de prebióticos de inulina y fructo-oligosacárido puede mejorar la recuperación de ambas especies tras la radioterapia.**

Registrado en el ClinicalTrials.gov con el identificador núm. NCT01549782.

(*Nutr Hosp.* 2012;27:1908-1915)

DOI:10.3305/nh.2012.27.6.5992

Palabras clave: *Prebióticos, Microflora, Radioterapia, Cáncer ginecológico.*

Introduction

The human intestine is home to several types of microorganisms, the most common of which is bacteria.[1-2]

It is estimated that a human being has 100 billion bacteria and that more than 95% of this population lives in the gastrointestinal tract, mainly in the colon.

The adult intestine contains 500-1,000 different species of bacteria, with 30-40 species comprising 99% of the total population.[2-3] Culture on selective media shows that strict anaerobic bacteria outnumber aerobes by a factor of 100 to 1,000. The most common genera are *Bacteroides, Bifidobacterium, Eubacterium, Clostridium, Lactobacillus, Fusobacterium*, and various anaerobic Gram-positive cocci. Enterococci and *Enterobacteriaceae* are present in lower numbers.[4]

Some intestinal bacteria strains are pathogenic or become pathogenic when the integrity of the mucosal barrier is broken. However, bacteria strains belonging to *Bifidobacterium* and *Lactobacillus* have been shown to be beneficial for the host.[5-8]

Bifidobacterium constitute up to 25% of the intestinal cultural microbiota of an adult.[9]

The main beneficial effects described in the literature include synthesis of vitamin B, pathogen growth inhibition, decreased intestinal pH and cholesterol levels, protection from intestinal infections, stimulation of intestinal function, and improved immune response.

The positive effects of *Lactobacillus*[10] include pathogen growth inhibition, decreased intestinal pH, and prevention of excessive growth of *Candida*, *Pseudomonas*, *Staphylococcus*, and *Escherichia coli* during antibiotic treatment.

Several disorders are associated with changes in the composition and metabolism of enteric flora.[10] For instance, many acute diarrhoeal diseases are caused by pathogens that proliferate and invade or produce toxins. Antibiotic-associated diarrhoea is due to an imbalance in the composition of intestinal flora with overgrowth of pathogenic species (eg, some strains of *Clostridium difficile)* that produce toxins and cause pseudomembranous colitis. Some authors have shown that putrefaction of proteins in the intestinal lumen is associated with the pathogenesis of hepatic encephalopathy in patients with chronic or acute liver failure.[1]

Abdominal and pelvic radiotherapy (RT) reduces the renewal capacity of the epithelium. Rectal biopsies obtained from patients receiving pelvic RT have revealed atrophy of surface epithelium, acute cryptitis, crypt abscesses, crypt distortion and atrophy, and stromal inflammation.[11] Modifications in intestinal microbiota, such as an increase in the number of pathogens, may contribute to intestinal injury. The factors involved include the volume of bowel in the radiation fields, the fractionation schedule used, the total dose, the radiation technique, and concurrent chemotherapy.

Gibson et al.,[12] recently redefined prebiotics as selectively fermented ingredients in the colon that produce specific changes in the composition and/or activity of gastrointestinal microbiota and have beneficial effects for host health. Therefore, the criteria for defining a prebiotic are resistance to digestion in the small intestine, hydrolyzation, fermentation by colonic microbiota, and selective stimulation of colonic bacteria.

The prebiotic effect of a carbohydrate is assessed by its capacity to stimulate the proliferation of healthy bacteria *(Bifidobacterium*, *Lactobacillus)* rather than pathogenic bacteria *(Clostridium*, *E. coli)*.[1,13] Not all carbohydrates have prebiotic activity,[12,14] and it seems that bacteria prefer to metabolize smaller carbohydrates (oligosaccharides) than larger carbohydrates (polysaccharides). Interest in the fructans inulin and fructo oligosaccharide (FOS) has recently been increasing because of their prebiotic effect, and some authors have demonstrated in vivo and in vitro their beneficial effect on intestinal microbiota.[15-20] Some recent studies suggest that prebiotics that have been designed to produce quite selective changes in the commensal flora may have benefits in irritable bowel syndrome[21-22] and on minimal hepatic encephalopathy.[23]

Our objective was to study the effect of pelvic RT on intestinal microbiota (especially *Lactobacillus* and *Bifidobacterium)* and the effects of a mixture of inulin and FOS on both populations and on the intestinal mucosa (desquamation, inflammation) by using both, cultural and molecular methods.

Subjects and methods

Study group

The inclusion criteria for participation in the study were female gender, age ≥ 18 years, and a diagnosis of

gynaecologic cancer requiring postoperative pelvic RT. The exclusion criteria were previous RT, previous or adjuvant chemotherapy, other types of pelvic tumours or other gynaecologic malignancies, antibiotic or inmunosuppressive treatment one week before inclusion or during treatment, and the presence of acute or chronic gastrointestinal disease contraindicating ingestion of the fibre. RT was administered using a linear accelerator (15 Mv). The patients were in the supine position when RT was delivered using a four-field technique or in the prone position when RT was delivered using a two-field technique. A pelvic plane computed tomography scan was performed with the patient in the treatment position and 5-mm slices were obtained.

The clinical volume was the surgical field and the areas potentially harbouring microscopic disease, namely, the vagina, the obturator externus, and the internal, external, common iliac, and presacral lymph node areas. Para-aortic areas were included when indicated (ie, when periaortic or iliac biopsy samples were positive and when no periaortic lymph node biopsy samples were available).

Patients received a dose of 1.8 Gy/d, five times weekly for 29 days. The total prescribed dose was 52.2 Gy. Heterogeneous dose distribution was ensured by following the International Commission on Radiation Units and Measurements (Report 50).

Brachytherapy was administered one week later at low doses and using individual moulds when there was involvement of the cervix or lymph-vascular space. When the results of peritoneal cytology or cytology for serous carcinoma were positive, we used whole abdominal radiation, limiting the renal dose to ≤ 20 Gy and the hepatic dose to ≤ 28 Gy at 0.8 Gy/fraction, two fractions daily, five days per week. The pelvic region was treated with 56 Gy using the same fractional dose (70 fractions, 35 days).[24]

All patients provided written informed consent to participate in the study. The study was performed in accordance with the Declaration of Helsinki and Spanish laws on scientific research, and was approved by the local Ethics Committee.

Clinical study

This was a randomised double-blind placebo-controlled clinical trial in two parallel groups.

At the first visit, patients were randomised to receive either 6 g twice daily for a mixture of fibre (50% inulin and 50% FOS) (Raftilose® Synergy 1 Orafti, Tienen, Belgium) or the same amount of matching placebo (maltodextrin). Both products were prepared by Vegenat SA (Badajoz, Spain) and supplied in coded sachets (double-blind study). Fibre and placebo in powder form were dissolved in 200 ml of water.

After randomisation, the patients underwent a 1-week run-in period before starting RT and continued taking the same products throughout the treatment course, until three weeks after RT was finished. Also, written recommendations including exclusion of fibre and lactose were given to all patients to homogenize their diet. Patients were not permitted to eat foods produced by fermentation during treatment. The use of other prebiotics and probiotics were excluded.

Concomitant pharmacotherapy with antimotility drugs, immunosuppressors, or antibiotics was not permitted. The need for any of these treatments led to the patient being withdrawn from the study.

Stool samples were collected four times: day –7 before starting RT, day 15 after starting RT, at the end of RT, and three weeks after RT was finished. The *Lactobacillus* and *Bifidobacterium* counts were analyzed to study changes in intestinal microbiota. Faecal calprotectin was measured as a marker of intes 163 tinal inflammation[25-26] and faecal DNA as a marker of epithelial desquamation.[27] Stool samples were rapidly frozen and conserved at -30º C.

Patients were followed weekly in a specific nutrition outpatient department for patients receiving radiotherapy. The total duration of the study for each patient was three months.

Microbiological studies

Enumeration of *Bifidobacterium* and *Lactobacillus* cells by culturing

Faeces diluted (1:10) in PBS 1x (130 mM sodium chloride, 10 mM sodium phosphate (pH 7.2) were homogenized in a stomacher Lab-Blender 400 (Seward Medical, London, UK) for 2 min. Serial dilutions ranging from 10-2 to 10-8 from homogenized fecal samples were plated on the appropriate agar media in duplicate. Lactobacilli were enumerated on MRS Agar (Man, Rogose and Sharpe, Merck) and incubated in a 5% CO2 atmosphere at 35° ± 2° C for 48 hours. Bifidobacteria were enumerated on selective media: BFM Agar[28] and Beerens agar (Oxoid). The plates were anaerobically incubated at 37° C for 72 hours. Duplicate plate values were averaged and bacterial densities were expressed as the log10 of the number of CFU/g wet weight of faeces.

Enumeration of *Bifidobacterium* and *Lactobacillus* cells by FISH

Total *Lactobacillus* and *Bifidobacterium* counts were also determined by fluorescent *in situ* hybridization using genus-specific probes.[29-30] The Bif164 genus specific probe was used to target all *Bifidobacterium* species and the LAC158 probe was selected for the specific hybridization of *Lactobacilli.*[31] Probes sequences were confirmed to match with *Lactobacilli*

and *Bifidobacterium* by the gapped Probe Match at RDP II (Michigan State University) and by a BLAST (National Center for Biotechnology Information [http://www.ncbi.nlm.nih.gov/blast/]) search. Although the LAC158 probe also measure enterococci, lactobacilli were discriminated from those because of the cell shape and size. The EUB 338 universal probe, complementary to a region of 16S rRNA of the domain *Eubacteria* was used only as a positive hibridization control to select all bacteria present in the sample.[32] Specificity of the probes was tested by fluorescent *in* situ hybridization (FISH) of different *Bifidobacterium*, lactic acid bacteria (LAB) reference strains and LAB isolates from dairy products. Probes were synthesized and labelled with FITC and CY3 by MOLBIOL (Berlin, Germany).

To establish the optimal conditions of FISH analysis, 1 g from each sample of faeces was diluted in 9 ml of PBS buffer (130 mM sodium chloride, 10 mM sodium phosphate, [pH 7.2]). 1 ml of the mixture was then centrifuged (1,000 x g, at 4°C for 10 min followed by 4,000 x g, at 4° C for 10 min), resuspended in PBS buffer and fixed with three volumes of 4% paraformaldehyde at 4º C for 2 h. Subsequently, fixed samples were centrifuged again, washed with PBS buffer and finally resuspended in 1:1 PBS/ethanol (vol/vol).

An aliquot of 5 l fixed bacteria was placed on a gelatine-coated slide, air dried, dehydrated (50, 80, 100% ethanol) and hybridized as described by Amann et al.[33] LAB fixed cells were permeabilized by adding 10 l of a 50 mg.ml-1 lysozyme solution for 30 minutes. To provide a specific hybridization to the target organisms, a final concentration of formamide was established at 20 % in the hybridization buffer (0.9 M NaCl, 0.01% SDS, 20 mM Tris-HCl, pH 7.6).

Slides were mounted with FluoroGuard Antifade Reagent (Bio-Rad) and visualized by Olympus BX50 microscopy system with filters U-MWIB and U-MWIG. Digital colour micrographs were done by PM10SP camera (Olympus Optical CO., Germany). A minimum of 20 fields were counted.

Effect on the inflammation

Calprotectin concentrations as a marker of inflammation were determined using a calprotectin enzyme-linked-immunosorbent assay that measured leucocytes in faeces.[34] The results are expressed as micrograms of calprotectin per gram of faeces.

Faecal DNA was quantified by real-time polymerase chain reaction of a sequence of the human β-globin gene,[27] which makes it possible to estimate the number of desquamated cells in stool. The results of DNA excretion in faeces are expressed as copies/g of dry faecal weight.

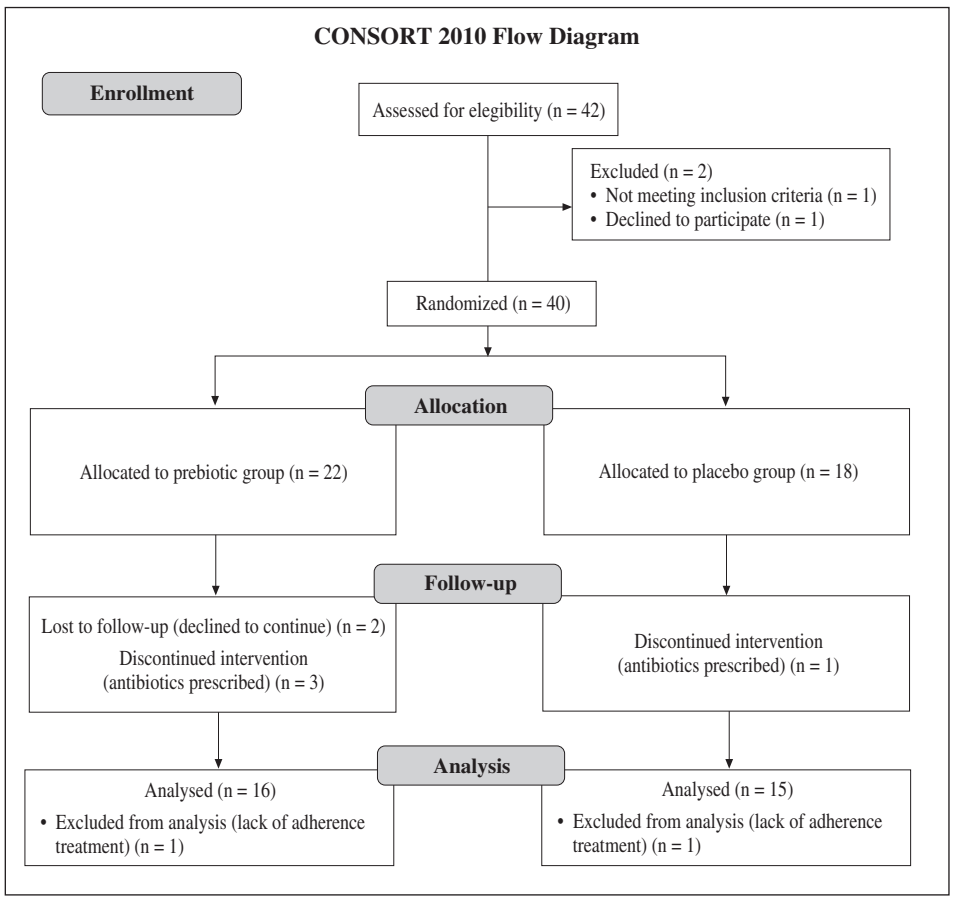


Fig. 1.—Flow chart.

Table I
Patient characteristics at baseline

	Prebiotic mixture group		*Placebo group*		*p*
	Patient (n)	*Median (range) or %*	*Patient (n)*	*Median (range) or %*	
Age (y)	16	59 (43-77)	15	59 (36-75)	0.19+
Weight (kg)	16	75.4 (54.4-98.2)	15	79 (65-91)	0.51+
Primary tumour site					0.21-
Endometrium	13/16	81.25	12/15	80	
Cervix	2/16	12.5	0/15	0	
Uterus	1/16	6.25	2/15	13.3	
Vulva-vagina	0/16	0	1/15	6.7	
Lymphadenectomy					1.0×
Yes	11/16	68.75	11/15	73.3	
No	5/16	31.25	4/15	26.7	

+Mann-Whitney U test.
-Likelihood ratio.
×Fisher exact test.

Statistical analysis

Categorical variables were expressed as relative frequencies and percentages. Quantitative variables were expressed as the median and range (maximum and minimum). The size of the *Lactobacillus* and *Bifidobacterium* counts was expressed logarithmically according to the type of data and in order to better appreciate the results.

Non-parametric tests were used due to the type of variable and the small sample size.

Statistical analysis was performed with the statistical package SAS, version 9.1.

Significance was set at $p < 0.05$.

Results

Between June 2005 and December 2007, a total of 40 patients were randomly allocated to the prebiotic mixture or placebo. Nine patients were excluded from the study: four because they were prescribed antibiotics, three for personal reasons, and two due to lack of adherence. Flow chart is showed in figure 1. The remaining 31 patients constituted the study population: 16 received the prebiotic mixture and 15 received the placebo. In general, the prebiotic mixture was well tolerated. Only one patient complained of abdominal distension.

Mean age was 58 years (36-77 years). All patients were diagnosed with gynaecological cancer and had undergone surgery. The baseline characteristics are shown in table I.

Both groups were well matched according to standard variables.

Our results show that RT negatively affected the *Lactobacillus* and *Bifidobacterium* viable counts in both groups. A statically significant decrease in *Lactobacillus* and *Bifidobacterium* counts was observed in both groups (table II). However, recovery of the *Lactobacillus* and *Bifidobacterium* viable counts was statistically significant in patients treated with the prebiotic mixture after three weeks of treatment (figs. 2 and 3).

Table II
Changes in the Lactobacillus *and* Bifidobacterium *counts*

	Day -7 before RT	*End of RT*	*p+*
Lactobacillus			
Prebiotic group	5.9 (3-7.4)	5.6 (2-7.1)	0.007
Placebo group	5.9 (3-7.9)	5 (2-7.1)	0.05
Bifidobacterium			
Prebiotic group	5.1 (2.8-7.9)	4.5 (3-7.2)	0.036
Placebo group	5.7 (1-8.1)	4.6 (3-7.3)	0.011

+Wilcoxon test.

Viable *Lactobacillus* counts between the both groups (fig. 2), show an statistically significant increase in viable

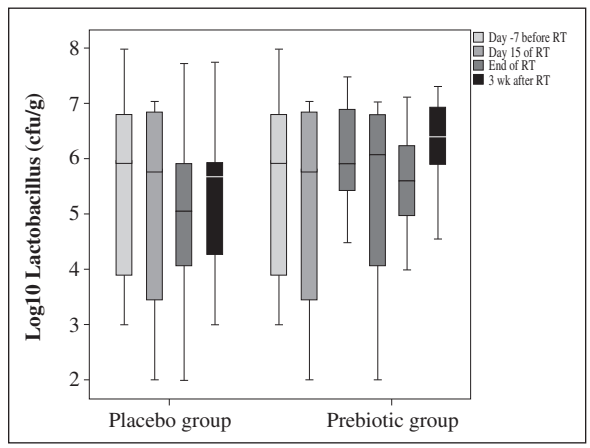


Fig. 2.—Changes in viable Lactobacillus during the study in both groups.

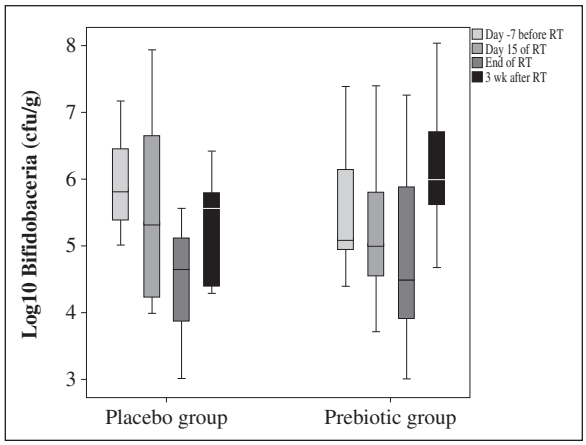


Fig. 3.—Changes in viable Bifidobacterium during the study in both groups.

Lactobacillus count for the prebiotic group at three weeks after RT. However, there were no differences in the total number of *Lactobacillus* cells measured by FISH (fig. 4).

Figure 3 shows the progress of viable *Bifidobacterium* counts in both groups during the study. Once again, we observed statistically significant differences 3 weeks after RT had finished. We did not observe differences in the total number of *Bifidobacterium* cells (fig. 5).

FISH enumeration showed that the prebiotic group maintained higher *Lactobacillus* and *Bifidobacterium* counts during treatment than the placebo group (figs. 4-5).

There were no statistically significant differences in calprotectin levels between the groups during treatment.

We did not observe statistically significant changes in DNA between the groups during treatment.

The patients were tested for the presence of *Clostridium difficile* and none were infected.

Discussion

Although no significant changes in the total number of *Lactobacillus* was observed along the treatment, there was a difference in the response of the viable counts indicating more resistance to RT or an increase of the rate of reproduction. Population levels of *Bifidobacterium* varied during the treatment period with a significant increase in both, viable and total counts. These results are in line with those obtained by Gibson et al.[17] who reported that prebiotics stimulate the multiplication or activity of some bacterial groups as *Lactobacilli* or *Bifidobacterium*. Other prebiotics are used to selectively stimulate the growth and activity of *Lactobacilli* and *bifidobacteria* in the colon. However, there is little infor-

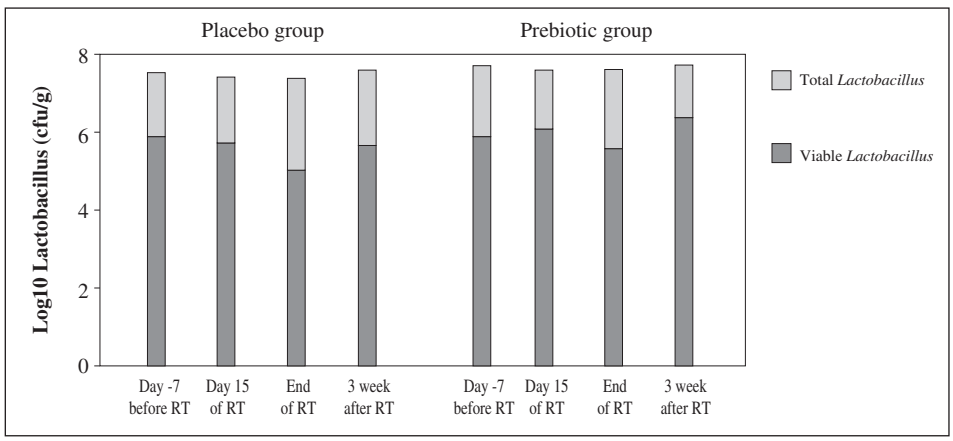


Fig. 4.—Evolution of Total and Viable Lactobacillus during the study.

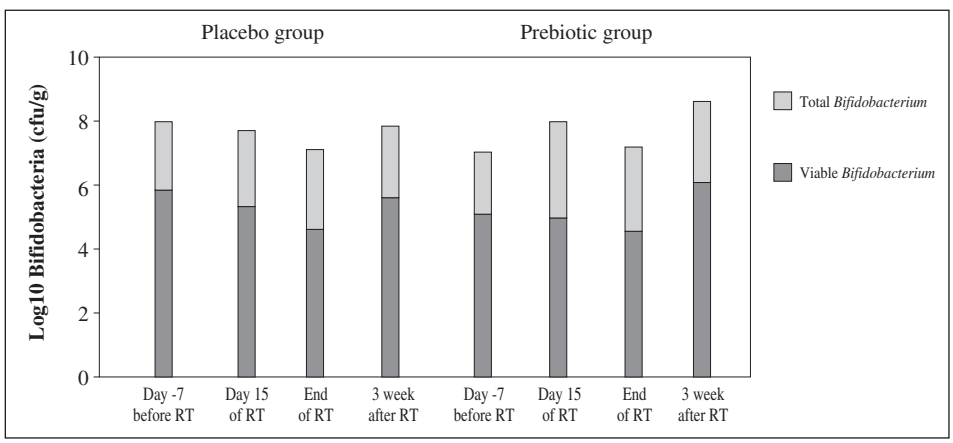


Fig. 5.—Evolution of Total and Viable Bifidobacterium during the study.

mation on the mechanisms whereby prebiotics exert their specific effects upon such microorganisms.[36]

Therefore, these results seem to indicate that, as soon as the microbiota recovers, the patient experiences fewer intestinal complications. Both inulin and FOS have proven beneficial in conditions such as pouchitis and ulcerative colititis. In one placebo controlled clinical trial 20, twenty patients with pouchitis received 24 g of inulin or placebo daily for three weeks. Dietary supplementation with inulin increased butyrate concentrations, lowered pH, decreased numbers of *Bacteroides fragilis*, and diminished concentrations of secondary bile acids in faeces. This was associated with a significant reduction in the endoscopic and histological scores of mucosal inflammation in the ileal reservoir. Furthermore, a recent study[37] analyzed a synbiotic preparation combining a probiotic *(Bifidobacterium longum)* and FOS-enriched inulin (12 g of Synergy 1 per day) in a one-month double-blind randomised controlled trial involving 18 patients with active ulcerative colitis. After treatment, expression of inflammatory cytokines in rectal biopsies was significantly reduced in the synbiotic group but not in the placebo group.

There were no statistically significant differences in calprotectin levels between the groups during treatment. Calprotectin is a calcium-binding protein found in neutrophilic granulocytes. It resists metabolic degradation and is easily measured in faeces. Faecal calprotectin levels can successfully predict relapses in patients with inflammatory bowel disease.[27]

Excretion of human DNA in faeces is another surrogate marker of intestinal inflammation.[38] We did not observe statistically significant changes in DNA between the groups during treatment.

In our opinion, the improvements in the radiotherapy techniques have influenced the results obtained in the markers of intestinal inflammation. So, patients presented less intestinal damage.

The mixture of inulin and FOS is used because these fibres are well-defined prebiotics that can increase *Lactobacillus* and *Bifidobacterium* counts in human colonic lumen.[29]

We used a mixture of 6 g of inulin and 6 g of FOS, which is similar to doses administered in other studies.[39-40] A number of controlled clinical trials have shown that prebiotics are safe and may be effective in the prevention of acute gastrointestinal conditions.[39,41-43]

Our study shows that Synergy 1 is well tolerated by patients.

Further studies with larger samples are needed to investigate the clinical effects of the prebiotic in patients receiving abdominal RT. Nowadays; our group is performing a study evaluating the clinical effects of prebiotics in gynaecological cancer patients treated with RT that includes clinical variables and a quality of life questionnaire.

In conclusions, results of our randomised controlled trial suggest that abdominal RT produces a significant decrease in *Lactobacillus* and *Bifidobacterium* counts. The prebiotic mixture Synergy 1 stimulates bacterial reactivation and enables both populations to recover at the end of RT.

Acknowledgements

This work was supported in part by grants from Vegenat (Spain).

Statement of authorship

PG designed the study, carried out the data analyses and drafted the manuscript. CV participated in the carried out of the study, performed the statistical analysis and helped to draft the manuscript. MAL was the patients' radiotherapist and participated in the design of the study. YM carried out the analysis of *Lactobacillus and Bifidobacterium*. LP carried out the study. CC participated in the design of the study and helped to draft the manuscript. MC and IB participated in the design of the study. JGH helped to draft the manuscript. FG participated in the design of the study and carried out with the analysis of calprotectin and DNA. MH participated in the design of the study and carried out with the analysis of *Lactobacillus and Bifidobacterium*.

All authors read and approved the final manuscript. Authors have no conflict of interest.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1916-1927
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Effects of dietary restriction combined with different exercise programs or physical activity recommendations on blood lipids in overweight adults

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Abstract

Background and aim: **Many exercise studies, although generally showing the beneficial effects of supervised aerobic, resistance or combined exercise on blood lipids, have sometimes reached equivocal conclusions. The aim of this study is to evaluate the impact of different programs that combined exercise and dietary restriction on blood lipids versus a clinical practice intervention for weight loss, in overweight adults.**

Methods: **For this study 66 subjects participated in a supervised 22 weeks training program, composed of three sessions per week and they were randomized in three groups: strength training (S; n = 19), endurance training (E; n = 25), a combination of E and S (SE; n = 22). Eighteen subjects served as physical activity group (PA) that followed a clinical intervention consisted of physical activity recommendations. All groups followed the same dietary treatment, and blood samples were obtained for lipids measurements, at the beginning and end of the study.**

Results: **Lipid profile improved in all groups. No significant differences for baseline and post-training values were observed between groups. In general, SE and PA decreased low-density lipoprotein cholesterol (LDL-C) values ($p < 0.01$). S decreased triglyceride levels ($p < 0.01$) and E, SE, and PA decreased total cholesterol levels ($p < 0.05$, $p < 0.01$ and $p < 0.01$, respectively).**

Conclusions: **These results suggest that an intervention program of supervised exercise combined with diet restriction did not achieved further improvements in blood lipid profile than diet restriction and physical activity recommendations, in overweight adults.**

(Clinical Trials gov number: NCT01116856).

(*Nutr Hosp.* 2012;27:1916-1927)

DOI:10.3305/nh.2012.27.6.6057

Key words: *Lipoprotein. Overweight. Strength training. Aerobic training. Combined training. Supervised exercise. Physical activities recommendations.*

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Recibido: 14-VII-2012.
Aceptado: 28-IX-2012.

EFECTOS DE LA RESTRICCIÓN DIETÉTICA COMBINADA CON DIFERENTES PROGRAMAS DE EJERCICIO O ACTIVIDAD FÍSICA SOBRE LOS LÍPIDOS SANGUÍNEOS EN ADULTOS CON SOBREPESO

Resumen

Antecedentes y objetivo: **Muchos estudios sobre ejercicio han proporcionado en ocasiones conclusiones equívocas, si bien, por lo general, han demostrado los efectos beneficiosos del ejercicio supervisado aeróbico, de resistencia o combinado. El propósito de este estudio fue evaluar el impacto de diferentes programas que combinan ejercicio y restricción dietética sobre los lípidos sanguíneos frente a una intervención de la práctica clínica de pérdida de ejercicio en los adultos con sobrepeso.**

Métodos: **En este estudio participaron 66 individuos en un programa de entrenamiento supervisado de 22 semanas, compuesto por tres sesiones semanales y, posteriormente, se les distribuyó al azar en tres grupos: entrenamiento de fuerza (F; n = 19), entrenamiento de resistencia (R; n = 25), o una combinación de R y F (FR; n = 22). Diecioho sujetos sirvieron como grupo de actividad física (AF) que siguió una intervención clínica que consistía en recomendaciones de actividad física. Todos los grupos siguieron el mismo tratamiento dietético y se obtuvieron muestras de sangre para medición de lípidos al inicio y al final del estudio.**

Resultados: **El perfil lipídico mejoró en todos los grupos. No se observaron diferencias significativas basales ni tras el entrenamiento entre los grupos. Por lo general, el FR y la AF disminuyeron los valores de lipoproteínas de densidad baja-colesterol (LDL-C) ($p < 0,01$). El F disminuyó los valores de triglicéridos ($p < 0,01$) y el R, FR y AF disminuyeron las concentraciones de colesterol total ($p < 0,05$, $p < 0,01$ y $p < 0,01$, respectivamente).**

Conclusiones: **Estos resultados sugieren que la intervención con un programa de ejercicio supervisado combinado con la restricción dietética no proporcionó mejorías en el perfil lipídico con respecto a la restricción dietética y las recomendaciones de actividad física, en adultos con sobrepeso.**

(Núm. de registro en Clinical Trials Gov: NCT01116856).

(*Nutr Hosp.* 2012;27:1916-1927)

DOI:10.3305/nh.2012.27.6.6057

Palabras clave: *Lipoproteína. Sobrepeso. Entrenamiento de fuerza. Entrenamiento aeróbico. Entrenamiento combinado. Ejercicio supervisado. Recomendaciones de actividades físicas.*

Abbreviations

S: Strength training group.
E: Endurance training group.
SE: Strength + Endurance combined training group.
PA: Diet and physical activity recommendations group.
VO_2peak: Peak oxygen uptake.
PRONAF: Programas de Nutrición y Actividad Física para el tratamiento del sobrepeso y la obesidad).
HULP: Hospital Universitario La Paz.
HRR: Heart rate reserve.
HRmax: Maximal heart rate.
RM: Repetition máximum.
DEE: Daily energy expenditure.
HPA: Physical activity

Introduction

Many exercise training studies, although generally showing the beneficial effects of aerobic, resistance or combined exercise on plasma lipids and lipoproteins, have sometimes reached equivocal conclusions. The results of initial studies of strength training in coronary risk factors showed evidence that high intensity strength training improved blood lipid profile, with any diet counseling.[1] Strength training protocol suggested that this exercise without diet could improve HDL-C levels in overweight and obesity men, while diet alone did not.[2] Other study without diet intervention have reported increases in HDL-C ranging from 9% to 15% with endurance training, while strength and combination did not results in any significant changes in any of the blood lipid variables [3]. Some investigators found no differences in the blood lipid profile improvements obtained among endurance, strength, combined training and diet and diet alone intervention.[4,5] Previous studies have suggested a relationship between endurance and combined training, without diet intervention, and favorable blood lipid profile in men and women.[6] On the other hand, dietary and caloric intake interventions alone have shown clinical evidence about its influence on plasma lipid and lipoprotein levels.[4,5,7,8]

At present there are many studies including behavior strategies based in diet and exercise advice, but there is limited evidence that such "standard lifestyle interventions" including specific recommendations for informal physical activity, improve metabolic abnormalities.[9,10] Therefore, it is not so far clear if supervised exercise may contribute to reach health goals better than following standard recommendations.

The PRONAF Study *(Programas de Nutrición y Actividad Física para el tratamiento del sobrepeso y la obesidad)* is a research project in nutrition and physical activity programs for overweight and obesity, developed in Spain in several years of intervention. The design and protocol includes three exercise modes (endurance, strength and combined training) and diet restriction, in a randomized control trial concerning diverse health status variables. A particular characteristic in the methodology is to include a group that follows the principles of hospital clinical practice for lifestyle changes (diet and physical activity recommendations) when treating patients for weight loss management. This way the PRONAF study will provide harmonized and comparable data on exercise effects on blood lipid profile, which is the purpose of this particular study here presented.

Therefore our study attempts to evaluate the impact of different supervised exercise modes with diet restriction on lipid profile versus the habitual weight loss intervention clinical practice with physical activity recommendations included, in overweight men and women.

Materials and methods

Participants

A group of 119 middle-aged (range 18-50 years) men (n = 46) and women (n = 73) volunteered to participate in this study (table I). Figure 1 shows the flow diagram of the PRONAF study. Of the initial 1568 subjects who reported to the advertisement, 84 only completed the study and were included in the final analysis. The subjects were recruited using a wide variety of techniques, including newspapers, radio, mailers, and posters. Inclusion criteria required to be healthy, overweight [body mass index (BMI) 25-29.9 $kg \cdot m^{-2}$], nonsmokers, sedentary (one or less exercise bout per week), not on a diet program, normoglycemic and women had regular menstrual cycles. The voluntary participants who fulfilled the inclusion criteria and passed the baseline physical examination were stratified by age and sex and randomly divided into four groups: diet and supervised strength training [strength training group (S)], diet and supervised endurance training [endurance training group (E)], diet and supervised combined strength and endurance training [combined strength and endurance training group (SE)] or diet and physical activity recommendations (PA).

After receiving written and oral information about the project and possible risks and benefits of the experimental protocol, the participants read and signed an institutionally approved informed consent document, in agreement with the guidelines of the Declaration of Helsinki regarding research on human subjects. The study was approved by the Human Research Review Committee of the *Hospital Universitario La Paz* (HULP) (PI-643).

Study design

This study was an intervention trial of 24 week duration. The measurements took place in the first week

Table I
Subjects' characteristics at baseline

	Men		*Women*		*Total*	
	n = 37		*n = 47*		*n = 84*	
	n	*Mean ± SD*	*n*	*Mean ± SD*	*n*	*Mean ± SD*
Age (years)						
S	7	35.5 ± 9.2	12	36.4 ± 8.6	19	36.1 ± 8.7
E	10	34.6 ± 8.3	15	36.4 ± 7.9	25	35.8 ± 8
SE	12	37.1 ± 7.7	10	34.7 ± 6.9	22	36 ± 7.3
PA	8	36.2 ± 8.6	10	37.2 ± 9.3	18	36.8 ± 8.9
Weight (kg)						
S		92.7 ± 10.7		76.2 ± 8.6		81.4 ± 12,0
E		89.3 ± 10		74.9 ± 6.6		80.1 ± 10.5
SE		86.1 ± 8.8		72.5 ± 7.6		79.6 ± 10.6
PA		88.1 ± 7.2		74.8 ± 5.8		80.4 ± 9.2
BMI (kg/m²)						
S		29.9 ± 2.7		29.8 ± 1.7		29.8 ± 2
E		29.2 ± 1.1		28.8 ± 1.9		29 ± 1.7
SE		28.2 ± 1.8		28.2 ± 1.5		28.2 ± 1.7
PA		29 ± 1.4		27.7 ± 1		28.3 ± 1.3
Body fat (%)						
S		39.5 ± 6.8		40.5 ± 6.8		40.1 ± 6.7
E		39.5 ± 5.7		39.9 ± 6.4		39.7 ± 6.1
SE		39.2 ± 6.8		36.5 ± 5.6		37.8 ± 6.2
PA		40.8 ± 3.2		40 ± 6.8		40.4 ± 5.2
Body fat free (kg)						
S		48.9 ± 9		46.1 ± 11.4		47.2 ± 10.4
E		44.9 ± 8.9		46 ± 8.8		45.6 ± 8.6
SE		45.4 ± 8.1		50.1 ± 10		47.8 ± 9.3
PA		45.6 ± 6.8		46.4 ± 9.2		46 ± 7.9
VO_{2peak} (mL/kg/min)						
S		36,0 ± 8.7		27.5 ± 3.6		30.5 ± 7.1
E		38.4 ± 4.7		27.1 ± 3.2		30.9 ± 6.5
SE		38.3 ± 5.3		29.5 ± 5.7		34.1 ± 7
PA		30.7 ± 6.1		30.7 ± 6.1		30.7 ± 6.1

Data are shown as mean ± SD.
S: Strength group; E: Endurance group; SE: Combined strength and endurance group; PA: Physical activity recommendations group. BMI: Body Mass Index; VO2peak: Peak oxygen uptake.

(baseline values) for all subjects before starting training, and 22 weeks of training later, in 24th week (post-training values). Once the first group started the pre-evaluation week, each group started sequentially (fig. 2) maintaining the same periodization. Adherence criteria for diet and exercise were took into account to determine final analyzed subjects (table I).

Diet

Diet prescription was performed for all patients by expert dieticians in the Nutrition Department of HULP. All groups underwent an individualized and hipocaloric diet (between 1,200 and 3,000 kcal). Diet was lowered a 25% from Daily Energy Expenditure (DEE)[11] measured using SenseWear Pro Armband™ data. Macronutrient distribution consisted of 29-34% of energy from fat, 12-18% from protein, and 50-55% from carbohydrates, according to recommendations.[12] A dietitian interviewed each participant at baseline, 3 months, and 6 months and reviewed a 3-day food record diary. An adherence to diet of 90% was elicited and was calculated with 72-hour recall.[13]

Exercise training

The different exercise groups followed the corresponding, supervised training program of 22 weeks, which consisted in all cases of three sessions per week. All training sessions were carefully supervised by certified personal trainers. An adherence to training of 90% was demanded. The exercise programs were designed taking into account each subject's muscle strength (MS) and the heart rate reserve (HRR). MS

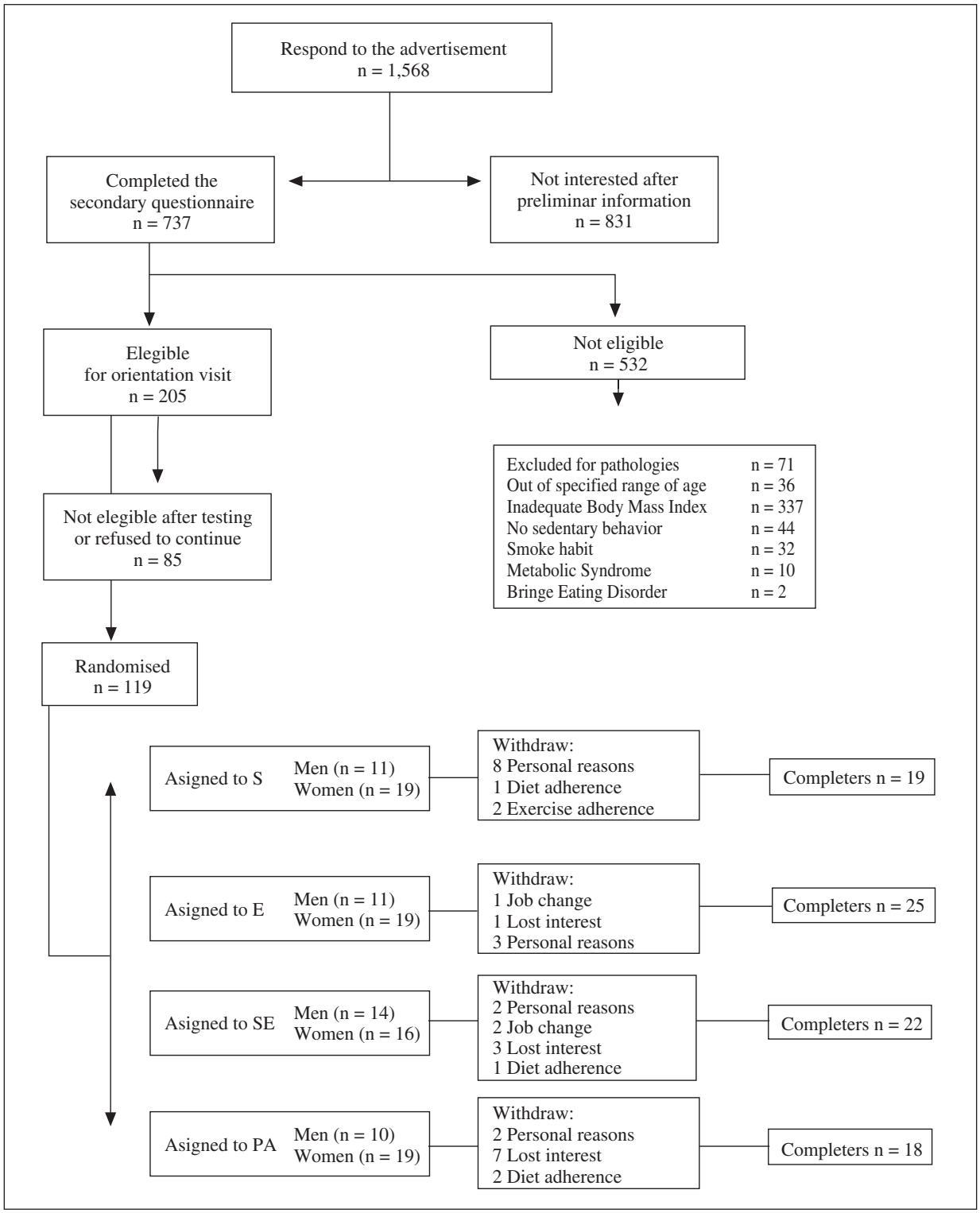


Fig. 1.—Participant flow diagram in the PRONAF study. A total of 1,568 were screened, of whom 119 were randomized into the PRONAF study. The dropout rates in the groups were: strength group (S) was 36.6%, endurance group (E) was 16.6%, combined group (SE) was 26.6% and physical activity recommendations group (PA) was 37.9%.

was measured using the 15-repetition maximum (15 RM) testing method,[14] in the S and SE groups (both of which involved strength training). The 15 RM for each exercise in each program was recorded twice on different days during the pre-intervention subject strength evaluation period. The intraclass correlation coefficient of reliability for all exercises was ICCr = 0.995 and ICCr = 0.994 for the men and women respectively (groups S and SE

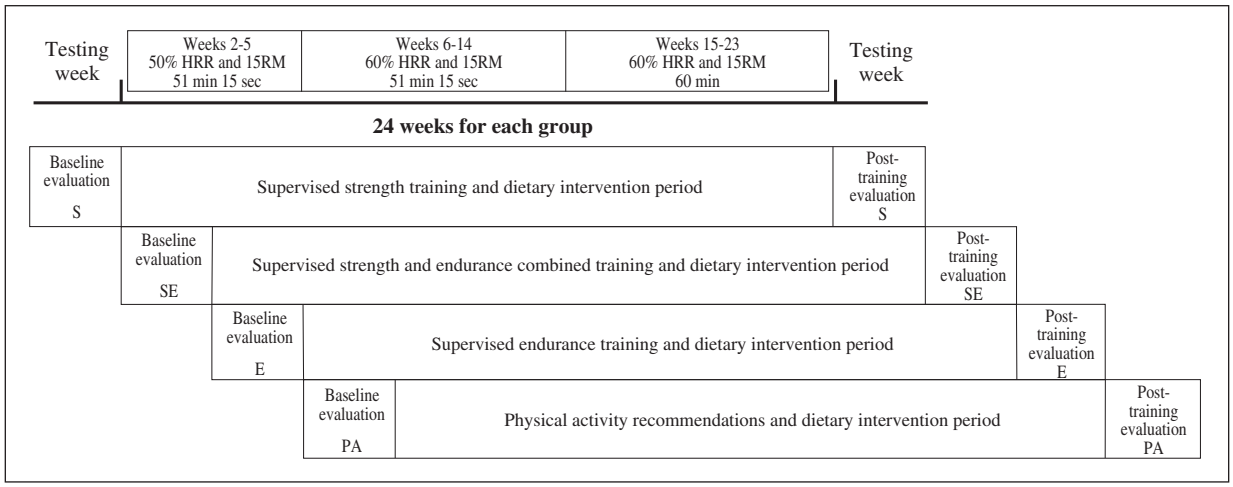


Fig. 2.—Study design. Pre and post-evaluation (baseline and post-training evaluation) week consisted of the same tests: peak oxygen uptake test (O_{2peak}) test, habitual physical activity, blood analysis, body composition, diet prescription and 15RM. Top bar shows intensity (HRR and RM) and volume (minutes) progression during 22 week.

subjects together). All the assessments and trainings were carried out with the same machines and free weights (Johnson Health Tech. Iberica, Matrix, Spain). Heart rate reserve (HRR) was also calculated to prescribe exercise intensity plus resting heart rate for E and SE interventions programs.[15,16]

The intensity of exercise was increased over the study period. In weeks 2-5 exercise was at an intensity of 50% of the 15RM and HRR, and lasted an overall 51 min and 15 s (twice around the circuit, lasting 7 min 45 s each lap). In weeks 6-14 exercise was performed at an intensity of 60% of 15RM and HRR, again with a duration of 51 min and 15 s (again, twice around the circuit). Finally, in weeks 15-23, exercise was performed at an intensity of 60% of 15RM and HRR, with a duration of 64 minutes (three times around the circuit). The recovery period between circuits was set at 5 min. Participants performed 15 repetitions (45 s) of each exercise with a rest period of 15 seconds between them.

Each training session for the strength, endurance + combined strength and endurance training commenced with a 5 min aerobic warm-up, followed by the main session exercises, and concluded with 5 min of cooling down and stretching exercises. In addition, each session was monitored for HR and Rate of Perceived Exertion (RPE) scale. In all sessions the exercise rhythm was controlled by instructions recorded on a compact disk. The cadence for the resistance exercises was fixed at 1:2 (concentric-eccentric phase).

Feedbacks for training loads were done once a month with the RPE to subjectively evaluate each session and determine where the participant considered the intensity to be at, following a similar methodology as used elsewhere.[17]

Endurance training group (E). The E group training involved the use of a treadmill, exercise bike or cross trainer.

Strength training group (S). The S group followed a circuit involving the following eight exercises: shoulder press, squat, barbell row, lateral split, bench press, front split, biceps curl, and French press for triceps.

Strength and endurance training group (SE). The SE group performed a combination of cycle ergometry, treadmill or cross trainer work, plus weight training with the following exercises intercalated: squat, row machine, bench press and front split.

Physical activity recommendations group (PA). These participants followed the habitual hospital clinical practice. This means the same dietary intervention as the training groups plus general recommendations in physical activity (ACSM),[18] without being supervised and regulated. The control of lifestyle changes was registered with accelerometer, just as real clinical health practitioners at hospital units.

Data collection

Body composition. Body composition was assessed by dual-energy x-ray absorptiometry DXA (GE Lunar Prodigy; GE Healthcare, Madison, WI, GE Encore 2002, version 6.10.029 software) and was used to measure total body fat (%) and body fat free (kg) mass.

Anthropometric measures included height (stadiometer SECA; range 80-200 cm), body mass (BC-420MA. Bio Lógica. Tecnología Médica SL) and body mass index (BMI) calculated as [body weight (kg)/(height (m))^2].

Peak oxygen uptake test. Peak oxygen uptake (O_{2peak}) was measured using the modified Bruce protocol. The test was conducted on a computerized treadmill (H/P/COSMOS 3P® 4.0, H/P/Cosmos Sports & Medical, Nussdorf-Traunstein, Germany). Volume and composition of expired gas measure was carried out with a gas analyzer Jaeger Oxycon Pro (Erich Jaeger, Viasys Healthcare, Germany) and continuous 12-lead electrocardiographic monitoring. The exercise test was maintained until exhaustion. The mean of the

last three highest rates of oxygen consumption was used as $O_{2peak.}$

Habitual physical activity. Habitual physical activity (HPA) was assessed with a SenseWear Pro3 Armband™ (Body Media, Pittsburgh, PA). DEE was calculated using a generalized proprietary algorithm (Innerview Research Software Version 6.0). Subjects were instructed to wear the monitors continuously for 5 days including weekend days and weekdays following general recommendations[19] at baseline and post-training intervention. Data was recorded by 15min intervals. All subjects were instructed to continue their habitual daily activities as before and were provided with an exercise and HPA diary to log the type, duration, and intensity of any physical activity or exercise undertaken during intervention.

Blood analysis. All blood samples were taken after 12 h fast between 7:00 and 9:00 a.m. at baseline and post-training intervention (week 1 and week 24). All post-training samples were obtained 72 hours after the last training day to avoid acute effects of training on blood lipids. All blood samples were drawn from the antecubital vein and handled according to standardized laboratory practice at HULP.

Blood lipids and lipoprotein. Serum biochemicals (total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were determined using enzymatic methods with Olympus reagents by automated spectrophotometry performed on Olympus AU 5400 (Olympus Diagnostica, Hamburg, Germany). Menstrual cycle was controlled by diary to define the follicular and luteal phases when blood samples were taken.[20]

Statistical analysis

SPSS version 15.0 for Windows was used for statistical analyses (SPSS Inc., Chicago, Illinois, USA). Standard statistical methods were used for the calculation of the means and standard deviation. Two way analysis of variance (ANOVA) (group x measurement [baseline-post]) for repeated measures was used to determine any differences between four groups and differences in baseline and post-training values in each group assessed. Bonferroni's post-hoc test was employed to locate specific differences. The delta percentage was calculated through the standard formula: change (%) = [(post-test score-pre-test score)/pre-test score] × 100. The effect of menstrual cycle on lipid profile was assessed by impaired T-test. The effect of ApoE on lipid profile was assessed by univariate analysis of variance (ANOVA). The significance level was set at $\alpha = 0.05$.

Results

Data is presented separated in men and women, and total. Even though the purpose of this study was not to observe gender differences, we decided to show both ways in order to discuss results clearly, taking into account that most of the previous studies are performed with only men or women.

Anthropometric and Fitness Measurements

Baseline characteristics of the participants revealed no significant differences for weight, percentage body fat, body fat free mass and O_{2peak}. Baseline BMI was significantly different between S and PA (table I). Weight change results showed a significant decrease in men and women of all groups ($p < 0.01$).

Blood lipids and lipoproteins

Table II shows changes in plasma lipid and lipoprotein concentrations in four groups before and after the intervention period. There were no statistically significant differences between groups at baseline and post-training values.

Significant changes can be observed between baseline and post-training values in each group. No significant changes were found in the HDL-C, LDL-C and CT levels in SE group, while a significant decrease was observed for TG levels (22.8%; $p < 0.01$). No significant changes were found in the HDL-C, LDL-C and TG levels in E group, but TC decreased significantly (4.4%; $p < 0.05$). For SE group, significant changes were found for LDL-C (10.6%; $p < 0.01$) and TC levels (8.8%; $p < 0.01$). LDL-C (10.4%; $p < 0.01$) and TC (7.6%; $p < 0.01$) levels significantly decreased in the PA group, with no significant changes in HDL-C and TG values.

There were no differences in lipid profile values between luteal and non-luteal (follicular) phase at baseline and post-training measurements (data not shown). Regarding ApoE groups, there were no differences in serum lipids and lipoprotein concentrations at baseline (data not shown).

Dietary analyses

Measurements on macronutrient and energy intakes at baseline and post-training are shown in table III. There were no statistically significant differences between groups at baseline and post-training values. Carbohydrate percentage intake increased significantly in S and E group ($p < 0.01$). The lipid percentage intake showed a significant decrease in all four groups $p < 0.01$). E and SE groups obtained significant increased levels of protein percentage intake ($p < 0.05$).

Daily Energy Expenditure

There were no differences between groups neither at baseline nor at post-training for daily energy expendi-

Table II
Changes in blood lipid profile

	Men					Women					Total				
	n = 37					n = 47					n = 84				
	n	Baseline Mean ± SD	Post-training Mean ± SD	Change (%)	P-value	n	Baseline Mean ± SD	Post-training Mean ± SD	Change (%)	P-value	n	Baseline Mean ± SD	Post-training Mean ± SD	Change (%)	P-value
HDL-C (mg/dL)															
S	7	41.9 ± 7.8	45 ± 9.3	7.4	0.18	12	59 ± 9.6	59.5 ± 12.2	0.8	0.77	19	53.5 ± 12.1	54.9 ± 13.1	2.6	0.35
E	10	48,0 ± 6.8	51.8 ± 5.4	7.9	0.07	15	54.3 ± 10.9	52.9 ± 9.8	-2.6	0.37	25	52 ± 10	52.5 ± 8.4	1	0.72
SE	12	47.1 ± 7.6	51.1 ± 6.7	8.5	**0.03**	10	62.3 ± 8.5	57.4 ± 8.9	-7.9	**0.01**	22	54 ± 11	54 ± 8.2	0	0.97
PA	8	46.1 ± 6.4	48.7 ± 8.4	5.6	0.27	10	57.4 ± 11.4	57.5 ± 12.5	0.2	0.92	18	53 ± 11.1	54.1 ± 11.7	2.1	0.47
LDL-C (mg/dL)															
S		138.2 ± 25.2	138.8 ± 24.9	0.4	0.91		121 ± 18.8	120.5 ± 23	-0.4	0.9		125.9 ± 21.7	125.8 ± 24.4	-0.1	0.97
E		128.9 ± 29	122.8 ± 26.8	-4.7	0.21		117.3 ± 26.3	127.9 ± 21.8	9	**0.01**		121.4 ± 27.3	126.1 ± 23.3	3.9	0.13
SE		142 ± 31.8	127 ± 29.9	-10.6	**0.01**		126.2 ± 19.7	112.8 ± 25.3	-10.6	**0.01**		134.8 ± 27.6	120.5 ± 28.2	-10.6	**0.01**
PA		144.9 ± 35.5	138.3 ± 36.1	-4.6	0.24		125.6 ± 25.9	107 ± 28.4	-14.8	**0.01**		133.1 ± 30.5	119.2 ± 34.4	-10.4	**0.01**
TG (mg/dL)															
S		158.3 ± 91.1	118.1 ± 70.8	-25.4	**0.02**		111.3 ± 45.7	87.8 ± 33.3	-21.1	0.05		126.3 ± 65.3	97.5 ± 48.8	-22.8	**0.01**
E		85.2 ± 12	85.6 ± 19.2	0.5	0.98		96.3 ± 44.3	94.4 ± 69.1	-2	0.87		92.3 ± 36.1	91.2 ± 55.9	-1.2	0.9
SE		114.3 ± 80	100.7 ± 38.6	-11.9	0.31		87 ± 20.7	84.4 ± 21.3	-3	0.86		101.9 ± 61.1	93.3 ± 32.3	-8.4	0.38
PA		120 ± 54.6	135.9 ± 63.4	13.3	0.36		114.2 ± 75.9	96.8 ± 48.9	-15.2	0.21		116.4 ± 66.7	112 ± 56.6	-3.8	0.68
TC (mg/dL)															
S		204.6 ± 26.4	192 ± 42.2	-6.2	0.15		197.7 ± 25.8	197.6 ± 32	-0.1	0.99		199.9 ± 25.6	195.8 ± 34.6	-2.1	0.42
E		209.8 ± 36.4	191.6 ± 26.1	-8.7	**0.02**		199.5 ± 38	197.4 ± 26.5	-1.1	0.72		203.2 ± 37	194.3 ± 26	-4.4	**0.02**
SE		213.5 ± 41.1	198.2 ± 29.6	-7.2	**0.02**		209.6 ± 25.8	187.1 ± 26.1	-10.7	**0.01**		211.7 ± 34.2	193.1 ± 28	-8.8	**0.01**
PA		218.3 ± 48.9	213.3 ± 49.7	-2.3	0.56		207.9 ± 32.9	184.6 ± 31.5	-11.2	**0.01**		211.9 ± 38.8	195.8 ± 40.8	-7.6	**0.01**

HDL-C: High density lipoprotein; LDL-C: Low density lipoprotein; TG: Triglycerides; TC: Total cholesterol. Significant difference with baseline ($p \leq 0.05$).
S: Strength group; E: Endurance group; SE: Strength and endurance group; PA: Physical activity recommendations group.

Table III
Changes in weight. Daily Energy Expenditure and diet macronutrient after intervention

	Men					Women					Total				
	n = 37					n = 47					n = 84				
	n	Baseline Mean ± SD	Post-training Mean ± SD	Change (%)	P-value	n	Baseline Mean ± SD	Post-training Mean ± SD	Change (%)	P-value	n	Baseline Mean ± SD	Post-training Mean ± SD	Change (%)	P-value
Weight (kg)															
S	7	92.7 ± 10.7	84.4 ± 9.5	-9	**0.01**	12	76.2 ± 8.6	70.6 ± 9.1	-7.3	**0.01**	19	81.4 ± 12	75 ± 11.1	-7.9	**0.01**
E	10	89.3 ± 10	80.9 ± 10.4	-9.4	**0.01**	15	74.9 ± 6.6	68.6 ± 7.8	-8.4	**0.01**	25	80.1 ± 10.5	73 ± 10.5	-8.9	**0.01**
SE	12	86.1 ± 8.8	77.1 ± 8.4	-10.5	**0.01**	10	72.5 ± 7.6	65.5 ± 9.2	-9.7	**0.01**	22	79.6 ± 10.6	71.6 ± 10.4	-10.1	**0.01**
PA	8	88.1 ± 7.2	81.4 ± 9	-7.6	**0.01**	10	74.8 ± 5.8	69.6 ± 7.2	-7.0	**0.01**	18	80.4 ± 9.2	74.5 ± 9.8	-7.3	**0.01**
Daily Energy Expenditure (kcal/d)															
S		3,024 ± 335.6	2,799 ± 335.1	-7.4	0.1		2,432 ± 331,3	2,354 ± 266.4	-3.2	0.4		2,621 ± 430	2,496 ± 352.8	-4.8	0.11
E		2,660[a] ± 317	2,935 ± 247.9	10.4	**0.02**		2,246 ± 285,1	2,209 ± 355.1	-1.6	0.69		2,401 ± 355.5	2,482 ± 476.7	3.3	0.28
SE		2,893 ± 387.8	2,872 ± 506.1	-0.7	0.84		2,273 ± 197.9	2,198 ± 276.9	-3.3	0.53		2,628 ± 443.9	2,583 ± 537	-1.7	0.57
PA		2,924 ± 434.9	2,672 ± 146.4	-8.6	**0.05**		2,403 ± 245	2,264 ± 343.3	-5.8	0.18		2,612 ± 415.7	2,427 ± 343.9	-7.1	**0.02**
Carbohydrate (%)															
S		41.4 ± 5.3	51 ± 7.2	23.2	**0.01**		39.1 ± 7.4	43.5 ± 5.5	11.3	**0.04**		39.8 ± 6.8	45.8 ± 6.9	15.1	**0.01**
E		38 ± 5.5	42.7 ± 5.4	12.4	0.1		36.5 ± 4.9	46.8 ± 7.5	28.2	**0.01**		37 ± 5.1	45.4 ± 7	22.7	**0.01**
SE		40.3 ± 7	44.2 ± 4.6	9.7	0.12		39.7 ± 4	41.9 ± 4.6	5.5	0.38		40 ± 5.5	43.1 ± 4.6	7.8	0.09
PA		33 ± 8.7	41 ± 5.8	24.2	**0.01**		37.8 ± 5.2	39.9 ± 4.7	5.6	0.44		35.4 ± 7.3	40.4 ± 5.1	14.1	0.01
Protein (%)															
S		17 ± 2.5	17.2 ± 0.7	1.2	0.93		17.3 ± 2.6	18.9 ± 2.7	9.2	0.22		17.2 ± 2.5	18.4 ± 2.4	7.0	0.28
E		17.7 ± 3.5	19.7 ± 2.8	11.3	0.23		16.3 ± 2.2	18.4 ± 3	12.9	0.09		16.8 ± 2.7	18.9 ± 2.9	12.5	**0.04**
SE		15.7 ± 2.4	17.8 ± 2.1	13.4	0.18		16.3 ± 2.6	19.5 ± 2.1	19.6	**0.04**		16 ± 2.4	18.6 ± 2.2	16.3	**0.02**
PA		21.9 ± 13.5	20.7 ± 2.8	-5.5	0.49		16.2 ± 3.1	19.4 ± 3	19.8	0.06		19 ± 9.9	20.1 ± 2.9	5.8	**0.01**
Fat (%)															
S		36.1 ± 7.1	27.9 ± 7.9	-22.7	**0.01**		39.1 ± 5.9	34.4 ± 4.6	-12,0	**0.03**		38.2 ± 6.3	32.4 ± 6.3	-15.2	**0.01**
E		38.7 ± 3.3	32.3 ± 7.7	-16.5	**0.02**		43.9 ± 5.1	30.5 ± 7.7	-30.5	**0.01**		42.1 ± 5.2	31.1 ± 7.5	-26.1	**0.01**
SE		39.5 ± 7.2	35 ± 3.5	-11.4	0.07		40.3 ± 5.5	35.2 ± 3.8	-12.7	**0.04**		39.9 ± 6.2	35.1 ± 3.6	-12,0	**0.01**
PA		41.1 ± 7.4	34.3 ± 5.4	-16.5	**0.02**		43.3 ± 6.3	37.5 ± 5.3	-13.4	**0.04**		42.2 ± 6.7	35.9 ± 5.4	-14.9	**0.01**

Significant difference with baseline ($p \leq 0.05$). [a]Significant difference with diet and physical activity recommendations group (C). $p \leq 0.05$.
S: Strength group; E: Endurance group; SE: Strength and endurance group; PA: Physical activity recommendations group.

ture (DEE). Table III shows data from daily energy expenditure without the supervised training sessions. No significant changes were found between baseline and post-training values for each group, except to PA group that decreased significantly ($p < 0.05$). When comparing these data adding the energy expenditure from the training sessions there were not significant differences: S ($p = 0.40$), E ($p = 0.33$), SE ($p = 0.26$).

Discussion

The main finding of the present study was that adding supervised training to diet restriction did not obtain further improvements on lipid profile versus diet restriction and physical activity recommendations usual in clinical practice.

Training effects on lipids

Effects on HDL-C concentration

Measurements on HDL-C in men, after 22 weeks intervention in this study, indicated a mild improvement in S, E and PA groups, and a significant increase in SE (8.5%). Previously, other studies had confirmed improvements in HDL-C with exercise programs, without following a hipocaloric diet.[2] These results suggest that exercise alone could improve HDL-C levels in overweight and obese men, but not diet alone. In contrast, women in our study after the intervention did not improve HDL-C levels as reported by other authors.[2] A relevant clinical review exposes that, on average, women have HDL-C levels approximately 10 mg/dL higher than men.[21] This higher initial value may be responsible for women not enhancing HDL-C levels in our study. Possibly, resistance training or endurance training are not an effective stimulus to increase HDL-C in women or subjects with high baseline values.[22] Nevertheless, the importance of increased HDL-C should be emphasized, even though these changes could not appear to be significant. The Framingham Heart Study concluded that for every 1 mg/dL rise in HDL-C levels, there was a 3% reduction in cardiovascular risk.[23]

Effects on LDL-C concentration

Measurements on LDL-C levels showed significant greater reductions in SE compared to the rest. A similar study reported significant improvements in LDL cholesterol in both diet-only and diet-plus exercise conditions in men and women.[4] The decrease in body fat percentage and increase in body fat free mass may explain the decrease observed in LDL.[24] A quantitative analysis in the study of Durstine et al. (2001), about adaptation of blood lipids and lipoproteins with contribution of exercise, suggest that LDL-C reductions could occur with intensities of exercise > 60% of maximal heart rate (HRmax).[25] Our results are in agreement with this observation except for E women. There are some studies which observed that LDL-C levels increased despite the contribution of exercise and the main reasons that seem to explain this result are related to LDL-C particle size and increased resistance to oxidation of LDL-C. These studies concluded that other factors than concentration must be considered when determining the efficacy of a given intervention, such as exercise training, on LDL.[26] On the other hand, our results showed greater improvements in LDL-C in the SE group, in agreement with others, where a combined exercise program demonstrated higher efficacy on LDL-C levels in subjects independently if they were engaged in a diet program.[27]

Effects on TG concentrations

The results of the present study exhibit a favorable response of TG levels both in men and women for exercise groups, but only S group obtained significant decreased levels. A recent review and meta-analyses[28] indicated that strength training leads to lower TG concentrations in men and women, independent of changes in body weight or body composition. It seems that strength training improves TG levels better than other exercise modalities but we should take into account also that in our study S group started with worst levels, fact that could have determined the significant changes.[29] A positive response of TG levels to exercise compared to diet alone has been observed previously.[30] In addition, it is necessary to refer to studies that show the efficacy of LDL-TG removal from circulation.[31] These suggest that there could be a increase of the triglyceride content of LDL secreted by the liver, which in turn may affect intravascular lipolysis of LDL-triglyceride and LDL-triglyceride plasma clearance, because larger, triglyceride-rich particles are more susceptible to lipolysis by lipoprotein lipase than smaller particles.[31]

Effects on TC concentration

In our study, TC levels after intervention were maintained or reduced in all groups compared with the data of pretraining time. Significant reductions were occurred in E, SE and PA groups. Several studies about blood lipid and exercise concluded that TC levels infrequently change with exercise training and, as happened with LDL levels, it appears to be an intensity threshold to obtain reductions.[25] Studies with similar protocols to our study[4,5] found no differences between groups, but also achieved significant changes in all groups between baseline and post-training values. On the other hand, diet intervention must be taken into account, following

previous study, where plasma TC levels were directly related to total fat intake.[32]. Therefore, reduction in blood TC seems to be attributable in a manner to dietary advice resulting to improvements in fat intake.[33]

Lipid profile and diet treatment

In our study, macronutrient components in the diet of all participants tended to improve the distribution towards the current recommendations. Even though changes in macronutrient distributions were only significantly different in women of E compared with PA ($p < 0.05$), general distribution improved in a great manner for all macronutrients in all groups getting closer to the ideal recommendations.[34]

There is considerable clinical evidence about the influence of changes in dietary and caloric intake on plasma lipid and lipoprotein levels.[8] In our study, all groups achieved to lose weight and to improve plasma lipid and lipoprotein concentrations. Our data are in agreement with similar studies[4,5] that presented 10-15% weight losses which obtained with diet alone and/or different exercise protocols and associated with significant improvements in serum lipid profiles.

Findings from accelerometer-measured daily physical activity indicated that there were not significant changes in any group (non-training activity) after 6 months of intervention, except for men in the E and PA ($p < 0.05$). No differences between groups were found, including PA. Even though participants in the PA group may have tried to engage in different activities following the ACSM recommendations received, it was not enough to increase their lifestyle activity significantly. On the other hand, training groups did not result in a more active lifestyle outside training intervention.

As the flow diagram shows, the PA group showed up with the highest dropouts percentage (37.9 %). Recent studies try to investigate predictive variables for weight loss programs abandons, meaning that is a big matter of concern.[35] Our results showed that supervised exercise did not obtain any additive effects to diet restriction and physical activity recommendations, but it seems that was helpful in sustaining adherence in order to finish the intervention program. Hospital units tend to supervise with often feedback the dietary modifications, but poor counseling in the exercise recommendation is done. When analyzing previous interventions developed to promote changes in diet and/or physical activity in adults it seems to be clear that the key elements to successful behavioral change are frequent contact and support.[36,37]

Menstruation and ApoE were measured as confounding variables. Previous studies suggest the existence of a variation in the blood lipid levels during the menstrual cycle, with increases in TC, LDL-C and HDL-C during the follicular phase when compared to the luteal phase.[20] On the other hand, ApoE is a glycoprotein that plays a fundamental role in the lipid metabolism. Many studies assessing the role of ApoE polymorphism on plasma lipids have shown that the presence of the 4 allele is associated with elevations in LDL-C, while the presence of 2 is associated with decreased levels of LDL-C.[38] Therefore, both menstruation and ApoE polymorphism were included in the statistical analysis allowing excluding these variables interference or influencing on the results obtained in this study. Given that there was no statistically significant difference when including menstrual cycle and ApoE, the alterations found after the intervention period would appear to have been caused by the diet and/or exercise program.

Unfortunately, our sample size could have turned to be too small to detect significant changes in all variables due to a higher experimental death than estimated. The sample size of the PRONAF study was calculated to detect a main effect of training and diet on body fat (%) with 80% statistical power at 5% significance, assuming a 0.80 correlation between repeated measures and an estimated percentage of experimental death. The strengths of the present study include the randomized-controlled design, the long supervised training period and the lifestyle and genetic factors controlled.

We also assumed that, as other studies suggested previously,[39] supervised training protocols may have not achieved enough intensity in order to obtain significant improvements versus diet and unsupervised regular physical activity recommendations. These could be due also because the baseline lipid profile concentrations in this study were considered as "low risk" according to the guidelines published by the expert panel report,[40] and it is known that better baseline values determine post-intervention changes.[29] Moreover, baseline macronutrient distribution of the subjects' diet was far away from recommended guidelines.[34] This means that a considerable lifestyle change was made in this way, dietary intake changed in all groups in great manner and diet adherence was also high. Although dieting alone generally achieves beneficial results, regular exercise add salutary effects and therefore both strategies support counseling by health practitioners.[41]

In conclusion, an intervention program of endurance, strength or combined supervised training protocol with diet restriction did not achieved further improvements in lipid profile than diet restriction and usual physical activity recommendations developed in clinical practice in overweight men and women. Future research is required in order to investigate if higher intensity of any supervised training protocol mode can add improvements to dietary modification.

Statement of authorship

The contributions of the authors to the manuscript are as follows. EMM: study design, data collection,

data analysis and writing of the manuscript; BRM, PJB and ABP.: study design and data collection; MGG, CGC and CFF reviewing the manuscript; PJB: study design and reviewing the manuscript. All authors read and approved the manuscript.

Acknowledgments

Funding for the PRONAF Study comes from the *Ministerio de Ciencia e Innovación, Convocatoria de Ayudas I + D 2008, Proyectos de Investigación Fundamental No Orientada, del VI Plan de Investigación Nacional 2008-2011* (Contract: DEP2008-06354-C04-01).

Study sponsors had no involvement in the study design, in the analysis and interpretation of data, in the writing of the manuscript or submit it.

Conflict of interest statement

The authors have no conflicts of interest.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1928-1935
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Induction of food craving experience; the role of mental imagery, dietary restraint, mood and coping strategies

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Abstract

Introduction: **Food craving consists of a strong motivational state whereby a person is driven to seek and ingest a specifically desired food.**

Objectives: **To explore the influence of mental imagery on the food craving experience as well as to analyse the role of different psychological variables.**

Methods: **Participants consisted of 65 normal weight undergraduate students. An experimental induction of food craving was analysed considering the actual previous craving and the induced one as a state food craving. Measures of trait food craving, imaging ability, dietary restraint, anxiety, depression, and coping strategies were considered.**

Results: **Sweet foods in general and chocolate in particular were the most craved foods. During the induction thoughts and images were the most highly rated triggers, and all the different sensory modalities were involved. Anxiety, depression, and negative coping strategies influenced the results with regards to the food craving.**

Discussion: **This study confirms the role of mental imagery, the correlation between state and trait food craving, and the influence of different psychological variables on the food craving.**

(*Nutr Hosp.* 2012;27:1928-1935)

DOI:10.3305/nh.2012.27.6.6043

Key words: *Food craving. Mental imagery. Dietary restraint. Mood. Coping strategies.*

INDUCCIÓN DE LA EXPERIENCIA DE "FOOD CRAVING"; PAPEL DE LAS IMÁGENES MENTALES, RESTRICCIÓN DIETÉTICA, HUMOR Y ESTRATEGIAS DE AFRONTAMIENTO

Resumen

Introducción: **El food craving se define como un fuerte estado motivacional por el que una persona se ve impulsada a buscar e ingerir un alimento específicamente deseado.**

Objetivos: **Explorar la influencia de las imágenes mentales sobre la experiencia de food craving, así como analizar el papel de diferentes variables psicológicas.**

Métodos: **Los participantes fueron 65 estudiantes de pregrado de peso normal. Se analizó un modelo de provocación experimental de food craving teniendo en cuenta el deseo real previo al experimento y el inducido durante el mismo como medida de estado. Medidas de food craving habitual, capacidad de formación de imágenes, restricción dietética, ansiedad, depresión y estrategias de afrontamiento fueron consideradas.**

Resultados: **Los alimentos dulces en general y el chocolate, en particular, fueron los alimentos más ansiados. Durante la inducción, los pensamientos y las imágenes fueron los desencadenantes más potentes y todas las modalidades sensoriales estuvieron involucradas. Las variables ansiedad, depresión y estrategias de afrontamiento negativas influyeron en los resultados con respecto al food craving inducido.**

Discusión: **Este estudio confirma el papel de las imágenes mentales, la correlación entre estado y rasgo de food craving y la influencia de diferentes variables psicológicas en el mismo.**

(*Nutr Hosp.* 2012;27:1928-1935)

DOI:10.3305/nh.2012.27.6.6043

Palabras clave: *Food craving. Imágenes mentales. Restricción dietética. Humor. Estrategias de afrontamiento.*

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Recibido: 5-VII-2012.
Aceptado: 12-IX-2012.

Introduction

Food craving consists of a strong motivational state whereby a person is driven to seek and ingest a specifically desired food.[1] Neurochemical and psychological (subjective) aspects are involved in the experience of craving[2] and this experience differs from ordinary food choices or hunger in its intensity and the specificity of the craved food.[3] Food craving occurs in non-clinical (as a normative everyday experience) and clinical groups (i.e., binge eating, bulimia nervosa, and obesity) and it has been associated with guilt, depression and impairment in cognitive performance.[1,4-7] Moreover, food craving usually precedes binge eating in bulimia nervosa and obesity, binge eating disorder, seasonal affective disorder, and premenstrual syndrome.[8]

Among the biological triggers of the food craving, hunger, nutritional deficits, and nutritional deprivation have been repeatedly considered, as well as the menstrual-related changes.[9,10] Nevertheless, other psychological (i.e., affective, cognitive) triggers have been mentioned, as for example negative mood states, expectations and cognitions.[1,11] It is important to mention that while associations between craving and binge eating have been reported, multiple observations indicate that not all those who experience food cravings binge on the desired food.[5] In fact, it has been assumed that craving would be an extreme instance of a range of normal phenomena associated with motivated consumption behaviours.[2] The role of dietary restraint in the experience of food craving is controversial and it has been suggested that the relationship between dietary restraint and food craving may be a function of how craving is operationalized (e.g., frequency, intensity), the dietary restraint being related to general or aggregated measures of food craving, rather than to single episodes.[12]

Cognitive psychology considers that phenomenological experiences can be measured with the method of the experimental psychology.[13] In this regard two main theories of the nature of everyday craving have emerged. On the one hand, Tiffany's theory (as expressed within the Interacting Cognitive Subsystems model) implies that craving episodes would be triggered by means of generated somatovisceral responses to high-level schematic thoughts about a substance (i.e. a specific food) or by a person noticing their overt behaviour. In this case, conscious inspection is possible, so the person is able to attribute the triggering causes of the craving.[2,14,15] On the other hand, the Elaborated Intrusion theory does not assume that people have any direct access to the processes that triggered an intrusive thought, and therefore suggests that people may often have little insight these triggers.[2,16] In the Elaborated Intrusion theory the imagery is a key element of craving, providing the subjective experience and mediating much of the associated disruption of concurrent cognition.[2]

The role of mental imagery in the experience of food craving episodes has been longer reported, the former studies reporting food-related images in craving experiences.[17] Food cravings may be induced by imagery instructions and the intensity of the craving may be increased following specific instructions to imagine a food script. In addition, a positive correlation between self-reported vividness of the imagined food script and the craving intensity has been found.[17-19] With respect to specific images, all the different sensory modalities have been, more or less, involved in the food craving experiences.[2]

In a study of everyday cravings, cravers tended not to attribute their thoughts about a substance to any identifiable cue in the environment, but reported them as spontaneous or due to somatovisceral sensations, and involving olfactory or visual imagery.[2] In other study on food cravings, the specific sensory modalities most involved were visual and gustatory, followed by olfactory.[12] There was little involvement of auditory or tactile modalities. Apart from the mental imagery, other psychopathological variables, as anxiety or depression have been widely related with food craving, especially in patients with bulimia nervosa.[20,21] From a psychophysiological point of view, a decreased reactiveness of the autonomic nervous system linked to a negative affect (anxiety and depression among others) has been reported in different psychopathological disorders included bulimia nervosa.[22]

The aim of the current study was to explore the role of the mental imagery in the food craving experience. The specific objectives were to explore: a) the relationship between the vividness of the mental images and the intensity of the craving; b) the possible relations between food craving and specific sensory modalities involved in those images; c) the role of the dietary restraint; and d) the influence of coping strategies, anxiety and depression on the relationship between mental imagery and food craving.

Method

Participants

The sample consisted of 65 normal weight undergraduate students (54 women, 11 men) at Pablo de Olavide University who participated in their established regular practices during the course 2010-2011. The range of age was 19-31 years, with M = 23.19 and SD = 3.74. None of the participants was suffering neither from an eating disorder nor any other psychological disorders at the moment of the study, this being assessed by means of a clinical interview. None of the participants was on diet and the level of hunger was fair (M = 6.2, SD = 1.8) and none had eaten within the three hours before the experiment.

Procedure

Students were asked to express an actual previous craving experience by way of a questionnaire. Then students filled in other different questionnaires administered randomly, thus reducing potential biases. After that, the experimental induction of food craving was analysed in the laboratory setting. Like other authors,[12] the actual previous craving and the induced one were considered as a state food craving. Finally, different measures were taken, including the trait food craving as well as imaging ability, dietary restraint, anxiety, depression, and coping strategies.

Instruments

a) The actual previous craving experience. After explaining in what the food craving consists of, students were asked to think back to the last time they had a food craving experience. The specific instruction was to recall the experience as clearly as they could, really putting themselves into the situation. After that, participants wrote a paragraph describing the experience in detail and were asked to score the intensity of their craving by means of a 10-point scale (from 1 = *very slight* to 10 = *overwhelming)* and to specify the food involved in the experience. In order to assess the triggers for the craving, a list with 14 different potential triggers[2,12] was administered and students were asked to rate each one on a 5-point Likert scale (from 1 = *not at all* to 5 = *definitely*). Potential triggers included biological (hunger), affective (stress), external cues (smelt the food), thoughts and mental imagery.

b) The induced food craving experience. Basically the induction consisted of asking participants to think about their favourite food and imagine they were eating it. Following the above-mentioned specific instruction, students were asked to bring the experience to mind as clearly as they could, in detail. Then, they were instructed to rate the vividness of their image (from 1 = *no image at all* to 10 = *image perfectly clear*). The current urge to eat the imagined food was rated too (from 1 = *no desire or urge* to 10 = *extremely strong desire or urge*), and students were instructed to describe the experience by scoring 10 descriptors[2,12] on 5-point scales (from 1 = *not at all* to 5 = *definitely*). Finally, participants rated the sensory descriptors (five sensory modalities) on 10-point scales (from 1 = *not at all* to 10 = *definitely*).

c) Other measures. Based on previous studies, the following measures were included, having been demonstrated some relationship with the phenomenon of food craving.

c1) Habitual food craving. The trait food craving was measured by means of the Spanish version of the Food Craving Inventory (FCI).[23,24] This version consists of 28 self reported items scored from 0 to 4 (where 0 = *never*; 1 = *rarely*; 2 = *sometimes*; 3 = *often*; and 4 = *always/almost every day*) according to the strength of the craving. The Spanish version of the FCI yielded three factors *(single sugars/trans fats, complex carbohydrates/proteins,* and *saturated fats/high calorie content —fast food—*) and showed adequate internal consistency (Cronbach's α coefficients between 0.91 and 0.95) and psychometric properties.

c2) Mental imagery. The Spanish version of the shortened form of Bett's Questionnaire Upon Mental Imagery was used.[25] This questionnaire assesses the general imaging ability with respect to the different sensory modalities (visual, auditory, cutaneous, kinaesthetic, gustatory, olfactory, and organic). Participants are asked to rate their thoughts with respect to the vividness of the resulting mental images (from 1 = *perfectly clear and as vivid as the actual experience* to 7 = *no image present at all, you only 'know' that you are thinking of the object*). The Spanish version of this questionnaire has shown an adequate internal consistency (Cronbach's coefficient = 0.92).

c3) Dietary restraint. It was measured by means of the Spanish version of the Revised Restraint Scale,[2,26] which consists of 10 items (e.g., *how often do you diet?*) measuring weight fluctuation (4 items) and concern for dieting (6 items), which are scored on a 4- or 5-point Likert scales (total score ranges from 0 to 35). The Spanish version of this scale has shown an adequate internal consistency (Cronbach's α coefficient = 0.78 for the concern for dieting subscale, and Cronbach's coefficient = 0.70 for the weight fluctuation subscale).

c4) Anxiety. Anxiety was measured by means of the Spanish version of the State-Trait Anxiety Inventory (STAI).[28,29] This is a 40-item self-report questionnaire, which measures state anxiety (STAI-S) and trait anxiety (STAI-T). Items are scored from 0 to 3, where 0 = *not at all* and 3 = *a lot*. As regards reliability and discriminant validity the STAI items show a sufficient ability to discriminate and differentiate (between age, sex and anxiety levels) and have a good internal consistency (between 0.90 and 0.93 for the STAI-S and between 0.84 and 0.87 for the STAI-T). The convergent validity with respect to other measures of anxiety ranges from 0.58 to 0.79.

c5) Depression. Depression was assessed by means of the Spanish version of the Beck Depression Inventory (BDI),[30,31] which measures the intensity of depression and is used as a screening test in the general population. It is a self-report instrument comprising 21 items and four response levels (0 to 3 for each item). The scores obtained are linked to three categories: absence of depression (0-9), dysthymia or mild depression (10-15) and depression (over 15). The BDI shows adequate reliability (0.93) and a convergent validity between 0.62 and 0.66.

c6) Coping Strategies. They were assessed by means of the Coping Strategies Inventory (CSI).[32,33] This instrument consists of a test in which eight primary strategies, four secondary and two tertiary are explored, on the basis of the description of a stressful situation. After that, the individual answers 40 items,

following a Likert scale consisting of 5 points so that they tell how often, in the described situation, they did what is expressed in each item. At the end they answer, in an item, about the perceived coping self-efficacy. Following a previous study,[34] two conditions were established in this one: a] "high/not high problem-focused engagement" (Percentile > 50/ ≤ 50) and b] "high/not high emotion-focused engagement" (Percentile > 50/ ≤ 50).

Statistical analyses

Conventional descriptive statistics (*M, SD*) were used to describe characteristics of the sample. Comparisons between groups were tested by means of an ANOVA and χ^2-test was used to determine differences with respect to categorical variables. Different associations among variables were analysed with the Pearson's correlation coefficient and a regression analysis was performed to test the possible predictors of the urge to eat the food during the favourite food craving experience.

Results

Considering the recall of the food craving experience detailed in the paragraph previously written, 38.46% of the participants imagined that they were "at home", followed by those who imagined themselves "walking in the street" (10.77%) and those who imagined themselves "in a cafeteria, restaurant or ice-cream saloon" (7.69%).

The main activities in which they were involved were "walking, waiting for the bus, in the car" (12.31%), "studying" (10.77%), "watching TV or a movie" (9.23%), "attending classes" (7.69%) or "travelling" (4.62%).

With regards to the imagined thoughts and/or feelings, they mainly referred "confusion" (12.31%), "recalls" (12.31%), "tiredness" (7.69%), "stress" (6.15%) or "feelings of guilt" (4.62%).

As examples of the consequences of their experience they mentioned "to eat" (41.54%), "to buy food" (15.38%) and "drinking water" (5.41").

Craving experience

With respect to the sweet and salty foods, sweet foods were the most craved ones (56.9%). Regarding the specific foods, chocolate was the most craved (21.5%), followed by other foods like pastries (12.3%). Among those who craved sweet foods, 52.31% were women ($\chi^2 = 0.27$; $df = 1$; $p = 0.05$), and among those who craved chocolate, 64.10% were women ($\chi^2 = 20.36$; $df = 10$; $p = 0.01$). With regards to other foods, more men craved a meal (e.g., meat) or fast foods (e.g., pizza). There was a significant difference between sweet and salty foods on the score of the *single sugars/trans fats* subscale of the FCI with a mean of 17.32 ($SD = 9.14$) for sweet foods and a mean of 11.93 ($SD = 8.76$) for salty foods ($F_{1,64} = 5.75$; $p < 0.01$).

Among the 14 studied triggers for the food craving experience, the highest mean score corresponded to *I imagined the smell/taste of it* ($M = 3.46$), followed by *I suddenly thought about the food* ($M = 3.38$), *I pictured myself having it* ($M = 2.91$) and *I felt hungry* ($M = 2.74$). The lowest scores were obtained for *I always have it at that time/place* ($M = 1.66$) and *I imagined the sound of myself having it* ($M = 1.66$).

Taking into account the craving intensity, different significant and positive correlations were found. Thus, the craving intensity was correlated with the following triggers: *I imagined the smell/taste of it* ($r = 0.41$; $p < 0.001$), *I pictured myself having it* ($r = 0.29$; $p < 0.05$), and *I saw it* ($r = 0.25$; $p < 0.05$). The mean craving intensity was 7.09 ($SD = 1.94$). Craving intensity did not correlate neither with the three subscales of the FCI nor with the total score on the FCI.

Correlations among the three factors of the FCI and the different triggers were also explored. These correlations are shown in table I (only the significant correlations are presented). The following triggers did not

Table I
Correlations among triggers and scores on PCI

	FC1	*FC2*	*FC3*	*Total FC*
I imagined the smell/taste of it	0.31*	0.01	0.17	0,26*
I pictured myself having it	0.29*	0.13	0.21	0.31*
I saw it	0.09	0.11	0.31*	0.19
I heard it	0.02	0.42**	0.21	0.25*
I smelt it	0.22	0.35**	0.25	0.36**
Other things I was thinking about reminded me of it	0.06	0.28*	0.13	0.20
I felt happy	0.17	0.19	0.31*	0.28*
I was really busy	0.32**	0.08	0.08	0.27*
I imagined the sound of myself having it	0.14	0.27*	0.21	0.26*

FC: Food craving; FCI: Food Craving Inventory; FC1: Single sugars/trans fats; FC2: Complex carbohydrates/proteins; FC3: Saturated fats/high calorie content —fast food—. *p < 0.05; **p < 0.01.

Table II
Correlations among descriptors of the favourite food imagining experience and scores on FCI

	FC1	*FC2*	*FC3*	*Total FC*
Current urge to eat the food	0.25*	0.16	0.31*	0,32**
I want the food because I am hungry	0.01	0.32**	0.20	0.19
Thinking how much better I would feel after				
I have eaten it	0.35**	0.37**	0.36**	0.48**
I am imagining the taste of it	0.25*	0.06	0.24*	0.26*
I would feel more relaxed if I ate it	0.23	0.17	0.22	0.29*
I can hear myself eating it	0.01	0.30*	0.03	0.13

FC: Food craving; FCI: Food Craving Inventory; FC1: Single sugars/trans fats; FC2: Complex carbohydrates/proteins; FC3: Saturated fats/high calorie content —fast food—. *$p < 0.05$; **$p < 0.01$.

correlate significantly with the scores on the FCI: *I suddenly thought about the food, I felt hungry, I had nothing else to do/I was bored, I felt stressed/anxious/sad, I always have it at that time/place.*

Favourite food induction

The mean of vividness imagining the favourite food was 7.09 (*SD* = 1.94) and the mean of the current urge to eat the food was 5.05 (*SD* = 2.62). With respect to the favourite food imagining experience, the mean ratings of the descriptors ranged between 1.23 (*I have it with me right now*) and 3.69 (*I am imagining the taste of it*). Following the latter highest score, the next two descriptors were also relevant (rates > 2.5): *If I don't think about it, my craving will go away*, and *I want the food because I am hungry*. The correlations among the different descriptors of the favourite food imagining experience and the three factors of the FCI were explored. Table II shows these correlations (only descriptors with significant correlations are presented).

Sensory modalities involved during the favourite food induction

The mean rates for the different sensory modalities involved during the favourite food induction ranged between 5.72 (*I tasted the food*) and 2.88 (*I heard myself eating the food*). Table III shows the correlations among the sensory modalities, the vividness and the urge to eat the food, and the three factors of the FCI.

Dietary restraint and craving experience

There was only one significant correlation between the score on the Revised Restraint Scale and the different triggers for the food craving experience, this correlation being that one established between the dietary restraint and the trigger *I felt stressed/anxious/sad* ($r = 0.37$; $p < 0.01$). There was no significant correlation between dietary restraint and the scores on the FCI.

Dietary restraint and favourite food imagining experience

The scores on dietary restraint were not correlated neither with the descriptors of the favourite food imagining experience nor with the sensory modalities involved during the experience.

General imaging ability, food craving experience and favourite food imagining experience

There was a significant and positive correlation between the score on the Bett's Questionnaire and the following triggers for the food craving experience: *I imagined the smell/taste of it* ($r = 0.26$; $p < 0.05$) and *I pictured myself having it* ($r = 0.27$; $p < 0.05$). With respect to the favourite food imagining experience, there was a significant and positive correlation between the score on the Bett's Questionnaire and the descriptor *I am imagining the taste of it* ($r = 0.36$; $p < 0.01$). Considering the different sensory modalities included in the Bett's Questionnaire and the sensory modalities descriptors during the favourite food imagining experience, the gustatory ($r = 0.41$; $p < 0.01$), olfactory ($r = 0.25$; $p < 0.05$), and organic ($r = 0.28$; $p < 0.05$) modalities were correlated with the urge to eat the imagined food. The descriptor *I saw the food* was correlated with gustatory ($r = 0.33$; $p < 0.01$) and organic ($r = 0.28$; $p < 0.05$) sensory modalities of the Bett's Questionnaire. The descriptor *I saw myself eating the food* was correlated with cutaneous ($r = 0.26$; $p < 0.05$), gustatory ($r = 0.46$; $p < 0.01$), and organic ($r = 0.28$; $p < 0.05$) sensory modalities. The descriptor *I smelt the food* was correlated with the organic modality ($r = 0.37$ $p < 0.01$), the descriptor *I tasted the food* was correlated with gustatory ($r = 0.35$; $p < 0.01$) and organic ($r = 0.28$; $p < 0.05$) modalities and, finally, the descriptor *I felt the texture of the food*

Table III
Correlations among the sensory modalities, the vividness and the urge to eat the food, and the three factors of the FCI

	Mean	*Vividness*	*Urge*	*FC1*	*FC2*	*FC3*	*Total FC*
I saw the food	5.66	0.33**	0.50**	0.15	0.10	0.11	0.09
I saw myself eating the food	5.20	0.29*	0.35**	0.21	0.01	0.17	0.19
I heard myself eating the food	2.88	0.21	0.18	0.13	0.15	0.17	0.19
I smelt the food	3.92	0.28*	0.42**	0.24	0.26*	0.33**	0.36**
I tasted the food	5.72	0.40**	0.49**	0.18	0.10	0.18	0.21
I felt the texture of the food in my mouth	5.52	0.40**	0.56**	0.16	0.17	0.20	0.23

FC: Food craving; FCI: Food Craving Inventory; FC1: Single sugars/trans fats; FC2: Complex carbohydrates/proteins; FC3: Saturated fats/high calorie content —fast food—. *p < 0.05; **p < 0.01.

in my mouth was correlated with the gustatory modality ($r = 0.31$; $p < 0.01$).

May the urge to eat the food during the favourite food induction experience be predicted?

A stepwise multiple regression analysis (entering as predictive variables age, sex, FCI scores, Bett's Questionnaire scores, descriptors of favourite food induction, sensory modalities descriptors, vividness during the favourite food induction, BDI scores and STAI scores) revealed the following to be predictors of the urge to eat the food during the favourite food induction experience: *I saw the food* ($b = 0.61$; $t = 4.95$; $p < 0.0001$), *I would feel more relaxed if I ate it* ($b = 0.40$; $t = 3.56$: $p < 0.001$), *I felt the texture of the food in my mouth* ($b = 0.29$; $t = 2.69$; $p < 0.01$), and *I smelt the food* ($b = 0.27$; $t = 2.44$; $p < 0.01$).

The role of psychological and psychopathological variables (anxiety, depression and coping strategies)

Anxiety symptoms, as measured by the STAI, were significantly correlated with dietary restraint considering the STAI-T ($r = 0.26$; $p < 0.05$), and with the second factor of the FCI (*complex carbohydrates/proteins*) considering the STAI-S ($r = 0.25$; $p < 0.05$). Depression symptoms were significantly correlated with dietary restraint ($r = 0.30$; $p < 0.05$). There was a positive and significant correlation between the trigger *I felt stressed/anxious/sad* and STAI-S ($r = 0.36$; $p < 0.01$), STAI-T ($r = 0.32$; $p < 0.05$), and BDI ($r = 0.25$; $p < 0.05$). There also were some significant correlations between anxiety/depression and different descriptors and sensory modalities of the favourite food imagining experience, which are shown in table IV. Taking into account the coping strategies, these showed no significant correlations neither with the variables associated with the craving experience nor with those variables related with the favourite food induction. Nevertheless, some correlations were found considering trait measures as dietary restraint and FCI. Thus, dietary restraint was negatively associated with social support ($r = -0.42$; $p < 0.01$), emotion-focused engagement ($r = -0.39$; $p < 0.01$) and engagement ($r = -0.39$; $p < 0.01$). Vice versa, dietary restraint was positively associated with social withdrawal ($r = 0.30$; $p < 0.01$). With respect to the scores on FCI, problem avoidance was associated with the third subscale of the FCI (*saturated fats/high calorie content —fast food—*) ($r = 0.31$; $p < 0.01$) and with FCI total score ($r = 0.26$; $p < 0.05$). Problem-focused disengagement was associated with

Table IV
Correlations among anxiety/depression and descriptors/sensory modalities of the favourite food imagining experience

	BDI	*STAI-S*	*STAI-T*
Descriptors			
Eating it would feel very comforting right now	0.28*	0.37**	0.28*
Thinking how much better I would feel after I have eaten it	0.21	0.38**	0.20
I would feel more relaxed if I ate it	0.34**	0.50**	0.31*
I am visualizing it	0.31*	0.37**	0.20
I am trying to resist eating it	0.19	0.31*	0.18
I can hear myself eating it	0.21	0.27*	0.20
Sensory modalities			
I smelt the food	0.18	0.29*	0.21
I tasted the food	0.29*	0.33**	0.19
I felt the texture of the food in my mouth	0.44**	0.39**	0.38**

BDI: Beck Depression Inventory; STAI-S: State Trait Anxiety Inventory (State); STAI-T: State Trait Anxiety Inventory (Trait).
*p < 0.05; **p < 0.01.

that third subscale ($r = 0.29$; $p < 0.05$) and with FCI total score ($r = 0.30$; $p < 0.01$). Finally, disengagement also was associated with the third subscale ($r = 0.33$; $p < 0.01$) and with FCI total score ($r = 0.25$; $p < 0.05$).

Discussion

Considering the description of craved foods, the fact that sweet foods were the most craved ones confirms other previous findings. The same applies in the case of chocolate as the most craved specific food, women being those who prefer this specific food.[1,11,12,23] Reasons based on sociocultural bases have been given in order to explain this preference, which is supported by the results of different cross-cultural studies among Western countries.[35]

During the food craving experience, thoughts and images were the most highly rated triggers, confirming previous results.[12] Moreover, those images were correlated with craving intensity. Taking into account that the experimental craving experience was a measure of state food cravings, our results show that this state is, to some extent, correlated with measures of trait food cravings. Seven out of the 14 triggers were significantly correlated with the total score on the FCI, this indicating that it is hardly difficult to separate the state and trait food craving experiences. On the other hand it seems that different triggers are correlated with specific trait food cravings. Thus, imagining the smell/taste of the food, picturing oneself having the food or being busy were correlated with the craving for *single sugars/trans fats*; other triggers like *I heard it, I smelt it* or *Other things I was thinking about reminded me of it* were correlated with the craving for *complex carbohydrates/proteins;* and finally, to see the food or feeling happy were correlated with the craving for *saturated fats/high calorie content —fast food—*.

With respect to sensory modalities, visualizing and imagining the taste of the food caused the most craving intensity, confirming previous results.[12] Imagining the taste of the food and the texture of the food in the mouth were highly correlated with the vividness of the experience. Finally visualizing the food, imagining the taste and smell of the food, and imagining the texture of the food in the mouth were highly correlated with the urge to eat the food. To some extent, these relations among imagining, vividness of the experience, and craving were previously reported.[26]

Dietary restraint does not seem to be specifically related to the state craving, except in case of the trigger *I felt stressed/anxious/sad.* This general absence of association between dietary restraint and state craving has been previously reported.[12] Apart from methodological differences among studies, the distinction between state craving and trait craving could explain different results with respect to the link between food craving and dietary restraint. In fact, a relationship between trait craving and dietary restraint has been reported,[12] that association not being confirmed in the current study. Based on the current results, feelings of stress, anxiety or sadness may be associated with state craving. Thus, these negative feelings might be correlated with single episodes of craving more than with global measures of food craving.

Considering the general imaging ability, this general ability was found correlated with the triggers, descriptors and sensory modalities taken into account in this study. The same applies to the different modalities considered in the assessment of imaging ability. Once again these results confirm those reported previously as well as the fact that the imagery is a key element of craving, providing the subjective experience and mediating much of the associated disruption of concurrent cognition as it has been noted by the Elaborated Intrusion theory.[2,12]

The most novel point about the current study is the analysis of the role of some psychological variables. Having in mind the results, state anxiety is the main variable associated with the descriptors and sensory modalities during the favourite food imagining experience. The descriptor *I would feel more relaxed if I ate it* is also significantly associated with symptoms of depression, and *to feel the texture of the food in the mouth* was associated with symptoms of depression too. The association of the food craving with different psychopathological syndromes and eating behaviour disorders has been widely reported.[5,36] In addition, high rates of psychopathology have been found in binge eaters and bulimia nervosa.[22]

The role of coping strategies appears to be more related with trait measures as dietary restraint and FCI. Considering the characteristic of personality, a previous study found that cravers have higher level of harm avoidance and lower level of self-directedness and persistence than controls. Moreover, food cravers who binge were characterized by a high level of dietary restraint and low self-directedness, existing true differences between cravers who do and do not binge.[5] The current results show that dietary restraint was negatively associated with social support, emotion-focused engagement. Vice versa, dietary restraint was positively associated with social withdrawal. These results indicate an association between dietary restraint and negative coping strategies. On the other hand a positive association between negative coping strategies and trait food craving was found. Summarizing, negative coping strategies are related to dietary restraint and trait food craving. In fact, inadequate coping skills have been found among binge eaters[37] and different subgroups of patients with eating disorders have been reported with regards to the characteristics of personality and coping strategies.[38]

The current results firstly confirm the role of mental imagery in the food craving experience with all the different sensory modalities involved to some extent. The correlation found between variables of state and trait food craving shows the difficulty to separate the two facets of the craving experience. Feelings of stress,

anxiety or sadness may be associated with state craving. Finally, the current study shows the role of anxiety during the food imagining experience, the association between the dietary restraint and negative coping strategies, and the link between those negative strategies and trait food craving.

This study has a number of limitations, the first with respect to the sample, which is a specific one comprising of only undergraduate students. Future studies should be included other type of non-clinical participants as well as patients with eating behaviour disorders (e.g., binge eaters). Due the relationship between the phenomenology of food craving and symptoms of anxiety and/or depression, other type of disorders should also be included in future designs. In order to analyse the theoretical, but controversial, relationship between food craving and eating behaviour it would be appropriate to include some behavioural measures besides the analysis of state and trait cravings. The influence of coping strategies, anxiety and depression on the relationship between relationship between mental imagery and food craving need to be better explored in future studies in order to clarify that role as mediator or modulator by means of tests of mediation.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1936-1939
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Dietary intake of cancer patients on radiotherapy

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Abstract

The dietary intake of cancer patients can affect their nutritional status.

Objectives: **To assess the dietary intake and nutritional status of head and neck cancer patients on radiotherapy.**

Methods: **24-hour recalls and anthropometric measures were taken during the first and third weeks of radiotherapy.**

Results: **Of the 62 patients, significant reductions were found in arm muscle area (p = 0.001) and arm muscle circumference (p < 0.001), and 69% of patients had an average weight loss of 5.7% in three weeks. With regards to their dietary intake, reductions were found in energy (26.5 kcal/kg/d-21.3 kcal/kg/d, p < 0.001), carbohydrate (196.9 g/d – 180.5 g/d, p = 0.020), protein (1.19 g/kg/d-0.93 g/kg/d, p = 0.009) and fat (44.4 g/d-33.1 g/d, p < 0.001) intakes during the study period.**

Discussion: **The changes that result from cancer radiotherapy led to reductions in dietary intake and negatively affected body composition measures.**

(*Nutr Hosp.* 2012;27:1936-1939)

DOI:10.3305/nh.2012.27.6.5958

Key words: *Nutritional status. Radiation therapy. Head and neck cancer.*

LA INGESTA DIETÉTICA DE LOS PACIENTES CON CÁNCER EN RADIOTERAPIA

Resumen

La ingesta dietética de los pacientes con cáncer pueden afectar su estado nutricional.

Objetivos: **Evaluar la ingesta alimentaria y el estado nutricional de los pacientes con cáncer de la cabeza y cuello de la radioterapia.**

Métodos: **Recuerdo de ingesta de 24 horas y valoración del status nutricional por antropometría fueron tomadas durante la primera semana y la tercera de la radioterapia.**

Resultados: **De los 62 pacientes, las reducciones significativas en el área muscular del brazo (p = 0,001) y la circunferencia muscular del brazo (p < 0,001), y el 69% de los pacientes tenían una pérdida de peso promedio de 5,7% en tres semanas. Con respecto a su ingesta, las reducciones fueron encontrados en la energía (26,5 kcal/kg/día-21,3 kcal/kg/día, p < 0,001), carbohidratos (196,9 g/día-180,5 g/día, p = 0,020), la proteína (1,19 g/kg/día-0,93 g/kg/día, p = 0,009) y grasas (44,4 g/día-33,1 g/día, p < 0,001) la ingesta durante el período de estudio.**

Discusión: **Los cambios resultan en reducciónde la ingesta alimentaria y las medidas del cuerpo afectado negativamente a la sua composición.**

(*Nutr Hosp.* 2012;27:1936-1939)

DOI:10.3305/nh.2012.27.6.5958

Palabras clave: *Estado nutricional. Radioterapia. Cáncer de cabeza y cuello.*

Abreviations

AI: Adequate intake.
MUAMA: Mid-upper arm muscle area.
MUAC: Mid-upper arm circumference.
MAMC: Mid-arm muscle circumference.
SD: Standard deviation.
EAR: Estimated Average Requirement.
CI: Confidence interval.
BMI: Body mass index.
kcal: Calories.
TAM: Thumb adductor muscle.
Md: Median.
TST: Triceps skinfold thickness.

Introduction

In Brazil, malignant cancers are the second leading cause of adult mortality, and their prevention is one of the biggest public health challenges of our time[1]. Cancer is a disease caused by the uncontrolled, rapid and invasive growth of cells with alterations in their DNA[2]. Many factors affect cancer development, such

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Recibido: 25-V-2012.
Aceptado: 17-IX-2012.

as the environment, specific habits and customs of a given location, as well as internal factors, which are genetically determined causes.[1]

Head and neck tumors represent approximately 4% of total cancers, and one of the main challenges in the treatment of affected patients is the deterioration of their nutritional status.[1] In particular, patients with cancers of the oral cavity, pharynx, larynx and esophagus have difficulty swallowing, which leads to reductions in dietary intake and consequently malnutrition.[2] These cancers are responsible for more than 90% of malignant neoplasms of the upper digestive and respiratory tract,[3] and their treatment involves chemotherapy, radiotherapy and in some cases, surgery.[4]

Malnutrition can lead to morphological and functional alterations, and can also affect the patient's immune system. In some cases, it can lead to prolonged hospital stays and increased risk of postoperative complications, which impact the patient's quality of life and treatment outcomes.[5]

Several studies indicate that malnutrition resulting from reductions in dietary intake occurs in 30 to 50% of patients with these cancers[3]. The effects of malnutrition increase the risk of postoperative complications and reduce patients' tolerance to radiotherapy and chemotherapy.[1,2] This study assessed the dietary intake and nutritional status of head and neck cancer patients during radiotherapy.

Methodology

This is a quantitative, longitudinal study in which 62 head and neck cancer patients undergoing radiotherapy were assessed. Patients were randomly selected at the radiotherapy unit of Hospital Santa Rita da Irmandade Santa Casa de Misericórdia in Porto Alegre, Brazil. The study was approved by Universidade Federal de Ciências da Saúde de Porto Alegre's Ethics in Research Committee (10-676). Pregnant women, patients unable to undergo anthropometric or nutritional assessment, patients with a different diagnosis than the aforementioned cancers, patients with ascites, edema and/or amputations were excluded from the study.

The assessments were conducted during the first and at the end of the third week of treatment. The following assessments and respective equipment were used: weight, Techline® personal scale; height, Seca® bodymeter 206 stadiometer; mid-upper arm circumference, non-stretchable tape measure; triceps skinfold thickness (TST) and thumb adductor muscle (TAM), both with a Cescorf® – Innovare caliper. Next, the body mass index (BMI), mid-arm muscle circumference (MAMC) and percent weight loss were calculated. Finally, patients' cachexia levels were classified.[6]

A 24-hour recall assessed patients' dietary macronutrient and fiber intakes. These records were then analysed using the Nutwin *Programa de Apoio à Nutrição* software, and compared to nutritional recommendations established in the Brazilian National Institute of Cancer's National Consensus on Oncological Nutrition[3]. The recommended energy intake was 30 kcal/kg/day, since this the upper limit for weight maintenance and the lower limit for weight gain[4]. Carbohydrate and protein intakes were compared to the EAR (Estimated Average Requirement)[7] for each patient's age and gender group. For fats, the average intake based on a 2000-calorie diet from the Brazilian Food Guide was used, irrespective of age and gender. Finally, the AI (Adequate Intake)[7] was used as the recommended dietary fiber intake.

Statistical analyses were conducted using version 17.0 of the SPSS software package. A 5% ($p \leq 0.05$) significance level was chosen. The Kolmogorov-Simrnov test and the Pearson correlation coefficients were used to test the distribution of the variables. The Student's t-test or the Wilcoxon test were used to compare the quantitative measures of patients' first and second assessments.

Results

Of the 62 patients, 46 (74.2%) were male. Patients' average height and weight were 1.68 ± 0.09 m and 58.0 ± 9.7 years, respectively. Of all head and neck cancers, laryngeal cancer had the highest prevalence (32.3%), followed by oropharyngeal cancer, tongue cancer (12.9%), and the remaining cancers represented 30.6%.

For the anthropometric assessment, comparative data from the first and the third week of radiotherapy were used, and an average 5.7% body weight loss was detected in 43 (69%) of patients. As shown in table I, patients' current body weight, mid-upper arm circumference, mid-arm muscle circumference, mid-upper arm muscle area, body mass index and triceps skinfold thickness were significantly reduced between the 2 weeks. The thumb adductor muscle was the only measure that did not change during the study period.

Patients' total daily meals were also reduced between weeks 1 and 3 (from 4.13 ± 1.3 to 3.98 ± 1.15, on the 1st and 3rd weeks, respectively). They also altered the consistency of their diet. At the beginning of the study period, 58.1% of patients were following a diet of normal consistency, 9.7% a soft diet, 4.8% a pureed diet, 4.8% a liquid diet and 22.6% of patients were receiving enteral tube feeding. After 3 weeks of treatment, 71% were following a normal consistency diet, 14.5% a pureed diet, 8.1% a soft diet, 4.8% a liquid diet and only 1.6% continued on enteral tube feeding.

Table II presents the results of the two 24-hour recalls, where a reduction in energy intake from carbohydrate, protein and fat was detected between weeks 1 and 3. Dietary fiber intake was lower than the AI[7], and the difference in intake between the 2 weeks was not statistically significant.

Table I
Anthropometric profile of patients on radiotherapy, comparison between treatment weeks 1 and 3

Variables	1st week	3rd week	p-value#
	Average ± SD	Average± SD	
Current body weight (kg)	65.6 ± 15.3	64.2 ± 15.7	< 0.001
Usual body weight (kg)	68.9 ± 16.0	–	–
TAM (mm)	11.0 ± 3.1	10.5 ± 2.8	0.09
BMI (kg/m2)	23.1 ± 4.5	22.6 ± 4.7	< 0.001
MAMC (cm)	24.1 ± 4.0	23.4 ± 4.3	< 0.001
MUAC (cm)	27.8 ± 4.8	27.0 ± 5.1	< 0.001
TST (mm)	12.0 ± 5.5	11.5 ± 5.4	0.006
MUAMA (mm^2)	4,725 ± 1581	4,477 ± 1629	0.001

t-test.

A positive correlation was detected between reductions in dietary energy intake and weight loss at week 3 of treatment (r = 0.420; p = 0.001). The same type of correlation was found for reductions in protein intake and mid-upper arm circumference (r = 0.287; p = 0.024).

The number of patients whose nutritional status was classified with cachexia also increased, from 30.6% at the beginning, to 41.9% during the third week of treatment, respectively.

Discussion

According to Brazilian estimates, cancers of the oral cavity have a higher prevalence in men. The findings of this study support these estimates, since most patients were male. They are also in accordance with the findings of Mendes et al.,[2] who assessed the nutritional status of 81 patients undergoing ambulatory treatment for head and neck cancer.

The nutritional assessments conducted at weeks 1 and 3 of radiotherapy found reductions in patients' dietary intake and consequently in their muscle mass stores (MUAC, MAMC and MUAMA) at week 3. This is indicative of sarcopenia, a condition that is highly prevalent in cancer patients and is characterized by muscle mass and skeletal muscle loss.[12] The reductions we observed in patients' BMI during the study period is in accordance with studies by Schantz et al.[9] and Mendes et al.[2], although because the BMI reflects total body mass, its applicability in patients with edema is limited. Another limitation is that body weight and BMI can be classified as normal despite underlying changes in patients' body mass.

Patients' body weight was reduced between weeks 1 and 3, which reflects the changes detected in anthropometric measures. The percent weight loss found in 63% of patients over a 3-week period was 5.7%, which is higher than reported by Hill et al.,[10] who detected a 5% weight loss in 11% of patients during the first 3 weeks of treatment. These weight fluctuations are known to occur during the initial stages of treatment due to reductions in dietary intake caused by a loss of appetite, metabolic alterations and cachexia.[10]

A study by Maio et al.[11] found that out of 48 oral cancer patients, 12% had severe weight loss in the

Table II
Dietary intake of patients on radiotherapy, dietary recommendations for the disease, comparison of dietary intake between treatment weeks 1 and 3

Variables	Daily recommendation	Intake		p-value#
		1st week	3rd week	
		Md (P25-P75)	Md (P25-P75)	
Energy (kcal/kg/day)*	30	26.5 (18.0-35.4)	21.3 (14.9-24.5)	< 0.001
Carbohydrate(g/day)**	100	196.9 (142.4-312.6)	180.5 (130.5-260.7)	0.020
Protein (g/kg/day)	1.0-1.8* 0.66**	1.19 (0.80-1.74)	0.93 (0.73-1.24)	0.009
Fat (g/day)£	50-61	44.4 (29.8-70.0)	33.1 (20.8-55.6)	< 0.001
Dietary fiber (g/day)***	21-30	12.6 (6.6-21.9)	12.4 (6.9-20.1)	0.294

*National Consensus on Oncological Nutrition (INCA, 2009).
**EAR-Estimated Average Requirement (DRIs, 2002).
***AI-Adequate intake (DRIs, 2002) – minimum recommendation for men and women, respectively.
£Brazilian Food Guide, 2006.
#Wilcoxon test.

months prior to surgery. This level of weight loss is clinically relevant, since it places patients in a higher risk group for severe postoperative complications, increased morbidity and mortality.[12]

The clinical manifestations of cancer, as well as the prescribed treatment scheme may have influenced patients' dietary intake during radiotherapy, since dietary energy and macronutrient intakes were significantly lower at week 3 compared to the start of treatment. Dietary fiber intake was lower than recommended by the AI (Adequate Intake),[7] and no statistically significant difference was detected during the study period.

It is important to emphasize, however, that the 24-hour recall method may underestimate or overestimate actual dietary intake. Similarly to Bosaeus et al.,[13] who reported a low energy intake in cancer patients using the same method, we found that patients' energy intakes were below established recommendations at the start of the study, and were reduced by nearly 20% at week 3.

Ravasco et al.[14] assessed the impact of nutrient supplementation and dietary counseling on head and neck cancer patients undergoing radiotherapy and found that energy and protein intakes increased in the study group, but decreased in the control group. These authors therefore underscore the importance of dietary counseling during radiotherapy treatment to prevent the deterioration of patients' nutritional status.

Radiotherapy is known to reduce patients' dietary intakes as a result of the effects of treatment on local tissues.[15] Side effects generally develop during the first weeks of treatment,[15] as observed in the present study. We found reductions in patients' dietary intake between weeks 1 and 3, as indicated by a reduction in the number of daily meals, thus leading to a deterioration of their nutritional status. It is important to consider that although cancer patients may be prescribed one or a combination of antineoplastic treatments —such as chemotherapy— and that these treatment schemes may further exacerbate the side effects that result in reduced dietary intake and body mass reserves, our patients were not questioned about whether or not they were receiving other treatments. The same consideration applies to the correlations found between protein/energy intake and body mass reserves (mid-arm muscle circumference and body weight) measured at week 3 of treatment, and which indicate the effects of reductions in dietary intake on patients' nutritional status. Moreover, a change in patients' diet consistency was detected, although many of them progressed to a diet of normal consistency during the third week of treatment. It seems, however, that this progression did not adequately restore energy and protein intakes.

These findings demonstrate that patients reduced both their dietary intake and body mass reserves during radiotherapy treatment. A significant number of them began their treatment with cachexia, which may be a contributing factor in the observed effects of radiotherapy on their dietary intake and body composition.

Acknowledgements

To the Radiotherapy Unit staff of Hospital Santa Rita da Irmandade Santa Casa de Misericórdia de Porto Alegre and to colleagues Juliana Ricardi e Luciane Pinheiro for their assistance and collaboration in the study.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1940-1944
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Lactancia materna en bebés pretérminos; cuidados centrados en el desarrollo en el contexto palestino

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Resumen

El contacto precoz piel a piel provee beneficios para la madre y para el bebé, además de tener un papel importante en el establecimiento de la lactancia materna.

Objetivo: **El objetivo de este estudio fue informar a las madres de bebés pretérmino sobre la importancia del contacto piel con piel para la implantación de la lactancia materna y para un mejor vínculo entre ellos (cuidados centrados en el desarrollo CCD).**

Material y método: **Se realizó un estudio de cohorte, prospectivo, en varios Hospitales de Cisjordania en Palestina, en el período de tiempo comprendido entre 2008 y 2011. El universo lo constituyó una estimación de un promedio de 2.500 partos anuales en cada hospital. Se determinó una población muestral de n = 252. Todos los recién nacidos tenían una edad gestacional inferior a 37 semanas y un peso inferior a 2.500 gramos y, por problemas de salud, fueron ingresados en unidades de encamación neonatal.**

Resultados: **Este estudio ha puesto de manifiesto que en Palestina las mujeres jóvenes practican el contacto piel con piel y la lactancia materna con mayor frecuencia que las mujeres mayores; una vez informada de sus ventajas, muestran mayor interés en aprender los cuidados de sus bebés en las propias unidades de encamación neonatal.**

Conclusiones: **La aplicación del contacto piel a piel (CCD) y la lactancia en bebés pretérmino ha sido posible mediante información e instrucción a las madres. Este estudio ha tenido una gran repercusión y ha sido muy bien aceptado por la población femenina. No existían estudios similares en ningún hospital de Palestina.**

(*Nutr Hosp.* 2012;27:1940-1944)

DOI:10.3305/nh.2012.27.6.5995

Palabras clave: *Lactancia materna. Prematuro. Apego. Cuidados.*

BREASTFEEDING IN PREMATURE BABIES; DEVELOPMENT-CENTERED CARE IN PALESTINE

Abstract

In addition to its important role in the initiation of breastfeeding, early skin-to-skin contact benefits both mothers and their babies.

Objective: **To inform all mothers of premature babies about the importance of skin-to-skin contact and breastfeeding in order to foment a closer bond between mother and child (development-centered care).**

Materials and method: **A prospective cohort study was conducted in various hospitals on the West Bank in Palestine during 2008-2011. The universe was made up of an estimated average of 2,500 childbirths per year in each hospital. All of the subjects in the sample population of n = 252 babies had a gestational age of less than 37 GWs, and had weighed less than 2,500 grams at birth. For health reasons, they were hospitalized in neonatal care units.**

Results: **The results obtained showed that in Palestine, young women tend to breastfeed their babies and have skin-to-skin contact with them more often than older mothers. Once the new mothers were informed of the advantages of these practices, they showed greater interest in learning how to care for their babies in the neonatal care units.**

Conclusions: **Breastfeeding premature babies as well as having skin-to-skin contact with them was made possible by informing and teaching new mothers about the advantages of this type of infant care. This research has had widespread impact and has been very well received by the female population in the country. This is the first study of its kind to be carried out in Palestine.**

(*Nutr Hosp.* 2012;27:1940-1944)

DOI:10.3305/nh.2012.27.6.5995

Key words: *Breastfeeding. Premature. Bonding. Care.*

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Recibido: 11-VI-2012.
Aceptado: 20-VI-2012.

Introducción

En muchas culturas, es frecuente que se sostenga a los recién nacidos desnudos contra el pecho desnudo de la madre ya desde el nacimiento. Históricamente, este procedimiento ha sido necesario para la supervivencia del neonato[1]. El contacto temprano piel con piel consiste en colocar al recién nacido desnudo en posición decúbito ventral sobre el torso desnudo de la madre, apenas nace o poco tiempo después. El método madre canguro se inició hace 30 años como una nueva forma de atender al recién nacido de bajo peso. Es un método sencillo, de fácil aplicación, de bajo coste y que ha producido unos excelentes resultados[1,2,3].

Los cuidados centrado en el desarrollo (CCD) constituyen un sistema de atención que pretenden mejorar el desarrollo del niño a través de intervenciones que favorezcan al recién nacido y a su familia, entendiéndolos a ambos como una unidad[4].

Las mujeres adolescentes necesitan un mayor apoyo en los primeros días de vida de su hijo en el medio hospitalario. Si las madres presentan alteraciones, se hará más difícil la aplicación de los cuidados centrados en su desarrollo en la unidad neonatal[5-8].

El mantenimiento del medio materno después del nacimiento es necesario para suscitar las conductas innatas del neonato y de la madre, que han de conducir a una lactancia satisfactoria y, por lo tanto, a la supervivencia. La separación de este medio produce un llanto inmediato por angustia y una conducta de "protesta o desesperación". Diversos autores han demostrado en sus investigaciones que el contacto piel con piel favorece un mejor vínculo y apego para las madres; otras ventajas son un mayor sentido del control y del autoperfeccionamiento, lo que genera una mayor confianza. El sentido del control y de la confianza son resultados pertinentes, porque predicen la duración de la lactancia. La lactancia materna presenta claros beneficios a corto, medio y largo plazo para la salud del bebé, sobre todo como protección contra la morbimortalidad por enfermedades infecciosas[9-12]. La leche humana es la mejor opción de alimentación del lactante, sobre todo en el primer año de vida. El dar el pecho tiene también ventajas para la madre, ya que se ha relacionado como un método eficaz en la prevención del cáncer de mama y también para la prevención de la hipertensión arterial y la obesidad maternas[13-16]. En un estudio se ha demostrado que el bebé prematuro tiene una necesidad superior de recibir lactancia materna. ya que la leche humana aporta al niño prematuro una mayor cantidad de poliaminas, lo que le ayuda en su proceso de maduración intestinal[17].

Otros estudios muestran que los niños nacidos de madres adolescentes suelen tener menor peso al nacer y un mayor riesgo de morbilidad que los de madres adultas. La alimentación con leche materna suele ser menos frecuente en los bebes de madres adolescentes. Parece que la edad de la madre condiciona la utilización del contacto piel con piel y la lactancia materna. También se ha establecido que la obesidad materna se relaciona con un menor tiempo de lactancia, tanto en mujeres adultas como en adolescentes[18-21].

En los hospitales en donde se llevó a cabo la investigación, la norma social era administrar lactancia materna sistemáticamente a los recién nacidos sanos. Sin embargo, con los bebés pretérmino no se hacía así; a las madres se les retiraba la leche en el posparto inmediato. Tampoco practicaban el contacto piel con piel, porque esa no era la costumbre.

Los niños eran ingresados y los padre volvían a sus domicilios hasta el alta hospitalaria del bebé y las visitas eran espaciadas en el tiempo. Por ello, la rotura del vínculo, sobre todo en los niños más pequeños, era muy frecuente.

El objetivo de este estudio fue informar a todas las madres de los bebés pretérmino sobre la importancia del contacto piel con piel para el establecimiento de la lactancia materna y de los CCD para lograr un mejor vínculo entre ellos.

Diseño metodológico

Se realizó un estudio de cohorte, prospectivo, en los Hospitales de Cisjordania en Palestina, en el período de tiempo comprendido entre los años 2008 y 2011.

El universo fue una estimación de un promedio de 2.500 partos anuales en cada hospital. Se determinó una población muestral de n = 252. Todos los recién nacidos tenían una edad gestacional inferior a las 37 semanas y un peso inferior a 2.500 gramos y, por algún problema de salud, fueron ingresados en unidades de encamación neonatal. Todos los padres autorizaron, mediante el escrito correspondiente, la participación en el estudio. Las variables estudiadas de todas las mujeres fueron las siguientes: biológicas maternas, sociales familiares y económicas, variables generales de seguimiento del bebé y de la evolución y días de estancia hospitalaria. También se facilitó información e instrucción mediante un cuestionario validado de los cuidados centrados en le desarrollo (CCD) a las madres en relación con la prematuridad, los beneficios del contacto piel con piel, la lactancia materna en los bebés pretérmino y la regulación térmica del neonato (incubadoras insuficientes). A todas las madres se les ofreció un ingreso hospitalario próximo a sus bebés durante los días de estancia, para que ellas se encargaran de los cuidados de sus hijos (CCD). En el protocolo se indicaban las horas que tenían que practicar el contacto piel con piel, la forma de colocarse al bebé para la lactancia, el mínimo estímulo, así como la importancia de su participación. También se les explican las ventajas de la lactancia para ella, como la prevención del cáncer de mama, la hipertensión y la obesidad.

Para la validación del cuestionario de los cuidados centrados en le desarrollo (CCD), se ha calculado el coeficiente Kappa de Fleiss (Fleiss, J. L. (1971) "Measuring nominal scale agreement among many raters."

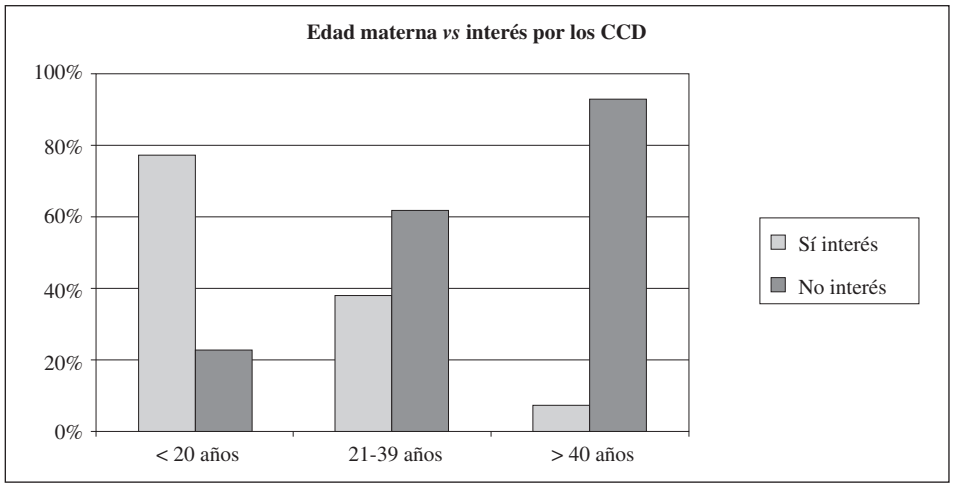


Fig. 1.—Edad de la madre e interés por los cuidados a su bebé (CCD).

Psychological Bulletin, Vol. 76, No. 5 pp. 378) para el acuerdo entre más de dos observadores. En nuestro caso hemos utilizado 30 evaluadores que han validado cada ítem como "correcto" o "incorrecto". El cálculo del coeficiente Kappa de Fleiss ha arrojado un resultado de 0,867. Según Landis y Koch (Landis, J. R. and Koch, G. G. (1977) "The measurement of observer agreement for categorical data" in Biometrics. Vol. 33, pp. 159|), este valor indica un grado de acuerdo casi perfecto respecto al acuerdo en la corrección de los ítems del cuestionario. Por lo tanto, se puede considerar que el cuestionario es suficientemente válido, de acuerdo con el procedimiento utilizado.

La recogida de información se realizó mediante los registros de formulario por el autor de la investigación. Para el procesamiento de los resultados se utilizaron los tests de chi2 y t de Student para determinar las diferencias entre variables, considerándose significativa una $p < 0,05$.

Resultados

Respecto a la relación entre la edad de la madre y el interés mostrado en los cuidados a su bebé, en la unidad de encamación neonatal las madres menores de 20 años muestran más interés que el resto de las madres estudiadas. ($\chi^2 = 30,247$; $p < 0,001$) La diferencia está a favor de las mujeres menores de 20 años con el 76%, frente a un 38% de las mujeres que no ofrecieron interés en los CCD ni en la hospitalización conjunta. Ellas decidieron continuar haciendo visitas esporádicas a la unidad de encamación neonatal para ver a sus hijos.

La edad de la madre también se encuentra asociada al contacto piel con piel ($\chi^2 = 18,997$; $p < 0,001$). Las madres menores de 20 años tienen contacto con sus bebés en mayor proporción que las madres entre 21 y 39 años y que las mayores de 40 años. Hay diferencias estadísticamente significativas entre la edad de las madres y el contacto piel con piel. La diferencia está a favor de las mujeres menores de 20 años, con el 70,2%. Valor que baja al 39,7%, para edades entre 20 y 39 años y todavía más, el 14,3%, para las mujeres con más de 40 años de edad.

Respecto a la relación entre la edad de la madre y la lactancia materna, las madres menores de 20 años dan al pecho a sus hijos en mayor proporción que el resto de las madres estudiadas (21-39 años) y mayores de 40 años ($\chi^2 = 40,987$; $p < 0,001$). La diferencia se inclina a

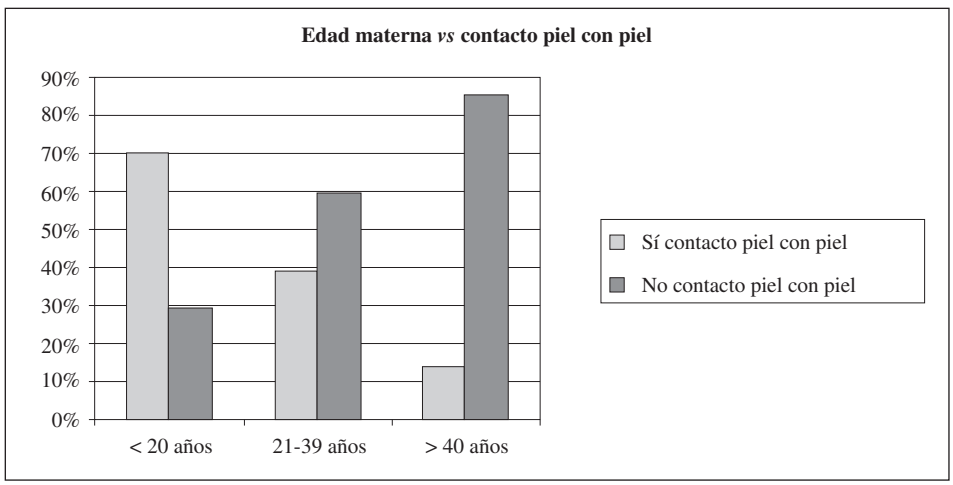


Fig. 2.—Edad de la madre y contacto piel con piel.

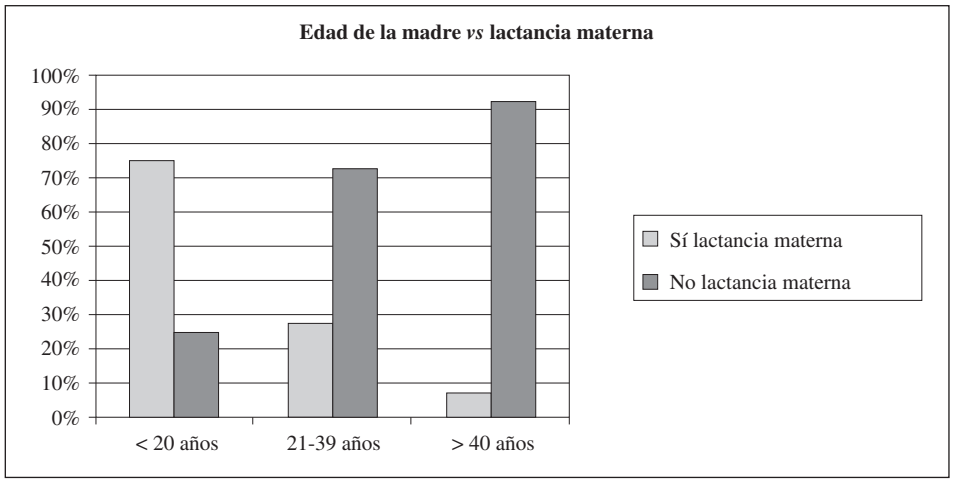


Fig. 3.—Edad de la madre y lactancia materna.

favor de las mujeres menores de 20 años, con el 73%, frente a un 27% de las mujeres que no amamantaban. Llamó poderosamente la atención que, de las mujeres mayores de 40 años, de las que hubo 14 en el estudio, solamente una dio el pecho. El resto no quiso información sobre el contacto piel con piel, ni de la lactancia materna, ni tampoco de los cuidados centrados en el desarrollo, como beneficio para su hijo.

Discusión

Los resultados obtenidos en relación con el interés de la madre por los cuidados centrados en el desarrollo de su bebé y la edad de la misma (χ^2 = 30,247; p < 0,001), difieren con los obtenidos en otros estudios, en los que la adolescencia es ya un factor de riesgo para el apego con su hijo. La mayoría de los autores coinciden en que la etapa de 21 a 34 años es la óptima para la concepción, pues la mujer ya ha completado su maduración biológica y social y está mejor preparada para la procreación, lo que no ocurre en las edades extremas de la vida.

Estos autores demuestran que las madres que reciben información adecuada sobre lactancia materna en etapas tempranas de su vida reproductiva son muy susceptibles de experimentar el deseo de la lactancia exclusiva[22].

Los resultados obtenidos en el estudio han demostrado que las mujeres menores de 20 años están preparadas para el cuidado de su hijo, siempre y cuando se les proporcione una información y un entrenamiento posnatal inmediato adecuado.

En lo que se refiere a la asociación entre la edad de la madre y el contacto piel con piel (χ^2 =18,997; p < 0,001), las madres menores de 20 años tienen contacto con sus bebés en mayor proporción que las madres de más edad. Y es que fueron más sensibles a la información que se le administró y practicaron más esta técnica. Igual que en la bibliografía que a continuación se describe, los bebés tuvieron mejor estabilidad cardiorrespiratoria, menos duración del llanto y mejor regulación térmica.

Una revisión de Cochrane, recientemente actualizada, sobre los efectos del contacto piel con piel, mostró una mejoría de las conductas de afecto y apego, tanto a corto plazo como a largo plazo y manifiestan ser duraderas en el tiempo. Las madres que tuvieron este contacto informaron tener menos dolor, debido a la ingurgitación mamaria, que generalmente ocurre al tercer día del parto. Otros beneficios del contacto piel con piel incluyen una mayor estabilidad cardiorrespiratoria en los recién nacidos prematuros y una menor duración del llanto, en comparación con los otros recién nacidos. La regulación térmica es un componente esencial para la prevención de la morbilidad neonatal, particularmente en los recién nacidos de muy bajo peso[22,23]. Otros autores afirman también que este procedimiento, además de lo anteriormente mencionado, mejora la estabilidad metabólica y hemodinámica del niño, disminuye las infecciones, tiene efectos analgésicos y mejora la tasa de lactancia y su duración, con todas las ventajas que ella implica[24,25,26,27,28].

En relación con la lactancia materna, y coincidiendo con otros autores[26,27,28], como forma de alimentación el bebé pretérmino, se obtuvieron resultados favorables en el grupo de mujeres jóvenes, donde las menores de 20 años dan al pecho a sus hijos en mayor proporción que las otras madres (χ^2 = 40,987; p < 0,001).

A diferencia de otros estudios que han demostrado que la alimentación con leche materna es menos frecuente en los bebes de madres adolescentes, parece que la edad de la madre condiciona la utilización del contacto piel con piel y a la lactancia materna[18-21].

El establecimiento de esta forma de alimentación depende de un proceso de adaptación y aprendizaje entre el bebé y su madre. En esta etapa de la vida, la mujer que se enfrenta por primera vez al embarazo se prepara con esmero y aprovecha todo el caudal de conocimientos e información que están a su disposición en este momento. Es una etapa en la que la mujer necesita elevar su autoestima y demostrar que es capaz de proporcionar a su bebé alimento y salud.

Conclusiones

Este estudio pone de manifiesto que en el contexto de los hospitales palestinos las mujeres jóvenes que dan a luz bebés pretérmino, si son informadas e instruidas, se sienten más motivadas para el cuidado de sus hijos durante la hospitalización. Practican más el contacto piel con piel (CCD) y la lactancia materna es más prolongada. Todo ello conlleva un alta hospitalaria más temprana.

No se han realizado estudios similares con anterioridad en este país. Los resultados de esta investigación denotan que, con una buena información a las madres, se favorece el método de los CCD, que constituye una forma de atención al bebé pretérmino, moderna, eficaz y beneficiosa, tanto para el niño como para sus padres.

Se recomienda desde aquí la continuación de este trabajo en otros hospitales de Palestina, antelos resultados tan favorables que se obtuvieron en relación con la lactancia materna y con las revisiones postnatales de las mujeres.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1945-1951
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Perfil de prescripción de nutrición parenteral en recién nacidos de muy bajo peso al nacer; período 2006 a 2010

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Resumen

Introducción: **Un aporte precoz de nutrientes en las cantidades adecuadas es de vital importancia para los recién nacidos prematuros ya que disminuye el tiempo en alcanzar el peso esperado y en tolerar por vía enteral, disminuyendo la estancia hospitalaria El objetivo principal de este estudio es analizar la prescripción de nutrición parenteral (NP) de pacientes con menos de 1.500 g al nacimiento en los primeros 7 días de vida durante los años 2006-2010 en nuestro hospital y la adecuación de dichas prescripciones a las recomendaciones.**

Material y métodos: **Se recogió el aporte de aminoácidos, glucosa, lípidos (g/kg/día) y calorías (kcal/kg/día) prescritos en la NP de la primera semana de vida.**

Resultados: **Se estudiaron 1.899 prescripciones de nutrición parenteral de los años 2006-2010 que correspondían a la primera semana de vida de 360 pacientes con menos de 1.500 g. El contenido calórico aumentó desde una media de 41,83 kcal/kg/día (1,89 g/kg/día de aminoácidos y 0,69 g/kg/día de lípidos) el primer día de vida hasta 80,61 kcal/kg/día (3,2 g/kg/día de aminoácidos y 2,4 g/kg/día de lípidos) el séptimo día. Cerca de un 70% de las prescripciones de los niños que tuvieron NP el primer día de vida llevaban lípidos. Pero cuando se considera todos los niños que tuvieron NP el cuarto día solo un 17% de dichos pacientes tuvieron aporte de lípidos el primer día de vida. Ninguna prescripción sobrepasaba 120 kcal/kg/día. Solamente un 17,9% de las del sexto día y 25.5% de las del séptimo día aportaban mas de 90 kcal/kg/día. En nuestro hospital no se preparan NP los domingos y festivos. 30,1% y 56,9% de los niños que nacieron en día laborable recibieron NP el primer y segundo día, frente 11,6% y 38,8% de los nacidos en festivo o víspera de festivo.**

Conclusiones: **Un alto porcentaje de niños prematuros no recibe las cantidades recomendadas de nutrientes en la primera semana de vida en nuestro hospital.**

(*Nutr Hosp.* 2012;27:1945-1951)

DOI:10.3305/nh.2012.27.6.6042

Palabras clave: *Prescripción. Nutrición parenteral. Pretérmino.*

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Recibido: 5-VII-2012.
Aceptado: 17-VII-2012.

PROFILE OF PARENTERAL NUTRITION PRESCRIPTION IN VERY LOW BIRTH WEIGHT INFANTS; PERIOD 2006 TO 2010

Abstract

Introduction: **Early administration of nutrients in adequate amounts is of vital importance to preterm infants because it decreases the time needed to reach the expected weight and tolerate enteral nutrition as well as reducing their hospital stay The main objective of this study was to analyze the prescription of parenteral nutrition (PN) in patients weighing less than 1,500 g at birth in their first 7 days of life during the years 2006-2010 in our hospital and the adequacy of those requirements to the recommendations.**

Materials and methods: **Amino acids, glucose, lipids (g/kg/day) and calories (kcal/kg/day) prescribed in the PN of the first week of life were collected.**

Results: **We studied 1899 parenteral nutrition prescriptions from 2006 to 2010 corresponding to the first week of life of 360 patients weighing less than 1,500 g. The caloric content increased from an average of 41.83 kcal/kg/day (1.89 g/kg/ day of amino acids and 0.69 g/kg/day lipids) on the first day of life to 80.61 kcal/kg/day (3.2 g/kg/day of amino acids and 2.4 g/kg/day of lipids) on the seventh day. About 70% of prescriptions for the children who had PN on the first day of life contained lipids. But when all children who had PN on the fourth day were considered, only 17% of these patients had lipid intake on the first day of life. No prescription exceeded 120 kcal/kg/day. Only 17.9% on the sixth day and 25.5% on the seventh day received more than 90 kcal/kg/day. In our hospital PN is not prepared on Sundays and holidays. 30.1% and 56.9% of children born on weekdays received PN the first and second day versus 11.6% and 38.8% of those born on a holiday or the day before holiday.**

Conclusions: **A high percentage of premature babies do not get the recommended amounts of nutrients in their first week of life in our hospital.**

(*Nutr Hosp.* 2012;27:1945-1951)

DOI:10.3305/nh.2012.27.6.6042

Key words: *Prescription. Parenteral nutrition. Preterm infant.*

Introducción

Durante la vida fetal es la madre, a través de la placenta y el cordón umbilical, quien garantiza de forma continua el aporte adecuado para el crecimiento y la maduración[1,2]. La insuficiencia placentaria produce rápidamente una restricción del crecimiento intrauterino y si se mantiene mucho tiempo puede condicionar la programación celular (fenotipo ahorrador), el neurodesarrollo e incluso producir la muerte fetal.

Cuanto más prematuro es un recién nacido, más repercusión tiene la restricción de nutrientes y más puede afectar al neurodesarrollo y al crecimiento[3,4,5,6,7,8]. Los prematuros nacidos antes de la semana 32 o con menos de 1.500 gramos (denominados de muy bajo peso) no toleran por vía enteral durante los primeros días todos los aportes de nutrientes que necesitan, lo que obliga a recurrir al aporte intravenoso total o parcial de agua y nutrientes. Aún así la desnutrición y el hipocrecimiento son habituales en los prematuros con muy bajo peso, especialmente en los nacidos con menos de 1.000 gramos[9,10,11,12].

La tendencia actual consiste en comenzar el aporte enteral y parenteral de nutrientes en las primeras horas de vida e incrementarlo lo más rápidamente posible según la tolerancia hasta alcanzar los aportes máximos recomendados[13,14,15,16]. La nutrición parenteral se retira cuando se ha alcanzado al menos el 75% de los aportes recomendados y es previsible que puedan seguir aumentándose. Estas prácticas han demostrado mejorar la nutrición y acortar la estancia hospitalaria[2].

Se ha dado gran importancia al aporte precoz suficiente de aminoácidos, en las primeras horas y días de vida, para permitir el crecimiento precoz postnatal y mejorar la tolerancia de la glucosa[17,18,19,20,21,22,23]. Hoy es bien conocido que los prematuros utilizan parte de los aminoácidos como sustrato energético, igual que el feto, y que el aporte insuficiente de este nutriente limita el crecimiento y posiblemente el neurodesarrollo, por el gran crecimiento cerebral en este período[24,25,26,27,28].

Pasados los primeros días de vida, puede ser necesario mantener una nutrición parenteral total o de apoyo en caso de intolerancia digestiva, enterocolitis necrotizante, obstrucción intestinal, cirugía intestinal o síndrome de intestino corto.

Por otro lado exceder los aportes recomendados de algunos nutrientes puede relacionarse con hepatotoxicidad y con excesiva ganancia de grasa visceral[29,30,31,32,33].

La prescripción de la nutrición parenteral (NP) en Neonatología es especialmente compleja, porque hay que diseñar cada solicitud en función de la edad, el tiempo de gestación, el peso, la patología del paciente, el tipo de acceso venoso (central o periférico) y los aportes que reciba por vía enteral[34]. Además hay que contemplar la prevención de las complicaciones evitables en cada caso (por ejemplo en pacientes con colestasis o insuficiencia renal).

Los protocolos de práctica clínica deben incluir toda la información necesaria para permitir una adecuada prescripción de la NP y maximizar el crecimiento del niño evitando complicaciones. Sin embargo, no siempre las prescripciones de adhieren al protocolo. Las razones pueden ser variadas, desde intolerancia metabólica, miedo a efectos adversos, imposibilidad del Servicio de Farmacia de preparar las nutriciones parenterales, sobrecarga de trabajo, olvidos, desconocimiento de los protocolos o errores en la prescripción.

El objetivo principal de este estudio es analizar la prescripción de NP de los pacientes con menos de 1.500 g al nacimiento en los primeros 7 días de vida durante los años 2006-2010 en nuestro hospital y la adecuación de dichas prescripciones a las recomendaciones, para buscar oportunidades de mejora en la prescripción.

Métodos

Estudio descriptivo retrospectivo de las prescripciones de nutrición parenteral para recién nacidos prematuros nacidos con menos de 1.500 gramos en un centro hospitalario de tercer nivel, durante los años 2006 a 2010 (ambos incluidos). Se incluyeron todas las prescripciones de los 7 primeros días de vida. Se excluyeron los pacientes con malformaciones graves. En este periodo el Servicio de Farmacia preparaba diariamente las nutriciones parenterales prescritas a diario en el Servicio de Neonatología, excepto los domingos y festivos. Todas las prescripciones se realizaron de 9 a 14 h. No se permitió prescribir en los turnos de tarde y noche.

Variables de estudio de las prescripciones

- Aporte diario de aminoácidos, glucosa y lípidos (g/kg/día).
- Aporte diario de calorías (kcal/kg/día).
- Vía de administración (solo a partir de la informatización de la prescripción).
- Tipo de día de nacimiento (laborable o festivo).

Fuentes de datos

Base de datos del programa de nutrición del Servicio de Farmacia:

- Prescripción médica en formato papel hasta abril de 2009.
- Prescripción médica electrónica a partir de abril de 2009.

Base de datos del Servicio de Neonatología para obtener el peso de los pacientes al nacimiento.

Cambios en el protocolo de nutrición parenteral del Servicio de Neonatología en el periodo 2006-2010

En los años 2006 y 2009 se revisó el protocolo de administración de NP. Para determinar la adecuación de las

Anexo I
Recomendaciones de los protocolos 2006

Peso (g)	*Aporte inicial (g/kg/día)*	*Aumento diario (g/kg/día)*	*Aporte máximo (g/kg/día)*
Aminoácidos			
500-999	1,5-3	0,5-1	3.5-38
1.000-2.499	1,5-2	0,5-1	3,5
Lípidos			
500-2.499	1	0,5	3

Anexo II
Recomendaciones de los protocolos 2009

Peso (g)	*Aporte inicial (g/kg/día)*	*Aumento diario (g/kg/día)*	*Aporte máximo (g/kg/día)*
Aminoácidos			
500-1.500	2-3	0,5-1	3.5-38
> 1.500	1,5-2,5	0,5-1	3
Lípidos			
500-2.499	1	0,5	3
≥ 2.500	1	0,5-1	3-3,5

prescripciones al protocolo estudiamos el seguimiento de las recomendaciones relativas a la composición de las NP los primeros días de vida en pacientes prematuros (anexos 1 y 2). Ambos protocolos recomendaban alcanzar 90-110 kcal/kg/día para conseguir un crecimiento adecuado.

Métodos estadísticos

Descripción de variables: las variables dicotómicas o categóricas se describen en porcentajes. Las variables continuas se describen con la media, mediana, desviación estándar y percentiles

Las comparaciones de medias se analizan con la prueba ANOVA, y las proporciones con la prueba Chi-cuadrado.

Resultados

Se estudiaron 1.899 NP prescritas en los años 2006-2010 en el Servicio de Neonatología del Hospital 12 de Octubre de Madrid que correspondían con la primera semana de vida de 360 pacientes con menos de 1.500 g al nacimiento y sin malformaciones graves.

El contenido calórico de las NP fue aumentando desde una media de 41,83 kcal/día en el primer día de vida hasta 80,61 en el séptimo día. Respecto a los aminoácidos se pautó una media de 1,89 g/kg/día el primer día de vida aumentando progresivamente hasta 3,2 el séptimo día. Los lípidos también se incrementaron desde 0,69 de media hasta 2,4. Las medias, desviaciones estándar y cuartiles de los aportes de macronutrientes de los siete primeros días de vida pueden verse en la tabla I.

Cerca de un 70% de las prescripciones de los niños que tuvieron NP el primer día de vida llevaban lípidos. Sin embargo, sólo el 17% pacientes con NP el cuarto día recibieron aporte de lípidos el primer día. En la tabla 2 se puede ver el porcentaje de pacientes que recibió lípidos los 3 primeros días de vida, respecto al total de NP prescritas cada día y en la tabla 3 respecto al número de prescripciones del cuarto día de vida.

Ninguna prescripción superó las 120 kcal/kg/día. Solamente un 17,9% de las del sexto día y 25,5% de las del séptimo día aportaban más de 90 kcal/kg/día. En la tabla 4 se describen los porcentajes de NP con más de 90 kcal/kg/día.

La vía de administración solamente se pudo obtener en las prescripciones realizadas electrónicamente, ya que esta variable no se introducía en el ordenador con la prescripción manual. De las 637 prescripciones realizadas por prescripción electrónica 87 (13,66%) fueron administradas por vía periférica. Si se compara la composición de las prescripciones para vía central y para vía periférica, solamente se encuentran diferencias estadísticamente significativas en el aporte de aminoácidos y en el aporte calórico ($p < 0,05$). En la tabla V se describen la media, mediana y desviación típica de las prescripciones electrónicas para administrar por vía central y periférica.

Si comparamos los pacientes que nacieron en día laborable con los que nacieron en festivo o el día previo, el 11,6% de los pacientes que nacieron en festivo recibió NP el primer día de vida frente al 30,1% de los nacidos en día laborable y un 50,4% de los pacientes nacidos en festivo recibió su primera NP los primeros dos días de vida frente a un 87% de los que nacieron en día laborable. En la tabla VI se muestra el porcentaje de

Tabla I
Medias, desviaciones estándar y cuartiles de los aportes de macronutrientes de los siete primeros días de vida

Días de vida (número de prescripciones)	*Calorías (kcal/kg/día)*	*Aminoácidos (g/kg/día)*	*Glucosa (g/kg/día)*	*Lípidos (g/kg/día)*
1 (n = 86)				
Media	41,83	1,89	6,84	0,69
Desviación típica	7,56	0,44	1,32	0,49
Percentiles				
25	36	1,5	6	0
50	42	2	6	1
75	46	2	8	1
2 (n = 264)				
Media	49,58	2,20	7,83	0,94
Desviación típica	9,913	0,528	1,83	0,50
Percentiles				
25	42	2	7	1
50	50	2	8	1
75	57	2,5	9	1
3 (n = 318)				
Media	60,55	2,60	9,04	1,4
Desviación típica	12,05	0,53	2,21	0,5
Percentiles				
25	53,75	2	8	1
50	59	2,5	9	1,5
75	67	3	10	1,5
4 (n = 337)				
Media	69,29	2,91	9,97	1,8
Desviación típica	12,87	0,53	2,37	0,54
Percentiles				
25	62	2,5	8	1,5
50	70	3	10	2
75	77	3,5	12	2
5 (n = 331)				
Media	74,09	3,01	10,4	2,04
Desviación típica	12,86	0,55	2,41	0,54
Percentiles				
25	66	3	9	1,5
50	74	3	10	2
75	83	3,5	12	2,5
6 (n=308)				
Media	77,99	3,14	10,8	2,23
Desviación típica	13,19	0,52	2,48	0,59
Percentiles				
25	70	3	9	2
50	78	3,5	11	2
75	88	3,5	12	2,5
7 (n = 255)				
Media	80,61	3,2	10,95	2,4
Desviación típica	12,92	0,48	2,47	0,56
Percentiles				
25	72	3	10	2
50	82	3,5	11	2,5
75	91	3,5	12	3

pacientes que iniciaron la NP en los tres primeros días de vida según nacieran en día laborable o festivo. La media del día de inicio de la NP fue de 0,95 para los que nacieron en laborable frente 1,56 los que lo hicieron en festivo o previo a festivo (Significación Anova 0,000).

Discusión

Aunque cada vez hay mas evidencia que es necesario un adecuado aporte proteico y calórico los primeros días de vida en pacientes prematuros, muchas

Tabla II
Porcentaje de pacientes que recibió lípidos los 3 primeros días de vida respecto al total de NP prescritas cada día

Días de vida	*Frecuencia Total*	*Porcentaje Total*	*Frecuencia Manual*	*Porcentaje Manual*	*Frecuencia Electrónica*	*Porcentaje Electrónica*
1 (n = 86)	60	69,77%	48	69,57%	12	70,59%
2 (n = 264)	220	83,33%	144	82,29%	76	85,39%
3 (n = 318)	309	97,17%	201	96,17%	108	99,08%

Tabla III
Porcentaje de aporte de lípidos respecto al número de prescripciones del cuarto día de vida

Días de vida	*Frecuencia Total*	*Porcentaje Total*	*Frecuencia Manual*	*Porcentaje Manual*	*Frecuencia Electrónica*	*Porcentaje Electrónica*
1	60	17,8%	48	21,64%	12	10,43%
2	220	65,28%	144	64,86%	76	66,09%
3	309	91,69%	201	90,54%	108	93,91%

Tabla IV
Frecuencia y porcentaje de las prescripciones con más de 90 kcal/kg/día

Días de vida	*Frecuencia total*	*Porcentaje total*
3	7	2,2%
4	19	5,6%
5	31	9,4%
6	55	17,9%
7	65	25,5%

veces la prescripción no se adecua a estas necesidades. Lapillonne y cols.[35] describen los resultados de una encuesta realizada en el año 2006 a la que contestan 172 unidades neonatales francesas. El aporte proteico no se iniciaba el primer día de vida en la mitad de las unidades encuestadas y el aporte lipídico se iniciaba como pronto el tercer día en mas del 50% de las unidades. Grover y cols.[36] también realizan una encuesta en los años 2005-2006 en Reino Unido a la que contestan 48 unidades. Encuentran que sólo un 54% de las unidades inician la NP el primer día de vida. La mediana en que se alcanzan todos los requerimientos es 6 días y un 25% de las Unidades lo alcanzan el séptimo día o más tarde. Solo un 39% de las Unidades prescriben lípidos el primer día de vida y un 23% retrasan su inicio hasta el tercer día. Hay que tener en cuanta que cuando se contesta una encuesta generalmente se responde de acuerdo a los protocolos en vigor. En nuestro caso existe una revisión periódica de los protocolos y como se puede ver en los anexos 1-2 y éstos se adecuan a las recomendaciones de las sociedades científicas, tanto las españolas SENPE, SEGHNP, SEFH[37] como las americanas ESPGHAN y ASPEN[38].

Sin embargo, cuando revisamos las prescripciones neonatales en nuestro hospital encontramos que muchas de ellas no alcanzaban las cantidades mínimas recomendadas. A pesar de que los protocolos recomiendan alcanzar las 90 kcal/kg/día al quinto o sexto día (anexo 1-2), un 82,1% de las prescripciones del sexto día de vida no alcanza las 90 kcal/kg/día y solo un 25,5% de las del séptimo día de vida las alcanzaban. Sólo podemos analizar la prescripción de NP, ya que no tenemos datos de las cantidades reales administradas, ni de la cantidad recibida por vía enteral.

Tabla V
Aporte de macronutrientes según la vía de administración

Vía	*Calorías (kcal/kg/día)*	*Aminoácidos (g/kg/día)*	*Glucosa (g/kg/día)*	*Lípidos (g/kg/día)*
Central (n = 550)				
Media	69,26	2,87	9,9	1,82
Mediana	70	3	10	2
Desviación típica	16,04	0,65	2,46	0,72
Periférica (n = 87)				
Media	64,82	2,32	9,73	1,66
Mediana	68	2	10	2
Desviación típica	14,466	0,65	1,84	0,77

Tabla VI
Porcentaje de pacientes que iniciaron la NP en los tres primeros días de vida según nacieran en día laborable o festivo (en este último se incluyen los nacidos los días previos a un festivo) (Chi-cuadrado 0,000)

	Primer día	*Segundo día*	*Tercer día*
Laborable (239)	30,1%	56,9%	2,9%
Festivos (121)	11,6%	38,8%	39,7%

Al ser la fuente de datos el programa de nutrición parenteral del Servicio de Farmacia, no están recogidos los aportes de aminoácidos o glucosa administrados antes de que fuera prescrita la NP. Sin embargo, a estos niños no se les aportaron lípidos y el aporte de aminoácidos añadidos al suero intravenoso no excedió de 1 g/kg/día habitualmente, por lo que es muy probable que el aporte calórico y de aminoácidos fuese menor al recomendado.

Un aspecto relevante es que sólo un 25,5% tuvieron NP prescrita el primer día y un 78,3% y 94% el segundo y tercer día. Además un 82,2% de los pacientes que recibieron NP el cuarto día no recibieron lípidos el primer día de vida y un 34,72% no lo recibieron el segundo día de vida. Este menor aporte de lípidos en los primeros días de vida tanto por no recibir parenteral, como por recibirla sin lípidos, puede explicar que los aportes calóricos sean menores a los recomendados en los dos primeros días de vida, ya que en estos primeros días, cuando el paciente recibe nutrición parenteral, los aportes proteicos y de hidratos de carbono se ajustan bastante a los requerimientos.

En el séptimo día de vida hay un alto porcentaje de pacientes que no alcanzaron los requerimientos. Aunque aminoácidos y lípidos no llegaban en la mayoría de las prescripciones a los aportes máximos, es el aporte de glucosa el que se diferenciaba más. Martin y cols. revisan 1.506 pacientes de 23-27 semanas de gestación que sobrevivieron más de 28 días, pertenecientes a 14 unidades neonatales durante los años 2002-2004 y describen también un déficit de carbohidratos en las NP prescritas responsable del déficit calórico encontrado[9]. Ellos encuentran una mediana de 9,3 g/kg/día de aporte total de carbohidratos (incluyendo enteral) al séptimo día, en nuestros pacientes el aporte es mayor (mediana de 11). Una de las causas posibles de este menor aporte de glucosa son los problemas metabólicos del paciente como hiperglucemia, acidosis o hipertrigliceridemia.

Otro dato que puede disminuir las calorías prescritas es la ausencia de vía central. El 13,7% de las prescripciones electrónicas se administraron por vía periférica lo que pudiera haber impedido administrar todos los aportes necesarios. Aunque la media de los aportes de todos los macronutrientes es menor cuando la vía es periférica, sólo alcanza significación estadística en el aporte proteico y calórico. Sin embargo, el porcentaje de prescripciones con vía periférica es demasiado pequeño para explicar la diferencia entre las cantidades pautadas y recomendadas.

Otra posible causa del lento incremento calórico en los primeros días puede ser la restricción hídrica que sufren los pacientes con conducto arterioso persistente con hiperaflujo pulmonar, que en nuestra muestra se aproxima al 25%.

En el Hospital 12 de Octubre solo se preparan NP los días laborables en horario de mañana. Este hecho puede haber determinado un inicio de la NP más tardío en muchos de los pacientes nacidos en días festivos o en laborables después de las 2 o 3 de la tarde. El porcentaje de pacientes que recibió NP el primer día de vida es solo del 30% en los pacientes nacidos en día laborable. Esto puede ser debido, en parte, a la falta de disponibilidad de NP durante la tarde y la noche. Este porcentaje disminuye hasta el 11,6% en los nacidos en festivo o en víspera de festivo, y hay un 36% menos de pacientes que reciben su primera NP en los dos primeros días de vida entre los nacidos en día festivo. Una clara oportunidad de mejora sería disponer de NP para el primer y segundo día de vida en los días festivos y durante las tardes y noches en los días laborables.

Otra posible estrategia para mejorar las prescripciones es disponer en el programa informatizado de prescripciones prediseñadas por días para los primeros 7 días de NP. De esta forma se facilitaría la adherencia al protocolo en el incremento de los aportes venciendo las resistencias, los miedos o los olvidos de los prescriptores.

La mayor limitación del estudio es no hemos podido estudiar los aportes de aminoácidos y glucosa por vía intravenosa y los de leche por vía enteral ya que no estaban recogidos informativamente. Esto hace que no conozcamos las calorías totales recibidas por los niños. Sin embargo los aportes son claramente inferiores a los recomendados.

Conclusiones

Un alto porcentaje de niños prematuros no recibe las cantidades recomendadas en la primera semana de vida en nuestro hospital. Esto es debido fundamentalmente a un escaso aporte los primeros días de vida y a un insuficiente incremento de las calorías los días posteriores. Las patologías propias de los prematuros de muy bajo peso condicionan con frecuencia el aporte nutricional, sin embargo, en nuestro caso, también ha influido significativamente la falta de disponibilidad de NP los domingos y festivos. Es necesario que haya disponibilidad de NP para que estos pacientes puedan recibir la NP desde el primer día y establecer estrategias de adherencia a los protocolos en cuanto al aporte adecuado de nutrientes.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1952-1959
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

¿Siguen patrones de dieta mediterránea los universitarios españoles?

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Resumen

Objetivo: **Determinar el patrón de consumo de alimentos del alumnado de la Universidad de Alicante (UA) mediante el grado de adecuación a la dieta mediterránea.**

Método: **Estudio transversal descriptivo para estimar la ingesta individual a través de un cuestionario de frecuencia de consumo de alimentos (CFCA) en una muestra representativa de 380 universitarios. Variables a estudio: edad, sexo, área geográfica de procedencia, peso y talla autoreferidos. Así como los alimentos y frecuencias de consumo que componen el CFCA. Se determinó el porcentaje de adecuación teniendo en cuenta, consumo real sobre consumo recomendado por la guía dieta mediterránea tradicional: (100 x raciones consumidas/raciones recomendadas). Se establecieron 5 rangos de porcentaje adecuación: consumo óptimo (80%-119%), consumo aceptable (60%-79%), consumo deficiente (40%-59%), consumo muy deficiente (< 39%), consumo excesivo (> 120%). Se realizó contraste de diferencia de proporciones y la prueba t-Student con EPIDAT 3.1, y SPSS 15.0.**

Resultados: **Prevalencia de sobrepeso-obesidad, es mayor en hombres (34,6%) que en mujeres (9,8%), p < 0,001. Mientras que las mujeres presentan mayor prevalencia de bajo peso (7,0%) que hombres (0,7%), p < 0,05. El consumo de cereales y derivados es muy deficiente (mujeres = 90,6; hombres = 94,9), y el consumo de carnes rojas (mujeres = 90,6; hombres = 92,7) y embutidos (mujeres = 95,9%, hombres = 96,3%) es excesivo. Ningún alumno cubre un "consumo óptimo" o un "consumo aceptable" de todos los grupos de alimentos (n = 12).**

Discusión: **El nivel educativo y el acceso a la información no protegen a la población universitaria de factores socioambientales que influencian sus hábitos alimentarios. Deben reforzarse estrategias de salud pública dirigidas a este grupo de población.**

(*Nutr Hosp.* 2012;27:1952-1959)

DOI:10.3305/nh.2012.27.6.6091

Palabras clave: *Dieta mediterránea. Cuestionario frecuencia de consumo. Guías alimentarias.*

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Recibido: 15-VI-2012.
1.ª Revisión: 31-VII-2012.
Aceptado: 7-VIII-2012.

DO THE SPANISH UNIVERSITY STUDENTS FOLLOW MEDITERRANEAN DIETARY PATTERNS?

Abstract

Objective: **To determine the pattern of food intake among the students of the University of Alicante (UA) by the level of adherence to the Mediterranean diet.**

Methods: **Descriptive trans-sectional study estimating the individual intake by means of a questionnaire of food intake frequency (QFIF) in a representative sample of 380 college students. Study variables: age, gender, geographical area of origin, self-communicated weight and height; types and intake frequencies of the foods included in the QFIF. The percentage of adherence was calculated taking into account the actual intake and the intake recommended in the guideline of traditional Mediterranean diet: 100 x servings consumed/recommended servings. We established 5 ranges of percentage of adherence: optimal intake (80%-119%), acceptable intake (60%-79%), deficient intake (40%-59%), very deficient intake (< 39%), excessive intake (> 120%). We analyzed the differences in proportions distribution and the Student's t test with EPIDAT 3.1 and SPSS 15.0.**

Results: **The prevalence of overweight/obesity is higher in men (34.6%) than in women (9.8%), p < 0.001, whereas women had higher prevalence of low weight (7.0%) than men (0.7%), p < 0.05. The consumption of grains and derivatives was very deficient (women = 90.6; men = 94.9) whereas the intake of red meats (women = 90.6; men = 92.7) and cold meats (women = 95.9%, men = 96.3%) was excessive. No student had an "optimal intake" or an "acceptable intake" of all the dietary groups (n = 12).**

Discussion: **The educational level and access to the information do not protect the university population from socio-environmental factors that have an influence on their dietary habits. The public health strategies focused on this population group should be strengthen.**

(*Nutr Hosp.* 2012;27:1952-1959)

DOI:10.3305/nh.2012.27.6.6091

Key words: *Mediterranean diets. Questionnaires of food intake frequency. dietary guidelines.*

Abreviaturas

UA: Universidad de Alicante.
CFCA: Cuestionario de Frecuencia de Consumo de Alimentos.
IMC: Índice Masa Corporal.
OMS: Organización Mundial de la Salud.
SENC: Sociedad Española de Nutrición Comunitaria.
CEDM: Comité de Expertos de Dieta Mediterránea.
NAOS: Nutrición, Actividad Física y Prevención de la Obesidad.
AESAN: Agencia Española de Seguridad Alimentaria y Nutrición.

Introducción

La dieta mediterránea ha sido reconocida como un modelo de alimentación saludable por su asociación a una mayor esperanza de vida y a su efecto protector frente a enfermedades crónicas. Se caracteriza por un alto consumo de vegetales crudos y cocidos, frutas frescas, legumbres y cereales, aceite de oliva; un moderado consumo de leche y productos lácteos; un bajo consumo de carne y un moderado consumo de alcohol, especialmente en forma de vino. En el caso de España, se añade, además, un alto consumo de pescado[1]. Este modelo alimentario se encuentra ampliamente difundido entre países meridionales de Europa como España, Grecia e Italia. No obstante, el consumo de alimentos en cada uno de ellos varía en función de su cultura y nivel socioeconómico[2,3].

Los efectos de la globalización están produciendo un cambio en los estilos de vida mediterráneos, especialmente notables en los hábitos alimentarios de la población joven, por ser los más expuestos a los diversos cambios transfronterizos[4]. Las transformaciones emocionales y fisiológicas propias de la juventud[5], las presiones publicitarias y los patrones estéticos actuales, son algunos de los factores que influyen en su adhesión a la dieta mediterránea. En el caso de la población universitaria, a todo esto se añade la asunción de nuevas responsabilidades en la compra de alimentos, la elaboración de sus menus[6] y la organización de unos horarios de comidas que resultan ser bastante irregulares[7]. De hecho, se han identificado entre los estudiantes deficiencias en el consumo de micronutrientes, que distan de las recomendaciones de la dieta mediterránea[7-8]. Este cambio en los hábitos de consumo puede repercutir en su salud. Estudios recientes han encontrado una asociación entre la frecuencia de consumo de alimentos de la población universitaria y la aparición de estrés, depresión[9] y obesidad[10].

En España, la dieta de la población universitaria se caracteriza por ser rica en proteínas y estar asociada a una elevada ingesta de colesterol y grasa saturada[5,11]. El objetivo de este estudio es determinar el patrón de consumo de alimentos de los alumnos de la Universidad de Alicante (UA), a través del grado de adecuación a la dieta mediterránea.

Método

Estudio transversal descriptivo del consumo de alimentos utilizando un método directo retrospectivo para estimar la ingesta individual a través del cuestionario de frecuencia de consumo de alimentos (CFCA) en población universitaria entre diciembre de 2009 y abril de 2010.

La población diana estuvo constituida por estudiantes de la Universidad de Alicante (UA) (n = 26.273). La muestra representativa correspondió a 380 estudiantes. Se utilizó como criterio de inclusión el ser alumnado de primer y segundo ciclo matriculado en la UA en el curso académico 2009-2010, y aceptar voluntariamente la participación en el estudio. Como criterio de exclusión, ser alumnado de tercer ciclo, o personal de administración y servicios, o personal docente y de investigación, aún cumpliendo el criterio de ser también estudiante, para evitar heterogeneidad en la muestra.

La encuesta se cumplimentó en puntos estratégicos de la UA, definidos como lugares de mayor concurrencia y seleccionados mediante un muestreo aleatorio simple. Se eligió un total de 20 lugares del campus, de los cuales se extrajeron de forma aleatoria 7: la entrada principal, la biblioteca general y sus jardines, el aulario II, el polideportivo, la escuela politécnica y sus exteriores, el club social I y sus alrededores y el acceso al centro comercial próximo a la universidad.

La elección de los estudiantes se realizó mediante un muestreo sistemático. Consistió en entrevistar al tercero de los estudiantes que pasó por alguno de estos lugares seguido del sexto, noveno y así, sucesivamente, hasta completar cinco encuestas diarias. Estas se realizaron de lunes a viernes en horarios de mañana y tarde, entre diciembre de 2009 y abril de 2010. Todos los entrevistados, formaron parte del alumnado de primer y segundo ciclo matriculado en la UA en el curso académico 2009-2010. Posteriormente, se excluyeron para el análisis los estudiantes extranjeros no residentes en España (n = 13), porque el objetivo era estudiar el patrón de consumo en la población universitaria española.

La información se recogió mediante una encuesta auto cumplimentada por los estudiantes universitarios, apoyados y orientados por una dietista-nutricionista del grupo de investigación (AZ). La encuesta consta de una primera parte, que incluye los objetivos del estudio, el consentimiento informado, la confidencialidad de la información, los datos del estudiante (sexo, edad y lugar de nacimiento) y preguntas referentes a su peso y talla. Estas preguntas se elaboraron a partir de la metodología empleada en la Encuesta de Nutrición y Salud de la Comunidad Valencia[12]. La segunda parte se corresponde con el instrumento propiamente dicho: el cuestionario de frecuencia de consumo de alimentos del estudio PREDIMED (CFCA-PREDIMED), validado para población general en España[13]. Para facilitar la cumplimentación del cuestionario, reducir sesgos de información y lograr una mayor precisión en las res-

Tabla I
Clasificación de los alimentos

1a) Cereales y derivados (8 raciones/día):	77. Pan blanco 78. Pan negro o integral 79. Cereales desayuno 80. Cereales integrales	81. Arroz blanco 82. Pasta 96. Galleta integral
1b) Cereales integrales y derivados (8 raciones/día):	78. Pan negro o integral 80. Cereales integrales 81. Arroz blanco	82. Pasta 96. Galleta integral
2) Frutas (3 raciones/día):	57. naranja, pomelo y mandarina 58. Plátano 59. Manzana o pera 60. Fresas 61. Cereza, picota, ciruela	62. Melocotón, albaricoque, nectarina 63. Sandia 64. Melón 65. Kiwi 66. Uva
3) Hortalizas (6 raciones/día):	39. Acelgas, espinacas 40. Col, coliflor, brócoles 41. Lechuga, endivia, escarola 42. Tomate crudo 43. Zanahoria, calabaza 44. Judías verdes 45. Berenjena, calabacín, pepino	46. Pimiento 47. Espárrago 48. Gazpacho andaluz 49. Otras verduras 50. Cebolla 51. Ajos
4) Productos lácteos (2 raciones/día):	1. Leche entera 2. Leche semidesnatada 3. Leche desnatada 6. Yogur entero 7. Yogur desnatado 8. Petit suisse	9. Requesón o cuajada 10. Queso en porciones o cremoso 11. Otros quesos 12. Queso blanco o fresco
5) Pescados (5-6 raciones/semana):	31. Pescado blanco 32. Pescado azul 33. Pescados salados	37. Pescado y marisco enlatado natural 38. Pescado y marisco en aceite
6) Aves (4 raciones/semana):	17. Pollo o pavo con piel	18. Pollo o pavo sin piel
7) Aceitunas, legumbres y frutos secos (3-4 raciones/semana)	67. Aceitunas 70. Almendra, cacahuete, avellana, pistacho, piñones 71. Nueces	73. Lentejas 74. Alubias 75. Garbanzos 76. Guisantes y habas
8) Patatas (3raciones/semana)	55. Patata asada o cocida	
9) Huevos (3 raciones/semana)	16. Huevo de gallina	
10) Dulces (3 raciones/semana)	14. Natilla, flan, pudding, 15. Helados 97. Galleta con chocolate 98. Repostería y bizcocho hecho en casa 99. Croissant, ensaimada, pastas te, bollería industrial 100. Donut 101. Magdalena	102. Pasteles 104. Chocolates y bombones 120. Bebidas carbonatadas con azúcar 115. Mermelada 116. Azúcar 117. Miel
11) Carnes rojas (mensual)	19. Carne ternera o vaca 20. Carne cerdo 21. Carne cordero 22. Conejo o liebre	23. Hígado 24. Otras vísceras 29. Hamburguesa
Embutidos (no están incluidos en la pirámide de la dieta mediterránea, pero su alto consumo justifica incluirlos): Y está registrado dentro de la pirámide de la SENC.	25. Jamón serrano o paletilla 26. Jamón cocido 27. Carnes procesadas (chorizo, salchichón, mortadela, morcilla, salchicha, butifarra, sobrasada)	28. Patés, foie-gras 30. Tocino, bacón, panceta

puestas, se enseñó a los participantes láminas y dibujos de alimentos y raciones.

Las variables estudiadas para la caracterización de la muestra fueron: edad (en años, desde la fecha de nacimiento a la fecha de realización de la encuesta), sexo (mujer, hombre), área geográfica de procedencia (lugar de nacimiento: provincia, ciudad, país), peso (kg) y talla (cm) autoreferidos. En relación a los alimentos (n = 140 alimentos incluidos en 9 grupos) y las frecuencias de consumo (n=9 ítems) se contemplaron las opciones incluidas en el CFCA-PREDIMED: 1) nunca o casi nunca, 2) 1-3 veces al mes, 3) 1 vez a la semana, 4) 2-4 veces a la semana, 5) 5-6 veces a la semana, 6) 1 vez al día, 7) 2-3 veces al día, 8) 4-6 veces al día y 9) más de 6 veces al día.

Los datos de peso y talla autoreferidos permitieron construir la variable índice de masa corporal o IMC (kg/m^2) y categorizar el estado nutricional de acuerdo con los criterios de la OMS[14]: bajo peso (IMC < 18,5 kg/m^2), normo-peso (IMC ≥ 18,5 kg/m^2 < 25 kg/m^2); sobrepeso (IMC ≥ 25 kg/m^2 < 30 kg/m^2), obesidad (IMC ≥ 30 kg/m^2). Para su posterior análisis, las dos últimas categorías sobrepeso y obesidad, se reagruparon en una sola (IMC ≥ 25 kg/m^2), quedando al final 3 categorías: bajo peso, normopeso y sobrepeso-obesidad.

Con la información de los alimentos incluidos en el CFCA-PREDIMED se crearon 13 grupos de alimentos (tabla I). Los 12 primeros corresponden a los grupos de alimentos que incluye la pirámide de la dieta mediterránea tradicional[15]. Además, se incluyó el grupo de los embutidos (aunque estos no están dentro de la dieta mediterránea tradicional), por ser alimentos de consumo habitual entre la población universitaria española y estar incluidos dentro de las recomendaciones de consumo mensual de la pirámide de la Sociedad Española de Nutrición Comunitaria (SENC)[16] y de la nueva pirámide de la Fundación Dieta Mediterránea[17].

Se realizó un análisis descriptivo por sexo, edad, área geográfica de procedencia y estado nutricional de la muestra. Para estudiar las diferencias entre estado nutricional y el sexo se usó el contraste de diferencia de proporciones y para identificar diferencias de edad por sexo se realizó la prueba t de Student.

Para el análisis del consumo de alimentos por grupos se contrastaron los resultados con las recomendaciones de las guías alimentarias referentes a la Dieta Mediterránea Tradicional[15]. Las variables relacionadas con la frecuencia de consumo de alimentos se convirtieron a consumo mensual, tomando de referencia 4 semanas por mes. El porcentaje de adecuación se determinó teniendo en cuenta el consumo real sobre el consumo recomendado por la guía alimentaria: (100 x raciones consumidas/raciones recomendadas). Se establecieron 5 rangos de porcentaje de adecuación: consumo óptimo (80%-119%), consumo aceptable (60%-79%), consumo deficiente (40%-59%), consumo muy deficiente (< 39%), consumo excesivo (> 120%). Se contrastaron las diferencias de los porcentajes de adecuación a la dieta mediterránea de hombres y mujeres mediante contraste de diferencia de proporciones.

Finalmente, para conocer el nivel de adecuación total al modelo de dieta mediterránea, se sumaron todos los alumnos que tenían un "consumo óptimo" o un "consumo aceptable" de cada uno de los grupos de alimentos (n = 12).

El análisis se realizó con los paquetes estadísticos EPIDAT 3.1, y SPSS 15.0.

Resultados

La muestra se distribuye en 244 mujeres (64,2%) y 136 hombres (35,8%), con edades comprendidas entre los 19 y los 55 años y una media de edad de 22 ± 3,5 años en mujeres y 24 ± 5,1 años en hombres, siendo la diferencia de edad por sexo estadísticamente significativa (p = 0,009).

La tabla II, representa la distribución de la población según sexo, área geográfica y estado nutricional.

Tabla II
Distribución de los universitarios por sexo según área geográfica de procedencia y estado nutricional

	Mujeres	*Hombres*	*Total*
	n (%)	*n (%)*	*n (%)*
CCAA			
C. Valenciana	195 (79,9)	109 (80,1)	304 (80)
Castilla-La Mancha	19 (7,8)	12 (8.8)	31 (8,2)
Otras CC.AA.	13 (5.3)	8 (5,9)	21 (5.5)
Murcia	11 (4.5)	6 (4.4)	17 (4.5)
Andalucía	6 (2.5)	1 (0.7)	7 (1.8)
Total	244	136	380
IMC			
Bajopeso*	17 (7.0)	1 (0.7)	18 (4.7)
Normopeso†	203 (83,2)	88 (64,7)	291 (76.6)
Sobrepeso/Obesidad†	24 (9.8)	47 (34,6)	71 (18.7)
Total	244	136	380

*p < 0,05; †p < 0,001.

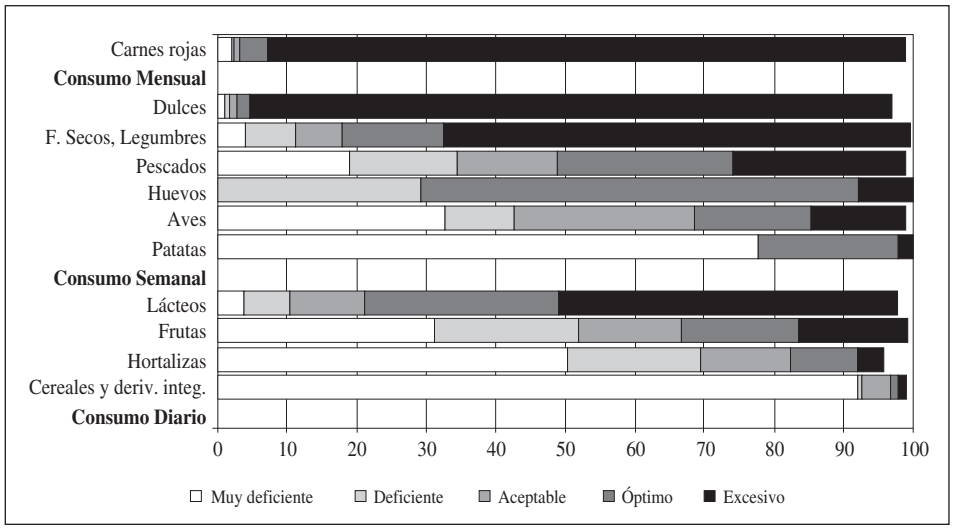


Fig. 1.—Distribución del porcentaje de adecuación de la dieta mediterránea de una muestra de alumnos españoles de la Universidad de Alicante. Año 2011.

Los resultados muestran que la Comunidad Valenciana es el lugar de mayor procedencia, con un 80%, seguida de Castilla-La Mancha, con un 8,2%.

En relación a la prevalencia de sobrepeso-obesidad, los hombres presentan una prevalencia del 34,6%, mayor que las mujeres (9,8%), siendo estadísticamente significativa, $p < 0,001$. Por el contrario, las mujeres presentan mayor prevalencia de bajo peso (7,0%) que hombres (0,7%), siendo también estadísticamente significativa ($p < 0,05$).

La figura 1, representa la distribución porcentual de la adecuación a la dieta mediterránea por grupos de alimentos. Se observa un consumo muy deficiente de cereales y derivados y un consumo excesivo de carnes rojas, en más del 90% de la población universitaria. Aproximadamente el 50% declara un consumo excesivo de lácteos y derivados. Al analizar el nivel de adecuación total al modelo de dieta mediterránea, ningún alumno cubre un "consumo óptimo" o un "consumo aceptable" de todos los grupos de alimentos ($n = 12$) en su conjunto.

En la tabla III, se representan los datos desagregados por sexo. Hay diferencias estadísticamente significativas entre mujeres y hombres en el consumo excesivo de frutas y en el consumo óptimo de patatas, aceitunas, frutos secos y legumbres. El 18,4% de las mujeres y el 10,3% de los hombres declaran tener un consumo excesivo de frutas ($p = 0,049$). Tienen un consumo óptimo de patatas el 23,8% de las mujeres y el 14,0% de los hombres ($p = 0,032$). Mientras que el 11,9% de las mujeres y el 19,9% de los hombres fueron clasificados con un consumo óptimo de aceitunas, frutos secos y legumbres ($p = 0,050$).

El consumo de embutidos es excesivo en más del 90% de la población universitaria, siendo ligeramente superior en los hombres (96,3%) que en las mujeres (95,9%), aunque esta diferencia no es estadísticamente significativa ($p = 0,9$).

Discusión

El patrón alimentario de los estudiantes de la Universidad de Alicante se encuentra alejado actualmente del patrón de dieta mediterránea. Se caracteriza por un consumo excesivo de carnes rojas y embutidos, y un consumo muy deficiente de cereales integrales y refinados. El consumo de forma óptima de patatas y en exceso de frutas, es mayor entre las estudiantes. La prevalencia de bajo peso en las estudiantes es mayor que la de los hombres pero ellos presentan mayor sobrepeso-obesidad. Se precisa reforzar la intervención dirigida a este grupo de población.

La caracterización del estado nutricional de estudios previos realizados tanto en el ámbito universitario español como en el europeo, es similar a la de nuestro estudio en cuanto a las altas prevalencias de sobrepeso y obesidad. En el País Vasco, el 17,5% de la población universitaria presenta sobrepeso-obesidad[18], mientras que en la Universidad de Navarra[4] la prevalencia es algo menor (13,4%). Población universitaria europea como la de la universidad de Wroclaw, Polonia[19], presenta una prevalencia de sobrepeso-obesidad del 10,3%, similar a la del estudio de la Universidad de Navarra[4]. Llama la atención que ambas instituciones (Wroclaw y Navarra) se encuentran alejadas geográficamente del área mediterránea, dado que se sitúan al norte de Polonia y España respectivamente. Así mismo, la diferencia en la prevalencia de sobrepeso-obesidad, mayor en hombres que en mujeres, es otro de los resultados de nuestro estudio que también coincide con los estudios citados anteriormente. En el caso del bajo peso hay que prestar especial atención a un posible riesgo de trastorno de la conducta alimentaria, preocupante sobre todo en el caso de las mujeres[7] dado que presentan un mayor porcentaje (7,0%) que el de los hombres (0,7%). Algunas publicaciones internacionales reportan datos de una prevalencia de bajo peso del 4%, similar a los resultados del presente estudio. Sin embargo, el estudio de la Universidad de Navarra

Tabla III

Distirbución porcentual de adecuación a la dieta mediterránea por grupos de alimentos de alumnos españoles por sexo, Universidad Alicante 2010

	Muy deficiente		*Deficiente*		*Aceptable*		*Óptimo*		*Excesivo*		*No Contesta*	
	Mujeres	*Hombres*	*Mujeres*	*Hombres*	*Mujeres*	*Hombres*	*Mujeres*	*Hombres*	*Mujeres*	*Hombres*	*Mujeres*	*Hombres*
	n = 244	*n = 136*	*n = 244*	*n = 136*	*n = 244*	*n = 136*	*n = 244*	*n = 136*	*n = 244*	*n = 136*	*n = 244*	*n = 136*
	n (%)	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*
Consumo Diario												
Lácteos	7 (2,9)	6 (4,4)	14 (5,7)	8,812 ()	29 (11,9)	12 (8,8)	70 (28,7)	37 (27,2)	114 (46,7)	69 (50,8)	10 (4,1)	0 (0,0)
Cereales y derivados	166 (68,0)	94 (69,1)	43 (17,6)	30 (22,1)	20 (8,2)	6 (4,4)	12 (4,9)	3 (2,2)	1 (0,4)	0 (0,0)	2 (0,9)	3 (2,2)
Cereales y derivados integrales	221 (90,6)	129 (94,9)	15 (6,1)	4 (2,9)	3 (1,2)	0 (0,0)	3 (1,2)	0 (0,0)	0 (0,0)	0 (0,0)	2 (0,9)	3 (2,2)
Frutas	72 (29,5)	47 (34,6)	49 (20,1)	29 (21,3)	31 (12,7)	25 (18,4)	45 (18,4)	20 (14,7)	45 (18,4)*	14 (10,3)*	2 (0,9)	1 (0,7)
Hortalizas	118 (48,4)	74 (54,4)	42 (17,2)	30 (22,1)	37 (15,2)	12 (8,8)	24 (9,8)	12 (8,8)	12 (4,9)	3 (2,2)	11 (4,5)	5 (3,7)
Consumo Semanal												
Pescados	47 (19,3)	24 (17,6)	36 (14,8)	24 (17,6)	38 (15,6)	17 (12,5)	64 (26,2)	32 (23,5)	56 (23,0)	38 (27,9)	3 (1,1)	1 (0,9)
Aves	81 (33,2)	44 (32,4)	22 (9,0)	16 (11,8)	64 (26,2)	33 (24,3)	38 (15,6)	26 (19,1)	34 (13,9)	17 (12,4)	5 (2,1)	0 (0,0)
Aceitunas, frutos secos y legumbres	11 (4,5)	4 (2,9)	22 (9,0)	6 (4,4)	18 (7,4)	7 (5,1)	29 (11,9)*	27 (19,9)*	163 (66,8)	91 (66,8)	1 (0,4)	1 (0,9)
Patatas	182 (74,7)	111 (81,6)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	58 (23,9)*	19 (14,0)*	4 (1,4)	6 (4,4)	0 (0,0)	0 (0,0)
Huevos	79 (32,4)	33 (24,3)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	149 (61,1)	89 (65,4)	16 (6,6)	14 (10,3)	0 (0,0)	0 (0,0)
Dulces	2 (0,8)	2 (1,5)	1 (0,4)	2 (1,5)	2 (0,8)	2 (1,5)	5 (2,0)	2 (1,5)	227 (93,0)	123 (90,3)	7 (3,0)	5 (3,7)
Consumo Mensual												
Carnes rojas	5 (2,0)	3 (2,2)	3 (1,2)	1 (0,7)	0 (0,0)	0 (0,0)	10 (4,1)	6 (4,4)	221 (90,6)	126 (92,7)	5 (2,1)	0 (0,0)
Embutidos†	3 (1,2)	2 (1,5)	1 (0,4)	0 (0,0)	0 (0,0)	0 (0,0)	1 (0,4)	1 (0,7)	234 (95,9)	131 (96,3)	5 (2,0)	2 (1,5)

Muy deficiente (< 39%); Deficiente (40% a 59%); Aceptable (60% a 79%); Óptimo (80% a 119%); Excesivo (< 120%).

*Diferencias por sexo estadísticamente significativas ($p < 0,05$).

†Los embutidos no están dentro de la Guía dieta mediterránea.

muestra una prevalencia mayor (7,6%). Con respecto a los países europeos, España se encuentra en niveles de sobrepeso-obesidad comparables, o incluso mayores, a los de Italia o Francia, mientras que estos niveles son inferiores en Alemania y otros países europeos[20].

El alumnado de la UA de nuestro estudio mantiene un consumo excesivo, de más del 90% de carnes rojas y de embutidos, que no coincide con las recomendación de consumo ocasional propuesta por el Comité de Expertos de Dieta Mediterránea (CEDM)[17]. Según este comité y apoyado por la evidencia de la literatura científica, existe una asociación entre el consumo elevado de estos alimentos proteicos con alto contenido en grasas saturadas y colesterol, y el riesgo de padecer enfermedades cardiovasculares[21-24]. Los resultados también muestran que aproximadamente un 50% del alumnado tiene un consumo excesivo en el caso de lácteos y derivados, y deficiente en el caso de cereales integrales, hortalizas y patatas. Estos resultados coinciden con los obtenidos en estudios similares realizados en el País Vasco, Navarra, Islas Baleares y Granada[8,18,25-26] y con otros del ámbito europeo[19,27-29]. Esto significa, que en la población universitaria, el valor calórico total proviene del aumento del consumo de grasas y proteínas, al tiempo que disminuye el consumo de los hidratos de carbono. Las recomendaciones del CEDM indican que los cereales integrales deben constituir la base de la pirámide de la dieta mediterránea y el principal grupo de alimentos de aporte energético. El resultado del consumo de cereales integrales y refinados analizados en este estudio, pone de manifiesto que es en ambos casos muy deficiente (92,1% y 68,4% respectivamente). Llama la atención, que los estudios revisados anteriormente no incluyan diferencias entre el consumo de cereales integrales y los refinados, dado que se ha evidenciado una relación de estos últimos con el posible riesgo a desarrollar distintos tipos de cáncer, diabetes y otras enfermedades crónicas[30-31].

A pesar de los beneficios que se han identificado en la dieta mediterránea para prevenir distintas enfermedades crónicas[32-36], los cambios en el perfil epidemiológico de consumo de alimentos y de los hábitos alimentarios están motivando una transición nutricional y un distanciamiento de la dieta mediterránea[20]. Precisamente en la Comunidad Valenciana, parece que se está perdiendo este modelo de dieta saludable[37-38]. En relación con la población universitaria, los resultados del presente estudio evidencian que esto es así entre los estudiantes universitarios de dicha comunidad, dado que más del 50% no llega a cumplir con las recomendaciones dietéticas. Pero además, estos resultados también son similares a los de otras comunidades españolas[4-8]. Algunos autores han explicado estos cambios, posiblemente y, entre otras causas, por la influencia del contexto social, cultural y educativo[6], así como por cambios macroestructurales relacionados con las políticas agrarias o las económicas, que influyen en la producción, disponibilidad y comercialización de alimentos[20,39] Además, la literatura científica reporta que estos patrones de consumo alimentario a través del tiempo van determinando los estilos de vida, el estado nutricional y de salud de las poblaciones[9,40]. El objetivo de la estrategia NAOS (Estrategia para la Nutrición, Actividad Física y Prevención de la Obesidad), puesta en marcha en 2005 desde el Ministerio de Sanidad y Consumo, a través de la Agencia Española de Seguridad Alimentaria y Nutrición (AESAN), ha sido impulsar todas las iniciativas necesarias para lograr que la población y en especial la infantil y juvenil adoptase una alimentación adecuada y la práctica regular de actividad física. Sin embargo, los resultados de este estudio muestran que estos esfuerzos han de incrementarse, dado que ningún alumno de la UA cubre el consumo de todos los grupos de alimentos en cantidad y frecuencia, cómo lo indica la pirámide dieta mediterránea.

Una de las limitaciones de cualquier estudio de evaluación del consumo de alimentos, es el propio cuestionario utilizado para la recogida de la información, ya que un solo método no es suficiente y se recomienda la complementación entre métodos. Sin embargo, la literatura reporta que el CFCA, es uno de los más utilizados en los estudios comunitarios, con buenos resultados en los estudios de validación, y permite obtener información sobre las veces que se consume un determinado alimento para poder compararlo con las recomendaciones nutricionales[41-42].

También hay que tener en cuenta el posible sesgo del voluntariado, ya que las personas voluntarias suelen tener un mejor estado de salud frente a las no voluntarias. Sin embargo, una alta tasa de respuesta garantiza que el sesgo de selección no es una amenaza para la validez interna del estudio[43]. Otra limitación es que los datos sobre el peso y la talla son autoreferidos por parte de los estudiantes, pudiendo subestimar o sobreestimar los datos reales. Estos datos antropométricos, están siendo utilizados con frecuencia para estimar el índice de masa corporal y valorar el estado nutricional con buenos resultados[44-45].

En definitiva, pese a que la población universitaria es un grupo aparentemente aventajado en cuanto al nivel educativo y el acceso a la información, existen factores socioambientales que les hace vulnerables en sus hábitos alimentarios. Deben reforzarse estrategias de salud pública dirigidas a este grupo de población que favorezcan su adecuación a una dieta saludable. Para ello deben integrarse esfuerzos y fomentar la participación lo más amplia posible de todos los componentes de la sociedad, esto es administraciones públicas, empresas del sector privado, consumidores y expertos de alimentación y nutrición.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1960-1965
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Análisis del estado nutricional en escolares; estudio por áreas geográficas de la provincia de Granada (España)

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Resumen

Introducción: **En España la prevalencia de obesidad muestra un patrón de distribución norte-sur. En la provincia de Granada se desconoce su distribución.**

Objetivos: **Los objetos del presente trabajo son estudiar la prevalencia de sobrepeso y obesidad en una población de escolares representativa de toda la provincia de Granada. Verificar diferencias significativas entre las comarcas de la provincia. Comprobar una correlación entre el estado nutricional de los alumnos y el de sus progenitores.**

Métodos: **977 escolares de entre 9 y 17 años de edad, pertenecientes a 13 centros educativos públicos de la provincia de Granada (España). Estudio analítico y multicéntrico, en el que se realizó una valoración del estado nutricional mediante antropometría. Además, mediante un cuestionario, se evaluó la existencia de antecedentes familiares de sobrepeso u obesidad.**

Resultados: **Se encontró una elevada prevalencia de sobrepeso y obesidad entre la población estudiada. En chicas, la mayor prevalencia tanto de sobrepeso como de obesidad se situaba entre los 12 y los 14 años de edad. En los chicos, se observó un repunte en la prevalencia de sobrepeso a los 12 años. Respecto de la obesidad, sus tasas fueron considerablemente inferiores a las descritas entre las chicas. Se encontraron diferencias estadísticamente significativas para el peso ($F = 4,154$; $p = 0,003$), pero no para la estatura ($F = 1,928$; $p = 0,105$). En cambio, para la variable IMC se observaron diferencias estadísticamente significativas ($F = 5,037$; $p < 0,001$) entre las diferentes comarcas geográficas estudiadas. Aquellos alumnos con antecedentes familiares de obesidad mostraron un significativo ($p < 0,01$) peor estado nutricional.**

Discusión: **Existe una elevada prevalencia de obesidad, especialmente entre las chicas. Existe un patrón de distribución geográfico posiblemente derivado de las características socioeconómicas de cada comarca. La existencia de antecedentes familiares de obesidad constituye un factor determinante para su desarrollo entre los jóvenes.**

(*Nutr Hosp.* 2012;27:1960-1965)

DOI:10.3305/nh.2012.27.6.6067

Palabras clave: *Escolares. Obesidad. Distribución geográfica. Obesidad parental.*

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Recibido: 27-V-2012.
1.ª Revisión: 19-VII-2012.
Aceptado: 7-VIII-2012.

ANALYSIS OF THE NUTRITIONAL STATE OF SCHOOL CHILDREN IN DIFFERENT DISTRICTS OF THE PROVINCE OF GRANADA (SPAIN)

Abstract

Background: **In Spain the prevalence of obesity shows a north-south distribution. In the province of Granada its distribution is unknown.**

Objectives: **(1) To study the prevalence of overweight and obesity in a sample population of school children and adolescents from different districts in the province of Granada. (2) To verify whether there are significant differences, depending on the district where the students reside. (3) To find a possible correlation between the nutritional state of the students and that of their parents.**

Methods: **The population sample was composed of 977 school children and adolescents from 9 to 17 years of age, attending 13 public elementary schools and high schools in the city and province of Granada (Spain). In this analytical and multicentric study, the nutritional state of the subjects was evaluated by means of anthropometric measurements. Furthermore, data were collected by means of questionnaire to discover whether the respondents had a family history of overweight or obesity.**

Results: **We found a high prevalence of overweight and obesity among the studied population. In girls, the greater prevalence of both overweight and obesity ranged from 12 to 14 years of age. In boys, there was an increase in the prevalence of overweight at twelve years of age. Regarding obesity, their rates were significantly lower than those described among girls. There were statistically significant differences for weight ($F = 4,154$; $p = 0,003$) but not for height ($F = 1,928$; $p = 0,105$). But for the variable BMI was statistically significant difference ($F = 5.037$; $P < 0.001$) between the studied geographical areas. The results showed that the nutritional state of students with a family history of obesity was significantly worse ($p < 0.01$).**

Discussion: **A high prevalence of obesity was found in the sample, especially among the girls. There exists a geographical distribution pattern, possibly derived from the socioeconomic characteristics of each area in the province. The existence of a family history of obesity is an important factor that can determine whether the child will also become obese in the future.**

(*Nutr Hosp.* 2012;27:1960-1965)

DOI:10.3305/nh.2012.27.6.6067

Key words: *School children. Obesity. Geographic distribution. Parental obesity.*

Introducción

Actualmente, en Europa 1 de cada 6 niños, o su equivalente casi el 20% padece sobrepeso, mientras que 1 de cada 20 adolescentes (el 5%) tiene obesidad[1,2]. El sobrepeso y en su caso la obesidad infantil constituyen el trastorno nutricional más frecuente en la sociedad de países subdesarrollados, afectando más a los niveles socioeconómicos más desfavorecidos, con peores estados nutricionales y obviamente formativos[3]. Factor, este último, importante pues en este tipo de sociedades la obesidad en la infancia es considerada como un indicador de elevado estatus social. En países en vías de desarrollo, por su parte, serán los niveles socioeconómicos más elevados quienes asignen este concepto equívoco a la obesidad infantil[4]. En el caso de España, se ha descrito un patrón de distribución norte-sur en la prevalencia de sobrepeso y obesidad[5]. Así, tenemos que la prevalencia de sobrepeso oscila en un rango que va desde un 22% para la región noreste, concretamente en la comunidad de Cataluña, hasta el 29% existente en la comunidad de Andalucía. No obstante, las cifras más elevadas son las referentes al archipiélago canario, en donde se ha descrito una tasa de prevalencia superior al 35%[6]. A pesar de no quedar claras las causas de esta distribución, parece encontrarse en los aspectos socioeconómicos propios de cada región española, el motivo que origina estas discordantes tasas de prevalencia[7]. Ahora bien, en el caso concreto de la provincia de Granada, diferentes estudios han tratado de valorar la prevalencia de sobrepeso y obesidad aunque ninguno de ellos con una muestra representativa de toda la provincia. Además, considerando las características de las diferentes áreas geográficas que la integran, resulta necesario plantearse verificar la existencia de posibles diferencias en cuanto a la prevalencia de sobrepeso y obesidad entre la población infantil y adolescente.

Otro aspecto a valorar en la patogenia del sobrepeso y la obesidad es el estado nutricional de los progenitores[8]. Se ha establecido una relación entre el sobrepeso o la obesidad parental y el riesgo de padecimiento de la misma por parte de la descendencia. Determinados autores postulan que si uno de los progenitores es obeso, el riesgo de sobrepeso-obesidad infantil entre su descendencia se multiplica por cuatro, y por ocho si son los dos[9].

Los objetivos de este trabajo fueron realizar una estimación precisa de la prevalencia de sobrepeso y obesidad entre una población de escolares representativa de toda la provincia de Granada, compuesta por 977 niños y adolescentes de entre 9 y 17 años de edad, pertenecientes a 13 centros educativos públicos. Asimismo, se pretendía verificar la existencia de diferencias significativas en términos del estado nutricional entre las distintas comarcas geográficas de la provincia granadina. Por último, analizar una posible relación entre el estado nutricional de los alumnos y el de sus progenitores.

Objetivos

Los objetivos propuestos a alcanzar con el desarrollo de este estudio fueron los siguientes:

- Determinar la prevalencia de sobrepeso y obesidad nutricionales entre la población de escolares valorada según el sexo y la edad.
- Verificar la existencia de diferencias significativas en términos del estado nutricional entre las distintas zonas geográficas de la provincia estudiadas.
- Comprobar la existencia de una correlación entre el estado nutricional de los alumnos y el de sus progenitores.

Métodos

La población de participantes en el estudio estaba referida a alumnos con edades comprendidas entre los 9 y los 17 años. Para poder participar en el estudio y a modo de criterio de inclusión, los alumnos dispuestos a participar debían carecer de patologías endocrinometabólicas tales como diabetes mellitus, entre otras. Para ello, fue condición indispensable que los alumnos aportaran un documento clínico donde su médico de referencia expusiese el no padecimiento por el alumno de ningún trastorno del tipo mencionado. En este sentido, fueron excluidos de participar en el estudio aquellos alumnos quienes no cumplieron dichos requisitos.

Con el fin de obtener un tamaño muestral representativo de toda la provincia de Granada, fue necesario realizar un análisis previo sobre la situación demográfica existente en la provincia en cuanto a número de niños y adolescentes según el sexo. Para ello se utilizó el Padrón Municipal de 2008, según el cual la población existente para ese intervalo de edad en ese periodo ascendía a 49.359 sujetos entre chicos y chicas. Distinguiendo entre sexos, 24.055 eran niños, esto es, el 48,7% del total de la población infantil en ese momento. En el caso de las niñas, su número ascendía a 25.304, el 51,3% del total de la población objeto del estudio. Teniendo en cuenta estos datos y asumiendo un error del 3%, la población de estudio quedó teóricamente fijada en 1044 participantes. Si bien, tras el procedimiento de solicitud de consentimiento informado a los padres y responsables de los alumnos, la muestra final de participantes quedó en 977 sujetos, de los cuales 524 fueron chicas y 452 chicos, con un error muestral asociado para la estimación de la proporción del 3,1%. Para la toma de datos, fue imprescindible contar con la colaboración del equipo de dirección de cada centro educativo, quienes colaboraron en todo momento con el equipo de investigadores en establecer reuniones con los padres y tutores de los alumnos, garantizando con ello una implicación máxima tanto de padres como de alumnos.

La selección de las últimas unidades fue proporcional al tamaño del municipio de residencia y el área geo-

gráfica en la que este se encontraba. Con esta premisa, se establecieron cinco zonas geográficas. La zona norte de la provincia, con los municipios de Guadix y Baza. Zona metropolitana, que comprendía escolares de la ciudad de Granada. La zona del extrarradio y cinturón de la capital, abarcando población escolar de los municipios de Santa Fe y Maracena. La Zona de la Alpujarra, con alumnos del municipio de Órgiva, la zona del Valle de Lecrín representada por alumnos del municipio del Padul y la zona de la costa tropical (región sur de la provincia de Granada), abarcando población escolar de los municipios de Salobreña y Almuñécar. De este modo, y atendiendo al volumen de población existente para este rango de edad en cada una de las zonas indicadas, fueron seleccionados un total de trece centros educativos. La elección de tales centros y no otros, tuvo como criterio la procedencia geográfica de sus alumnos.

Para analizar el estado nutricional fue necesario realizar una evaluación antropométrica completa, siguiendo en este caso, las recomendaciones del Protocolo Pediátrico Europeo *(Body Composition Analyzing Protocol)*. Dicha valoración se realizó a todos los alumnos en dos momentos distintos del curso académico 2008-2009. La primera durante el mes de octubre de 2008 y la segunda en el mes de mayo de 2009, todo ello con el fin de garantizar el máximo de fiabilidad y objetividad en los datos obtenidos. La evaluación fue llevada a cabo por miembros del equipo investigador, debidamente instruidos al respecto. Para su realización, cada centro educativo colaboró proporcionando al equipo investigador un habitáculo (gimnasio, aula, biblioteca) donde poder realizar todas las determinaciones garantizando con ello condiciones de intimidad para los alumnos participantes. En dicha evaluación fueron valoradas las variables peso, estatura y a partir de estas, el índice de masa corporal. La determinación del peso de los sujetos se llevó a cabo mediante una balanza electrónica de fabricación alemana (marca Seca®, modelo 861*) autocalibrable y dotada de una precisión de hasta cien gramos. Para medir la estatura de los sujetos se utilizó un antropómetro de la marca Seca®, modelo 214*. Para determinar la estatura, el sujeto debía situarse en posición antropométrica con la cabeza orientada según el plano de Frankfort. El dorso del tronco y la pelvis del sujeto debían de permanecer en continuo contacto con la rama vertical del antropómetro. Una vez colocado en esta posición, se procedía a aplicar la rama horizontal del antropómetro sobre el vértex o punto más alto del cráneo. También fueron evaluados seis pliegues cutáneos (pliegue tricipital, bicipital, subescapular, suprailíaco, pliegue del muslo y de la pantorrilla). Para ello se utilizó un plicómetro de la marca Holtain® con una precisión de entre 0,1-0,2 mm. Además, fueron evaluados los perímetros de la cintura y de la cadera, para lo que se utilizó una cinta métrica flexible e inextensible, cuya precisión era de 1 mm.

Para definir estados de sobrepeso y obesidad, se tomaron como referencia los estándares proporcionados por el estudio ENKID (1998-2000)[10], definiendo sobrepeso como aquellos valores comprendidos entre los percentiles 85 y 95 de índice de masa corporal, y obesidad aquellas cifras iguales o superiores al percentil 95 de índice de masa corporal. Una vez realizada la evaluación del estado nutricional, y con objeto de poder valorar la existencia o no de antecedentes familiares de sobrepeso u obesidad, se hizo uso de un cuestionario específicamente elaborado y validado previamente por el equipo investigador. En dicho cuestionario, no sólo se recogía información relativa a aspectos del entorno familiar de éstos sino también información relativa a frecuencia de consumo de alimentos y práctica de actividad física. Para facilitar la cumplimentación de dicho cuestionario, y al objeto de atender posibles dudas, a nivel de cada centro se realizó una reunión con todos los padres durante la cual éstos cumplimentarían el cuestionario.

Para las variables consideradas, se aplicaron sendos análisis de la varianza considerando el factor comarca, utilizando el método de Tukey para la comparación post-hoc de los distintos niveles, y un análisis de la varianza a dos vías con los factores antecedentes familiares y sexo para la variable estado nutricional.

Resultados

El análisis de los valores observados en el índice de masa corporal confirma la existencia de una elevada prevalencia de sobrepeso y obesidad entre la población de escolares estudiada. Entre las chicas, la mayor prevalencia tanto de sobrepeso como de obesidad se situaba entre los 12 y los 14 años de edad. En el caso de los chicos, se observa un repunte en la prevalencia de sobrepeso a la edad de 12 años que tenderá a suavizarse con la edad. Con relación a la prevalencia de obesidad, sus tasas son considerablemente inferiores a las descritas entre las chicas. Estos resultados se muestran más claramente en la tabla I y la figura 1.

Relativo al estudio de las variables peso, estatura e índice de masa corporal, en la tabla II se muestran los valores observados en las diferentes comarcas geográficas estudiadas. No se encontraron diferencias estadísticamente significativas para la estatura y sí para el peso ($F = 4,154$; $p = 0,003$) y el IMC ($F = 5,037$; $p < 0,001$), entre las diferentes comarcas geográficas estudiadas. Las mayores diferencias en peso e IMC se encontraron entre la población de alumnos valorados en los centros escolares de Granada capital.

Como estudio complementario en la población general estudiada (723 alumnos, ya que 254 no facilitaron dicha información), se consideró si podían existir diferencias significativas en relación con la existencia o no de antecedentes familiares de sobrepeso u obesidad. Los resultados obtenidos ponen de manifiesto que el factor de antecedentes familiares (presencia de antecedentes de familiares de primer y segundo grado con sobrepeso u obesidad) es significativo ($F = 4,27$; $p < 0,01$) respecto del estado nutri-

Tabla I
Percentiles 85 y 95 de IMC para sobrepeso y obesidad en función de la edad y sexo

Edad	*N*	*Enkid (85%)*	*n*	*Media*	*D. T.*	*Enkid (95%)*	*n*	*Media*	*D. T.*
Chicas									
≤ 10	**6**	20,90	1	23,75	–	22,92	1	23,75	–
11	**17**	21,52	4	26,38	1,95	23,62	4	26,38	1,95
11	**136**	22,14	32	25,72	2,82	24,28	18	27,03	2,29
13	**147**	22,72	49	25,63	2,51	24,89	22	27,58	2,15
14	**132**	23,21	25	26,78	2,81	25,39	14	28,72	1,97
15	**72**	23,61	17	25,2	1,66	25,79	2	27,84	2,72
≥ 16	**14**	23,91	3	26,49	1,61	26,13	1	27,24	–
Total	**524**		**131**				**62**		
Chicos									
≤ 10	**10**	21,77	2	23,29	1,4	24,01	0	–	–
11	**19**	22,57	5	23,99	1,34	25,02	0	–	–
11	**129**	23,38	36	26,46	3,36	26,04	11	29,92	3,63
13	**117**	24,15	28	26,81	2,09	26,97	10	28,99	1,31
14	**112**	24,82	29	29,08	3,48	27,75	14	31,28	3,16
15	**57**	25,34	6	29,14	1,95	28,31	3	29,79	1,5
≥ 16	**9**	25,71	1	26,26	–	28,62	0	–	–
Total	**453**		**107**				**38**		

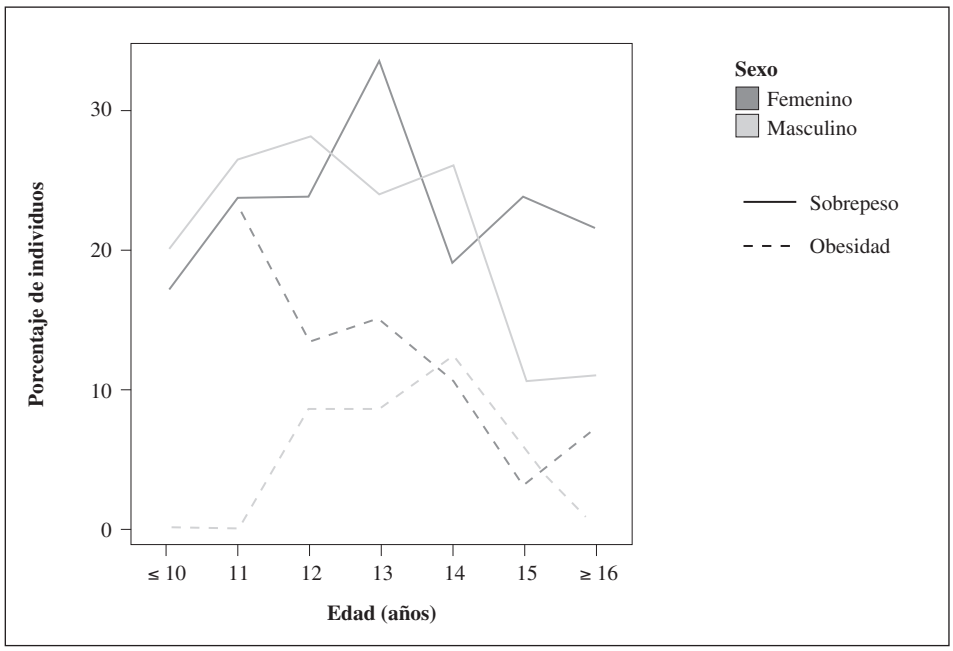


Fig. 1.—Prevalencia de sobrepeso y obesidad según edad y sexo.

cional (IMC) de los alumnos valorados, no así el factor sexo. En la figura 2 puede observarse cómo de los dos grupos (con antecedentes y sin antecedentes) el grupo con antecedentes familiares para sobrepeso y obesidad fueron quienes mayores tasas de índice de masa corporal obtuvieron y por ende aquellos con un estado nutricional más inadecuado para su sexo y edad, situándose en éstos la media para dicho índice en 24,18 frente a 20,05 para aquellos sin antecedentes. Esta circunstancia se hizo más representativa entre los alumnos con edades comprendidas desde los 12 años en adelante, alcanzando valores máximos para el índice de masa corporal a los 14 años.

Discusión

Respecto de la variable índice de masa corporal, los datos obtenidos en el estudio muestran una más que preocupante tendencia al sobrepeso entre la población escolar

Tabla II
Valores medios de peso, estatura e IMC en las comarcas geográficas estudiadas

Comarca		*Peso*		*Estatura*		*IMC*	
	N	*Media*	*D. T.*	*Media*	*D. T.*	*Media*	*D. T.*
Granada capital	76	61,82 (a)	9,955	159,70	9,120	24,14 (a)	2,076
Extrarradio-Cinturón	72	68,47 (b)	12,817	162,79	9,076	25,66 (b)	2,929
V. Lecrín y Alpujarra	84	67,61 (b)	11,334	162,73	8,035	25,41 (b)	3,101
Norte de la provincia	200	67,45 (b)	11,612	161,88	8,683	25,60 (b)	2,879
Costa de la provincia	44	68,11 (b)	14,259	160,23	8,268	26,32 (b)	3,748
Total	476	66,80	11,933	161,67	8,702	25,41	2,958
		F = 4,154	**p = 0,003**	F = 1,928	**p = 0,105**	F = 5,037	**p < 0,001**

**Los códigos asociados a los valores medios de cada nivel indican los subgrupos homogéneos en caso de diferencias significativas (método de Takey).

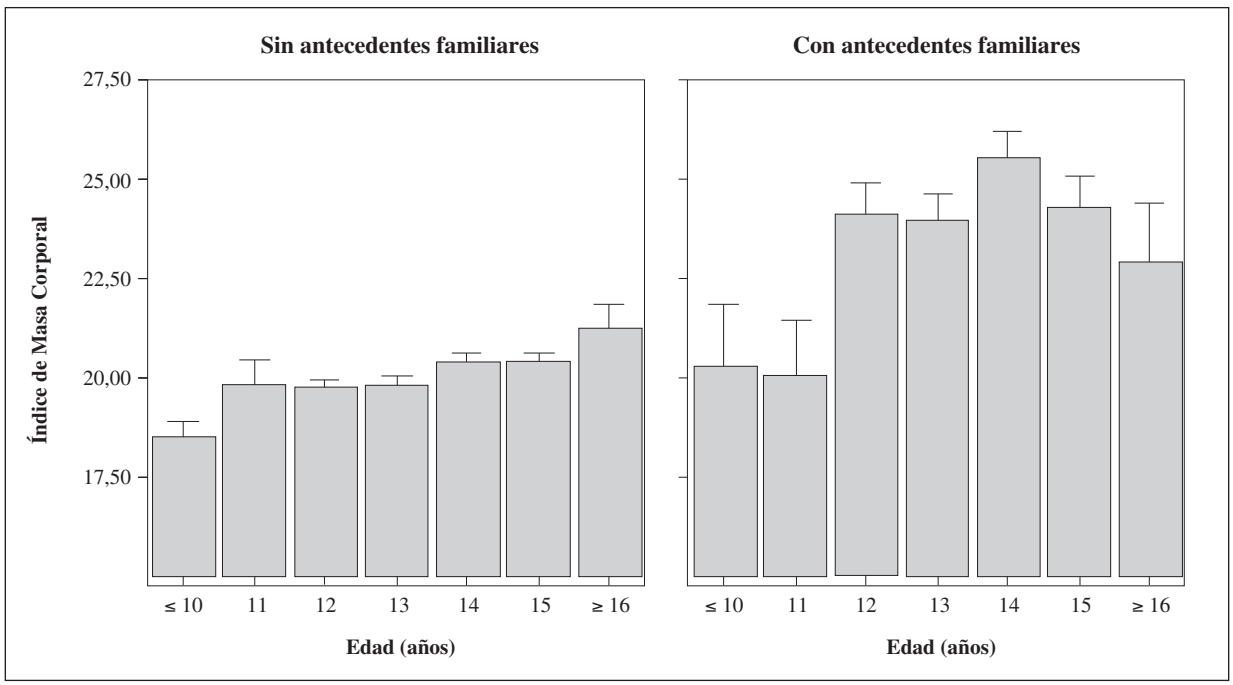


Fig. 2.—Estado nutricional y su relación con la existencia o no de antecedentes familiares de obesidad.

valorada. Ello implica replantearse qué está ocurriendo en términos de alimentación y ejercicio físico entre la población infantil y juvenil. Estableciendo una comparación con datos del estudio ENKID[10], en los resultados aquí presentados se observa un marcado incremento general en la prevalencia de sobrepeso y obesidad. Mientras que en el estudio ENKID se obtuvo una prevalencia de sobrepeso general del 12,4%, en este estudio dicha cifra se vió incrementada considerablemente. Por su parte, respecto de la prevalencia de obesidad es cierto que los datos obtenidos en este estudio resultan en el caso de las chicas muy similares a los reportados en su momento por el estudio ENKID donde la tasa de obesidad en chicas se estimó en un 12%. En cuanto a la prevalencia de obesidad, en este estudio, las mayores diferencias comparativamente con el estudio ENKID se encontraron entre los chicos, con una menor prevalencia de obesidad para todas las edades estudiadas.

Comparando los resultados obtenidos con los alcanzados por Meléndez en Granada (2002)[11], cabe resaltar un incremento tanto de sobrepeso como de obesidad entre la población valorada. Teniendo en cuenta que la población estudiada por Meléndez comprendía población de entre 4 y 12 años de edad se estimó una prevalencia de sobrepeso en chicos del 8,4% y del 9,8% en chicas frente a una tasa de obesidad en chicos del 15,3% y del 16,9% en chicas. Estos resultados contrastan igualmente con los obtenidos en el presente estudio en donde la prevalencia de sobrepeso superó considerablemente estos valores. En el caso de la prevalencia de obesidad la situación resultó ser a la inversa, esto es, las tasas de obesidad encontradas en este estudio resultaron inferiores a las descritas por Meléndez. No obstante, cabe tener en consideración las diferencias en cuanto a los intervalos de edades valoradas, circunstancia que implica la necesidad de interpretar estos datos y sus diferencias con cautela. Estos resultados son coinci-

dentes con los reportados por otros estudios, como el desarrollado por García y cols. (2010)[12], en el cual a partir de una muestra de 111 escolares se determinó una prevalencia de sobrepeso u obesidad del 38,7%, siendo esta mayor entre las chicas. Por otra parte, otros estudios como el desarrollado por Puig Mojer y colaboradores (2002)[13] o Martín Acero y cols. (2000)[14], concuerdan con los datos aquí presentados de mayor prevalencia de obesidad en chicas. Si bien, otros estudios no muestran diferencias significativas en los porcentajes de sobrepeso y obesidad entre ambos sexos, independientemente de la edad de los sujetos[15,16,17]. Estos resultados ponen de manifiesto el imparable ascenso que las tasas de sobrepeso y obesidad muestran actualmente entre la población infantil y adolescente. De estos resultados se puede deducir en principio la dudosa eficacia que los programas de acción propuestos por los diferentes gobiernos en materia de prevención del sobrepeso y la obesidad están teniendo entre los menores.

Respecto al estudio de la prevalencia de sobrepeso y obesidad en las distintas comarcas geográficas de la provincia de Granada, los resultados confirman una mayor prevalencia de obesidad entre los escolares de los municipios del extrarradio-cinturón de la Capital así como de la comarca norte de la provincia. Por otra parte, sería en Granada capital donde los valores medios de IMC tomarían valores más cercanos a la normalidad. Estos resultados sugieren que los hábitos de alimentación y probablemente de actividad física se alejan de los recomendados para estas edades siendo además muy variables en las diferentes comarcas granadinas estudiadas.

Según Aguilar y cols. (2011)[18], la existencia de un mejor estado nutricional entre el grupo de alumnos de Granada capital, podría tener su explicación en un mayor nivel cultural y socioeconómico por parte de sus familias de. En cualquier caso, la existencia de diferencias significativas en el estado nutricional de alumnos de las distintas comarcas que integran la provincia de Granada, es cuanto menos indicativo de patrones de alimentación y hábitos de actividad física muy distintos dependiendo de cada territorio. Ello deberá ser objeto de análisis profundo por estudios posteriores.

Con relación a si el estado nutricional de los progenitores supone o no un factor vinculante al desarrollo de obesidad en sus hijos, los resultados obtenidos confirman dicha hipótesis. Estos resultados coinciden plenamente con lo descrito por otros estudios previos[19,20]. No obstante, existe cierta controversia al respecto, esto es, si el desarrollo de sobrepeso y obesidad puede venir condicionado por el estado nutricional de los padres. En cualquier caso, serán necesarios nuevos estudios a partir de grupos poblacionales más amplios donde se analice dicha cuestión.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1966-1972
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Body weight perception among adolescents in Dubai, United Arab Emirates

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Abstract

This study investigated the body image perceptions among adolescents in Dubai, United Arab Emirates (UAE). A cross-sectional survey was conducted amongst 661 adolescents (324 males; 337 females) aged 12-17 years selected from government schools using a multistage stratified random sampling technique. A pretested validated questionnaire was employed to determine the perception of adolescents toward their weight status. A nine figure silhouette illustration was used to measure perceptions of their ideal body image and how it compares with their current body weight. The results reveled that overweight (18.5%) and obesity (27.2%) were higher among males than in females (13.1% and 20.5% respectively). A high proportion of overweight males and females considered themselves as average (45.0% and 52.3%, respectively). Similarly, 56.9% of obese male and 46.4% of females considered themselves as average weight. Of non-overweight/obese males and females, 27.6% and 39.3% respectively, were pressured by parents to gain weight (p > 0.000). In general overweight and obese adolescents were more likely to face pressure from their parents and teased by friends than non-overweight/obese adolescents. Compared to their current body image, overweight and obese adolescents chose a significantly lighter figure as their ideal (p < 0.000). It is suggested that the current health education curriculum should include information related to healthy body weight and appropriate diet and lifestyle so as to minimize risk of developing distorted body image concerns in adolescence and beyond.

(*Nutr Hosp.* 2012;27:1966-1972)

DOI:10.3305/nh.2012.27.6.5830

Key words: *Adolescents. Perception. Ideal body weight. Current body weight. UAE.*

PERCEPCIÓN DEL PESO CORPORAL EN LOS ADOLESCENTES DE DUBAI, EMIRATOS ÁRABES UNIDOS

Resumen

Este estudio investigaba la percepción de la imagen corporal en los adolescentes de Dubái, Emiratos Árabes Unidos (EAU). Se realizó una encuesta transversal entre 661 adolescentes (324 chicos; 337 chicas) con edades de 12-17 años, seleccionados de colegios públicos utilizando una técnica de muestreo aleatorio estratificado en varias etapas. Se empleó un cuestionario validado y previamente testado para determinar la percepción de los adolescentes con respecto a su peso. Se usó la ilustración de una silueta de los nueves para medir las percepciones de su imagen corporal ideal y cómo se comparaba con su peso corporal real. Los resultados mostraron que el sobrepeso (18,5%) y la obesidad (27,2%) fueron superiores entre los chicos que entre las chicas (13,1% y 20,5%, respectivamente). Una proporción alta de chicos y chicas con sobrepeso se consideró a sí mismos en el promedio (45,0% y 52,3%, respectivamente). De forma similar, el 56,9% de los chicos obesos y el 46,4 % de las chicas obesas se consideraron dentro del promedio. El 27,6% y el 39,3S% de los chicos y chicas, respectivamente, sin sobrepeso ni obesidad eran presionados por sus padres para ganar peso (p > 0,000). Por lo general, los adolescentes con sobrepeso u obesidad tenían una mayor probabilidad de recibir presiones de sus padres y burlas de sus compañeros que los adolescentes sin sobrepeso ni obesidad. En comparación con su imagen corporal actual, los adolescentes con sobrepeso u obesidad eligieron un número significativamente menor como su peso ideal (p < 0,000). Se sugiere que el currículo educativo sanitario actual debería incluir información relacionada con el peso corporal saludable y una dieta y estilo de vida apropiados para minimizar el riesgo de desarrollar preocupaciones sobre una imagen corporal distorsionada en la adolescencia y más allá.

(*Nutr Hosp.* 2012;27:1966-1972)

DOI:10.3305/nh.2012.27.6.5830

Palabras clave: *Adolescentes. Percepción. Peso corporal ideal. Peso corporal real. UAE.*

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Recibido: 10-VI-2012.
Aceptado: 7-VIII-2012.

Introduction

Adolescence represents a period of marked physical changes that are associated with changes in body perception.[1] Body image focuses on both how we feel about the size and shape of our bodies and how accurately we perceive our body size.[2] Perception towards body weight is a strong determinant of the dietary habits and weight management amongst adolescents.[3] The perception of being overweight rather than actually being overweight has been associated with eating disorder tendencies.[4] It has now become more apparent that body image disturbance and concerns about body shape and size are formed very early in life and are often well formed by mid childhood.[5] There is overwhelmingly evidence that body image is intrinsically linked with self-esteem[6] and the society's emphasis on how we look also seems to affect the way people feel about themselves.[7]

Studies in Western countries have shown that there are many socio-cultural, biological and interpersonal factors that influence body dissatisfaction with gender difference.[8-10] In the Arab culture, thinness has been regarded as socially undesirable, whereas plumpness is regarded as a symbol of fertility and womanhood.[11] However in the past three decades, the oil rich Arab Gulf countries, including the United Arab Emirates (UAE), has undergone rapid and extensive economic and socio-cultural modernization. This has resulted in a clash of cultures, and studies indicate that a clash between a traditional culture and adopted culture may heighten the risk for eating and body image disturbances in susceptible individuals.[12]

While most previous studies in the UAE have focused on high prevalence of overweight and obesity among adolescents,[13-15] few studies have investigated the weight related beliefs and body perceptions amongst this population. In the UAE, one of the early evidence of eating disorder as a result of increasing globalization was reported by Abou-Saleh, et al.[16] A body image perception study among adolescents in Bahrain showed that many overweight and obese adolescents failed to perceive themselves as such, and many normal weight adolescents reported previous attempts at weight loss.[17] A study by Nasser[18] among Egyptian secondary school girls has confirmed that morbid eating patterns are emerging in Egyptian culture, with similar rates to those in western society.

Addressing issues of body image are important since body image disturbance is a fairly stable belief pattern, as children who exhibit higher levels of body dissatisfaction will tend to continue to express this into adolescence and young adulthood, which could ultimately result in eating disorders.[19] Hence, we have sought to examine body weight perception and some associated factors among adolescents attending preparatory and secondary government schools in Dubai, UAE. This may identify areas to formulate suitable intervention strategies and promote healthy body image among the adolescent population.

Materials and methods

Sampling

The study population included Dubai national male and female adolescents aged between 12 to 17 years selected from the government schools. A sample of these children (324 males and 337 females) was selected by means of a multistage stratified random sampling technique in schools and stratified by sex and type of school (preparatory and secondary). Dubai was first divided into four administrative areas. One preparatory and one secondary school for each sex were then selected by a simple random method from each area. One class from each educational level (3 for preparatory and 3 for secondary) were then selected from each school by a simple random method, and only Emirati adolescents were included in the study. Student reported age and date of birth were verified against the school records, which in turn were based on the birth certificate. The study was approved by the Research Ethics Committee of the Ministry of Health, Dubai Medical District. All adolescents, parents and teachers were clearly informed about the purpose and content of the study and written consent was obtained from parents.

Anthropometric measurements

Weight and height were measured as described by Gibson.[20] Weight was measured to the nearest 0.1 kg using an electronic portable scale (Seca). To ensure accuracy in measurement the scale was checked for zero reading before each weighing and calibrated with a known weight on the morning of each data collection. Student height was measured, in the standing position, to the nearest 0.1 cm using a portable stadiometer which was attached to the "Seca" weighing scale. The student was asked to stand without shoes and socks, back against the scale, heels together and head in the upright position. The movable headboard was lowered until it firmly touched the upper part of the subjects head and a direct reading of height was obtained. From these measurements the body mass index (BMI) (weight in kilograms divided by height in meters squared) was computed.

Questionnaire

The participants were given a questionnaire previously validated and used by Al-Sendi et al.[17] among adolescents in Bahraini (an Arab Gulf country) to assess the adolescent's perceptions of their body

Table I
Prevalence of weight status using BMI categories among adolescents in Dubai, UAE

Weight status	*Males*		*Females*		*p-value*
	n	*%*	*n*	*%*	
Non-overweight/obese	192	59.3	224	66.4	> 0.1859
Overweight	60	18.5	44	13.1	
Obese	72	22.2	69	20.5	
Total	**324**	**100.0**	**337**	**100.0**	

image. Perceptual body image was explored with questions aimed towards assessing the adolescent's knowledge of their weight status, height, parents and friends attitudes towards their body size. To measure adolescent's perceptions of ideal body image and how it compares with their current body image, we used the nine figure silhouettes developed by Stunkard, et al.[21] Illustrations of male and female body shapes ranging from very thin to grossly obese were shown to the adolescents, and they were asked to circle the male/female that looks most like them now (current), and the male/female that they wanted to look like (ideal). The subjects were asked to select only one silhouette which was coded from one (thinnest) to nine (heaviest).

Statistical analysis

Data were entered and analyzed using the SPSS statistical package. The association between perception of weight and actual weight status was examined using contingency tables. Based on the World Health Organization recommendations[22] and using the age and gender specific BMI data of the NHANES1[23] the participants were classified into three groups according to their BMI percentile categories as follows: non-overweight/obese: < 85th percentile of BMI for age; Overweight: 85th to < 95th percentile of BMI for age and Obese: ≥ 95th percentile of BMI for age. Due to small sample size of underweight adolescents, they were combined with normal weight, and called non-overweight/obese adolescents.

The means and standard deviations of the adolescent's perceptions of their current and ideal figures, as measured by the nine figures silhouettes of Stunkard et al.[21] were then calculated, and the difference between perceived current and ideal body figure were tested for statistical significance using students paired t-test

Results

The prevalence of weight status among the Dubai adolescents by age and sex is presented in table I. The percentages of overweight (18.5%) and obesity (27.2%) among males were higher than that among females (13.1% and 20.5% respectively).

The perceptions and attitudes towards body weight amongst male and females adolescents are presented in table II. Among males, about 45% of overweight considered themselves as average and 22% as obese. Similar was the case with 52.3% of overweight females were considered themselves as an average and 20.4% as obese. As weight status of adolescents increased, the pressure of parents of adolescents to lose their weight incresed. Of overweight adolescents, 25% of males and 31.8% of females forced by parents to lose weight. The proportion increased to 52.8% and 53.6% among obese males and females, respectively. Additionally, 33.3% and 36.4% of overweight and 50% and 47.8% of obese males and females, respectively were teased by friends about their weight status ($p < 0.000$). Of overweight males and females, 51.7% and 70.5% had undertaken dietary programme. The proportion reached to 63.9% and 68.1% of obese males and females, respectively. In general, the association of weight perception and weight status was statistically significant in all items.

Tables III and IV show the perceptions of adolescent's current and ideal body shape preference according to the nine figure silhouette for males and females, respectively. Most of the non-overweight/obese boys perceived themselves as normal (32.2% and 26%, selected figures 4 and 5, respectively), in contrast 26.2% and 35.2% of non-overweight/obese girls perceived themselves as thin (selected figs. 2 and 3, respectively). Overweight boys were more likely to perceive themselves as overweight than girls. As for ideal body weight preferred by adolescents, figures number 4 and 5 were mostly selected by boys (27.9% and 45.1%), whereas in girls, figures number 3 and 4 were the most ideal figures preferred (39.9% and 30.7% respectively). In general, girls were more likely to select thinness figures than boys with surprising results that a high percentage of non-overweight/obese girls preferred the thin figures (figs. 1, 2 and 3). This phenomenon was very low among boys.

The mean and the standard deviations of the adolescent's perceptions of their current and ideal figures measured using the nine figure silhouettes are presented according to actual weight category in table V. Compared to their current body image, non-overweight/obese adolescent males chose a significantly heavier body figure as their ideal ($p < 0.002$), but this was not the case for girls, as they selected similar figure. In the overweight

Table II
Perceptions of/and attitudes to body weight among male and female adolescents in relation to their actual weight status (BMI percentile)

Perception/attitudes	*Adolescent's actual weight status*						*p-value*
	Non-overweight/obese		*Overweight*		*Obese*		
	n	*%*	*n*	*%*	*n*	*%*	
Male adolescents							
How do you consider yourself?							
Don't know	29	16.0	8	14.0	10	14.0	
Thin	27	14.1	12	20.0	10	14.0	
Average	92	48.0	27	45.0	41	56.9	< 0.6895
Obese	44	22.9	13	22.0	11	15.1	
Parents force you to lose weight							
No	178	92.7	45	75.0	34	47.2	
Yes	14	7.3	15	25.0	38	52.8	< 0.0000
Parents force you to increase weight							
No	139	72.4	55	91.7	69	95.8	< 0.0000
Yes	53	27.6	5	8.3	3	4.2	
Friends tease you for being obese							
No	175	91.1	40	66.7	36	50.0	< 0.0000
Yes	17	8.9	20	33.3	36	50.0	
Did you do any dietary programs before to reduce your weight?							
No	160	83.3	29	48.3	26	36.1	< 0.0000
Yes	32	16.7	31	51.7	46	63.9	
Female adolescents							
How do you consider yourself?							
Don't know	27	12.1	4	9.1	12	17.4	
Thin	35	15.6	8	18.2	12	17.4	< 0.7395
Average	104	46.4	23	52.3	32	46.4	
Obese	58	25.9	9	20.4	13	18.8	
Parents force you to lose weight							
No	211	94.2	30	68.2	32	46.4	
Yes	13	5.8	14	31.8	37	53.6	< 0.0000
Parents force you to increase weight							
No	136	60.7	43	97.7	62	89.9	
Yes	88	39.3	1	2.3	7	10.1	< 0.0000
Friends tease you for being obese							
No	211	94.2	28	63.6	36	52.2	
Yes	13	5.8	16	36.4	33	47.8	< 0.0000
Did you do any dietary programs before to reduce your weight?							
No	166	74.1	13	29.5	22	31.9	
Yes	58	25.9	31	70.5	47	68.1	< 0.0000

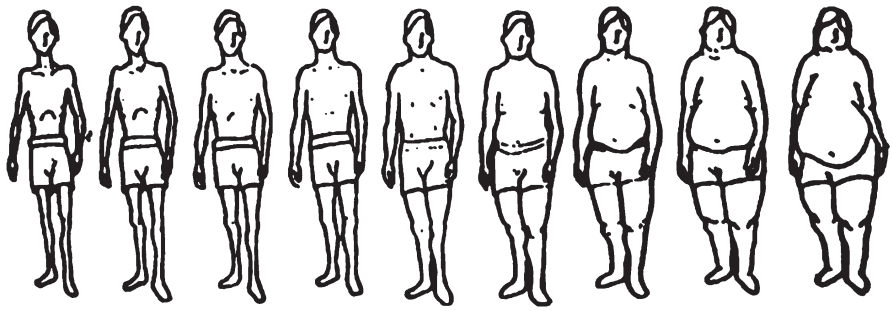
and obese category both set of genders chose a significantly lighter figure as their ideal ($p < 0.000$).

Discussion

The trends towards higher BMI status amongst the Dubai adolescents as seen in this study have been well documented by many researchers in the region.[15,17,24] It is clear from the results of the current study that conscious weight perceptions and weight concerns are present among adolescents in Dubai. Both overweight and underweight concerns have public health importance. Of particular concern is that this study supports the finding that there is a tendency for teenagers to overestimate/underestimate their body weight as evident by normal weight adolescents perceiving themselves as obese or thin. Previous studies among Bahraini adolescents have reported similar existence of a distorted body image as reflected by failure of many overweight or obese adolescents to perceive themselves as such.[17] It has been reported that, in girls, the strongest predictor of body dissatisfaction was internalization, while for boys the strongest predictor was pressure.[25]

Table III

Percentages of adolescents' current body weight status and ideal body figure preference by male adolescents in Dubai, UAE

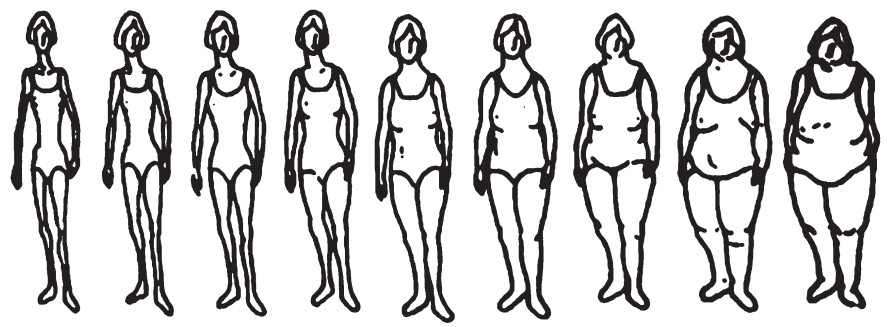


Body status (No.)		*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
		%	*%*	*%*	*%*	*%*	*%*	*%*	*%*	*%*
Non-overweight/obese	Current	2.5	10.4	21.3	32.3	26.0	6.3	1.2	0.0	0.0
(192)	Ideal	3.1	4.7	10.0	26.1	49.5	5.7	0.0	0.0	1.0
Overweight	Current	1.7	0.0	1.7	10.5	40.6	37.2	8.3	0.0	0.0
(60)	Ideal	1.7	6.7	18.9	28.9	38.9	5.0	0.0	0.0	0.0
Obese	Current	1.4	0.0	0.0	2.8	9.7	36.7	35.1	14.3	0.0
(72)	Ideal	6.9	1.4	12.5	31.9	40.3	5.6	0.0	1.4	0.0
Total	Current	2.2	6.2	12.7	21.7	25.7	19.2	9.6	2.8	0.0
(324)	Ideal	3.7	4.3	12.4	27.7	45.1	5.6	0.3	0.3	0.6

Another interesting finding of this study and an area of concern was that parents of about 27.6% and 39.3% of non-overweight/obese, males and female adolescents wanted them to gain weight. Haines et al.[26] suggest that parents may indirectly teach their adolescents to be dissatisfied with their bodies by modeling body dissatisfaction and dieting behavior. It is reported that society provides message about how people should

Table IV

Percentages of adolescents' current body weight status and ideal body figure preference by female adolescents in Dubai, UAE



Weight status (No.)		*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
		%	*%*	*%*	*%*	*%*	*%*	*%*	*%*	*%*
Non-overweight/obese	Current	5.9	26.2	35.2	24.6	7.1	1.0	0.0	0.0	0.0
(224)	Ideal	10.6	16.5	42.9	23.6	5.4	1.0	0.0	0.0	0.0
Overweight	Current	2.3	0.0	2.3	20.5	36.4	31.8	6.8	0.0	0.0
(44)	Ideal	2.3	9.1	38.6	50.0	0.0	0.0	0.0	0.0	0.0
Obese	Current	0.0	0.0	2.9	5.8	20.8	36.6	25.2	2.9	5.8
(69)	Ideal	4.3	7.2	30.5	39.7	12.6	4.3	1.4	0.0	0.0
Total	Current	4.2	17.6	24.7	20.9	13.4	11.9	5.6	0.6	1.2
(337)	Ideal	8.0	13.8	39.9	30.7	5.9	1.5	0.3	0.0	0.0

Table V
Means and standard deviations for male and female adolescent's perceptions of current and ideal body figure

Actual weight category	n	Body image (mean ± SD)		p-value
		Current	Ideal	
Males				
Non-overweight/obese	192	3.8 ± 1.41	4.28 ± 1.39	< 0.000
Overweight	60	5.00 ± 1.68	3.85 ± 1.49	< 0.000
Obese	72	6.03 ± 1.85	4.21 ± 1.28	< 0.000
Females				
Non-overweight/obese	224	2.98 ± 1.10	2.93 ± 1.11	< 0.6321
Overweight	44	5.11 ± 1.13	3.36 ± 0.75	< 0.000
Obese	69	5.72 ± 1.90	3.51 ± 1.37	< 0.000

ideally look and parental message were the strongest influence on body image.[9] Hodes, et al.[27] in their study to determine cultural variation in mothers' attitudes to children's body shape have reported that mothers of adolescents in non-Western countries express more positive attitudes regarding the need for children to gain. This finding is especially important to health professionals as the existing problems of overweight and obesity are quite high amongst the UAE adolescents. On the other end of the spectrum is the fact that more than one-half of the obese adolescents in this study were forced by their parents to lose weight. This could indicate changing attitudes in the Arab communities towards fatness, which so far was generally considered as desirable. In recent years the UAE has undergone rapid socioeconomic transition and adoption of western lifestyle could have brought about this change.[28]

Another outcome from this study was that there was a greater concern with body shape and a desire to be thin in females than in males as evident from the silhouettes[21] used to obtain information about ideal and current body image. It should be noted that although the scales used here are more for adults rather than for adolescents, the figures have been used previously in numerous studies as they adequately demonstrate the shape of the body among adolescents.[17,29] This preference for western thin body image as obvious amongst the normal weight adolescents in this study has also been made among other Arab women in the region.[30-31] Until the early 1990s, it was generally accepted that the thin body ideal, and widespread body dissatisfaction, were culturally linked phenomena that were limited to Western Europe and North America. Non-Western societies, particularly African and Middle Eastern, were thought to be relatively free from body dissatisfaction, disordered eating, and obsessions with weight.[32] However, in the past three decades, the Arab Gulf region has undergone rapid and extensive economic and socio-cultural modernization, resulting in a Western influence on the Arab adolescent's lifestyle. This adoption of a thin body figure due to westernization has been demonstrated in a study by Ford, et al.[33] where it was found that Arab students indicated a clear preference for thinness as a result of exposure to Westernized society thereby causing internalization of Western attitudes concerning eating and body shape. As reported by Gleaves et al.[34] awareness of a thin western ideal is becoming more accessible to non-western cultures through mediums like the internet, television, movies, direct travel accessibility, and music. As this dissemination of information occurs, western cultural values and attitudes spread to non-western cultures, which often results in an adoption of some aspects of westernisation. Although the data in this study indicates preference for a lighter weight among females than essential, it does not allow concluding that there is evidence of eating disorder amongst the female adolescents.

In contrast to the girls who wanted a lighter weight, boys preferred heavier weight as their ideal. Studies indicate that adolescent boys although are concerned about body weight and shape, wish to increase weight and thereby muscularity, rather than lose weight.[35] It is however important to note that many adolescent boys may find themselves pursuing a body type that is impossible to obtain the consequence of which could be an eating disorder such as bulimia, or an image disorder, such as muscle dysmorphia.[36] Finally, it is important to keep in mind that poor body image is associated with unhealthy weight control behaviors among both the children and adolescents.[37]

Studies in the UAE and other Arab Gulf countries have shown that that obesity has reached an epidemic level and potential for increase in obesity level continues to rise as the UAE continues to urbanize further.[15] Hence, the finding in this study that boys and parents alike favored a heavier weight needs to be dealt with at the earliest. In contrast, the findings that girls favour a lower body weight could be a step in the right direction, although it needs to be noted that in recent years there are reports of the emergence of abnormal eating behavior among adolescents in this region.[38-39] It is suggested that health education related to an awareness of a healthy

body weight, appropriate eating and exercise behavior should be integrated within the current health education curriculum, to minimize risk of developing distorted body image concerns in adolescence and beyond.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1973-1980
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Characteristics of newly diagnosed women with breast cancer; a comparison with the recommendations of the WCRF/AICR Second Report

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Abstract

Introduction: **The Second Expert Report, Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective from World Cancer Research Fund/ American Institute for Cancer Research (WCRF/AICR), features general and special recommendations for cancer prevention.**

Objective: To evaluate nutritional and lifestyle characteristics of newly diagnosed women with breast cancer according to WCRF/AICR Second Report recommendations.

Methods: **This is a cross-sectional study with a sample of 133 women. Diet data were obtained from a food frequency questionnaire and anthropometric data by standard procedures. The characteristics of study population were evaluated in comparison with the recommendations of the WCRF/AICR Second Report.**

Results: **Mean age of participants was 51.6 ± 10.98 (range 28-78) years; 35% was obese and 51% had waist circumference higher than the maximum cut-off value. Regarding life style, 80% of participants were sedentary, 89% reported diet presenting energy density higher than 125 kcal/100 g, 51% reported consumption of fruits and vegetables lower than 400 g/day, and 47% reported high consumption of red or processed meat (≥ 500 g per week). Just 3% related consumption of alcoholic beverages above the recommendation (15 g/day), 82% presented the intake of sodium lower than the limit recommended (2.4 g/day), and the use of dietary supplements was reported by 11% of the subjects. Finally 51% of women reported breast feeding for less than 6 months.**

Conclusion: **Inadequacies were observed related to behavior factors that can result in weight gain, such as inadequate physical activity and high energy density diet.**

(*Nutr Hosp.* 2012;27:1973-1980)

DOI:10.3305/nh.2012.27.6.6006

Key words: *Breast neoplasms. Prevention & control. Life style. Food. Nutritional status. Physical activity.*

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Recibido: 22-V-2012.
1.ª Revisión: 14-VI-2012.
Aceptado: 7-VIII-2012.

CARACTERÍSTICAS DE LAS MUJERES CON DIAGNÓSTICO RECIENTE DE CÁNCER DE MAMA: UNA COMPARACIÓN CON LAS RECOMENDACIONES DEL SEGUNDO INFORME DE LA WCRF/AICR

Resumen

Introducción: **El Segundo Informe Pericial, Alimentación, Nutrición, Actividad Física y la prevención del cáncer: una perspectiva global de la Fundación Mundial para la Investigación del Cáncer del Instituto Americano para la Investigación del Cáncer (WCRF / AICR), incluye recomendaciones generales y especiales para la prevención del cáncer.**

Objetivo: **Evaluar las características nutricionales y del estilo de vida de las mujeres con diagnóstico reciente de cáncer de mama según el recomendaciones del Segundo Informe de la WCRF/AICR.**

Métodos: **Este estudio transversal se realizó en una muestra de 133 mujeres. Los datos de la dieta se obtuvieron mediante cuestionario de frecuencia de alimentos y los datos antropométricos mediante procedimientos estándar. Las características de la población de estudio fueron evaluados en comparación con las recomendaciones del Segundo Informe de la WCRF/AICR.**

Resultados: **La edad media de los participantes fue de 51,6 ± 10,98 (rango 28-78) año; 35% era obeso y 51% tenía la circunferencia de cintura mayor que el máximo valor recomendado. En cuanto a estilo de vida, 80% de los participantes eran sedentarios, 89% tenía una dieta con densidad de energía mayor que 125 kcal/100 g, 51% informó el consumo de frutas y verduras más bajo que 400 g/día, y 47% informó de un consumo elevado de carne roja o procesada (≥ 500 g por semana). Sólo 3% tenía del consumo de bebidas alcohólicas encima del recomendado (15 g/día), 82% presentó la ingesta de sodio por debajo del límite recomendado (2,4 g/día), y el uso de suplementos dietéticos que fue reportado por 11% de los sujetos. Por último 51% de las mujeres reportaron la lactancia materna por menos de 6 meses.**

Conclusión: **Se observaron deficiencias relacionadas con factores de comportamiento que pueden resultar en el aumento de peso, tales como la inactividad física y la dieta de alta densidad de energía.**

(*Nutr Hosp.* 2012;27:1973-1980)

DOI:10.3305/nh.2012.27.6.6006

Palabras clave: *Cáncer de mama. Prevención y control. Estilo de vida. Alimentación. Estado nutricional. Actividad física.*

Abbreviations

AICR: American Institute for Cancer Research.
BMI: Body mass index.
FFQ: Food frequency questionnaire.
PAL: Physical activity level.
WC: Waist circumference.
WCRF: World Cancer Research Fund.

Introduction

Breast cancer is the most commonly diagnosed cancer and the second most common cause of cancer mortality among women worldwide, both in developed and developing regions.[1] The incidence rates vary from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe.[2]

Both, genetic and environmental influences may be involved in its etiology, however genetic account for only 5-10% of all breast cancer cases, suggesting the potential role of external factors in the development of this disease.[3] Modifiable risk factors for breast cancer include being overweight or obese (for postmenopausal breast cancer), physical inactivity, and consumption of one or more alcoholic drinks per day. [4] In addition, migration data has shown nutrition to be one of the most important external factors.[5]

Although, the role of nutrition in breast cancer risk is strongly suggested by a lot of researches, the combined evidence from epidemiological studies is inconclusive for most diet aspects[1]. As a result, according to the World Cancer Report[6] several studies have been conducted to investigate whether the intake of fruit, vegetables and related micronutrients, dietary fiber, total and saturated fats, dairy products, and others, has an influence on breast cancer risk.

According to the Second Expert Report *"Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective",* the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) have declared that about one third of the most common cancers could be prevented through a healthy diet, being physically active and maintaining a healthy weight.[1]

This document[1], first published in 1997, was recognized as the most authoritative and influential report in its field and helped to highlight the importance of research in this crucial area. The second report presents eight general and two special recommendations that help people to reduce the risk of developing cancer.

The eight general recommendations are: be as lean as possible within the normal range of body weight; be physically active as part of daily life; limit the consumption of energy dense foods, avoid sugary drinks; eat mostly plant foods; limit the intake of red meat and avoid processed meats; limit alcoholic beverages; limit consumption of salt, avoid mouldy cereals (grains) or pulses (legumes); and aim to meet nutritional needs through diet alone, not supplements. It has also two specific recommendations: mothers should practice breastfeeding and children should be breastfed, and finally, cancer survivors should follow the same recommendations for cancer prevention.[1]

In order to establish intervention strategies on the modifiable risk factors related to lifestyle it is essential to know the distribution pattern of risk factors associated with breast cancer in groups that have propensity or already have developed the disease. In this context, this study aimed to evaluate the nutritional and lifestyle characteristics of newly diagnosed women with breast cancer according to WCRF/AICR Second Report[1] recommendations.

Study population and methods

Study characterization and design

The population of this cross-sectional study was selected from a convenience sample of 176 women admitted to breast surgery, between October 2006 and June 2010, at the Hospital *Maternidade Carmela Dutra* (HMCD), Florianopolis, Brazil. Data from 41 women (23.2%) with confirmed benign tumors and 2 (1.1%) with missing data were excluded. Finally, 133 women with breast cancer diagnosis confirmed by pathological examinations were included in the study. All the participants were evaluated anatomopathologically according to the Tumor-Node-Metastasis system classification of malignant tumours.[7]

The study was approved by the Ethics Committee of the Federal University of Santa Catarina (protocol 145/06 and 099/08) and by the MCDH, and the written informed consent was obtained. All participants were interviewed after admission and before surgery by professional and nutrition students previously trained, using a study adapted questionnaire.[8]

Nutritional parameters

The food consumption data was obtained from a food frequency questionnaire (FFQ), for the preceding year, adapted from a FFQ previously validated in Brazil,[9] containing 112 food items, classified into seven groups: cereals and pulses (legumes), meats (including eggs and processed meat), dairy products, fruits, vegetables, oils and fat, sweet foods and others (alcoholic and non-alcoholic beverages, processed foods).

A photographic record of dietary surveys and household items of various sizes were used to assist respondents in identifying the portions consumed.[10] The amounts of food reported as household measures were converted into their respective weights and volumes, in grams (g) or milliliters (mL), respectively, as previously described.[11,12]

Weight, height and waist circumference (WC) were measured according to standard procedures,[13] using the

anthropometric Filizola® scale and an inelastic tape. Nutritional status was assessed by body mass index (BMI) and classified according to categories defined by the World Health Organization, which is recommended by WCRF/ AICR Second Report.[1]

Recommendations of WCRF/AICR Second Report

Both, nutritional and lifestyle characteristics of the study population were evaluated according to the recommendations of the WCRF/AICR Second Report[1]: The mean adult body mass index (BMI) should be between 21 and 23 kg/m^2, depending on the normal range for different populations. For this study, we adopted the following classification: underweight (< 18.5), normal weight (18.5 to 24.9), overweight (25.0 to 29.9) and obese (≥ 30 kg/m^2).[14]

The physical activity of patients was assessed based on the physical activity level (PAL) recommended to be above 1.6. This is a way to represent the average intensity of daily physical activity. PAL is calculate as the ratio of total energy expenditure to basal energy expenditure.[15] The results were divided in sedentary (PAL ≤ 1.39), e.g. housework, walking to the bus; low active (1.40 to 1.59), e.g. walking at 5-7 km/h for 30-60min daily; active (1.60 to 1.89), e.g. at least 60 minutes of daily moderate activity.[15]

Regarding food intake the WCRF/AICR Second Report[1] recommends that the diet should contain an energy density lower than 125 kcal/100 g, excluding all liquids, so it is recommended avoid sugary drinks and fruit juices should also be limited[1]. Thus, the drinks that are part of the FFQ, such as, whole milk and skim milk, soy drinks, artificial juices, soft drinks, coffee, tea, mate and alcohol were excluded from the calculation of energy density (ED), by equation: ED = total calories (kcal)/ total weight (grams) x 100. Subsequently, the women were grouped according to the ED < 125 kcal/100 g and ED ≥ 125 kcal/100 g.

For plant foods the recommended consumption is 400 g or 14 oz per day of a variety. The consumption of plant foods (groups of fruits and non-starchy vegetables) were classified in > 400 g/day and ≤ 400 g/day. For animal source food the recommendation is to limit the intake of red (beef, pork, lamb, and goat) and processed meat (preserved by smoking, curing or salting, or addition of chemical preservatives).[1] The recommendation for animal source foods is 500 g per week, so we analyze the total grams of this food available in our FFQ.

For the consumption of alcoholic drinks, the recommendations were based on grams of ethanol (1 "drink" contains 10 to 15 grams of ethanol). For women, the recommendation is limited to consumption of no more than one drink per day. So, we evaluated the alcoholic drinks available in our FFQ (beer, wine and whisky) per grams of ethanol and classified the daily consumption as: not drink ≤ 9 g, 10 to 15 g, and ≥ 16 g. To assess sodium intake, only the intrinsic grams of sodium in foods reported were analyzed on the FFQ. The daily intake was classified in ≤ 2.4g (recommended amount) and > 2.4g.[1]

The use of dietary supplements was assessed by a question about the current consumption, once this is not recommended for cancer prevention according to WCRF/AICR Second Report.[1] Finally, women were asked if they breastfed their babies for six months or longer (yes/no), according to the report.

Table I
Demographic and clinical characteristics of newly diagnosed breast cancer women (n = 133), Florianópolis, SC-Brazil

Variables	*n (%)*
Age (years)	
28-39	18 (14)
40-49	40 (30)
50-59	46 (34)
≥ 60	29 (22)
Ethnicity	
White	124 (93)
No White	9 (7)
Tumor classification	
Invasive carcinoma	119 (89)
Carcinoma in situ	14 (11)
Tumor stage	
0	6 (5)
I	46 (34)
II A/B	47 (35)
III A/B/C	34 (26)

Statistical Analysis

Data was typed in a double entry database for later statistical analysis with Statistical 7.0 software, and in all cases the level of significance was established at 5%. Continuous data was presented as mean, standard deviation, median and range, and categorical data as absolute and relative frequency. Normality of data distribution was assessed by the *Shapiro-Wilk test*.

To evaluate the correlation between BMI, WC, PAL, intake of total energy, plant foods, animal source foods, ethanol, sodium and dietary energy density, the *Spearman correlation coefficients (r)* was used and classified according to Callegari-Jacques.[16] Mann-Whitney U test was used to evaluate the association between the total energy variables and energy density with the variables of dietary intake.

Results

The mean age of the participants was 51.6 ± 10.98 (median = 51, range 28-78) years and 93% were Caucasians. There was a high prevalence of women with invasive carcinoma (89%), stage I or II tumor (69%) (table I).

Table II
Anthropometry, physical activity levels and dietary variables of newly diagnosed women with breast cancer according to WCRF/AICR Second Report[1] (n = 133), Florianópolis, SC-Brazil

Variables	*N (%)*	*Mean ± DP*	*Median*	*Range*
Nutritional status (BMI)		28.13 ± 4.97	27.83	17.75-41.25
Underweight (≤ 18.5 kg/m²)	3 (2)			
Normal weight (18.5-24.9 kg/m²)	41 (31)			
Overweight (25-29.9 kg/m²)	42 (32)			
Obese (BMI ≥ 30 kg/m²)	47 (35)			
Waist circumference (cm)		90.36 ± 13.22	88.0	64.00-125.00
< 80	27 (20)			
80-88	39 (29)			
≥ 88	67 (51)			
Physical activity levels (PAL)		1.35 ± 0.10	1.33	1.20-1.78
Sedentary (1.0-1.39)	106 (80)			
Low active (1.40-1.59)	22 (16)			
Active (1.6-1.89)	5 (4)			
Energy density of diet (kcal/100 g/day)		175.46 ± 41.50	172.53	101.0-305.87
< 125	15 (11)			
≥ 125	118 (89)			
Plant foods (g/day)		466,27 ± 263,92	392.47	26,59-1406,39
< 400	67 (51)			
≥ 400	66 (49)			
Animal foods (g/week)		583.72 ± 391.29	485.00	0-1716.53
< 500	70 (53)			
≥ 500	63 (47)			
Alcoholic drinks (g of ethanol/day)		1.82 ± 5.55	0.00	0.00-40.67
No	99 (74)			
≤ 9	25 (19)			
10-15	5 (4)			
≥ 16	4 (3)			
Sodium Intake (g/day)		1.66 ± 0.99	1.40	0.48-6.18
≤ 2,4	109 (82)			
> 2,4	24 (18)			
Dietary supplements				
Yes	14 (11)			
No	119 (89)			
Breastfeeding (up to six months)				
Yes	66 (49)			
No	67 (51)			

Table II shows the distribution of the study participants according to WCRF/AICR Second Report[1] recommendations. According to BMI, 32% of women were overweight, 35% were obese and 50% had WC higher than the maximum cut-off value of 88 cm. Regarding the physical activity level (PAL), 80% were sedentary and 89% of women had food intake with energy density higher than 125 kcal per 100 g.

The consumption of plant foods was less than 400 g per day in 51% of women and 47% consumed more than 500 g per week of animal source foods (red or processed meats). An alcoholic beverage was null in 74% of women and only 3% had alcohol intake above of the recommendation. In addition, the intake of sodium was lower than the limit recommended in 82% of the sample and the use of dietary supplements was

Table III
Correlation table between anthropometric data, lifestyle and food consumption in women with breast cancer (n = 133), Florianópolis, SC-Brazil

	BMI	*WC*	*PAL*	*Total energy*	*Plant foods*	*Animal foods*	*Ethanol*	*Sodium*
WC	0.874*							
PAL	-0.587*	-0.581*						
Total energy	-0.047	-0.114	0.127					
Plant foods	0.156	-0.164	0.049	0.042				
Animal foods	-0.042	-0.072	0.173	0.469*	0.006			
Ethanol	-0.020	-0.053	0.055	0.099	-0.049	0.234		
Sodium	0.134	0.053	0.039	0.680*	0.090	0.390	0,128	
Density energy	0.043	0.005	-0.018	0.299	-0.343*	0.153	0.044	0.298

*Moderate or high Spearman correlation ($p < 0.001$); BMI: Body mass index; WC: Waist circumference; PAL: Physical activity level.

reported by only 11% of subjects. According to the recommendation for breastfeeding, approximately 50% reported that they breastfed their babies for longer than 6 months (table II).

Table III shows the correlation analysis between the nutritionals and physical activity variables. According to the expected, a positive correlation between BMI and WC was found. In addition, an inverse correlation was seen between PAL and BMI, and between PAL and WC, both significant. Furthermore, a significant positive correlation between the total energy and animal source foods and between total energy and sodium was found, while an inverse correlation between plant foods and energy density was obtained.

To reinforce the above highlighted findings, the consumption was measured for vegetables (g/d), food products of animal origin (g/s) and sodium (mg/d) in relation to the total dietary energy (kcal/day) and the density energy diet (kcal/100 g). It was observed that women with higher total daily energy intake (> 2,280 kcal or > 50th percentile) showed significantly higher consumption of plant foods (fruits and vegetables), animal source foods and sodium. In contrast, when measured by the diet energy density, it was observed that women who had a diet with higher energy density (> 172.53 kcal/100 g) had a significant lower consumption of plant foods, and highly significant consumption of animal source foods and sodium. The food intrinsic sodium consumption was significantly higher among women with higher energy intake and also among women with higher energy density diet. However, between these two groups, sodium consumption was higher among women with higher energy intake compared to women with higher energy density diet (table IV).

Discussion

According to the findings of this study, modified risk factors for breast cancer were confirmed among newly diagnosed women with the disease, highlighting high prevalence of sedentarism, high rate of overweight and obesity, and waist circumference values above the recommended. These factors are known to be strongly associated with a poor diet.[17]

In relation to food consumption, low consumption of fruits and vegetables, high consumption of red/processed meats and concomitantly, high energy density diet were observed in this study. However, fruit juice consumption should be controlled because they may contribute to increase the total energy consumption of the diet. On the other hand, red/processed meat should be consumed within recommendations.[17]

Table IV
Dietary intake variables associated with total energy and density energy in newly diagnosed women with breast cancer (n = 133), Florianópolis, SC-Brazil

Dietary intake		*Total energy (kcal)*		*Density energy of diet (kcal)*	
		≤ 50th	*> 50th (> 2,280)*	*≥ 50th*	*> 50th (> 172.53)*
	N	*67*	*66*	*67*	*66*
Plant Foods (g/d)		451.7	579.6**	647.8	370.7*
Animal foods (g/week)		392.0	700.1*	450.3	507.8***
Sodium (g/d)		1.09	2.05*	1.28	1 .57**

Data are expressed as median. *$p < 0.001$; **$p < 0.005$; ***$p < 0.05$ (compared with daily dietary intake < 50th percentile). Mann-Whitney U test.

Thus, it is believed that knowing the nutritional status and dietary habits of women with breast cancer before treatment can help establish and maintain intervention strategies that promote a healthy weight through diet and physical activity with the intention of reducing the risk of cancer recurrence.

According to the case-control study of Felden and Figueiredo,[18] 42.4% and 30.3% of participants were overweight during pre and postmenopausal periods, and 30.3% and 45.5% were obese in pre and post menopausal, respectively. A similar result was found in our study, where overweight was observed in 34% of premenopausal women and 29% of postmenopausal, and obesity was seen in 27% and 42% of women pre and postmenopausal, respectively (data not shown).

A systematic review[19] on risk and protective factors for cancer indicated that weight gain has been demonstrated to be a risk factor for breast malignancy, and that body fat as indicated by the WCRF and AICR as a risk factor for promoting breast cancer in postmenopausal women, and probably a protective factor for premenopausal women. The role of high BMI for breast cancer risk is probably due to its effect on endogenous estrogen concentrations, since women who have high BMI and adipose tissue have higher concentrations of aromatase, an enzyme that catalyzes the conversion of androgens to estrogens.[20]

Magnetic et al.[21] in a literature review on the relationship between breast cancer and lifestyle, has shown that physical activity is a modifiable factor that may have a beneficial effect on survival by reducing body fat, once it helps regulate the metabolism of sex hormones, insulin sensitivity and immunization routes. The authors state that proper diet and regular physical activity can reduce the risk of death related to cancer. Although the underlying mechanisms are not clear yet, growing clinical evidence support the inclusion of low to moderate intensity physical activity as a preventive measure.

Eight percent of women of this study were classified as sedentary and only 4% were considered physically active, and therefore in disagreement with the recommendation of WCRF/AICR Second Report.[1] Furthermore, as expected, the data shows a moderate negative correlation of the BMI and of WC with the PAL. In case-control study in Southern Brazil, the authors also concluded that most women diagnosed with breast cancer, were sedentary.[18]

The recommended daily intake of 400 g, or at least five servings of fruits and vegetables, which usually have low energy density, was inadequate in 67 (51%) of the studied women. Masala et al.[22] when evaluating the association between consumption of fruits and vegetables and breast cancer risk based on data from the European Prospective Investigation into Cancer and Nutrition - EPIC study also noted the low consumption of vegetables (< 190 g/day) and fruits (< 360 g/day) in women.

As expected, it was found that the daily consumption of vegetables was lower than recommended in women with higher energy density diet (percentile > 50) than among those with lower density (370 g *vs.* 647 g/ day). Thus, it can be confirmed that a diet rich in fruits and vegetables contributed to reducing the total energy density of the diet.

Most food standards that protect against cancer consist mainly of a plant food rich diet[1]. Fruits and vegetables are rich sources of a variety of antioxidants such as carotenoids, tocopherols and ascorbic acid. Also, the consumption of fruits and vegetables provide other compounds that have been associated with the prevention of cancer, for example, the lignans.[23]

With respect to the consumption of plant foods with the goal of preventing breast cancer recurrence, the Second Expert Report advises that the same behavior in relation to primary prevention should be taken with regard to prevention of disease recurrence.

Thus, in a narrative review[24] on the diet modification in women after treatment for breast cancer, the author concluded that in terms of individual components of the diet —recommended by several guidelines— eating a variety of fruits, vegetables and grains are important for several reasons. For example, they contain fiber, which improves the feeling of satiety and, therefore, may help reduce fat intake, thereby to reduce the diet energy density. These foods are also abundant in micronutrients vital for optimal cellular function and besides help minimizing fatigue.

Epidemiological studies also indicate a possible correlation between the consumption of red/processed meat and breast cancer, suggesting the presence of factors in red meat that result in damage to biological components[25]. In this sense during year of 2007, our research group in order to determine possible associations between the risk of breast cancer and dietary factors, showed that weekly consumption of red meat and fat in the form of lard was associated with occurrence of breast cancer in women in southern Brazil.[8]

It was observed that 47% of women reported consuming more than the recommended limit of 500 g of red/processed meat per week and, when analyzing the correlation coefficients, it was found that the intake of foods of animal origin showed positive regular correlation with the total energy in the diet. Corroborating this finding, the consumption of red and processed meats was analyzed in relation to the percentile of total energy and energy density of the diet, which alerts us to reduce the consumption of foods from this group.

The relationship between red/processed meat intake and breast cancer[8,25] is possibly to the hypothesis of red meat compounds and its oxidative processes in our body. Red meats have heterocyclic amines, which contain mutagenic and carcinogenic[23,26] compounds. Although studies have observed this effect,[8,25] results from a meta-analysis did not demonstrate an independent association.[27]

The grilled or roasted meat consumption can increase the risk of breast cancer and its recurrence by

greater exposure to heterocyclic amines and polycyclic aromatic hydrocarbons, and other potent carcinogens.[23,26] In addition, fats, found in red and processed meats, by induction of lipid peroxidation, mediated by free radicals would be another mechanism by which a fat diet may promote carcinogenesis and contribute to increase the risk of such disease recurrence.[28]

Considering alcohol consumption a satisfactory result was found. However, according to Qureshi et al.[28] there is great difficulty in investigating alcohol consumption, and consequently the association between alcohol and breast cancer risk studies because of the possibility of recall bias and selection bias, quite common in studies for this purpose. Moreover, in the "Second Expert Report," convincing evidence was shown only for high alcohol consumption (≥ 2 drinks/day).[29]

In contrast, a collaborative reanalysis of individual data from 53 epidemiological studies, including 58.515 women with breast cancer and 95.067 women without the disease, Hamajima et al.[30] estimated that each additional drink per day increases the relative risk of breast cancer in 7.1%, and that 4% of breast cancer cases in developed countries could be attributed to alcohol.

Another important finding was that sodium intake was adequate in much of the present study sample, despite the limitation in the assessment of sodium intake. According to the WHO[31] food frequency questionnaires are not particularly useful for measuring sodium intake by assessing food intake in full. Still, the Second Expert Report highlights that sodium intake is related to stomach cancer,[1,32] and there are few studies on the relationship between sodium intake and breast cancer. Thus it can be said that this increased consumption was due to the inclusion of beverages —which are rich in sodium[33]— in the diet total energy calculation.

Regarding the use of dietary supplements the vast majority reported not using these supplements. About this, some epidemiological studies associated the antioxidants intake —that can be taken via supplementation— with a reduced risk of certain cancers.[34] A meta-analysis of cohort and case-control studies to assess the intake of multivitamins and its relation to the risk of breast cancer, showed inconsistent results in epidemiologic studies. The authors concluded that the use of multivitamins is not demonstrably associated with breast cancer risk increment/reduction, but these results highlight the need for further case-control studies or randomized controlled trials to examine deeply this relationship.[35]

The Second Expert Report [1] does not recommend the use of dietary supplements, because there is no consensus among studies. The guide indicates that, in general, for healthy people, the inadequate intake of nutrients must be supplied from a diet rich in nutrients and not supplements, because this way it is also acquired other potentially beneficial[1] dietary components.

Finally, the Second Expert Report[1] is the first major report which sets out the recommendations on breastfeeding for prevention of breast cancer in mothers and to prevent overweight and obesity in children. A recent systematic review[19] on risk and protective factors for breast cancer concluded that breastfeeding was a protective factor against breast cancer. The breastfeeding time is also important. In the study by Felden and Figueiredo[18], women which didn't breastfeed for five months are 84% more likely to develop the disease compared to those which nurse for over six months or longer.

Conclusion

In this study, high rates of overweight and waist circumference values were observed above the recommendation, indicating abdominal obesity. It is also stressed that most women practice insufficient physical activity, and present a diet with high energy density.

Based on these results, intervention strategies —based mainly on modifiable risk factors mentioned above— should be prioritized. Moreover, it is important to encourage the maintenance of healthy habits and dietary quality among patients with breast cancer which contributes to the treatment success and prevention of disease recurrence.

Acknowledgements

The authors would like to thank the Brazilian Federal Agency for Support and Evaluation of Graduate Education (CAPES), Program for the Restructuring and Expansion of Federal Universities (REUNI), Foundation for the Support of Scientific and Technological Research of the State of Santa Catarina (FAPESC), Carmela Dutra Maternity Hospital, Nutrition Post-Graduate Program at the Federal University of Santa Catarina and the National Council for Scientific and Technological Development (CNPq) for the support given to this research.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1981-1986
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Effect of vitamin A supplementation on clinical evolution in patients undergoing coronary artery bypass grafting, according to serum levels of zinc

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Abstract

Vitamin A and zinc are powerful antioxidants with synergy between them, thus protecting the organism against oxidative stress during the pre and postoperative periods. Our aim was to investigate the evolution clinical in patients undergoing coronary artery bypass grafting while receiving vitamin A supplements according to their zinc nutritional status. They were randomly divided into two groups (2:1): Control group (G1 = 60); and Supplemented group (G2 = 30) and subdivided according to the nutritional status of zinc. Serum concentrations of retinol, β-carotene, zinc and levels of malondialdehyde were measured prior to (T0) and on the 21st day (T1) following surgery. After surgery, was found a significant difference between G1 and G2 when comparing retinol (G1 = 38.7 ± 17.1 µg/dL and G2 = 62.1 ± 20.3 µg/dL; p < 0.001) and β-carotene (G1 = 12.3 ± 5.7 µg/dL and G2 = 53.5 ± 20.9 µg/dL; p < 0.001) in the patients with adequate concentrations of zinc. Analyzing the evolution clinical, operative mortality was 8.33% in G1 and 3.33% in G2. Hospitalization time significantly smaller in the G2 was found in the patients who had adequate concentrations of zinc (p = 0.001), as well as time in the intensive care unit both in those with adequate and inadequate levels of zinc (p = 0.047; p = 0.039). Such results may indicate that vitamin A supplementation may have a positive impact in combating the oxidative stress to which these patients are exposed above all in patients with adequate levels of zinc.

(*Nutr Hosp.* 2012;27:1981-1986)

DOI:10.3305/nh.2012.27.6.5891

Key words: *Vitamin A. Zinc. Coronary artery bypass grafting.*

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Recibido: 7-IV-2012.
Aceptado: 7-VIII-2012.

EFECTO DE LA SUPLEMENTACIÓN CON VITAMINA A SOBRE LA EVOLUCIÓN CLÍNICA EN PACIENTES SOMETIDOS A CIRUGÍA DE REVASCULARIZACIÓN MIOCÁRDICA, DE ACUERDO CON LOS NIVELES SÉRICOS DE ZINC

Resumen

La vitamina A y zinc son antioxidantes de gran alcance con la sinergia entre ellos, lo que protege el organismo contra el estrés oxidativo durante los períodos pre y postoperatorio. Nuestro objetivo fue investigar la evolución clínica en pacientes sometidos a cirugía miocárdica, mientras que recibir suplementos de vitamina A en función de su estado nutricional de zinc. Ellos fueron divididos aleatoriamente en dos grupos (2:1): grupo control (G1 = 60) y el grupo suplementado (G2 = 30) y se subdividen de acuerdo con el estado nutricional de zinc. Las concentraciones séricas de retinol, β-caroteno, el zinc y los niveles de malondialdehído se midieron antes (T0) y el día 21 (T1) después de la cirugía. Después de la cirugía, se encontró una diferencia significativa entre G1 y G2, al comparar el retinol (G1 = 38,7 ± 17,1 mg / dl y G2 = 62,1 ± 20,3 mg/dl, p <0,001) y el β-caroteno (G1 = 12,3 + 5,7 g/dl y G2 = 53,5 ± 20,9 mg/dl, p <0,001) en los pacientes con concentraciones adecuadas de zinc. El análisis de la evolución clínica, la mortalidad operatoria fue del 8,33% en el G1 y el 3,33% en el G2. El tiempo de hospitalización significativamente menor en el G2 se encontró en los pacientes que tenían concentraciones adecuadas de zinc (p = 0,001), así como el tiempo en la unidad de cuidados intensivos, tanto en aquellos con niveles adecuados e inadecuados de zinc (p = 0,047, p = 0,039). Estos resultados podrían indicar que suplementos de vitamina A puede tener un impacto positivo en la lucha contra el estrés oxidativo al que estos pacientes están expuestos, sobre todo en pacientes con niveles adecuados de zinc.

(*Nutr Hosp.* 2012;27:1981-1986)

DOI:10.3305/nh.2012.27.6.5891

Palabras clave: *Vitamina A. Zinc. Revascularización miocárdica.*

Introduction

Cardiovascular diseases (CVD) are regarded as a major global health issue,[1] being the world's leading cause of death.[2] The World Health Organization (2012)[2] estimates that 17.1 million people die of CVD per year and, if appropriate measures are not taken, the number of deaths stemming from such illnesses will rise to around 23.6 million per year by 2030.

Coronary artery bypass grafting (CABG) is standard treatment for ischaemic heart disease in a number of subgroups [3]. It is a major surgical procedure known to have a high rate of morbidity and operative mortality, and it is much more costly than therapeutic medication.[4]

The rise in oxidative stress in patients who undergo heart surgery is well documented,[5] as are the undesirable consequences such operations provoke[6] – with a drop in immunological response[7] and the onset of postoperative complications.[6]

One of the most used indicators for the assessment of oxidative stress is the malondialdehyde (MDA), which is a product of lipid peroxidation, in which is estimated by measurement of thiobarbituric acid reactive substances (TBARS nmol/L), the method most used in studies of lipid peroxidation due to be simple and sensitive.[8]

Vitamin A and zinc are not just potent antioxidants that work in synergy,[9] they are also closely linked to the immunological system,[10] protecting the organism against oxidative stress and the postoperative complications associated with heart surgery.

In recent years conflicting findings have surfaced in studies associating vitamin A with a reduction in oxidative stress and cardiovascular diseases[1,11] however, these studies did not investigate the relationship between this vitamin and zinc nutritional status. Hence, we investigated the clinical evolution in patients undergoing CABG receiving vitamin A supplementation according to zinc nutritional status.

Patients and methods

The participants in this study were adult patients undergoing CABG at a public hospital in the city of Rio de Janeiro between July 2008 and December 2009. This research was approved by the research ethics committee of the National Cardiology Institute of Laranjeiras.

Were used as inclusion criteria patients hospitalized to elective surgery of CABG, age ≥ 20 years[12] and that they gave their formal authorization to take part in the study by signing the Consent Form (Free and Clear). We excluded patients who were suffering from malabsorption syndromes, acute and chronic infections, kidney diseases, alcoholism, acquired immune deficiency syndrome (AIDS), took medication or vitamin supplements containing vitamin A or zinc over the last six months, and who had previously undergone CABG.

This study was composed of 90 patients distributed, through randomized table 2:1, into two groups: Control group (G1 = 60), made up of patients given a standard hospital diet; and supplemented group (G2 = 30), made up of patients who were given vitamin A supplementation of 5,000 IU, daily for 21 days, in the form of retinol palmitate. These groups were subdivided in those with adequate zinc concentrations and inadequate.

Supplementation in the form of a single pill began immediately after a blood sample was taken before surgery (T0). The patients from both groups were accompanied for 21 days, the second blood sample was taken, 21 days post surgery (T1).

The method for determining serum retinol and -carotene levels was high performance liquid chromatography (HPLC).[13] We adopted the cut points < 30 μg/dl for inadequate serum retinol levels and ≤ 40 μg/dL for inadequate serum β-carotene levels.[14,15]

Zinc was measured using atomic absorption spectrometry, with values < 0.7 mg/L deemed to be inadequate.[16]

The levels of MDA were evaluated through Spectrophotometry[17]. In addition, it was analyzed through the HPLC-UV method also.[18]

In considering the intraoperative period, we evaluated duration of surgery, duration of extracorporeal circulation (T CEC), clamp duration (T clamp), and the number of grafts of each patient. We took note of: time hospitalized, in the intensive care unit (ICU), and on breathing support (BS) through visits and by checking the patients' medical records. All deaths to occurring during the length of hospital stay or the 1st month post surgery were counted as operative mortality.

In analyzing the data, quantitative variables were expressed as mean and standard deviation and qualitative variables as percentages. The Kolmogorov-Smirnov test was used to test the normality of the continuous variables. For variables with normal distribution was used the t-Student test and for variables with non-normal distribution, the Mann-Whitney test was used to compare two groups. Was employed the Chi-square test, for assessing the association between categorical variables, as well as Spearman's correlation coefficient. The level of significance adopted was 5% ($p < 0.05$). The analyses were performed on the SPSS program version 15.0.

Results

The sample group was comprised of 90 patients. Following a randomization procedure (2:1), G1 (control) was comprised of 60 patients, while G2 (supplemented), 30 patients.

Average age was 65.06 ± 9.81 in G1 and 63.06 ± 9.3 in G2. It wasn't observed any significant difference between the groups according to the intra-operative

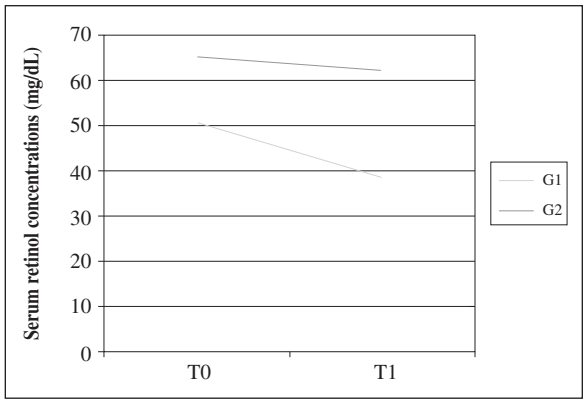


Fig. 1.—Serum retinol concentrations pre and post CABG in patients with adequate levels of zinc.

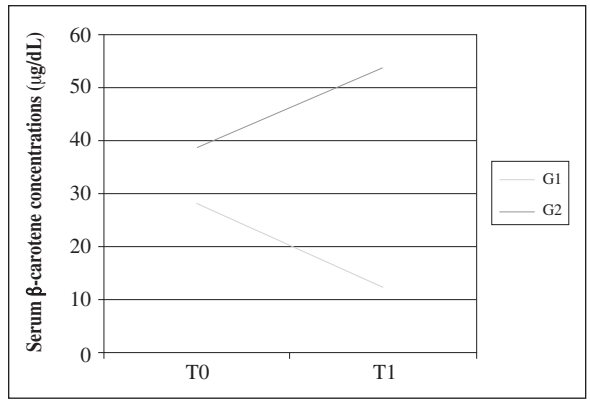


Fig. 2.—Serum β-carotene concentrations pre and post CABG in patients with adequate levels of zinc.

profile: duration of surgery (p = 0.93), extracorporeal circulation (p = 0.41), clamp time (p = 0.29), and number of grafts (p = 0.91).

When assessing the Vitamin A serum level (retinol and -carotene), there was no significant difference between the groups at T0 among the individuals who presented adequate zinc concentrations (G1 = 50.4 ± 14.6 µg/dL and G2 = 65.3 ± 15.7 µg/dL; p = 0.051) to retinol and (G1 = 28.1 ± 8.98 µg/dL and G2 = 38.5 ± 13.1 µg/dL; p = 0.051) to β-carotene, as well as inadequate (G1 = 44.5 ± 17.3 µg/dL and G2 = 52.1 ± 17.7 µg/dL; p = 0.052) to retinol and (G1 = 25 ± 0,1 µg/dL and G2 = 31.6 ± 6.7 µg/dL; p = 0.06) to β-carotene, respectively.

After surgery, was found a significant difference between G1 and G2 when comparing retinol (G1 = 38.7 ± 17.1 µg/dL and G2 = 62.1 ± 20.3 µg/dL; p < 0.001) and β-carotene (G1 = 12.3 ± 5.7 µg/dL and G2 = 53.5 ± 20.9 µg/dL; p < 0.001) in the patients with adequate concentrations of zinc (figs. 1 and 2).

A strong and positive correlation was found between concentrations of serum retinol and β-carotene following supplementation, in patients with adequate serum concentrations of zinc (r = 0.852 and p = 0.014).

After surgery, MDA concentrations were significantly higher at T1 in patients with inadequate serum levels of zinc (G1 = 3.5 ± 2.8 nmol/L and G2 = 2.6 ± 1.6 nmol/L) compared to those with adequate concentrations (G1 = 3.0 ± 1.5 nmol/L and G2 = 1.6 ± 1.1 nmol/L), in both groups, G1 and G2 (p < 0.001 and p = 0.002), respectively (fig. III). At T0 there was not significance difference between this variables in G1 (p = 0.48) and G2 (p = 0.053).

In analyzing evolution clinical, operative mortality was found to be 8.33% in G1 and 3.33% in G2. We noted a significant difference in time hospitalized between the control and supplemented groups, in patients with adequate levels of zinc (p = 0.001), and in time in ICU, both in those with adequate and inadequate levels of zinc (p = 0.047; p = 0.039). Now as for time on breathing support, no significant difference was found between the groups according to zinc nutritional status (table I).

Discussion

Intense study into the involvement of oxidative stress in the etiology of cardiovascular diseases has

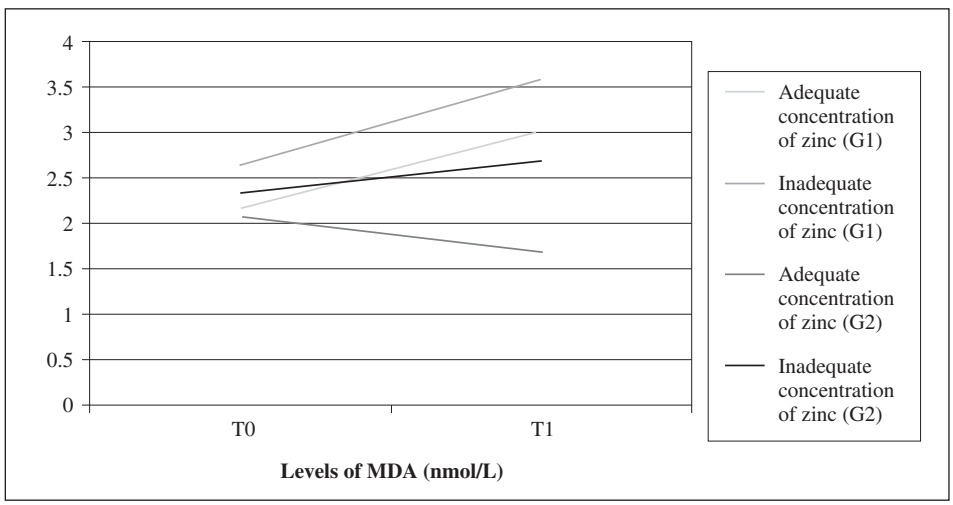


Fig. 3.—Average concentrations of levels of malondialdehyde (nmol/L) according to zinc nutritional status in G1 and G2 pre and post CABG.

Table I
Mean values of evolution clinical factors according to serum zinc concentrations in G1 and G2 post CABG

		G1		G2		
	Zinc concentrations	*Mean*	*SD*	*Mean*	*SD*	*p*
T* hospitalized (days)	Adequate	25.4	17.3	13.4	9.4	0.001
	Inadequate	30.8	50.1	13.7	10.0	0.205
T ICU** (days)	Adequate	8.5	9.9	4.6	6.4	0.047
	Inadequate	8.7	10.5	2.7	0.4	0.039
T BS*** (days)	Adequate	2.7	5.2	2.1	3.4	0.631
	Inadequate	3.8	6.1	1	0	0.08

*Time.
**Intensive care unit.
***Breathing support.

been undertaken,[19,20] however, the effect of the deficiency of micronutrients with antioxidant properties, like vitamin A and zinc, is so far not well established for cardiac patients, especially those undergoing surgical treatment.

CABG is one of the surgical procedures performed most frequently around the world.[21] This procedure exposes patients to powerful oxidative stress[5] with a subsequent rise in demand for antioxidants; not to mention it having undesirable consequences for the patient,[6] like weakened immune response,[7] harmed production and performance of T- and natural killer cells,[22] and the onset of postoperative complications.[6]

Morbimortality post myocardial revascularization surgery is of great interest, having given rise to several postoperative management protocols and risk models with the aim of curtailing cardiovascular complications.[23] In our research operative mortality was found to be 8.33% in the control group – a rate similar to that reported for Brazil (7.2%). In the supplemented group a death rate of 3.33% was found, which is quite a satisfactory result given how close it is to the mortality rate (2.9%) documented in developed nations.[24,25]

The patients exhibiting adequate zinc levels who were given vitamin A supplementation saw a significant drop in concentrations of MDA compared to those deficient in zinc, suggesting that adequate vitamin A and zinc concentrations are indeed effective in combating oxidative stress. This finding may indicate a relationship between zinc and vitamin A nutritional status in the patients from the study. There is research showing that zinc deficiency can hinder retinol-binding protein (RBP) synthesis, resulting in secondary vitamin A deficiency.[26]

By analyzing patients' clinical progression according to zinc nutritional status, we noticed a significantly shorter time in hospital among those from the supplemented group with adequate zinc levels ($p = 0.001$), with no significance found in the zinc-deficient patients. This finding suggests that vitamin A supplementation had no effect on zinc-deficient patients. Furthermore, significantly greater concentrations of vitamin A were found in the supplemented group, mainly among those with adequate levels of zinc, showing that the dosages proposed for keeping serum vitamin A concentrations were sufficient above all in the patients without hypozincemia. In a cross-sectional study performed by Wahed et al. (2008)[27] on children suffering pneumonia, a significant difference in time hospitalized ($p < 0.01$) was found between the control group and the group supplemented with antioxidants, among them vitamin A and zinc. Mda et al. (2010)[28] described a significantly shorter hospital stay in HIV-infected children who were given supplements containing vitamin A and zinc compared to those given placebo ($p < 0.05$).

As for time in the ICU, there was a significant difference between the groups both in patients with adequate zinc concentrations ($p = 0.047$) and inadequate zinc concentrations ($p = 0.039$) – that is, vitamin A supplementation was shown to have a positive effect regardless of zinc concentrations. These findings are similar to those of Heyland et al. (2008),[29] who found no significant association between zinc supplementation and the time patients in critical condition spent in the ICU ($p = 0.17$). Within this context, Robbins & Fletcher (1993)[30] found a significant reduction in length of stay at a neonatal ICU in the group supplemented with 2,500 IU of vitamin A, however, the study did not take into account the zinc nutritional status of these patients.

As for time on breathing support, no significant difference was found between the groups according to zinc concentrations. Though no significance was found according to zinc nutritional status, we must stress that a drop in zinc concentrations may lead to a drop in retinol concentrations and consequently affect β-carotene concentrations, seeing as we found a positive and significant correlation between retinol and β-carotene, suggesting that the more retinol available the less β-carotene is converted into retinol, preserving its important antioxidant function of battling free radicals in the patients studied. These finding corroborate those of Mecocci et al. (2000)[31,] who reported that vitamin A

nutritional status lowers bioconversion of carotenoids into retinol, revealing a relationship between retinol and carotenoid nutritional status exists.

Vitamin's A role in the regeneration of pulmonary epithelium has been thoroughly emphasized[32], as has its involvement in regulating the genes needed for pulmonary growth and increasing surfactant production in animal models.[33]. Supplementation of this vitamin may have been beneficial because of how the nutrient interferes with epithelial cell differentiation and integrity, and a deficiency of it is associated with the loss of ciliar cells and metaplasia in squamous cell lung tissue[34]. Robbins & Fletcher (1993)[30] found a lesser tendency towards breathing support in the group supplemented with vitamin A. Chuwers et al. (1997)[35] suggests β-carotene and retinol supplementation had a protective effect on ventilatory function in 816 patients.

Vitamin A supplementation may have improved the clinical progression of patients undergoing CABG especially in patients with adequate levels of zinc. Such findings are significant in that they bring us to reflect on the little-explored interaction between vitamin A and zinc in these patients, which may better equip clinical practice to deal with the powerful oxidative stress to which these patients are exposed.

Acknowledgments

This work was supported by National Counsel of Technological and Scientific Development – CNPq and Foundation for Research of the State of Rio de Janeiro – FAPERJ.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1987-1992
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Dietary vitamin K intake and stability of anticoagulation with coumarins; evidence derived from a clinical trial

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Abstract

Background: **Dietary vitamin K intake has been considered a major factor that influences stability of oral anticoagulation (OA) with coumarins. Few studies have evaluated the relationship between amounts of dietary vitamin K intake and stability of anticoagulation.**

Objective: **To assess whether high dietary vitamin K intake is associated to stability of International Normalized Ratio (INR) of the prothrombin time.**

Methods: **We performed a sub-analysis of a randomized clinical trial involving outpatients from the anticoagulation clinic of a university hospital. INR and vitamin K intake were prospectively collected at baseline, 15, 30, 60 and 90 days after randomization. Patients were considered with a stable anticoagulation when their INR coefficient of variation was less than 10%. Dietary vitamin K intake was assessed by a food frequency questionnair and a score of intake was derived.**

Results: **We studied 132 patients on chronic OA (57 ± 13 years; 55% males); 23 patients (17%) were achieved stable anticoagulation. Stable and unstable patients had no significant differences in baseline characteristics. The dietary vitamin K score over the entire follow-up for stable patients was significantly lower than that for unstable patients (p = 0.012).**

Discussion: **Our findings suggest that INR stability could be achieved with relatively low amounts of dietary vitamin K.**

(*Nutr Hosp.* 2012;27:1987-1992)

DOI:10.3305/nh.2012.27.6.6068

Key words: *Vitamin K. Warfarin. Food consumption. Anticoagulants. Coumarin.*

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Recibido: 21-V-2012.
1.ª Revisión: 19-VII-2012.
Aceptado: 7-VIII-2012.

EL CONSUMO DE VITAMINA K Y LA ESTABILIDAD DE LA ANTICOAGULACIÓN CON CUMARÍNICOS; EVIDENCIA DERIVADA DE ENSAYO CLÍNICO

Resumen

Introducción: **El consumo dietético de vitamina K ha sido considerado un factor importante que influye en la estabilidad de la anticoagulación oral (AO) con cumarina. Pocos estudios han evaluado la relación entre el consumo dietético de vitamina K y la estabilidad de la anticoagulación.**

Objetivo: **Evaluar la relación existente entre la alta ingesta de vitamina K y el mantenimiento de la estabilidade del la Razón Normalizada Internacional RNI.**

Métodos: **Se realizó una subanálisis de un ensayo clínico aleatorizado con pacientes ambulatórios de la clínica de anticoagulación de un hospital universitario. Los datos acerca del RNI y la ingesta de vitamina K fueron recogidos prospectivamente al inicio del estudio, y en los días 15, 30, 60 y 90. Los pacientes fueron considerados estables cuando su coeficiente de variación del RNI fue menor de 10%. La evaluacion de la dieta y la ingesta de vitamina K se obtuvo mediante un cuestionario de frecuencia alimentaria y un sistema de puntuación fue creado para esto.**

Resultados: **Se estudiaron 132 pacientes en tratamiento crónico (57 ± 13 años, el 55% masculino), 23 pacientes (17%) lograron anticoagulación estable. Con relación a las características basales, no hubo diferencias entre los sujetos con anticoagulación estable o inestable. La puntuación de la vitamina K de la dieta durante todo el seguimiento de los pacientes se mantuvo significativamente menor entre aquellos con RNI estable cuándo comparado con los inestables (p = 0,012).**

Discusión: **Nuestros hallazgos sugieren que con cantidades relativamente bajas de vitamina K podremos obtener la estabilidad de RNI.**

(*Nutr Hosp.* 2012;27:1987-1992)

DOI:10.3305/nh.2012.27.6.6068

Palabras clave: *Vitamina K. Warfarina. Consumo de alimentos. Anticoagulantes. Cumarina.*

Introduction

Chronic oral anticoagulation (OA) therapy has been extensively used in the primary and secondary prevention of thromboembolic events in several cardiovascular conditions.[1,2] However, a substantial percentage of patients who use coumarin derivatives cannot be maintained within the recommended therapeutic range evaluated by the International Normalized Ratio (INR) of the prothrombin time.[3,4] Adverse events are relatively common and frequently associated to anticoagulation instability. Therefore, there is a recognized risk of bleeding or thromboembolism, as a result of over- or under-anticoagulation, respectively.[5,6]

Several factors can be related to instability in chronic OA therapy, as drug interactions,[7] associated diseases and clinical co-morbidities,[2] drug-nutrient interactions[8] and use of medication.[9] Dietary vitamin K content has been studied as a central factor that influences anticoagulation stability.[10,11,12] Although strong evidences from clinical studies suggest that this relationship can be considered a fundamental and independent factor that interferes in chronic OA therapy,[10,13] there is still no consensus on the amount of dietary vitamin K that should be recommended to patients undergoing this therapy.

Few studies have directly studied the relationship between specific amounts of dietary vitamin K intake and stability of chronic anticoagulation with coumarins. Previous investigators have suggested that a constant high intake of vitamin K could provide INR stability.[14] Vitamin K supplementation has been reported to promote longer periods of time in the therapeutic target,[15] or to have less INR variation[16]. In addition, patients with lower vitamin K intake seem to have a higher risk of a subtherapeutic INR value.[13] However, there is also evidence showing no association between dietary vitamin K intake and stability.[17]

Our group has recently published a randomized clinical trial demonstrating that an intervention designed to modify dietary vitamin K intake would be an alternative and effective strategy to manage anticoagulated patients with minor INR instability.[11] In the present prespecified sub-study, we conducted an in-depth analysis about the relationship between dietary vitamin K intake and stability of OA, based on prospective sequential data on INR values and vitamin K intake collected before and after randomization.

Methods

Patients and study design

Data on INR values and semi-quantitatively vitamin K intake used for the present analysis were derived from a randomized clinical trial in which 132 patients were evaluated from the anticoagulation clinic of a university tertiary care hospital in Porto Alegre, Brazil. Patients were randomized into a control group (a strategy treatment based on conventional dose adjustment of oral anticoagulants) and an intervention group (a strategy treatment based on pragmatic changes on dietary vitamin K intake according to INR values). The protocol was registered at ClinicalTrials.gov (http:// clinicaltrials.gov) as NCT00355290. Detailed data from the study protocol is described in the original publication.[12] Briefly, prospective and sequential data on INR values and vitamin K intake was collected at baseline, 15, 30, 60 and 90 days after randomization.

Vitamin K intake

The consumption of vitamin K was evaluated by a Food Frequency Questionnaire consisted of foods with content of vitamin K ranging from about 20 mg to 700 mg per 100g of food. The Food Frequency Questionnaire was divided into foods with a high content of vitamin K (380 g to 712 g per 100 g): green tea, turnip greens and spinach; foods with moderate to high content (120 g to 180 g per 100 g): broccoli, brussels sprouts, cabbage, lettuce crisp, soybean or canola oil; and foods with moderate content (20 g to 95 g per 100 g): beef liver, asparagus, watercress, lettuce, peas, cabbage, cauliflower, arugula and cucumber with peel raw. Patients were instructed to answer the questionnaire about their consumption in the week before the prothrombin time test (INR). Our group has already tested and modified this questionnaire in a survey protocol with patients from our anticoagulation clinic, aiming to demonstrate the relationship between vitamin K intake and different levels of anticoagulation.[10]

Considering that the Food Frequency Questionnaire carries out a qualitative analysis of vitamin K consumption, we transformed the raw data from the questionnaire into a score of vitamin K intake, where food items were rated according to their content of vitamin K: those with high content received a score of 3, those with moderate to high content received a score of 2 points, and those with moderate content received a score of 1. This score was created to perform a semi-quantitative evaluation of the overall content of dietary vitamin K, but not aimed to quantify the content of vitamin K in mg/day.

Anticoagulation stability

Anticoagulation stability was assessed by calculating the coefficient of variation (CV) of INR measurements, calculated as the standard deviation divided by the average INR measured in the four moments after the baseline assessment (day 15, day 30, day 60, day 90). This formula has generated a percentage of variation for the entire follow-up time. For statistical analysis, we consider patients with stable anticoagulation those who

had a variation less than or equal to 10% in the INR CV, and patients with unstable anticoagulation those with CVs higher than 10%. This definition is relatively arbitrary, but aims to identify patients on chronic OA therapy with minimal variations on anticoagulation parameters (highly stable patients).

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median and interquartile range and categorical variables were expressed as absolute number and percentage. For comparison between groups (categorical variables), the χ^2 test was used. For analysis of vitamin K intake between different time periods and between groups we used Student's *t* test for normally distributed variables and the Mann-Whitney test for nonparametric variables. A two-tailed P value < 0.05 was considered statistically significant. Analysis was performed using the ProgramPASW® Statistics 18 (SPSS Inc., Chicago, IL).

Results

Studied population

Between March 2006 to September 2007, potentially eligible patients were recruited: 132 subjects fulfilled the entry criteria and consented to participate in the protocol, detailed clinical data of the enrolled patients was previously described.[12] The study population included predominantly male patients with indication for anticoagulation therapy predominantly because of mechanical valve prosthesis (57%) or atrial fibrillation (35%) as demonstrated at table I.

Patients with stable chronic OA

For analysis of INR stability, the whole sample of 132 patients was classified as stable (INR CV ≤10%) or unstable (INR CV > 10%). We found 23 (17.4%) patients with stable anticoagulation, evenly distributed in the 2 groups (intervention and control) of the orig-

Table I
Clinical characteristics and comparison between stable an unstable patients on crhonic oral anticoagulation

Clinical variable	*All n = 132*	*Stable patients n = 23*	*Unstable patients n = 109*	*P*
Age, years	57.2 ± 13	59 ± 13	56 ± 7	0.4
Sex (male)	73 (55)	11 (48)	62 (57)	0.3
Group				0.3
Control	66 (50)	10 (43)	56 (51)	
Body mass Index	26.7 ± 4.8	26.9 ± 4.6	26.7 ± 4.0	0.8
Education				0.6
Illiterate	5 (3.6)	–	5 (5)	
Elementary	102 (73.4)	19 (83)	83 (75)	
High School or more	25 (18)	4 (17)	21 (20)	
Comorbities				
Heart failure	26 (18.7)	2 (8.7)	24 (22)	0.1
Diabetes Mellitus	21 (15.1)	3 (13)	18 (16)	0.5
Ischemic heart disease	20 (14.4)	2 (8.7)	18 (16)	0.3
COPD	2 (1.4)	0 (0)	2 (1.8)	0.7
Indication for oral anticoagulation				0.7
Chronic atrial fibrillation	46 (35)	11 (48)	35 (32)	
Mitral mechanical valve	37 (28)	5 (22)	32 (29)	
Aortic mechanical valve	39 (29)	6 (26)	33 (30)	
Others	10 (8)	1 (4)	9 (17)	
Anticoagulant drugs				0.04
Warfarin	112 (85)	16 (69)	96 (88)	
Phenprocoumon	20 (15)	7 (30)	13 (12)	
Baseline anticoagulation dose				
Warfarin	30 (22-41)	35 (18.75-40)	30 (22.5-42.5)	0.5
Phenprocoumon	12 (8.4-15)	9 (7.5-19.5)	13.5 (11.25-15)	0.4
Baseline INR	2.41 (1.77-3.23)	2.26 (1.88-3.42)	2.07 (1.77-3.20)	0.5
INR Coefficient of Variation (%)	17.97 (11.5-25.63)	6.47 (3.76-8.78)	19.9 (14.9-28.1)	< 0.001

Values presented as n (%) or as median (25th percentile, 75th percentile). COPD: Chronic obstructive pulmonary disease.

Table II
Consumption frequency of vitamin K rich foods

Consumption of vitamin K rich foods	*All n = 132*	*Stable patients n = 23*	*Unstable patients n = 109*	*P*
High content (times/week)	0.7 (0-1.4)	0.4 (0-1.4)	0.4 (0-1.4)	0.8
Moderate to high content (times/week)	3.5 (1.8-5.0)	2.8 (1.6-4.6)	3.6 (1.8-5.1)*	0.2
Moderate content (times/week)	1.9 (0.8-3.2)	2.2 (0.8-2.6)	1.8 (0.8-3.3)	0.8

Values presented median (25th percentile, 75th percentile).
High content of vitamin K (380 g to 712 g per 100 g): green tea, turnip greens and spinach; moderate to high content (120 g to 180 g per 100 g): broccoli, brussels sprouts, cabbage, lettuce crisp, soybean or canola oil; moderate content (20 g to 95 g per 100 g): beef liver, asparagus, watercress, lettuce, peas, cabbage, cauliflower, arugula and cucumber with peel raw.

inal clinical trial. Patients classified as stable or unstable OA had similar clinical characteristics including age, gender, medical comorbidities, education, clinical indication for anticoagulation therapy, basal INR and baseline anticoagulation dose (table I). In both groups the majority of patients were using warfarin as the anticoagulant drug; however phenprocumon was used more frequently among stable patients (30% *versus* 12%, p = 0.04). Moreover, the CV of INR was different between the groups, as expected.

Relationship between stability and consumption of vitamin K

Dietary intake of foods with different contents of vitamin K was analyzed using the Food Frequency Questionnaire. In both groups the most representative food items of vitamin K intake were those with moderate to high content. Over the 90 days of follow-up the group of stable patients had a lower consumption of moderate to high content food and a slightly less consumption of low content food, although without statistical significance (table II).

In order to evaluate the relationship between OA stability and consumption of vitamin K we compared the score of vitamin K intake in patients classified as on stable anticoagulation with unstable patients over the entire follow-up time. Figure 1 demonstrates that the median vitamin K intake score was lower among patients who had less variation on INR (CV <10%) compared to unstable patients (CV >10%) [12 (7-14) versus 14 (7-19), respectively, P = 0.012].

When analyzing the scores of vitamin K for each moment individually, the same trends were observed (fig. 2). We also evaluated patients stratified by group of intervention of the original trial, and the same trends were observed (data not shown).

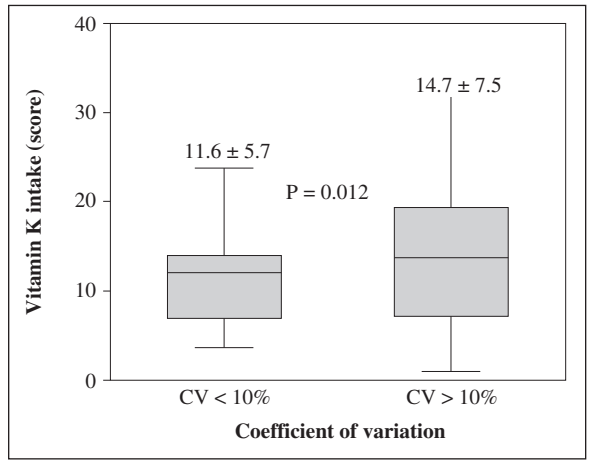


Fig. 1.—Overall score of vitamin K consumption over time during the entire follow-up according to the INR coefficient of variation (CV). Box plots represent median and interquartile range.

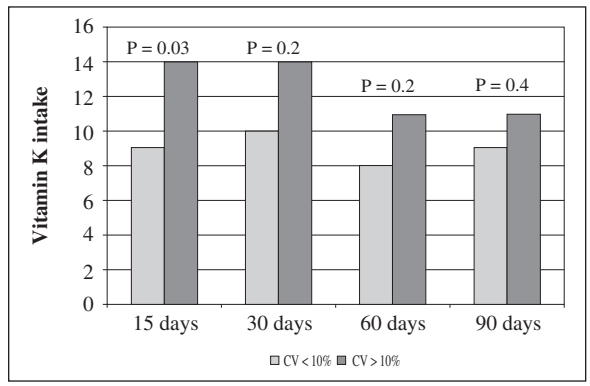


Fig. 2.—Vitamin K consumption in 4 moments of the study according to INR coefficient of variation (CV) for all randomized patients.

Discussion

There is a growing interest on the influences of the consumption of food items rich in vitamin K on the stability and effectiveness of oral anticoagulants. The interaction of this micronutrient with the pharmacologic effects of coumarin derivatives is well-known,[10,11,18] but the amount of vitamin K that should be ingested has not been precisely defined for patients on chronic OA. Previous studies have suggested that a high vitamin K intake could be associated with anticoagulation stability.[13,14,19] Our results questioned this hypothesis, showing that patients with very stable INRs (CF ≤ 10%) had, in fact, lower consumption of vitamin K rich foods.

In this study we have found that patients who were managed with pre-defined modifications in oral vitamin K intake were more likely to reach the desired target INR when compared to the conventional management (increases and decreases in oral anticoagulant dose). Although these results substantiate the interaction between dietary vitamin K and the effect of coumarin derived anticoagulants, they do not clarify the everyday dilemma about the amount of vitamin K intake that should be recommended for patients in chronic OA.

Studies that have evaluated the relationship between usual consumption of vitamin K and long-term stability of oral anticoagulants are scarce. A recent study suggested that supplementation with low dose vitamin K[1] resulted in an improvement of time that anticoagulation was within the therapeutic range in patients starting vitamin K antagonists.[20] However, other evidence shows the opposite relationship. Sconce et al. demonstrated that patients with stable anticoagulation (variation of less than 0.5 in the INR value) had significantly higher vitamin K intake compared to unstable patients.[14] Similarly, a recent report by Rombouts et al. found that patients with higher consumption of vitamin K rich foods had a lower risk of having sub-therapeutic INRs.[13] Finally, Kim et al. observed an inverse correlation between the CV of the INR and vitamin K intake,[19] suggesting that a higher vitamin K consumption would be associated to less INR variation. Although the overall trend of these studies indicates a potential beneficial effect of maintaining a "high" intake of vitamin K, the clinical applicability of this information might be limited, because of the heterogeneity in the definition of anticoagulation stability, as well as in the cut-off points to classify vitamin K intake. Unexpectedly, the present study does not confirm previous findings. Our results demonstrate that INR stability could be achieved even in patients taking lower amounts of vitamin K. Our strict definition of stable anticoagulation, based on lower than 10% changes in INR CV, restricted our analysis to a group of patients who maintains minimal change in INR values during follow-up, unlike other studies that defined stability as patients that varied less than 0.5 in INR values[14] or patients who have a sequence of INR values within the target.[13] Moreover, detailed knowledge of the content of vitamin K among different vegetables is difficult to be assimilated among healthcare professionals[21] and might be even more challenging to anticoagulated patients. One could speculate that the maintenance of a stable dietary intake of foods with a relatively low content of vitamin K would implicate in a smaller risk of unintentional large absolute variations in the consumption of this vitamin, a hypothesis that needs prospective confirmation. We have previously demonstrated that even brief periods of increased or decreased vitamin K intake might have a pronounced effect on coagulation parameters.[10]

Some methodological aspects of our study design deserve careful consideration. As the present analysis was derived from a clinical trial in which there was an intervention that modulated vitamin K intake, our results might be biased. However, analysis restricted to the group of patients managed conventionally demonstrated the same trends (data not shown). In the original protocol, we deliberately opted to use a semi-quantitative evaluation of vitamin K that does not precisely estimate daily consumption. A more detailed assessment and modulation of vitamin K ingestion would limit the clinical applicability of the proposed strategy, but could unravel more accurately the relationship between this micronutrient and OA stability. In addition, the relatively short-term follow-up of the original protocol limits the evaluation of the impact of vitamin K consumption over long-term OA stability.

Achieving oral anticoagulation stability over time is a challenging task. There is solid prospective clinical evidence demonstrating that changes in dietary vitamin K play a major, independent role in INR fluctuations in patients taking oral anticoagulants.[8,11,18,22] Thus, stable vitamin K intake is an essential aspect of anticoagulation therapy that must be actively pursued by clinicians, nurses, dietitians, and pharmacists. The present sub-analysis indicates that INR stability could be achieved with relatively low amounts of dietary vitamin K. However, we should not send the wrong message of indiscriminately decreasing dietary vegetable content because the background message of most studies is that anticoagulated patients should maintain a steady intake of vitamin K, once INR stability has been achieved. Our findings suggest that a reasonable target would be to pursue a daily vitamin K consumption near (just above) the internationally accepted RDA (90-120 µg/day), avoiding much higher intakes. However, prospective studies testing this strategy will be needed to determine the best dietary advice offered to patients in this scenario.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1993-1998
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Evaluación de la exposición solar, ingesta y actividad física en relación con el estado sérico de vitamina D en niñas prepúberes españolas

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Resumen

Antecedentes: **Los niveles adecuados de vitamina D y calcio en la infancia determinan el desarrollo adecuado de la masa ósea. En la actualidad se ha detectado déficit de vitamina D en determinadas poblaciones infantojuveniles, como en lactantes y adolescentes pero existe información insuficiente respecto al estado de la vitamina D en niños de otras edades.**

Objetivo: **Determinar los niveles séricos de vitamina D en niñas prepuberales sanas de una ciudad del sur de Europa y estudiar el efecto de la exposición solar, la actividad física y la ingesta.**

Métodos: **Se estudiaron 56 niñas caucasianas, sanas y prepúberes entre 7-10 años. Se recogieron datos sobre ingesta nutricional y actividad física. Las muestras de sangre se obtuvieron en diciembre.**

Resultados: **La ingesta de vitamina D fue significativamente menor a las recomendaciones internacionales. Los niveles medios de calcidiol fueron de 40,07 ± 10,49 ng/ ml. Ninguna niña presentó un nivel inferior a 20 ng/ml; un 25% (14 niñas) tenían unos niveles entre 20-30 ng/ml, y un 75 % superiores a 30 ng/ml. No hemos encontrado diferencias en los niveles de vitamina D entre las niñas que realizaban actividad física, y las sedentarias.**

Conclusión: **Los niveles de vitamina D en niñas prepúberes que viven al sur de España al inicio del invierno son adecuados. No obstante, se debe asegurar una ingesta adecuada de vitamina D, así como una exposición solar suficiente y realizar seguimiento en estas edades para evitar deficiencias.**

(*Nutr Hosp.* 2012;27:1993-1998)

DOI:10.3305/nh.2012.27.6.6065

Palabras clave: *Vitamina D. Prepuberal. Actividad física. Nutrición.*

EVALUATION OF SOLAR EXPOSURE, INTAKE AND PHYSICAL ACTIVITY IN RELATION WITH VITAMIN D SERUM STATUS IN SPANISH PREPUBERTAL GIRLS

Abstract

Background: **Vitamin D and calcium play an important role in peak bone mass acquisition. Recent studies have suggested that vitamin D deficiency in children is widespread, mainly during infancy and adolescent years. However, the vitamin D status at others ages is unsufficiently investigated.**

Objectives: **To determine the vitamin D status in prepubertal, healthy South European girls, and to examine the relationship between serum vitamin D concentrations, sun exposure, physical activity and dietary intake.**

Methods: **A cross-sectional observational study was conducted on 56 Caucasian; healthy and pre-pubertal girls aged 7-10 years. Dietary information, amount of sunlight exposure and activity were estimated. Blood samples were extracted in the first week of December.**

Results: **Vitamin D intake was below the international recommended references. Mean serum vitamin D was 40.07 ± 10.49 ng/ml. No girl presented a level lower than 20 ng/ml; 25% had levels between 20-30 ng/ml and 75% above 30 ng/ml. We have not found differences in vitamin D levels from the girls who did sport and those who were sedentary.**

Conclusions: **Vitamin D status is suitable for prepubertal girls living in the South of Spain at the beginning of winter. However, it is necessary to follow-up girls and check and adequate vitamin D intake, as well as sufficient sun exposure.**

(*Nutr Hosp.* 2012;27:1993-1998)

DOI:10.3305/nh.2012.27.6.6065

Key words: *Vitamin D. Prepubertal. Physical activity. Nutrition.*

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Recibido: 18-VII-2012.
Aceptado: 23-VII-2012.

Introducción

Los niveles adecuados de vitamina D y calcio en la infancia determinan el desarrollo adecuado de la masa ósea y la prevención de enfermedades como la osteoporosis en etapas adultas. Estos niveles, entre otros factores, pueden estar condicionados por la ingesta del calcio y la vitamina D[1] pero también por la influencia de factores como la genética o la edad de la menarquía en las mujeres[2]. Por otra parte, los hábitos sociales y culturales actuales favorecen la vida sedentaria limitando la exposición al sol de los niños y la práctica de actividad física, pudiendo condicionar deficiencia de vitamina D y afectar la formación de la masa ósea[3]. De hecho, durante los periodos de crecimiento, este déficit puede tener una influencia negativa en el desarrollo óseo, causando no sólo raquitismo, que es el resultado final de la deficiencia severa de vitamina D, sino en la talla establecida genéticamente y en la masa ósea final[4].

Las mujeres son la población más afectada por enfermedad ósea, favorecida además, por los cambios hormonales propios de la menopausia[5]. Hasta el 90% de la masa ósea máxima se adquiere antes de los 18 años en las niñas, por lo que se considera la infancia un momento crítico para promover conductas que mejoren la salud ósea[1,6].

En la actualidad se ha detectado deficiencia o insuficiencia en los niveles de vitamina D en determinadas poblaciones infantojuveniles como resultado de múltiples factores[7-9]. Ello ha condicionado nuevas investigaciones en relación con la acción de esta vitamina sobre la mineralización ósea. Además, el déficit de este nutriente, se ha relacionado también con diversas patologías, como diabetes, esclerosis múltiple y cáncer[10-11].

Los estilos actuales de vida sedentarios junto a las recomendaciones de protección solar para reducir la incidencia de cáncer de piel, pueden condicionar unos niveles de vitamina D inadecuados. Igualmente, en la mayoría de las encuestas alimentarias realizadas en España y otros países, la ingesta de vitamina D en la infancia es menor a las recomendaciones internacionales establecidas[12-13].

Actualmente no hay consenso sobre cuáles deben ser las recomendaciones diarias en la ingesta, o si debe hacerse profilaxis con vitamina D, sobre todo en países en los que hay mayor exposición a la radiación solar. La mayoría de los trabajos sobre la evaluación del estado de la vitamina D en la infancia incluyen las dos etapas donde más aumentan las necesidades; la etapa de lactancia[14] y la de la adolescencia[15]. No obstante, aún existe información insuficiente respecto al estado de la vitamina D en niños de otras edades, y la influencia de determinados factores sobre sus niveles y funciones. Por ello, el objetivo de este trabajo es determinar los niveles séricos de vitamina D en niñas prepuberales sanas de una ciudad del sur de Europa (latitud 30º N), y estudiar el efecto de factores influyentes como la exposición solar, la actividad física, o la ingesta. Los resultados de este trabajo pueden aportar información para conocer las circunstancias que afectan el metabolismo de la vitamina D en niñas en edad temprana y la utilidad de diseñar proyectos dirigidos a la prevención de deficiencia de vitamina D antes de la etapa puberal y edad adulta.

Material y métodos

Sujetos

Se estudiaron 56 niñas caucasianas prepúberes con edades comprendidas entre 7-10 años. Se eligió al azar un colegio de Córdoba, al sur de España (latitud: 37.8º N), seleccionando a las 16 primeras niñas por orden de lista de varias clases de educación primaria. En el caso de que algún padre denegara el consentimiento para formar parte del estudio o la niña no cumpliera los criterios de inclusión, se le ofreció a la siguiente de la lista. Se incorporaron al estudio tras la aceptación del menor y la obtención del consentimiento informado del responsable legal. El estudio de investigación se llevó a cabo en la Unidad de Metabolismo e Investigación Pediátrica del Servicio de Pediatría del Hospital Universitario Reina Sofía de Córdoba, y fue aprobado por el Comité Local de Bioética e Investigación Clínica.

Los criterios de inclusión fueron: niñas sanas de 7-10 años con medidas antropométricas y de tensión arterial en el p50 ± 1DS, y en estadio puberal de Tanner I[16]. Se excluyeron las niñas que estuvieran en otro rango de edad al establecido, en percentiles de medidas antropométricas < P10 o > P90, con patología crónica o con signos clínicos o analíticos de desarrollo puberal.

Valoración antropométrica, hemodinámica, nutricional y de actividad física

Se realizó una historia clínica con una exploración física completa, valorando los antecedentes personales y familiares, así como la existencia de patología previa o tratamientos farmacológicos. Se determinaron parámetros antropométricos como la talla, el peso y el perímetro de la cintura; posteriormente se calculó el índice de masa corporal (IMC): peso (kg)/ talla^2 (m). Para la medida del peso y talla se utilizó una báscula y tallímetro SECA (SECA, Hamburg, Germany). El perímetro de cintura se midió con una cinta métrica siguiendo un método estandarizado. Se realizó una exploración física exhaustiva para valorar la etapa de desarrollo puberal según Tanner[16].

La valoración nutricional se realizó mediante una encuesta de frecuencia de alimentos, analizando el aporte nutricional estimado por día para energía, macronutrientes, calcio, fósforo, magnesio y vitamina D, según la tabla de composición de alimentos española[17] y el sistema equivalente de alimentos[18]. La ingesta media fue comparada con las de referencia internacionales (Dietary Reference Intakes: DRIs) para niñas de 7 a 10 años[19].

La actividad física practicada fuera del horario escolar se evaluó mediante cuestionarios diseñados de acuerdo con la "Lista de Actividad Ayer", validado para la población española[20]. Se registraron datos de horario y duración, vestimenta utilizada, y lugar (interior o exterior) en el que se realizaba la actividad. Las encuestas fueron realizadas a las propias niñas.

Toma de muestras y análisis en sangre

Las extracciones se realizaron en situación de reposo tras 12 h de ayuno, durante la primera semana de diciembre. Se realizó una hematimetría y un análisis bioquímico general. En el estudio hormonal básico se midieron: FSH (Hormona folículo estimulante) (mU/L), LH (Hormona luteinizante) (mU/L), estradiol (mU/L) y testosterona (mU/L). Además se midió calcio y calcio corregido con proteínas (mg/ dl), calcidiol (ng/ml) y calcitriol (pg/ml). Los niveles plasmáticos de vitamina D se evaluaron mediante radioinmunoanálisis (RIA) con el analizador contador gamma PACKARD Cobre II E 5005. Con este método se cuantifican los dos derivados (D2 y D3) de la vitamina D. Para evaluar los niveles de calcidiol se utilizaron los puntos de corte basados en varios estudios[21-23] que describen los valores adecuados como aquellos superiores a 30 ng/ ml (> 75 nmol/L); insuficientes entre 20-30 ng/ml (50-75 nmol/L), y deficientes por debajo de 20 ng/ ml (< 50 nmol/L).

Análisis estadístico

El análisis estadístico se realizó con el programa SPSS versión 18.0 de software. Se realizó un análisis descriptivo para variables cuantitativas mediante el cálculo de media (m) y desviación típica o standard (DS); y para las variables cualitativas mediante el cálculo de proporciones (%). La determinación de la bondad de ajuste a una distribución normal (datos normales) se hizo mediante la prueba de Shapiro-Wilk. Si las muestras seguían una distribución normal y las varianzas eran homogéneas se aplicaron test paramétricos, en caso contrario se utilizaron test no paramétricos. La comparación de los valores medios de las variables cuantitativas entre dos grupos (deporte sí/no), se realizó mediante pruebas t de Student para grupos independientes (prueba paramétrica); o pruebas U de Mann-Whitney (prueba no paramétrica).

Tabla I
Características demográficas y antropométricas del grupo de 56 niñas prepúberes

Variable	*Media*	*DE*
Edad (años)	8,8	0,9
Peso (kg)	36,8	9,2
Talla (cm)	138,6	6,2
IMC (kg/m^2)	19	3,7
PC (mm)	63,8	8,6
TAS (mmHg)	115,3	13,2
TAD (mmHg)	63,8	10

IMC: Índice de masa corporal; PC: Perímetro de cintura; TAS: Tensión arterial sistólica; TAD: Tensión arterial diastólica. Los datos se expresan como media ± DE.

Tabla II
Valores medios de ingesta alimentaria vs DRI en niñas prepúberes de 7 a 10 años de edad

	Media ingesta/día	*DRIs*	*P*
Energía (kcal)	1.749,43 ± 572,15	2.000	< 0,002
Proteínas (g)	107,78 ± 44,33	34	< 0,001
Grasas (g)	55,29 ± 17,11	35	ns
Carbohidratos (g)	243,74 ± 92,97	100	< 0,001
Calcio (mg)	1.211,69 ± 346,82	1.300	0,062
Fósforo (mg)	1.922,43 ± 651,15	1.250	ns
Vitamina D (UI)	161,39 ± 64,70	200	< 0,001

DRIs: Dietary Reference Intakes[19]. Los datos se expresan como media ± DE. Significación: P ≤ 0,05; ns: no significativo.

Tabla III
Niveles séricos de calcio y vitamina D vs valores de referencia del laboratorio en 56 niñas prepúberes de 7 a 10 años de edad, y niveles de calcidiol por grupos de práctica de actividad física

Variable	*Media*	*Valor referencia*
Calcio (mg/ dl) (N = 56)	10,2 ± 0,3	8,4 ± 10,2
Calcio corregido (mg/dl) (N = 56)	10 ± 0,3	8,5 ± 10,5
Calcitriol (pg/ml) (N = 56)	70,89 ± 14,34	18-71
Calcidiol (ng/ml) (N = 56)	40,07 ± 10,49	20-100
Práctica deporte (N = 29)	41,48 ± 10,11	
No práctica deporte (N = 26)	37,8 ± 11,4	

Los datos se expresan como media ± DE. P = 0,098 al comparar los niveles séricos de calcidiol entre niñas con práctica deportiva o sin práctica de deporte.

Resultados

Todas las niñas del estudio presentaron una talla, peso e IMC así como valores de tensión arterial, en percentiles adecuados para su sexo y edad (tabla I).

Respecto a la valoración de nutrientes, se observó que la media de ingesta de calorías/día fue menor a la establecida en las DRIs[19] aunque la ingesta de macronutrientes fue mucho mayor (tabla II). En relación con la ingesta diaria de calcio no hubo diferencias significativas respecto a las recomendaciones pero la ingesta de vitamina D fue inferior.

En la tabla III se muestran los niveles medios de calcio sérico, calcio corregido con las proteínas totales y los de calcidiol y calcitriol, que se encontraron dentro del rango establecido como normal por el laboratorio.

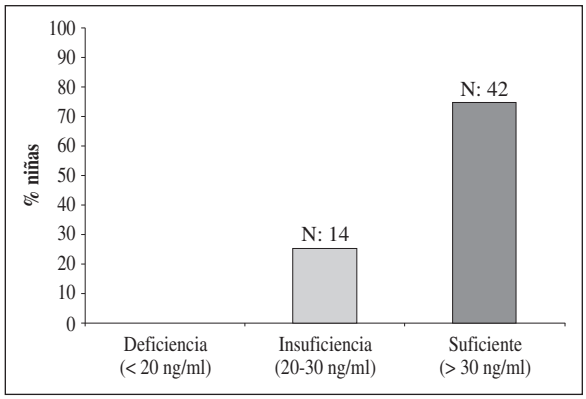


Fig. 1.—Porcentaje de niñas con diferentes niveles séricos de vitamina D.

En relación a los puntos de corte establecidos en la literatura para los niveles de vitamina D[7,15,21-24], ninguna niña presentó un nivel menor de 20 ng/ml (50 nmol/L), un 25% tenían unos niveles entre 20-30 ng/ml que se consideran como insuficientes y el 75 % restante superiores a 30 ng/ml que son niveles óptimos (fig. 1). Si se hubiera considerado el rango referido para adultos en 32 ng/ml[23,25] como insuficiente un 28% estaría dentro de estos límites.

La práctica de actividad física fuera del horario escolar se evaluó en 55 niñas, de las cuales el 52,7% (n = 29) sí realizaba deporte fuera del horario escolar, y el 47,3% (n = 26) tan sólo realizaba las 2 horas de deporte escolar obligatorio. La actividad deportiva extraescolar fue generalmente baloncesto, al aire libre durante 3 horas semanales, en horario de tarde. La actividad física escolar obligatoria fue de 2 horas a la semana en horario de mañana. Ambas se realizaban, si no llovía, al aire libre, utilizando normalmente una camiseta de manga corta y un pantalón corto. Entre ambos grupos, no existieron diferencias significativas de niveles de la vitamina D séricos (tabla III).

Discusión

Los resultados de este estudio indican que las niñas españolas prepúberes que viven en el sur no presentan deficiencia de vitamina D al inicio del invierno aunque la ingesta de este micronutriente fuera menor a la recomendada, sin encontrar tampoco diferencias en relación con la práctica deportiva.

En los últimos años se ha detectado un aumento en la prevalencia del déficit de vitamina D durante diferentes etapas de la infancia y adolescencia, surgiendo nuevos estudios que intentan clarificar la necesidad de uso de suplementos como profilaxis o tratamiento[23,26]. Durante los primeros años de vida es fundamental mantener unos niveles adecuados de vitamina D para conseguir un pico de masa ósea correcto, existiendo dos periodos críticos para la obtención de este pico, durante los tres primeros años de vida, y en la pubertad. Por eso, la mayoría de los artículos pediátricos se centran en estudiar el metabolismo óseo y de la vitamina D, y los factores que los condicionan en ambas etapas[15,27]. No obstante, es plausible pensar que las deficiencias que se detectan en la adolescencia procedan de etapas previas. Por ello, en este trabajo se ha abordado la etapa prepuberal, previa al inicio de un crecimiento acelerado, en la que aún existen escasos datos sobre el estado sérico de la vitamina D en niñas sanas.

Los niveles de vitamina D están influidos por numerosos factores entre los que destacan la ingesta, edad, sexo, tipo de piel, exposición solar, vestimenta, actividad física, y principalmente, la latitud y la estación del año[23]. En algunos estudios realizados se plantea una interpretación difícil al coexistir estos elementos de confusión u otros como la obesidad, la suplementación farmacológica, o la práctica de actividad física al aire libre o en ambientes cerrados[27]. Para tratar de limitar la interacción de estos factores, en este trabajo se ha estudiado una muestra homogénea seleccionando sólo niñas y en estado prepúber. Además, el sexo femenino tiene niveles más bajos de vitamina D[28] y estos valores, sobre todo en las deficiencias, condicionan la edad de la menarquia[29], siendo el sexo más afectado por la osteoporosis del adulto[5]. Por otra parte, todas ellas eran sanas con IMC normal, excluyendo a aquéllas con fallo de medro, desnutrición u obesidad, ya que en la mayoría de los estudios se ha establecido una relación inversa entre la adiposidad y los niveles de vitamina D[30]. Para que el efecto estacional estuviera controlado, todas las muestras se extrajeron durante la misma semana.

La comparación de los resultados entre los artículos se dificulta además por las diferencias metodológicas en las técnicas de medición de la vitamina D y en la falta de consenso para definir el punto de corte entre deficiencia y normalidad vitamínica en relación con la edad y el sexo[7,15,21-24]. Las diferentes pruebas de laboratorio difieren por su grado de precisión, siendo importante que se cuantifiquen los dos metabolitos de la vitamina D (D2 y D3), ya que se puede llegar a un diagnóstico incorrecto de deficiencia al despreciar los niveles de vitamina D2[23]. Aunque la espectroscopia en tándem de masas es considerada la prueba oro para la medición de vitamina D, los resultados obtenidos por RIA son satisfactoriamente comparables. Para la evaluación de los niveles séricos de vitamina D, se recomienda medir los niveles de 25-(OH)D ó calcidiol, metabolito que presenta una vida media de 30 días y que posteriormente se convierte a la forma activa 1,25 dihidroxi-colecalciferol, habiéndose demostrado además su correlación con el grado de mineralización ósea[31].

Por otra parte, existen diferencias para establecer el rango de normalidad sérico de la vitamina D. En niños se siguen considerando como suficientes unos niveles por encima de 20 ng/ml[24]. No obstante, en los últimos años también se ha destacado en los adultos que cuando existen valores de vitamina D por debajo de 32 ng/ml, se altera la absorción del calcio y la densidad mineral ósea baja por lo que se está considerando este valor como punto límite de la normalidad incluso en la infancia[25,32].

Considerando lo anteriormente expuesto, y tomando como rango de referencia el del laboratorio utilizado, no se ha detectado deficiencia de vitamina D3 en esta muestra de niñas prepúberes, aunque un 25% de ellas podrían presentar unos niveles insuficientes de vitamina D. No obstante estos resultados varían respecto a los de otros trabajos publicados en poblaciones similares. En un estudio realizado en Madrid (España) durante 1 año encontraron que un 51% de los niños presentaron niveles por debajo de 20 ng/ml en relación a un bajo consumo de vitamina D[33]. En el trabajo de Mansbach y cols.[7], realizado durante 5 años en USA observaron que en niñas entre los 6-11 años, hasta un 75% tenían niveles de vitamina D menores a 30 ng/ml. Otro estudio realizado en Reino Unido[34] con 7.500 niños con una edad media de 9,9 años, un 29% presentaban niveles de vitamina D3 menores a 20 ng/ml. Las diferencias en los niveles de vitamina D en todos estos estudios, pueden explicarse en relación a las razones expuestas anteriormente: poblaciones con rangos de edad, grupos étnicos, hábitos culturales, de ingesta, o de actividad física diferentes, o toma de muestras y evaluaciones durante distintas estaciones del año, y con diferencias en la exposición solar. Por ello, probablemente no se pueden establecer recomendaciones generales para la detección de deficiencias o para el uso de suplementos, sino que deberá hacerse una evaluación individual buscando aquéllos grupos de riesgo.

Al medir los niveles en sangre de calcidiol se evalúa no sólo la cantidad de vitamina D procedente de la dieta sino también la de la síntesis cutánea[21]. Esta última podría condicionar que existieran unos niveles séricos de vitamina D adecuados, a pesar de que la ingesta de esta vitamina fuera inferior a la recomendada. La síntesis cutánea depende de múltiples factores: exposición al sol, ubicación geográfica y época del año. La longitud de onda de los rayos ultravioletas B no está presente en la luz solar durante los meses de invierno. En múltiples estudios relacionan los niveles de vitamina D con la estación del año[9,30] presentando niveles más elevados en las muestras tomadas en los meses de Junio a Noviembre. Es importante recordar que las recomendaciones de ingesta de vitamina D de 600 UI al día para niños de 6 a 10 años se realizan asumiendo una mínima exposición solar[24]. Sin embargo, en zonas como la referida en este estudio, en el Sur de España, que está a una latitud de 37º N y con veranos calurosos donde las actividades al aire libre y la exposición solar son frecuentes, probablemente esta recomendación de ingesta estaría sobreestimada. En el trabajo de Rodriguez y cols.[33], indican que consumiendo un 67% de las DRI[19], se consiguen unos niveles adecuados en sangre de vitamina D en niños escolares.

En relación con la práctica de actividad física, no se han observado diferencias significativas en los niveles de vitamina D. Este resultado podría indicar por un lado, que la exposición por un tiempo más prolongado al aire libre no parece tener una gran influencia en que haya niveles más elevados de vitamina D, a diferencia de lo descrito en otras publicaciones[8,34] donde realizar una actividad al aire libre durante más de 1/2 hora es un factor protector de la deficiencia de vitamina D. Quizás la situación geográfica es la que dar explicación a estas diferencias. Así, en nuestra localización estarían justificadas las recomendaciones de una exposición moderada (en cara y extremidades) de 5-10 minutos, 2 ó 3 veces a la semana para mantener unos niveles adecuados de vitamina D[21] (y que cumplieron los dos grupos de niñas). Por otra parte, en este trabajo no se asocia la práctica de actividad física per se con mayores niveles de vitamina D, como se ha observado en estudios en adultos y adolescentes[28,35]. No obstante, no se ha monitorizado la intensidad del deporte y ello podría constituir una limitación a encontrar asociación.

Tras los resultados del presente estudio, se puede concluir que los niveles de vitamina D en niñas prepúberes que viven al sur de España al inicio del invierno son adecuados. No obstante, existe un grupo de riesgo en el que se debería realizar un seguimiento y asegurar una ingesta adecuada de vitamina D, así como una exposición solar suficiente. Probablemente en estos grupos en los que se puede asegurar la acción de factores protectores, no habría que plantear la administración de vitamina D en forma de suplemento. Aún así, sigue siendo necesario realizar más estudios en diferentes poblaciones para indicar cuáles son los niveles adecuados de vitamina D y seleccionar los grupos de riesgo que se beneficiarían de los suplementos de vitamina D sin intentar generalizar esta práctica a toda la población, ya que unos niveles elevados no estarían exentos de problemas de salud.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):1999-2005
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Body fat assessment by bioelectrical impedance and its correlation with anthropometric indicators

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Abstract

Introduction: **Since the excess of body fat is associated with higher morbid-mortality rates (mainly in adults), precise, reliable, cost-effective, and broadly applicable methods are necessary for its assessment in population-based studies and in clinical practice.**

Objective: **To evaluate the correlation between body fat estimated either by bioelectrical impedance or by the sum of skinfold thicknesses and anthropometric indicators of fat distribution.**

Methods: **A cross-sectional study was conducted enrolled 348 undergraduate students (median 21 years), from the Federal University of Pernambuco, Northeast Brazil. Results: 262 of the subjects were women. Mean body fat assessed by bioelectrical impedance was 22.3 ± 6.2% in women and 15.2 ± 4.2% in men. Body fat obtained by the sum of skinfold thicknesses was similar to that assessed by bioelectrical impedance only in men. A strong correlation was observed between body fat assessed by bioelectrical impedance and that assessed by the sum of the skinfold thicknesses, waist circumference and waist-to-height ratio. Regarding the conicity index, there was a moderate correlation for men and a weak correlation for women.**

Conclusions: **The sum of skinfold thicknesses surrogate of body fat percentage and can be used to assess body fat when BIA is not available in the field. Additional information about central fat distribution can be supply by measuring the waist circumference or waist-to-height ratio.**

(*Nutr Hosp.* 2012;27:1999-2005)

DOI:10.3305/nh.2012.27.6.6073

Key words: *Body fat. Bioelectrical impedance. Skinfold thicknesses. Waist circumference. Wais-to-height ratio.*

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Recibido: 7-IV-2012.
1.ª Revisión: 21-VII-2012.
Aceptado: 23-VII-2012.

EVALUACIÓN DE LA GRASA CORPORAL POR IMPEDANCIA BIOELÉCTRICA Y SU CORRELACIÓN CON INDICADORES ANTROPOMÉTRICOS

Resumen

Introducción: **Desde que el exceso de grasa corporal se asocia con mayores tasas de morbi-mortalidad (sobre todo en los adultos), los métodos precisos y fiables, rentables, y aplicables en términos generales son necesarios para su evaluación en estudios basados en población y en la práctica clínica.**

Objetivo: **Evaluar la correlación entre la grasa corporal estimada, ya sea por impedancia bioeléctrica o por la suma de pliegues cutáneos y los indicadores antropométricos de la distribución de la grasa.**

Métodos: **Un estudio transversal se realizó con 348 estudiantes, con una edad promedio de 21 años, de la Universidad Federal de Pernambuco, nordeste de Brasil. La grasa corporal se evaluó mediante impedancia bioeléctrica y la suma de pliegues cutáneos. Circunferencia de la cintura, la relación cintura-altura y el índice de conicidad fueron utilizados como indicadores centrales de distribución de grasa**

Resultados: **262 de los sujetos eran mujeres. Media de la grasa corporal por impedancia bioeléctrica evaluados fue de 22,3 ± 6,2% en mujeres y 15,2 ± 4,2% en los hombres. Grasa corporal obtenida mediante la suma de pliegues cutáneos fue similar a la evaluada por impedancia bioeléctrica sólo en los hombres. Una fuerte correlación se observó entre la grasa corporal evaluada por impedancia bioeléctrica y espesores de los evaluados por la suma de los pliegues cutáneos, circunferencia de la cintura y relación cintura-altura. En cuanto al índice de conicidad, se observó una correlación moderada para los hombres y una correlación débil para las mujeres.**

Conclusiones: **La suma de pliegues cutáneos se puede utilizar para evaluar la grasa corporal en la ausencia de la impedancia bioeléctrica. Información adicional sobre la distribución de la grasa central puede ser la oferta mediante la medición del circunferencia de la cintura o la relación cintura-altura.**

(*Nutr Hosp.* 2012;27:1999-2005)

DOI:10.3305/nh.2012.27.6.6073

Palabras clave: *Grasa corporal. Impedancia bioeléctrica. Pliegues cutáneos. Circunferencia de la cintura. Relación cintura-altura.*

List of abreviations

BMI: Body mass index.
BIA: Bioelectrical impedance.
WC: Waist circumference.
WHtR: Waist-to-height ratio.
CI: Conicity index.
FatBIA: Body fat assessed by bioelectrical impedance.
UFPE: Federal University of Pernambuco.
WHO: World Health Organization.
DXA: Dual energy absorptiometry.

Introduction

Overweight and obesity are important public health problems worldwide. The percentage of the world population diagnosed with overweight is alarmingly increasing. In 2005, about 1.6 billion adults (> 15 years) were overweight (BMI 25-30 Kg/m^2), and 400 million were obese (BMI > 30 Kg/m^2). By 2015, 2.3 billion people will be overweight and more than 700 million obese.[1]

Research has shown that, in Brazil, 12.4% of men and 16.9% of women are obese. The sum of overweight and obesity reaches 50.1% for men and 48.9% for women.[2]

Studies have shown that the amount of adipose tissue and, mainly, its central distribution are associated with high blood pressure, dyslipidemia, impaired fasting glucose, and insulin resistance, which lead to an increase risk of cardiovascular disease.[3,4]

Assuming that body fat excess seems to be associated with higher morbidity and mortality rates (mainly in adults), precise, reliable, cost-effective, and broadly applicable screening tools are necessary for its assessment in population field studies and in clinical practice.[5] Anthropometry and bioelectrical impedance (BIA) have been widely used because they are simple techniques and have significant correlation with body fat.[6]

The BIA estimates total body fat by sending a low electrical current throughout the body. It is a fast, non-invasive, painless, and cost-effective method to assess body composition.[7] However, in Northeast Brazil, the BIA is not widely used in clinical practice because this device is not available in most of the health care providers.

The skinfold thickness is, among the anthropometric measurements, the most frequently used diagnostic tool in the assessment of body fat percentage due to its low cost and feasibility.[8] Because there is a relationship between subcutaneous fat and total body fat, the sum of several skinfold thicknesses can be used to predict total body fat.[9]

In order to assess central fat, anthropometric indices such as waist circumference (WC) and waist-to-height ratio (WHtR) are commonly used due to their low cost and because more sensitive methods, such as computed tomography and nuclear magnetic resonance imaging, are far expensive.[10] The Conicity Index (CI) is known to be an accurate indicator of central fat. It provides an indicator of fat located in the central region of the trunk. It is based on the concept that people tend to accumulate fat in the central region of the trunk resembling a double-cone body shape, i.e two cones with a common base at the waist, while those with less amount of fat in this region have a cylindrical body shape.[11]

The purpose of the study was to assess the correlation between body fat assessed either by bioelectrical impedance (FatBIA) or by the sum of skinfold thicknesses and anthropometric indicators of central fat distribution (WC, CI and WHtR), in order to indentify the most suitable method to asses body fat and central fat distribution in clinical practice and field studies.

Methods

Study design and sample

A cross-sectional study was carried out in 2008, enrolling undergraduate students selected from the Health Sciences Center of the Federal University of Pernambuco (UFPE), Northeast Brazil.

The sample size was estimated by gathering data from a pilot study, in which the prevalence of overweight was 18.0%, with a precision of 4.0% and a confidence limit of 95.0%. Sample size calculation was performed by using the formula proposed by Lwanga & Tye.[12] Therefore, the sample was composed of 348 subjects, selected by convenience. Pregnant or lactating women, those with chronic diseases or disabilities which could affect the anthropometric measurements were identified in the interview and excluded from the study.

Data collection

The biosocial variables analyzed were: age and sex of students and physical activity, classified in sedentary, low active, active and very active followed the criteria of the Institute of Medicine.[13]

The following measurements were obtained: weight, height, skinfold thicknesses (triceps, biceps, suprailiac and subscapular), WC and FatBIA. Weight was measured on a digital electronic scale with maximum capacity of 150 kg and precision of 100 g. Subjects were barefoot and wearing light clothes. Height was measured with a portable stadiometer (Ghrum Polar Manufacture, Switzerland) fixed on a plain wall, with 2.00 m long, with precision in millimeters. Both weight and height were measured according to techniques described by Lohman et al.[14] BMI was obtained by weight in kg divided by height squared in meters. The World Health Organization (WHO) cutoff points for

BMI were used as follows: low weight (BMI < 18.5 kg/m^2); eutrophy (BMI 18.5-24.9 kg/m^2), overweight (BMI 25.0-29.9 kg/m^2) and obesity (BMI ≥ 30 kg/m^2)[15].

Triceps, biceps, subscapular and supra-iliac skinfold thicknesses were obtained according to Lohman et al.[14] standardization, using the Cescorf Scientific Adipometer (precision of 0.05mm). Body fat percentage was estimated by the sum of the four skinfold thicknesses according to Durnin & Womersley's[16] table, for age and sex.

To assess fat distribution, WC was measured in standing position by using a non-extensible tape at the midpoint between the iliac crest and the last rib. WHO cutoff points were used as follows: high risk (WC ≥ 80 cm for females and WC ≥ 94 cm for males), and very high risk (WC ≥ 88 cm for females and WC ≥ 102 cm for males).[17]

The WHtR, a simple and effective measurement, was obtained by dividing WC (cm) by height (cm), using 0.5 as a cutoff point for males and females.[18]

The CI, which is used to assess obesity and body fat distribution, was determined by weight, height and WC with the following equation: CI = Waist Circumference (cm)/0.109√Weight (kg)/Height (m). The constant 0.109 resulted from the root of the ratio between 4π and the average density of the human body (1,050 Kg/m^3). The cutoff points adopted were 1.25 for males and 1.18 for females.[11]

BIA measurements were performed with Maltron BF-906 (Maltron, United Kingdom), with 50Hz of frequency in alternate chain of four electrodes. The device provides the percentage of fat throughout equations already programmed. The measurements were performed with the subject laid in supine position on a non-conductive surface (gym mats), with legs and arms abducted to 45º, without using jewelry or metal objects. In order to assure the accuracy of the measurements, the following recommendations were required: 4 hours of absolute fasting; not perform vigorous exercise 12 hours before; not drink alcohol 48 hours before; not use medication that could influence the hydroelectrolytic balance 7 days before, and urinate at least 30 minutes before testing.[9]

Body fat excess for males and females was defined as those with values of 16% and 24%, respectively. These cuttoff points were used because the subjects in our study were mostly young, healthy and eutrophic.

Statistical analysis and ethical considerations

The statistical analysis was performed by using the Epi-Info software version 6.04 (WHO/CDE, Atlanta, GE, USA) and the Statistical Package for Social Sciences version 12.0 software (SPSS Inc., Chicago, IL, USA). Kolmogorov-Smirnov test was used to check the normality of data, and only FatBIA was normally distributed. Correlation between FatBIA and other anthropometric indices was assessed by Spearman's correlation test. All reported *P*-values were two tailed, and those with < 0.05 were considered statistically significant.

Table I
Anthropometrics characteristics of undergraduate students from the Health Sciences Center of the Federal University of Pernambuco (UFPE), Northeast Brazil, 2008

Variables	*Men* *Md (P_{25} e P_{75})*	*Women* *Md (P_{25} e P_{75})*
Age (years)	21 (20-24)	21 (20-23)
BMI (k/mg)	22,8 (21,3-24,5)	20,4 (19,1-24,3)
Body fat assessed by skinfold (%)	15,9 (12,3-20,2)	26,5 (23,4-29,6)*
Conicity Index	1,14 (1,11-1,19)	1,08 (1,05-1,11)
Waist Circumference (cm)	77,8 (73,3-84,4)	67,7 (64,2-72,9)
Waist-to-height ratio	0,45 (0,42-0,47)	0,42 (0,40-0,44)
% Fat BIA	15,2 ± 3,6°	22,3 ± 6,2°*

°Mean Values and standard deviation (normal distribution).
*Comparison of two means. p = 0.000, U test of Mann-Whitney.

The study protocol was approved by the Ethics Committee of the Federal University of Pernambuco (process 478789/2007-6) and each participant signed a written informed consent.

Results

A total of 348 subjects (75.2% females) were included in the study. The average age was 21 years (P_{25}20 years and P_{75}23 years) for both genders. Anthropometric characteristics of participants are shown in Table 1. Regarding to physical activity, 46.6% women and 32.6% of men were classified as sedentary (p = 0.031).

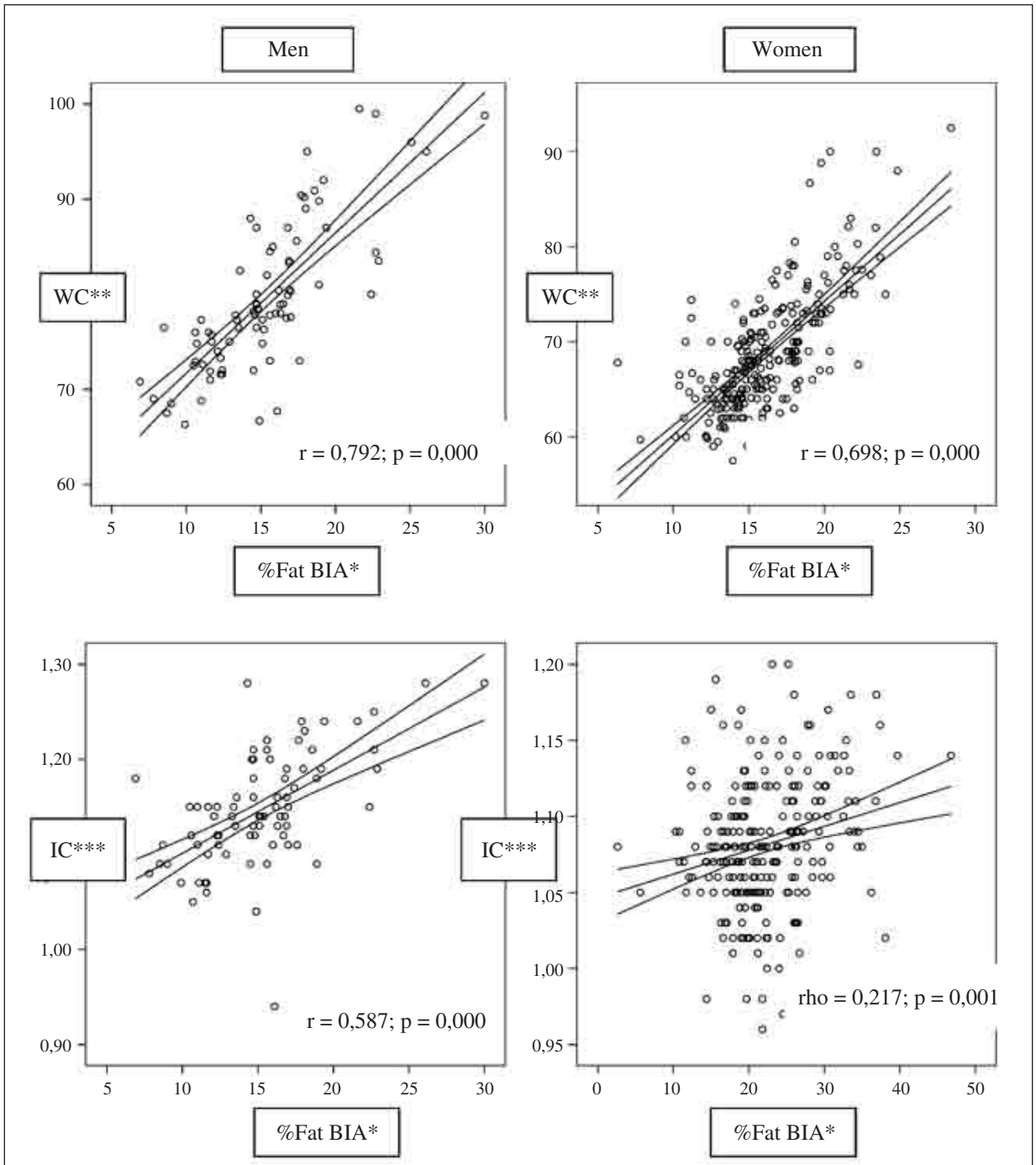
According to BMI, of the 262 women, 10.3% were underweight, 8.8% were overweight and 1.9% was obese.. In relation to the BIA, 27.4 and 7.3% of the women had ≥ 24% e ≥ 32% of body fat, respectively.

According to the BMI classification, 19.8% of males were overweight and only one was obese. In relation to the BIA, 27.4 % and 7.3% of females presented ≥ 24% e ≥ 32% of body fat, respectively.

Mean FatBIA was 22.3 ± 6.2% in females and 15.2 ± 4.2% in males, both within normality range. The percentage of body fat assessed by the sum of skinfold thicknesses was 15.9% in males and 26.5% in females (table I).

According to reference values for BMI classification, both men and women presented themselves in terms of median, in the range of normal weight. Regarding WC, WHtR and CI, the values found in terms of median, for both sexes, are below the range of risk (table I).

There was a strong correlation between FatBIA and fat assessed by the skinfold thickness, WHtR and WC. However, there was a moderate correlation for men and



**Waist circumference; *Fat percentage assessed by the BIA; ***Conicity Index; Rho Spearman's correlation test.

Fig. 1.—Correlation between fat percentage assessed by BIA (%FatBIA) WC and CI, according to sex in undergraduate students from the Health Sciences Center of the Federal University of Pernambuco, Northeast Brazil, 2008

a weak correlation for women regarding CI and FatBIA (Figs. 1 and 2).

Discussion

The significant correlation observed between either FatBIA or fat obtained by the sum of skinfold thickness and anthropometric indices (WC, WHtR and CI) was observed in our study population, even when adjusted for gender.

In a study designed to evaluate WC and WHtR in children and adolescents aged between 2-19 years, higher adiposity was observed between ages 18 to 19.[18] This result is in agreement with the Behavioral Risk Factor Surveillance System data that reported greater

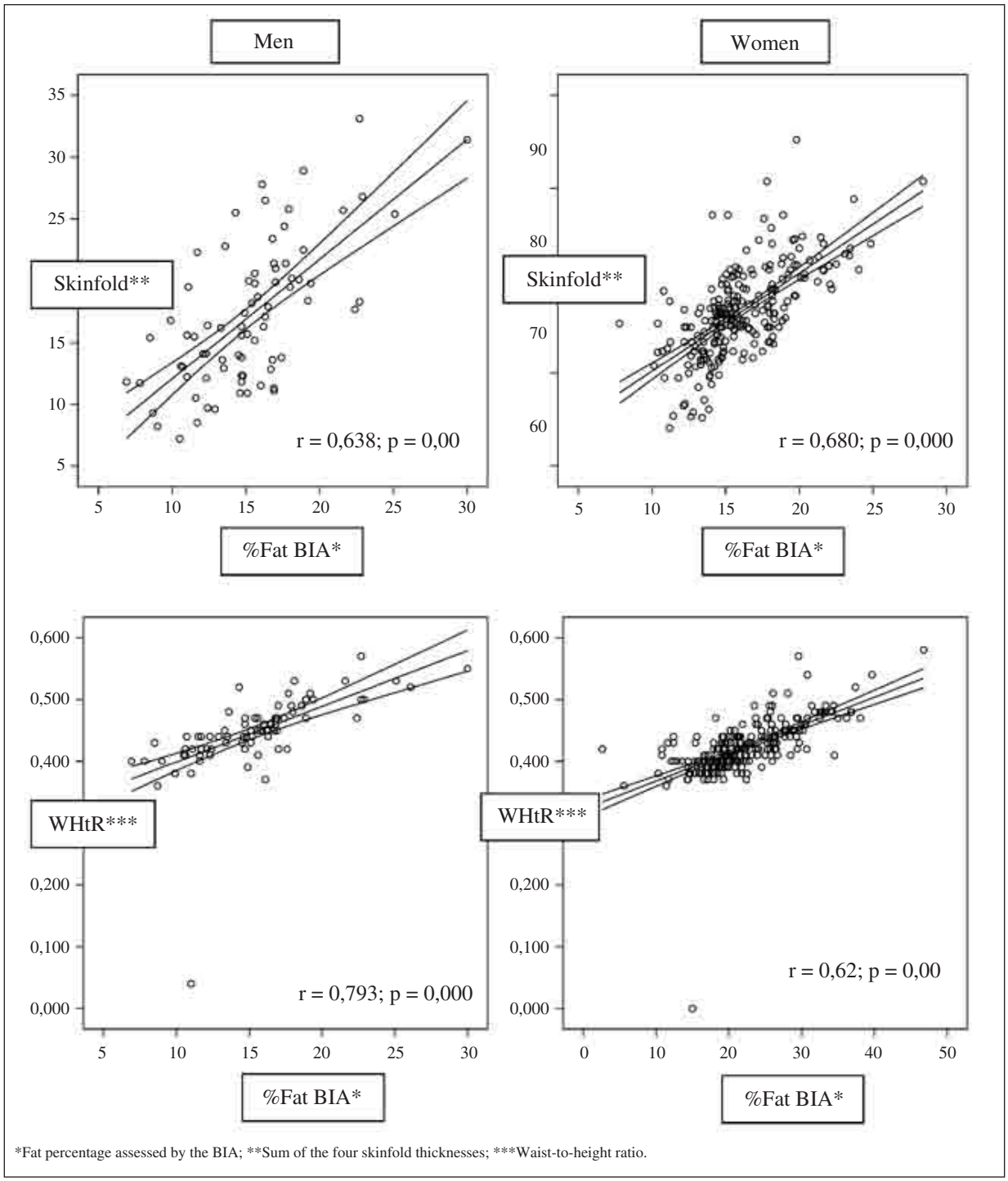


Fig. 2.—Correlation between fat percentage assessed either by BIA (%FatBIA) or by skinfold thickness and WHtR, according to sex in undergraduate students from the Health Sciences Center of the Federal University of Pernambuco, Northeast, Brazil, 2008.

increase in the prevalence of obesity between 1991 and 1998 in subjects aged between 18 to 29 years.[19] Therefore, the fact of our study have included similar young healthy adults considering that this population must be a priority in interventions regarding fat loss, mainly in the abdomen.

The subjects of the present study were young, homogeneous, and healthy, within normality ranges of BMI, body fat, WC, WHtR, and CI, except the body fat obtained by the sum of skinfold thicknesses in women and the physical activity. In fact, the highest percentage of women among sedentary students was similar to results reported by other authors. Guedes,[20] analyzing levels of habitual physical activity in adolescents found that boys were consistently more physically active than girls.

Fernandes et al. analyzed the effectiveness of the BIA by for assessing the excess of visceral and subcutaneous fat comparing WC and triceps skinfold thickness among adolescents aged 11-17 years, and found a strong correlation between FatBIA and triceps skinfold thickness in both genders (r = 0.76 for males and r = 0.77 for females).[6]

WC and WtHR are anthropometric indices largely used to predict the risk of cardiovascular diseases since they are simple and effective indicators of abdominal obesity.[17] Our findings show that both WC and WTHT had a strong correlation with FatBIA in both sexes. Fernandes et al found similar results using WC in adolescents aged 11-17 years (r = 0.82 for both sexes).[6] A higher correlation was also found by Eisenmann among children aged 3-8 years (r = 0.84).[21]

Abdominal obesity is composed of two distinct compartments of fat: subcutaneous and visceral, and the latter has a stronger association with the majority of metabolic risk factors when compared to subcutaneous abdominal adipose tissue.[22] However, in spite of different anthropometric indices are available to assess abdominal fat such as WC, WHtR, sagittal abdominal diameter (SAD), CI and waist-hip ratio (WHR),[23] these measurements represent the total abdominal area, and not the area of visceral adipose tissue in particular,[24] not being able to identify separately subcutaneous abdominal from visceral fat.[25]

Recent studies have reported that SAD is a predictor of visceral fat that shows strong correlation with cardiovascular risk factors, such as insulin resistance,[26,27,28] elevated levels of lipids and uric acid, blood pressure and metabolic syndrome[27,29]. A limitation of the use of SAD in clinical practice is the lack of consensus on the cutoffs adopted and the lack of definition of measurement protocols that best discriminate the risk of cardiovascular disease.[28]

Flegal et al.[30] observed a strong correlation between fat assessed by the dual energy absorptiometry (DXA) and WC (r = 0.85 for males and r = 0.80 for females) as well as between DXA and WHtR (r = 0.87 for males and r = 0.82 for females). WHtR showed a slightly better correlation with body fat percentage compared to WC.

A study carried out to compare different anatomic sites of WC measurements, in order to identify the most suitable site to predict FatBIA showed that the measurement performed at the midpoint between the iliac crest and the last rib (protocol recommended by the WHO) provided the best correlation,[31] which supported the use of this anatomic location when measuring WC in our study.

Several studies[18,30,31] have shown that WHtR is a better indicator for central obesity compared to WC, since it takes into account the individual's height. In our study, WHtR was more strongly correlated with FatBIA in males compared to WC. However, this result was not observed in females.

It is worth noting that participants in our study were too homogenous in terms of age and ethnic distribution, which may limit the external validity of results. Therefore, the study needs to be re-investigated in other aged groups and ethnic populations.

Conclusions

In this study the anthropometric parameters skingold thickness, WHtR and WC showed a significant correlation with BIA and can be used as proxies to identify body fat excess in young adults. Since abdominal fat is strongly associated with the risk for cardiovascular diseases, prospective studies addressing the cardiovascular outcomes in subjects with anthropometric indexes of total and central obesity altered are warranted.

Acknowledgments

The authors declare that there are no conflicts of interest.

The study represents a original work that has not been published previously and is not been considered by another journal.

Sources of funding: The study was funded by the National Council for Scientific and Technological Development - CNPq

Authors' contributions: MLD Araujo revised the literature, wrote the preliminary version of the manuscript and analyzed the data/PC Cabral contributed with data analyses, revised the final version of the manuscript and assisted the statistical analysis; IKG Arruda, APST Falcão and AS Diniz reviewed the final version of the manuscript and assisted the statistical analysis.

Acknowledgements: the authors are thankful to all the students who participated in the data collection, making possible the accomplishment of the present study.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2006-2014
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Evaluación del estado nutricional de pacientes con cirrosis hepática alcohólica atendidos en la Clínica de Hígado del Hospital General de México

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Resumen

La desnutrición en el paciente cirrótico se asocia a mayor morbi-mortalidad; sin embargo, su diagnóstico es complejo por lo que el objetivo del estudio fue evaluar el estado nutricional empleando distintos métodos.

Se evaluaron pacientes adultos con cirrosis hepática de origen alcohólico que acudieron a la Clínica de Hígado del Hospital General de México. Se aplicó un recordatorio de 24 horas y antropometría, herramientas de tamizaje (Malnutrition Universal Screening Tool, Nutritional Risk Screening-2002) y de diagnóstico nutricional específica para pacientes con cirrosis hepática (Royal Free Hospital Global Assessment).

Se incluyeron 62 pacientes y 51,6% fueron hombres. La desnutrición por área muscular de brazo fue de 31,3% en hombres y de 10% en mujeres, y por área grasa de brazo fue de 23,3% en mujeres y 3,1% en hombres ($p < 0,05$). Con las herramientas de tamizaje se obtuvieron porcentajes de riesgo de desnutrición de 43,5% y 54,8% respectivamente, *vs* 1,6% identificado con peso bajo por Índice de Masa Corporal. Con la herramienta de diagnóstico nutricional Royal Free Hospital Global Assessment se identificó 45,2% de pacientes con desnutrición. Los pacientes con desnutrición tuvieron un aporte energético y proteico significativamente menor respecto a los bien nutridos: 19,7 kcal/kg y 0,89 g/kg *vs* 30 kcal/kg y 1,25 g/kg respectivamente ($p < 0,005$).

La desnutrición es una complicación frecuente en los pacientes con cirrosis hepática. Los hombres presentan mayor afección en la reserva muscular y las mujeres en la reserva de tejido adiposo corporal. El Índice de Masa Corporal no es una buena herramienta para la detección de desnutrición. Es recomendable emplear herramientas con indicadores de composición corporal como el Royal Free Hospital Global Assessment.

(*Nutr Hosp.* 2012;27:2006-2014)

DOI:10.3305/nh.2012.27.6.6070

Palabras clave: *Estado nutricional. Evaluación nutricional. Cirrosis hepática.*

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Recibido: 30-IV-2012.
1.ª Revisión: 31-V-2012.
2.ª Revisión: 19-VII-2012.
Aceptado: 7-VIII-2012.

NUTRITIONAL ASSESSMENT OF ALCOHOLIC LIVER CIRRHOTIC PATIENTS TREATED IN THE LIVER CLINIC OF THE MEXICO'S GENERAL HOSPITAL

Abstract

Malnutrition in the cirrhotic patient is associated to a higher morbidity and mortality rate; however, the diagnosis is complex, so the study objective was to assess the nutritional status using different methods.

Adult patients with alcoholic liver cirrhosis treated in the Liver Clinic of the Mexico's General Hospital were evaluated. Anthropometric measurements and a 24 hours recall were made; screening tools (Malnutrition Universal Screening Tool, Nutritional Risk Screening-2002) and a method for assessing nutritional status specifically in cirrhotic patients (Royal Free Hospital Global Assessment) were used.

We included 62 patients, 51.6% of them were men. Malnutrition by arm muscle area was 31.3% in men and 10% in women, and by arm fat area was 23.3% in women and 3.1% in men ($p < 0.05$). With the screening tools the percentages of malnutrition risk were 43.5% and 54.8% respectively, *vs.* 1.6% identified as "low weight" with the Body Mass Index. With the Royal Free Hospital Global Assessment tool the percentage of malnutrition was 45.2%. Patients with malnutrition had an energy and protein intake significantly lower than the well-nourished: 19.7 kcal/kg and 0.89 g/kg *vs* 30 kcal/kg and 1.25 g/kg ($p < 0.005$).

Malnutrition is a common complication in patients with liver cirrhosis. Men have higher depletion of muscle mass and women a higher loss of body fat. The Body Mass Index is not a reliable tool for assessing malnutrition. It's advisable to use tools with indicators of body composition such as the Royal Free Hospital Global Assessment.

(*Nutr Hosp.* 2012;27:2006-2014)

DOI:10.3305/nh.2012.27.6.6070

Key words: *Nutritional status. Nutrition assessment. Liver cirrhosis.*

Abbreviations

DN: Desnutrición.
CH: Cirrosis hepática.
IMC: Índice de Masa Corporal.
MUST Malnutrition Universal Screening Tool.
NRS-2002: Nutritional Risk Screening 2002.
RFH-GA: Royal Free Hospital Global Assessment.

Introducción

La desnutrición (DN) es común en la enfermedad hepática crónica, identificándose hasta el momento una gran variedad de factores que influyen en su desarrollo tales como ingestión dietética deficiente, malabsorción, alteraciones en el metabolismo de los nutrimentos e hipermetabolismo[1,2].

La ingestión dietética deficiente es de origen multifactorial. Algunas causas frecuentes son la falta de apetito, disgeusia por deficiencia de vitamina A, zinc y/o magnesio, remplazo del consumo de alimentos por bebidas alcohólicas, saciedad temprana por compresión en casos de ascitis a tensión, así como esofagitis y gastritis originadas por el daño directo del alcohol a la mucosa del tubo digestivo alto, ocasionando dolor abdominal, náusea y vómito. Todo lo anterior aunado a la presencia de síntomas frecuentes como debilidad, fatiga y encefalopatía hepática leve contribuyen a disminuir la ingestión de alimentos[3,4].

La malabsorción puede ocurrir por colestasis, pancreatitis crónica, disminución en la reserva de sales biliares, enteropatía portal hipertensiva, uso de fármacos para el tratamiento de la encefalopatía hepática (por ejemplo la neomicina), así como también por alteraciones morfológicas y funcionales de la mucosa intestinal[5].

Los pacientes con cirrosis hepática (CH) frecuentemente desarrollan resistencia a la insulina, lo cual afecta la captación de glucosa en las células musculares y disminuye las reservas de glucógeno. También presentan un patrón de consumo energético alterado, en el cual ocurre una transición rápida del uso de hidratos de carbono al de lípidos como sustrato energético para el metabolismo. Se ha observado que durante el ayuno nocturno se presenta un rápido inicio del proceso de gluconeogénesis a partir de aminoácidos y que el 58% de la energía proviene de la oxidación de lípidos, mientras que en controles sanos el 55% de la energía se obtiene a partir de hidratos de carbono[6].

La prevalencia de hipermetabolismo es de aproximadamente 34% entre los pacientes con CH, con un gasto energético basal del 120% del valor esperado. No se conoce la causa exacta del hipermetabolismo, pero se han identificado como factores predisponentes las infecciones, ascitis e hipertensión portal[2,7].

La prevalencia de DN en pacientes con CH reportada en la literatura varía desde 25% hasta 80%, dependiendo de la gravedad clínica de la enfermedad y del método de evaluación empleado[8-10]; así como también de la etiología, ya que los pacientes con cirrosis alcohólica presentan mayor prevalencia y grado de DN respecto a otras etiologías como las virales[11].

Múltiples autores han referido que la DN en el paciente cirrótico se asocia a un mayor riesgo de complicaciones y muerte[8,10,12], por lo que la valoración del estado nutricional del paciente con enfermedad hepática crónica ha tomado gran importancia por su valor pronóstico. Se ha encontrado en los pacientes con CH y DN un riesgo hasta 4 veces mayor de desarrollar complicaciones como encefalopatía hepática recurrente, sangrado de tubo digestivo, ascitis e infecciones en comparación con aquéllos sin DN. En cuanto a mortalidad se ha reportado que un individuo cirrótico desnutrido tiene hasta 17 veces más probabilidades de fallecer que uno sin DN[9,13].

El impacto de la DN en el paciente con CH es de gran relevancia; sin embargo, establecer el método de valoración nutricional apropiado es una tarea difícil debido a que los indicadores empleados frecuentemente tienen menor fiabilidad por diversas condiciones asociadas a la enfermedad. En estos enfermos, el peso se ve afectado por fluctuaciones de ascitis y edema, así como ajustes en la dosis de diuréticos; el uso de impedancia bioeléctrica resulta controversial debido a la retención de líquidos, y las proteínas plasmáticas, como la albúmina, reflejan en mayor medida la disminución en la capacidad de síntesis hepática que las reservas asociadas al estado nutricional[14].

Por otro lado, en cuanto a la intervención en materia de alimentación, la restricción dietética de proteína en los pacientes con CH fue una práctica común en los años 1970-1980, periodo en el cual la creación quirúrgica de una derivación porto-sistémica era frecuentemente el único tratamiento exitoso para el sangrado de várices esofágicas. Tras este procedimiento algunos pacientes desarrollaban encefalopatía hepática como resultado del paso directo de la sangre rica en proteínas a la circulación sistémica. En esas condiciones se observó que la restricción de proteína en la dieta disminuía la encefalopatía hepática y esta práctica se expandió al manejo de todos los pacientes con cirrosis[15].

La investigación posterior ha demostrado que los requerimientos de proteína de los pacientes con CH están incrementados, que dietas normo e hiper-proteicas resultan favorables clínica y nutricionalmente siendo bien toleradas por los pacientes, así como también que las restricciones en casos graves de encefalopatía deben ser temporales[16]. Por lo anterior, las guías publicadas por la Sociedad Europea de Nutrición Enteral y Parenteral (ESPEN, por sus siglas en inglés) en 1997 plantearon la necesidad de abandonar las prácticas tradicionales de restricción proteica[17]. No obstante, los profesionales de la salud aún siguen incurriendo en prácticas inadecuadas al recomendar restricciones dietéticas innecesarias sin tomar en cuenta la evidencia actual ni las condiciones clínicas y nutricionales del paciente[15,16,18].

Objetivo

Evaluar el estado nutricional de pacientes con CH alcohólica atendidos de manera ambulatoria en la Clínica de Hígado del servicio de Gastroenterología del Hospital General de México, empleando distintas herramientas de tamizaje y diagnóstico nutricional.

Objetivo secundario

Citar las recomendaciones nutricionales para el paciente con CH de acuerdo a su estado clínico-nutricional y la evidencia actual.

Métodos

Diseño

Estudio descriptivo, observacional, y transversal.

Participantes

Se realizó la evaluación nutricional a los pacientes con diagnóstico de CH alcohólica que acudieron a consulta de seguimiento en la Clínica de Hígado del Hospital General de México de enero a junio del 2011. Se excluyeron pacientes con diagnóstico de insuficiencia renal o cáncer, así como aquéllos con alguna complicación aguda de la enfermedad (sangrado de tubo digestivo, peritonitis, infecciones, encefalopatía).

Análisis estadístico

Se utilizaron medidas de tendencia central y dispersión para las variables cuantitativas; las frecuencias se expresaron en términos de proporción y se escribieron entre paréntesis. Para comparar los grupos de variables categóricas se usaron como pruebas de hipótesis la chi cuadrada (χ^2) y la de la probabilidad exacta de Fisher; se aplicó t de Student o la U de Mann-Whitney para datos cuantitativos.

El nivel de significancia se consideró con un valor de $p < 0,05$ (dos colas). Se usó el paquete estadístico SPSS versión 16.0.

Procedimiento

Al término de la consulta médica de cada paciente en la Clínica de Hígado, se registraron los datos demográficos y clínicos relevantes para la descripción del estado actual del paciente como la gravedad de la enfermedad según los criterios de Child-Pugh que considera: la presencia y gravedad de ascitis, encefalopatía, y variables bioquímicas como albúmina, bilirrubina total, porcentaje del tiempo de protrombina e INR (International Normalized Ratio)[19].

– *Evaluación nutricional:* La evaluación dietética y antropométrica de todos los pacientes fue realizada por una licenciada en nutrición, en las instalaciones de la Clínica de Hígado, al término de la consulta del personal médico.

Como método de estimación del consumo de alimentos se aplicó un recordatorio de 24 horas con el cual se calculó aproximadamente el aporte energético y de proteínas de la dieta tomando como referencia las cantidades y valor nutricional de los alimentos referidos en el Sistema Mexicano de Equivalentes[20,21]. Se calculó el requerimiento energético aplicando las fórmulas modificadas por Schofield de Harris Benedict[11], y se evaluó el aporte dietético actual comparándolo con las recomendaciones establecidas por la ESPEN[17].

Se realizaron mediciones antropométricas (peso, talla, circunferencia media de brazo y pliegue cutáneo tricipital) con las técnicas descritas por Lohman[23]. Las herramientas utilizadas fueron: una báscula de balanza con tallímetro integrado marca BAME con precisión de 100 gramos y 1 cm respectivamente, una cinta para medición de circunferencias marca SECA modelo 201 con precisión de 1 mm y un plicómetro marca LANGE con precisión de 1 mm.

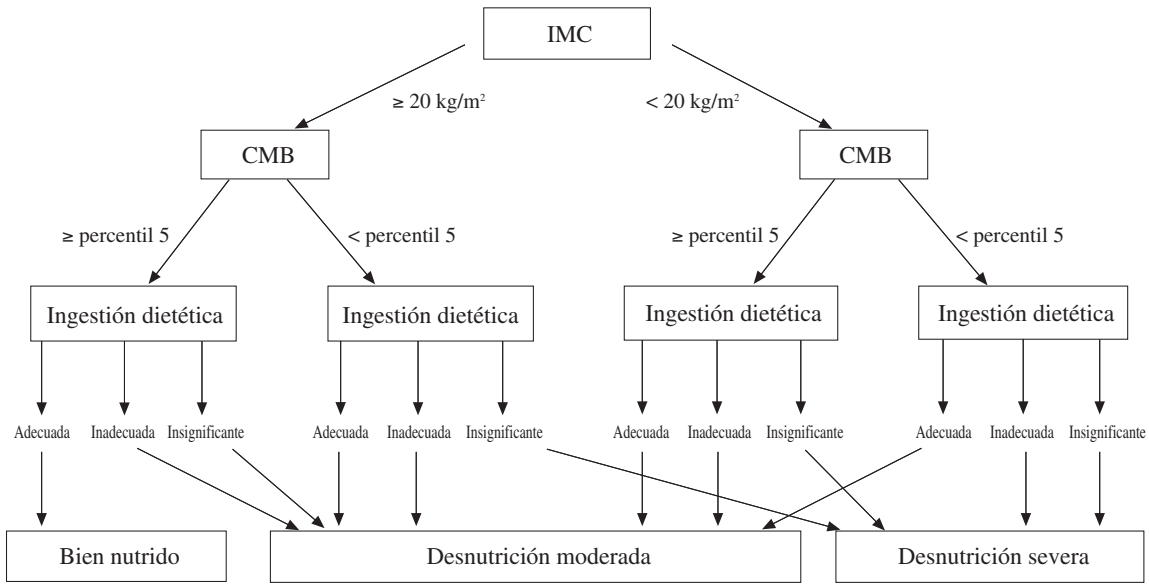
Con los datos antropométricos se calculó el índice de masa corporal (IMC), la circunferencia muscular de brazo (CMB), área muscular de brazo y área grasa de brazo. Los resultados obtenidos con la antropometría de brazo se evaluaron con los datos de las tablas de Frisancho[24].

Se emplearon 2 herramientas de tamizaje del estado nutricional (que permiten detectar a los pacientes en riesgo de DN): MUST (Malnutrition Universal Screening Tool)[25] y NRS-2002 (Nutritional Risk Screening 2002)[26], así como una herramienta de diagnóstico nutricional desarrollada específicamente para pacientes con CH, el RFH-GA (Royal Free Hospital Global Assessment)[27].

MUST. Esta herramienta fue desarrollada por el Malnutrition Advisory Group de la British Association for Parenteral and Enteral Nutrition; se ha recomendado para el tamizaje del estado nutricional en comunidad. Evalúa la pérdida de peso corporal, el IMC, la posibilidad de que el paciente ayune y la gravedad de la enfermedad. Como resultado clasifica a los pacientes en tres categorías: riesgo bajo, medio o alto de DN[25].

NRS-2002. Esta herramienta se emplea principalmente para el tamizaje nutricional de pacientes hospitalizados. Fue desarrollada por la ESPEN y evalúa el IMC, la disminución en la ingestión dietética, la pérdida de peso corporal, la gravedad de la enfermedad y la edad; clasifica a los pacientes en tres categorías: sin riesgo nutricional, con riesgo nutricional pero que aún no requieren intervención (sólo recomendación de revisión semanal) y pacientes con riesgo nutricional (que requieren intervención inmediata)[26].

RFH-GA. Esta herramienta se desarrolló específicamente para ser utilizada en pacientes con CH. Eva-



En esta figura se presenta el esquema de la herramienta Royal Free Hospital Global Assessment desarrollada específicamente para el diagnóstico nutricional de los pacientes con cirrosis hepática.
CMB: Circunferencia muscular del brazo.
IMC: Índice de masa corporal.
Adaptado de Morgan MY, Madden AM, Soulsby CT, Morris RW. Derivation and validation of a new global method for assessing nutritional status in patients with cirrhosis. *Hepatology* 2006; 44: 825-35.

Fig. 1.—Esquema del Royal Free Hospital Global Assessment.

lúa el IMC, la circunferencia muscular de brazo y la ingestión dietética, la cual se califica como *adecuada* si cubre los requerimientos estimados, *inadecuada* si no los cubre pero es mayor a 500 kcal/día e *insignificante* si es menor a 500 kcal/día; así mismo, admite una modificación subjetiva de la clasificación del estado nutricional sobre la base de factores dietéticos. Se presenta el esquema de esta herramienta en la figura 1[27].

Normas éticas

El diseño del estudio se apega a los preceptos de la Ley General de Salud de la República Mexicana, la Declaración de Helsinki de la Asociación Médica Mundial, y las buenas prácticas de investigación clínica, tal como lo estipula la Conferencia Internacional de Armonización. Este protocolo fue sometido a revisión y aprobación por el Comité de Investigación del Hospital General de México.

Resultados

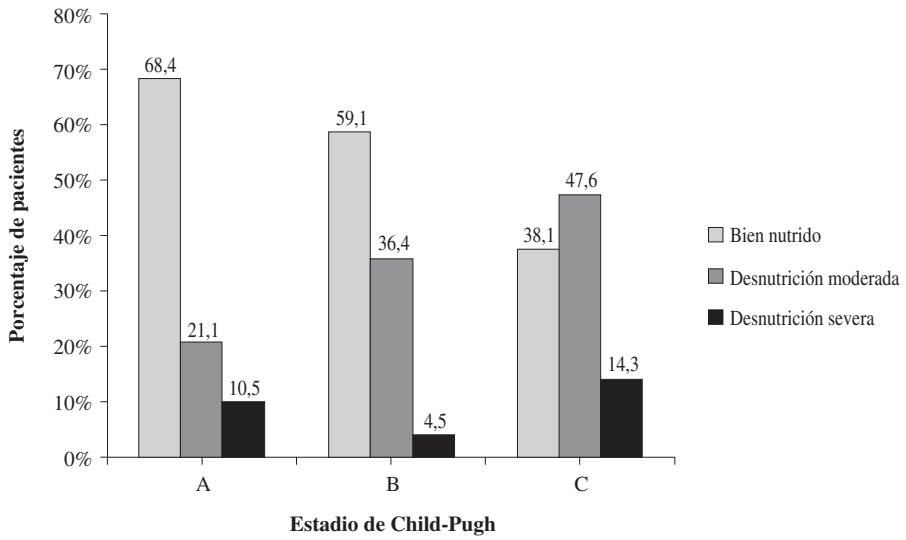
Se incluyeron un total de 62 pacientes, el 51,6% (n = 32) fueron hombres. La media de edad fue de 55 años (29-74 años).

El 30,6% (n = 19) de los pacientes se encontraban en estadio A de Child-Pugh, 35,5% (n = 22) en B y 33,9% (n = 21) en C. El 48,4% de los pacientes presentaban ascitis, de los cuales el 10% (n = 3) se encontraba en grado 1, 70% (n = 21) en grado 2, y 20% (n = 6) en grado 3.

Se encontraban con DN moderada o severa el 31,6% (n = 6) de los pacientes en estadio A de Child-Pugh, el 40,9% (n = 9) de los clasificados en estadio B y el 61,9% (n = 13) de los clasificados en estadio C. En la figura 2 se presentan estos resultados del estado nutricional de los pacientes estratificados por estadio de Child-Pugh.

Los porcentajes de DN por área muscular de brazo (< percentil 5) fueron 10% en mujeres *vs* 31,1% en hombres, y por área grasa de brazo (< percentil 5) fueron 23,3% en mujeres y 3,1% en hombres (ambos con $p < 0,05$).

Con los resultados de las herramientas de tamizaje MUST y NRS-2002 se detectó 56,5% (n = 35) y 45,2% (n = 28) de pacientes sin riesgo de DN, respectivamente. En la tabla I se presenta el desglose de los resultados de estas herramientas comparados con los obtenidos al utilizar el IMC como único indicador del estado nutricional, con el cuál sólo se encontró 1 paciente con peso bajo. En la figura 3 se agruparon los resultados en pacientes con riesgo y sin riesgo de DN de tal manera que las tres herramientas (MUST, NRS-2002 e IMC) fueran comparables de manera visual.



En esta gráfica se aprecia la diferencia porcentual de pacientes bien nutridos y desnutridos entre los grupos estratificados por la escala de gravedad clínica de la enfermedad de Child-Pugh.

Fig. 2.—Estado nutricional relacionado con el estadio de Child-Pugh.

Tabla I
Resultados de las herramientas de tamizaje y el IMC

MUST		*NRS 2002*		*IMC*	
Riesgo de desnutrición	*n (%)*	*Riesgo de desnutrición*	*n (%)*	*Riesgo de desnutrición*	*n (%)*
Bajo	35 (56,5)	Sin riesgo nutricional	28 (45,2)	Sobrepeso/obesidad	35 (56,5)
Medio	17 (27,4)	Reevaluaciones preventivas	26 (41,9)	Peso normal	26 (41,9)
Alto	10 (16,1)	Riesgo nutricional	8 (12,9)	Peso bajo	1 (1,6)

Se presenta la clasificación de los pacientes empleando herramientas de tamizaje del estado nutricional, comparada con el uso del IMC.
MUST: Malnutrition Universal Screening Tool; NRS-2002: Nutritional Risk Screening 2002; IMC: Índice de Masa Corporal.

La media de IMC de la población evaluada fue 26,84 ± 5 kg/m^2 (25,6 ± 4,6 kg/m^2 en mujeres, 28 ± 5,2 kg/m^2 en hombres). Tan sólo un paciente tuvo un IMC por debajo de 18,5 kg/m^2; el RFH-GA considera factor de riesgo de DN un IMC < 20 kg/m^2 y el NRS-2002 < 20,5 kg/m^2, encontrándose tan sólo dos pacientes bajo dichas cifras.

El 27,4% (n = 17) de los pacientes tuvo una pérdida de peso corporal del 5 al 10 % y 16,1% (n = 10) mayor a 10% en los últimos 6 meses. El 21% (n = 13) de los pacientes redujo la ingestión de alimentos en la última semana.

Con la herramienta RFH-GA para diagnóstico nutricional de los pacientes cirróticos se detectó 45,2% (n = 28) de DN, contribuyendo el IMC con la detección de 2 (3,2%) pacientes desnutridos, la circunferencia muscular de brazo con la detección de 13 (21%) y la ingestión energética de 15 (24,2%). En la tabla II se presentan los resultados de esta herramienta y se desglosan los 3 rubros que evalúa.

El gasto energético basal estimado con la fórmula predictiva de Harris-Benedict corregida por Schofield fue de 1.185,6 ± 91,2 kcal al día en mujeres y de 1.439,6 ± 166 kcal al día en hombres.

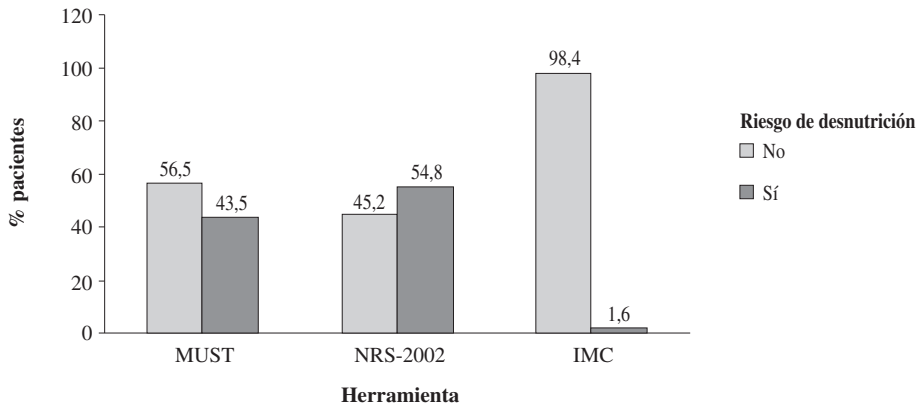
La media de ingestión de proteína de los pacientes evaluados fue de 0,9 ± 0,3 g/kg de peso corporal; la media de kcal por kg de peso fue de 21,9 ± 6,8.

Se compararon los resultados de las variables dietéticas (aporte de proteína y energía) en los tres grupos de pacientes definidos según su estado nutricional por la herramienta RFH-GA y se obtuvo como resultado que el consumo de proteína en g/kg de peso fue de 1,25 ± 0,27 en el grupo de pacientes bien nutridos, 0,97 ± 0,29 en pacientes con DN moderada y 0,89 ± 0,34 en aquéllos con DN severa (p < 0,005). En cuanto al aporte energético de la dieta (kcal/kg) se encontró una ingestión de 30,05 ± 5,93, 24,88 ± 7,70 y 19,77 ± 3,89 respectivamente en los grupos de pacientes mencionados con anterioridad (p < 0,001).

Discusión

El etilismo crónico es la principal causa de CH en México[28]. En todos los pacientes evaluados la etiología de la cirrosis fue por consumo de alcohol.

La relación positiva entre el grado de DN y la gravedad clínica de la CH ha sido estudiada en distintas publicacio-



Se presenta el porcentaje de pacientes con riesgo y sin riesgo de desnutrición obtenido al emplear herramientas de tamizaje del estado nutricional, comparado con el encontrado al utilizar el IMC.
MUST: Malnutrition Universal Screening Tool; NRS-2002: Nutritional Risk Screening 2002; IMC: Índice de Masa Corporal.

Fig. 3.—Riesgo de desnutrición utilizando herramientas de tamizaje e IMC.

Tabla II
Resultados del RFH-GA

IMC (kg/m²)		*CMB*		*Ingestión energética*		*Diagnóstico nutricional por RFH-GA*	
≥ 20	60 (96,8)	**> percentil 5**	49 (79)	**Adecuada**	47 (75.8)		
				Inadecuada	14 (22,6)	**Bien nutrido**	34 (54,8)
						Desnutrición moderada	22 (35,5)
< 20	2 (3,2)	**< percentil 5**	13 (21)	**Insignificante**	1 (1,6)	***Desnutrición severa***	6 (9,7)

Las cifras se presentan en n (%). En este cuadro se pueden apreciar los resultados obtenidos en los tres indicadores que considera la herramienta RFH-GA para emitir como resultado final el diagnóstico nutricional, que se muestra en la extrema derecha.
RFH-GA: Royal Free Hospital Global Assessment; IMC: Índice de Masa Corporal; CMB: Circunferencia muscular de brazo.

nes[1,8,10,12]. En este estudio no se obtuvieron diferencias estadísticamente significativas; sin embargo, es probable que se deba al número de participantes y podrían obtenerse al incrementar el tamaño de la muestra.

Empleando el IMC como herramienta de diagnóstico nutricional, sólo se pudo detectar a un paciente con DN, por lo que no es útil en estos casos ya que no permite detectar alteraciones en la composición corporal, como la pérdida de masa muscular. La baja sensibilidad del IMC para la detección de DN se ha descrito en diversos artículos donde se establece que no es una herramienta útil para la evaluación nutricional cuando existen cambios en la composición corporal (depleción grasa, sarcopenia, exceso de masa grasa, edema) subestimando la prevalencia de DN[29-31].

Para el cálculo del IMC se requiere conocer el peso corporal, resultando necesario calcular el peso seco en pacientes con retención hídrica, siendo finalmente un dato difícil de obtener. Gunsar y cols. proponen calcular el peso seco según los litros de líquido de ascitis obtenidos por paracentesis[12]; no obstante, considerando que los pacientes evaluados en este estudio se atienden de manera ambulatoria y no se cuenta con ese dato, fue necesario estimarlo de acuerdo a la gravedad de la ascitis, restando 2 kg en los pacientes con ascitis grado 1, 4 kg con grado 2 y 8 kg con grado 3[32].

Las herramientas de tamizaje utilizadas en este estudio permitieron detectar un alto porcentaje de pacientes en riesgo de DN, específicamente 43,5% (n = 27) con el MUST y 54,8% (n = 34) con el NRS-2002, a diferencia de los resultados obtenidos con el IMC (herramienta de diagnóstico nutricional, no de tamizaje) con el cual sólo se clasificó un paciente en la categoría de peso bajo. Con lo anterior reiteramos que el uso del IMC como única herramienta para emitir un diagnóstico nutricional resulta impreciso y poco útil, ya que el peso corporal no es fidedigno por la retención hídrica y además no se consideran variables de composición corporal ni dietéticas, que pueden reflejar con mayor precisión alteraciones en el estado nutricional.

Con el MUST se obtuvo un mayor porcentaje de pacientes sin riesgo nutricional que con el NRS-2002, principalmente debido a que no evalúa el consumo reciente de alimentos, por lo que no permite clasificar en riesgo a aquellos pacientes que presentan disminución en el apetito o reducción en la ingestión de alimentos.

Una ventaja significativa de la utilización de las herramientas de tamizaje es la facilidad y rapidez de su

Tabla III
Recomendaciones nutricionales en pacientes con enfermedad hepática crónica

Condición clínica	*Energía no proteica (kcal/kg/d)*	*Proteínas (g/kg/d)*
Cirrosis compensada	25-35	1,0-1,2
Complicaciones:		
– Ingestión inadecuada	35-40	1,5
– Desnutrición	35-40	1,5
– Encefalopatía I-II	25-35	0,5 de forma transitoria y posteriormente de 1-1,5 (en caso de intolerancia a la proteína utilizar proteína de origen vegetal o AACR)
– Encefalopatía III-IV	25-35	0,5-1,2 enriquecer con AACR

aplicación, ya que no evalúan plicometría u otras mediciones antropométricas que requieran capacitación; sin embargo, es importante considerar que en los pacientes con CH existe pérdida de masa magra aún antes de reflejar afección en pérdida de apetito o peso corporal, por lo que la herramienta para diagnóstico nutricional RFH-GA, que es específica para éstos pacientes, tiene la ventaja de incluir como indicador la CMB y con esto detectar pacientes con depleción que requieren de intervención nutricional.

Con la herramienta RFH-GA se detectó un 45,2% (n = 28) de pacientes en DN moderada o severa, cifras similares a las encontradas en otras publicaciones donde se evalúa el estado nutricional de pacientes cirróticos[10,12]. De las variables que se consideran dentro de esta herramienta, la que contribuyó en menor medida para la detección de los pacientes con DN fue el IMC (punto de corte 20 kg/m^2), siendo de mayor importancia la disminución en la ingestión dietética y la afección en la CMB.

Aunque el RFH-GA es una buena herramienta de diagnóstico nutricional, en estudios realizados con técnicas avanzadas de composición corporal se ha establecido que utilizar técnicas comunes de evaluación del estado nutricional en pacientes cirróticos puede ocasionar que se subestime la DN, principalmente en pacientes con insuficiencia hepática en estadios A y B de Child-Pugh, debido a que la DN es mucho más evidente en pacientes en estadio C de dicha clasificación[8].

Podría pensarse que los indicadores de mayor importancia son los que brindan información sobre la composición corporal del paciente, pero debe recordarse que los valores de referencia establecidos por las técnicas de composición corporal parten de supuestos universales aplicables en personas sanas, y se desconoce la variabilidad de la composición corporal en los diferentes tejidos en pacientes con CH. Por otro lado, aunque los indicadores dietéticos resultan muy subjetivos o sujetos a errores tanto por parte del paciente que informa su consumo dietético como de quien intenta obtener la información, se ha recomendado que en el caso de los pacientes con enfermedad hepática crónica, en quienes se ha encontrado asociación entre la baja ingestión de alimentos y un mal pronóstico, este aspecto sea valorado para poder brindar una orientación alimentaria dirigida considerando los hábitos de alimentación y el estado nutricional actual del paciente[17].

En los pacientes evaluados en este estudio, la media de ingestión de proteína en gramos por kg de peso corporal fue de 0,9, encontrándose por debajo de la cantidad recomendada de 1,2-1,5 g/kg (tabla III)[3,16,17].

Además de la falta de apetito, la recomendación innecesaria de disminuir el consumo de proteína en los pacientes con CH continúa siendo una práctica frecuente entre los responsables de establecer pautas de alimentación en estos pacientes[15,16,33].

La media de kcal por kg de peso fue de 21,9 ± 6,8, siendo la recomendación de 30-35 kcal/kg, lo cual indica que el aporte energético de la dieta de la población de pacientes con CH estudiados es insuficiente para cubrir sus requerimientos[17].

Se pudo observar que la dieta de los pacientes clasificados como "bien nutridos" aporta mayor energía (kcal/kg) y proteína (g/kg) que la de los pacientes con DN severa, como se ha encontrado en otros estudios[11,34,35], lo cual puede contribuir con el deterioro del estado nutricional.

Algunos autores no han encontrado diferencia en el aporte energético o de proteínas entre los pacientes con DN y sin ésta[1,36]. Riggio y cols. evaluaron el balance energético (ingestión menos gasto energético) y encontraron que los pacientes cirróticos compensados y con DN no presentaban un balance energético negativo; sin embargo, los pacientes evaluados —a pesar de estar desnutridos— se encontraban en condiciones nutricionales estables, lo cual se define como fluctuaciones menores a 5% en el peso corporal en los últimos 6 meses, por lo que probablemente ya se encontraban en un período de adaptación metabólica al momento de ser evaluados[36].

Se ha encontrado un mayor consumo de hidratos de carbono y menor de proteína y lípidos en los pacientes con CH al compararse con controles sanos, atribuyéndose este patrón dietético a alteraciones en la percepción de sabores y, más que nada, a restricciones dietéticas recomendadas por personal de salud o familiares[2,36].

Desde los años cincuenta se observó que algunos pacientes desarrollaban alteraciones mentales o hasta un "estado comatoso" al administrárseles algunas "sustancias nitrogenadas", incluyendo un exceso de proteí-

nas en la dieta[37]. Como se comentó en la introducción del trabajo, en los años 1970-1980, dicha complicación neurológica fue observada con mayor frecuencia como resultado de la derivación quirúrgica porto-sistémica, por lo que se recomendaban restricciones severas de proteína[15].

En 1997 la ESPEN publicó las guías para la nutrición en enfermedades hepáticas y trasplante, en las cuáles se recomiendan dietas con mayor aporte de proteínas y se señala la importancia de abandonar las restricciones dietéticas que pueden afectar el estado nutricional del paciente[17].

Soulsby y cols. realizaron un estudio en el Reino Unido dos años después de la publicación de las guías, en el cual aplicaron cuestionarios anónimos a dietistas del área hospitalaria y obtuvieron información de la intervención nutricional realizada en 1046 pacientes con CH. Reportaron que en el 73% de los pacientes (n = 759) se restringió el aporte dietético de proteína y además, en la mayoría de los casos, por tiempo prolongado[18]. En el año 2006, Heyman y cols. realizaron un estudio similar en Australia, reportando que tan sólo 10 (36%) de los 28 dietistas encuestados recomendaban una ingestión de proteínas adecuada para el paciente cirrótico con encefalopatía.[15] En ambos estudios concluyen que el personal de salud debe poner en práctica las recomendaciones nutricionales basadas en evidencia para evitar restricciones que resultan perjudiciales y difíciles para el paciente[15,18].

En el grupo de pacientes evaluados en este estudio, algunos refirieron tener menor consumo de alimentos por falta de apetito, pero también fue común que mencionaran haber disminuido la ingestión por recomendación del personal de salud o de sus familiares, lo cual recalca la relevancia de evaluar previamente el estado nutricional y los hábitos del paciente para realizar una recomendación dietética.

Considerando que ya se ha establecido que las técnicas indirectas subestiman la presencia de DN en pacientes cirróticos, principalmente en aquéllos en estadios A y B de Child-Pugh, resulta de suma importancia realizar una intervención alimentaria temprana antes de que la afección al estado nutricional sea de mayor gravedad. Durante la ejecución de este estudio, a todos los pacientes valorados se les brindó orientación alimentaria dirigida y adaptada a las condiciones nutricionales identificadas; resultaría importante valorar el impacto que puede tener este tipo de intervención en el estado nutricional, principalmente en pacientes de escasos recursos económicos como los evaluados en este estudio, quienes, en su mayoría, no cuentan con los medios para adquirir complementos alimenticios.

Los resultados de la antropometría de brazo reflejaron que la reserva muscular se encontró mayormente afectada en los pacientes hombres, lo cual coincide con lo informado en otros estudios[1,10,13,38]. Se ha atribuido la observada conservación de masa muscular en mujeres a la mayor presencia de tejido adiposo previo a la enfermedad; también se considera que en los hombres las alteraciones en hormonas sexuales que ocurren en la enfermedad hepática avanzada y ocasionan feminización (ginecomastia, hipogonadismo), podrían contribuir a la mayor pérdida de masa muscular[1].

La DN es un predictor independiente de complicaciones y muerte en pacientes con CH[39], e incluso se ha publicado que existe una mejoría en la precisión pronóstica de las escalas utilizadas para evaluar la gravedad de la enfermedad, como en la escala de Child-Pugh, cuando se agregan variables antropométricas[12] por lo que la valoración nutricional y, por ende, la intervención en materia de alimentación deben implementarse en todos los centros de salud que atienden a personas que padecen esta enfermedad.

Conclusión

La DN es una complicación frecuente en los pacientes con CH, presentando los hombres mayor afección en la reserva muscular y las mujeres en la reserva de tejido adiposo corporal.

Es recomendable emplear herramientas que valoren indicadores de composición corporal, principalmente la pérdida de masa muscular, debido a que los pacientes suelen presentar depleción de la misma sin aún reflejar cambios en apetito o en peso corporal. Es conveniente recordar que la gran mayoría de los indicadores antropométricos y bioquímicos del estado de nutrición se encuentran alterados por condiciones inherentes a la enfermedad y no reflejan el estado nutricional del paciente. Así mismo, es importante evaluar indicadores dietéticos que permitan realizar una intervención acertada en materia de alimentación evitando restricciones innecesarias que pueden afectar el aporte energético y de nutrimentos de la dieta del paciente.

Agradecimientos

Al personal del servicio de Gastroenterología del Hospital General de México por las facilidades otorgadas.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2015-2019
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Nutritional screening in clinical patients at a University Hospital in Northeastern Brazil

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Abstract

Objectives: **According to the Brazilian Hospital Nutritional Assessment Inquiry, malnutrition in hospitals reaches 48.1% in Brazil, with this figure reaching as high as 63.9% in the northern and northeastern regions of the country. Despite its high prevalence, hospital malnutrition is not well identified by the majority of professionals on healthcare teams. The aim of the present study was to identify nutritional risk in patients hospitalized for clinical conditions.**

Method: **This study was conducted at a university hospital in northeastern Brazil. Data were collected using the NRS 2002 screening tool (score ≥ 3 for nutritional risk) within 48 hours after admission to hospital.**

Results: **Ninety-nine patients (44.4% men and 55.6% women; 58.6% elderly individuals and 41.4%) were studied between April and October 2010. Nutritional risk was identified in 39.4% upon admission to hospital. Reduced food intake and body mass index were associated with nutritional risk.**

Conclusions: **A high percentage of clinical patients were at nutritional risk, which corroborates findings described in the literature. Low food intake was associated with nutritional risk. These results underscore the importance of nutritional care upon admission to hospital, which can contribute to improving or maintaining nutritional status and the avoidance of complications throughout the hospitalization period.**

(*Nutr Hosp.* 2012;27:2015-2019)

DOI:10.3305/nh.2012.27.6.6009

Key words: *Nutritional risk. Malnutrition. Nutritional risk screening. NRS 2002. Nutritional screening.*

EVALUACIÓN NUTRICIONAL EN PACIENTES CLÍNICOS EN UN HOSPITAL UNIVERSITARIO EN EL NORESTE DE BRASIL

Resumen

Objetivos: **De acuerdo con la Encuesta de Evaluación Nutricional del Hospital de Brasil, la desnutrición en los hospitales alcanza el 48,1% en Brasil, esta cifra alcanza hasta el 63,9% en las regiones del norte y noreste del país. A pesar de su elevada prevalencia, la desnutrición hospitalaria no está bien identificado por la mayoría de los profesionales en los equipos de salud. El objetivo del presente estudio fue identificar el riesgo nutricional en pacientes hospitalizados por cuadros clínicos.**

Método: **El estudio se llevó a cabo en un hospital universitario en el noreste de Brasil. Los datos fueron recolectados a través de la herramienta de detección NRS 2002 (puntuación ≥ 3 para riesgo nutricional) dentro de las 48 horas después del ingreso al hospital.**

Resultados: **Noventa y nueve pacientes (44,4% los hombres y las mujeres 55,6%, 58,6% personas de edad avanzada y 41,4%) fueron estudiados entre abril y octubre de 2010. El riesgo nutricional fue identificado en 39,4% al momento del ingreso al hospital. Reducción de la ingesta de alimentos y el índice de masa corporal se asoció con riesgo nutricional.**

Conclusiones: **Un alto porcentaje de pacientes clínicos estaban en riesgo nutricional, lo que corrobora los hallazgos descritos en la literatura. Baja ingesta de alimentos se asoció con riesgo nutricional. Estos resultados subrayan la importancia de la atención nutricional al ingreso en el hospital, que puede contribuir a mejorar o mantener el estado nutricional y la prevención de complicaciones durante el período de hospitalización.**

(*Nutr Hosp.* 2012;27:2015-2019)

DOI:10.3305/nh.2012.27.6.6009

Palabras clave: *Riesgo nutricional. Desnutrición. Detección de riesgo nutricional NRS 2002. Cribado nutricional.*

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Recibido: 15-VI-2012.
Aceptado: 7-VIII-2012.

Introduction

Although not well identified by professionals on healthcare teams, malnutrition is highly prevalent in hospitals.[1] According to Ferreira and França, malnutrition affects 15 to 20% of hospitalized patients in developed countries.[2] The following are among the problems that contribute to hospital malnutrition: a lack of nutritional screening upon admission; highly restrictive non-supplemented diets for long periods; meals not served due to interference by medical procedures and clinical tests; and a non-monitored lack of appetite in patients.[3,4]

The American Dietetic Association (ADA), Joint Commission on Accreditation of Healthcare Organizations and the Nutritional Screening Initiative define nutritional screening as the identification of characteristics associated with dietary or nutritional problems.[6] Nutritional screening consists of a simple inquiry directed at the patient or family members with the aim of determining nutritional risk, changes in the heath condition that affect nutritional status and factors that can lead to nutrition-related problems.[6,7] The European Society for Parenteral and Enteral Nutrition (2002) recommends the use of two screening tools for the adult population in Europe: the Malnutrition Universal Screening Tool and Nutritional Risk Screening 2002 (NRS 2002).[8]

There is a need to administer nutritional screening in hospitalized patients to optimize early nutritional care. Thus, the aim of the present study was to identify nutritional risk in patients hospitalized for clinical conditions.

Materials and methods

Study design and patients

This study was conducted at the hospital of the *Universidade Federal de Pernambuco* (UFPE, Brazil), involving 99 male and female adult and elderly patients interned in the medical clinic infirmary between April and October 2010. The study received approval from the UFPE Human Research Ethics Committee and all participants signed a statement of informed consent. The minimum age for inclusion in the study was 16 years. Patients with terminal diseases under palliative treatment, those unable to answer the questionnaire or had no caregiver available to answer the questionnaire, those having been hospitalized in the previous six months and those who refused to participate were excluded from the study.

Assessment methods

Data were collected using a chart with information on patient name, age, weight, height, body mass index (BMI), weight loss and food intake in the week prior to admission. This chart was filled out only by the researcher within 48 hours after admission to hospital. The information from this chart was used to fill out the NRS 2002, which is composed of questions on BMI, unintentional weight loss in the previous three months, appetite, food intake and absorption and stress stemming from illness. In this type of screening, age over 70 years is considered an important additional risk factor. Nutritional risk was defined by a cutoff point of ≥ 3.[8]

Weight and height were determined using a Filizola® scale (capacity: 150 kg) and stadiometer. These data were used to determine the BMI, with nutritional status determined based on Lipchitz (1994)[9] for elderly individuals and the World Health Organization (2000)[10] for adults. Adjustments were made for patients with swelling in the upper and/or lower limbs, ascitis and/or anasarca based on Rosa et al. (2008).[11]

Statistical analysis

The Excel 2003 program was used for the construction of the databank. The statistical analysis was performed using the Statistical Package for Social Sciences, version 13.0 for Windows (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to determine the normality of the distribution of the continuous variables. The results are presented in tables with respective absolute and relative frequencies. Either the chi-squared test or Fisher's exact test were used, when appropriate, to determine statistically significant associations, with the level of significance set to 5% ($p < 0.05$).

Results

Ninety-nine patients were included in the present study. Mean age was 53.91 ± 19 years (range: 17 to 90 years); mean weight was 58.07 ± 15 kg and mean BMI was 22.77 ± 5.3 kg/m^2. Table I displays the characteristics of the sample regarding gender, age, base disease, weight loss and nutritional status. The highest percentage of risk was found in patients diagnosed with neoplasm (38.4%), followed by patients with conditions classified as "others" (conditions with a low incidence in the infirmary throughout the study period). Upon admission to hospital, 39.4% (n = 39) of the patients were at nutritional risk.

Table II displays the association between nutritional risk and the variables addressed on the NRS 2002. Reduced food intake ($p < 0.001$), reduced BMI ($p = 0.004$) and unintentional weight loss ($p = 0.01$) were significantly associated with nutritional risk. Age, gender and base disease were not associated with nutritional risk. Figure 1 displays the distribution by age. Nutritional risk was detected in 19 adult patients (48.7%) and 20 (51.3%) elderly patients.

Table I
Characterization of sample according to gender, age, base disease, food intake, weight loss and nutritional status

Variables	*n*	*%*
Gender		
Male	44	44.4
Female	55	55.6
Age (years)		
< 60	58	58.6
≥ 60	41	41.4
Base disease		
Kidney disease	7	7.1
Infectious disease	7	7.1
Rheumatic disease	8	8.1
Heart disease	8	8.1
Lung disease	12	12.1
Liver disease	14	14.1
Others*	20	20.2
Neoplasm	23	23.2
Food intake		
0-25%	9	9.1
26-50%	22	22.2
51-75%	26	26.3
76-100%	42	42.4
Weight loss		
Present	60	60.6
Absent	26	26.3
Unknown	13	13.1
Nutritional risk		
Present	39	39.4
Absent	60	60.6
BMI		
Underweight	30	30.3
Ideal weight range	43	43.4
Overweight/obese	26	26.3

*Hereditary, gastric, neurologic, endocrine diseases and other less frequent conditions.

Discussion

Based on the results of the internationally validated NRS 2002 screening tool, 39.4% of clinical patients at the UFPE hospital were at nutritional risk. Underweight, reduced food intake and unintentional weight loss were significantly associated with this risk. These findings underscore the importance of establishing nutritional screening as a routine in Brazilian hospitals, as the country does not yet employ a single validated method that can contribute toward the prevention of hospital malnutrition.

The present study allows an understanding of the nutritional status of patients upon admission to university hospitals in northeastern Brazil. There are few studies in the country addressing the detection of nutritional risk upon admission to hospital. In contrast, a number of centers in other countries have performed this type of analysis. Data from the literature demonstrate variable degrees of malnutrition upon admission to hospital, with the frequency ranging from 10 to 67.4%.[12,13,14] According to Beghetto (2008), the Subjective Global Assessment is not the best predictor for the determination of hospital malnutrition or nutritional risk.[15] A trial conducted at the hospital of the *Universidade de São Paulo* involving the assessment of malnutrition using the Subjective Global Assessment reports a 7.5% frequency of moderate malnutrition among clinical patients.[16] A study carried out in Portugal reports a 58.4% frequency of malnutrition among clinical patients using the BMI, arm muscle circumference and triceps skinfold as the assessment parameters.[17] In the present study, the BMI classification revealed a 30.3% frequency of malnutrition. This difference likely occurred due to the limitation of the BMI when used alone in comparison to other methods employed for the diagnostic criteria of nutritional status.

Exclusively analyzing surgery patients, a number of studies have screened for malnutrition using different methods (Subjective Global Assessment, Nutritional Risk Index) and report different percentages (10-67.4%, 58.3%, respectively).[18,19] These figures are higher than those found in the present study (hospital malnutrition: 30.3%; nutritional risk: 39.4%).

There are few studies on the detection of nutritional risk that offer data for the purposes of comparison. Screening for nutritional risk in elderly individuals with a mean age of 82.1 years in the United Kingdom, Sarah et al. (2008)[18] found that different methodologies revealed different risk percentages, with 10.43% determined to be at risk using the Malnutrition Universal Screening Tool and 6.69% at risk using the Birmingham Nutrition Risk score. Moreover, the authors found that 17.39% were at risk when using both methods and concluded that the Malnutrition Universal Screening Tool is specific for predicting mortality among elderly individuals, which was not true for the Birmingham Nutrition Risk score or BMI. In the present study, a 48.78% frequency of nutritional risk was found among elderly individuals (≥ 60 years), which may be explained by difficulties regarding access to health care and the precarious socioeconomic status of the population studied.

A study carried out in Austria involving elderly individuals (≥ 65 years) found a 28% frequency of nutritional risk using the Short Form of the Mini Nutritional Assessment, with malnutrition associated with depression, hematocrit, fasting blood glucose and daily activities.[19] The authors concluded that the individuals had an increased risk due to the effect of preexisting conditions that are common in this age group, along with physical dependence, resulting in inadequate food intake. In comparison, the present study found a higher frequency of nutritional risk among elderly individuals (48.78%).

Studies involving the NRS 2002 for the detection of nutritional risk report frequencies greater than 30%

Table II
Association between nutritional risk, nutritional assessment variables and base disease

Variables	Nutritional risk				p-value
	Present		Absent		
	n	%	n	%	
Gender					
Male	20	51.3	24	40.0	0.370*
Female	19	48.7	36	60.0	
Age (years)					
< 60	19	48.7	39	65.0	0.162*
≥ 60	20	51.3	21	35.0	
Base disease					
Heart disease	3	7.7	5	8.3	0.054**
Lung disease	5	12.8	7	11.7	
Kidney disease	3	7.7	4	6.7	
Liver disease	4	10.3	10	16.7	
Rheumatic disease	0	0.0	8	13.3	
Infectious disease	3	7.7	4	6.7	
Neoplasm	15	38.4	8	13.3	
Others	6	15.4	14	23.3	
Food intake					
0-25%	9	23.1	0	0.0	< 0.001*
26-50%	14	35.9	8	13.3	
51-75%	10	25.6	16	26.7	
76-100%	6	15.4	36	60.0	
Weight loss					
Present	31	86.1	29	58.0	0.010*
Absent	5	13.9	21	42.0	
BMI					
Underweight	19	45.2	11	19.3	0.004*
Ideal weight range	18	42.9	25	43.9	
Overweight/obesity	5	11.9	21	36.8	

*Chi-squared test.
**Fisher's exact test.

among hospitalized patients,[17,20,21] which is in agreement with the percentage in the present study. In contrast, a study carried out in Denmark[22] and a publication from the European continent[23] report somewhat lower percentages of nutritional risk (20% and 27%, respectively). A cohort study carried out for the validation of the NRS 2002 as a nutritional screening tool in Turkey found a 15% frequency of nutritional risk.[12] A study carried out at five public hospitals in Portugal reports a 64.1% frequency of clinical patients at nutritional risk,[17] which is much higher than the figure found in the present study. Such divergences may be attributed to differences in population characteristics, socioeconomic status, sample size and age. The higher percentage of individuals at risk in northeastern Brazil likely occurs due to difficulties regarding access to healthcare services as well as a lack of awareness on the part of professionals on healthcare teams regarding the importance of determining nutritional status upon admission to the clinical evolution of patients.

In the present study, no statistically significant associations were found between nutritional risk and gender, base disease or age. These findings may be explained by the sample size, the considerable variability in diseases and the homogeneity of the sample in terms of age.

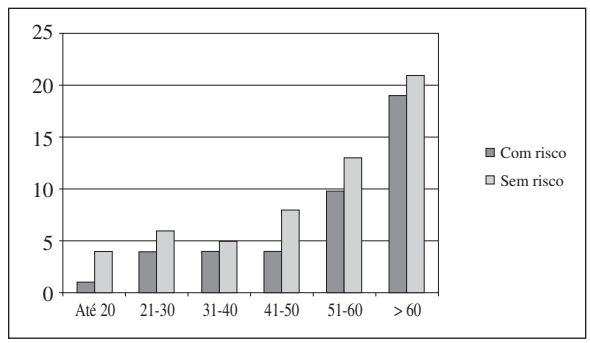


Fig. 1.—Distribution of nutritional risk according to age group among clinical patients at a university hospital in northeastern Brazil, 2010.

The present study offers an outline of the nutritional status of clinical patients upon admission to a university hospital in northeastern Brazil. The results of this

study may serve as the basis for comparisons with subsequent studies involving a larger sample and other hospital institutions. This issue is of considerable importance to the scientific community as well as patients who will benefit from the most adequate treatment strategy.

Conclusion

A high percentage of clinical patients in the present study were at nutritional risk, which corroborates findings described in the literature. Nutritional risk was associated with low food intake, underweight and unintentional weight loss. These results underscore the importance of nutritional care upon admission to hospital, which can contribute to improving or maintaining nutritional status and the avoidance of complications throughout the hospitalization period.

Acknowledgements

The authors are grateful to the Pernambuco State Secretary of Health, the Residency Program of the UFPE Department of Nutrition and the UFPE hospital for allowing the execution of this study.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2020-2027
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Factores fisiológicos y sociales asociados a la masa corporal de jóvenes mexicanos con discapacidad intelectual

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Resumen

Introducción: **Estudios sobre el estado de salud y nutrición de Mexicanos con discapacidad intelectual (DI) incluyendo aquellos con Síndrome de Down (SD), son escasos.**

Objetivo: **Analizar algunos factores fisiológicos y sociales asociados a la masa corporal de jóvenes con DI del norte de México.**

Métodos: **A 57 jóvenes con DI (17 ± 5 años, SD = 16%) y al menos uno de sus tutores, se les midió su peso, talla, y otras variables antropométricas. Se determinó su IMC (kg/m²), somatotipo y estado nutricio mediante 3 criterios internacionales y glucosa, colesterol total y triacilglicéridos plasmáticos. Al tutor se le aplicó un cuestionario socioeconómico, de inseguridad alimentaria y conocimientos de nutrición.**

Resultados: **Los participantes con SD eran 12 cm más pequeños y median 6 mm más de pliegue subscapular (PSECP) que aquellos con otra DI (p < 0,05). El sobrepeso-obesidad estuvo presente en 70 y 44%, respectivamente. Los parámetros bioquímicos fueron similares entre grupos, pero 25% tenía alguna dislipidemia. El IMC del participante correlacionó (p < 0,01) con varios indicadores antropométricos y de adiposidad (r = 0,40 a 0,88), plasmáticos [triacilglicéridos (r = 0,48), colesterol total (r = 0,44)] y edad del participante y tutor (r = 0,35). El gasto en alimentos correlaciono con PSECP del participante (r = -0,33, p < 0,05). La circunferencia de cadera, cintura, pantorrilla y PSECP, explicaron el 89% de la varianza del IMC.**

Conclusión: **La masa corporal de jóvenes con DI del norte de México se relaciona fuertemente con el grado de adiposidad corporal, con dislipidemias y con factores socioeconómicos de su entorno familiar.**

(*Nutr Hosp.* 2012;27:2020-2027)

DOI:10.3305/nh.2012.27.6.6062

Palabras clave: *Discapacidad intelectual. Síndrome de Down. Índice de masa corporal. Determinantes epidemiológicos. Antropometría.*

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Recibido: 9-VI-2012.
1.ª Revisión: 15-VII-2012.
Aceptado: 7-VIII-2012.

PHYSIOLOGICAL AND SOCIAL FACTORS ASSOCIATED WITH INCREMENTS OF BODY MASS OF MEXICAN YOUNG PEOPLE WITH INTELLECTUAL DISABILITIES

Abstract

Introduction: **Studies on the state of health and nutrition of Mexicans with intellectual disability (ID) including those with Down syndrome (DS), are scarce.**

Objective: **To analyze some physiological and social factors associated with the body mass of young people with ID from northern México.**

Methods: **Body weight, height and other anthropometric values were measured in fifty seven young (17 ± 5 years) participants with ID (DS,16%) and at least one guardian. BMI (kg/m²), somatotype and nutritional status were established by three international standards and total blood glucose, cholesterol & triacylglycerides, were also analyzed. Guardian's socio-economic, household food insecurity and nutrition literacy status were estimated with validated questionnaires by direct interview.**

Results: **Participants with SD were 12 cm smaller but subscapular skinfold (SECPS) was 6 mm thicker than that from other ID participants (p < 0.05). Prevalence of overweight/obesity was 70 and 44%, respectively. Blood biochemicals were similar between groups, but 25% had dyslipidemias. Participant's BMI correlated (p < 0,01) with several anthropometric & adiposity indicators (r = 0,40 a 0,88), blood triglycerides (r = 0,48) and cholesterol (r = 0,44) and guardians & participants' age (r = 0,35). The spending in food correlated (p < 0.05) with participant's SECPS (r = -0.33). The circumference of the waist, hip, calf and PSECP, 89% of the variance of the BMI explained.**

Conclusion: **The body mass of young people with DI from northern Mexico, is strongly related to the degree of body adiposity, dyslipidemias, and some socio-economic factors of their family environment.**

(*Nutr Hosp.* 2012;27:2020-2027)

DOI:10.3305/nh.2012.27.6.6062

Key words: *Intellectual disability. Down syndrome. Body mass index. Epidemiological determinant. Anthropometry.*

Abreviaturas

CBN: Conocimientos básicos en nutrición.
CSN: Conocimientos sobre la relación salud-nutrición.
DI: Discapacidad intelectual.
IMC: Índice de masa corporal.
ISAK: Society for the Advancement of Kineanthropometry.
PSCEP: Pliegue sub escapular.
R^2: Coeficiente de determinación.
SD: Síndrome de Down.
SPSS: Statistical Package for the Social Sciences.
χ^2: Prueba de Chi cuadrada.

Introducción

De acuerdo con la *Clasificación Internacional del Funcionamiento, de la Discapacidad y de la Salud*[1], las personas con discapacidad son aquellas que tienen una o más deficiencias físicas, mentales, intelectuales o sensoriales que al interactuar con el entorno social pueden impedir su participación plena y efectiva en igualdad de condiciones a las demás personas en una sociedad. En el *Informe Mundial sobre la Discapacidad 2011*[2], se informó que más de mil millones de personas viven en todo el mundo con alguna forma de discapacidad y casi 200 millones de ellas experimentan dificultades considerables en su funcionamiento. Para el caso Mexicano, en el 2000 se reportaron casi dos millones de personas con discapacidad (1,8% de la población total, 52,6 hombres y 47,4% mujeres), siendo mayormente personas entre 10 a 14 y de 60 a 79 años[3]. En ese año, 45,3, 26,0, 15,7, 16,1, y 4,9% de los casos fueron reportados con discapacidad motora, visual, auditiva, mental y del lenguaje respectivamente, siendo los últimos dos tipos más prevalentes en niños y jóvenes. Para el 2010, poco mas de 5,7 millones de personas (5,1% de la población total) se reportaron con discapacidad, siendo 8,5 y 8,3% los casos por discapacidad mental [actualmente considerada discapacidad intelectual (DI)] y del lenguaje, respectivamente y mayormente en población entre 30 a 59 años y de 60 a 84 años.[4]

La DI se caracteriza por un funcionamiento intelectual inferior al del promedio (coeficiente intelectual < 86%), que generalmente coexiste con dificultades en el comportamiento adaptativo y diversas limitaciones, entre ellas en la comunicación, el auto cuidado, la vida en el hogar, las habilidades sociales, la autodirección, las habilidades académicas y en el trabajo, entre otras[5,6]. Esta discapacidad es característica de diversos síndromes neurológicos entre ellos el de Asperger, Rett, Dravet, Prader-Willi, Klinefleter y Down (SD)[7,8]. Sin embargo, la DI no es una enfermedad por lo que no existen tratamientos para erradicarla, sino metodologías que ayudan a las personas, en la medida de sus capacidades, a funcionar mejor socialmente y a ser independientes. Así, un adecuado y temprano diagnóstico, además de una atención afectiva, educativa y social aplicada desde los primeros años influirá en forma decisiva en el desarrollo de las potencialidades de estos individuos, mismas que generalmente son subestimadas por nuestro entorno social[8,9].

Por otra parte, los graves problemas socioeconómicos aunados a los factores genéticos que condicionan al sobrepeso y obesidad, están afectando la salud y estado nutricional de los mexicanos[10]. Este fenómeno impacta de forma más decisiva en aquellos con DI, aunque su prevalencia y características no se conocen del todo en nuestro país. Físicamente, las personas con DI presentan talla más baja que la población general[11] y durante el segundo o tercer año de vida, muchos niños con SD u otras DI comienzan a ganar peso, convirtiéndose con los años el sobrepeso en un problema de salud[12]. El peso ideal de los niños con DI debe estar en proporción a la talla y no a la edad, como lo establecen las curvas de crecimiento para el niño, pues existen componentes genéticos ligados al aumento de peso y el crecimiento estatural[13,14]. En esta población existen además problemas psicomotores poco estudiados y arraigados, mitos acerca de que estas personas no pueden realizar actividad física de manera sistemática, agrandando con ello los problemas nutricionales arriba señalados[15,16]. Por si esto fuera poco, un componente que impacta en la desnutrición de estas personas es la incapacidad que tienen para seleccionar sus alimentos de manera adecuada.

El propósito de este trabajo fue el evaluar de una forma sistemática algunos determinantes socio demográficos y fisiológicos asociados a la masa corporal de 57 jóvenes con DI del norte de México, con especial interés en aquellos relacionados a la presencia de obesidad. A saber, este es el primer reporte sobre la asociación de los factores fisiológicos y ambientales con el incremento del Índice de masa corporal (IMC) en mexicanos con DI.

Métodos

Sujetos

Se realizó un estudio descriptivo transversal en 57 jóvenes (17 ± 5 años) de ambos sexos con SD y otras formas de DI (autismo y otros trastornos provocados por factores congénitos y perinatales no definidos), que se encontraban adscritos a 4 escuelas de atención especial en Ciudad Juárez (Chihuahua, México). Se reclutaron sólo aquellos sujetos que presentaban alguna forma de DI y en los que se consiguió la autorización por escrito de los padres. El protocolo de estudio fue aprobado por el comité de ética de la Universidad Autónoma de Ciudad Juárez y por las autoridades de las escuelas participantes, siguiendo las recomendaciones de la declaración de Helsinki[17], para la experimentación con humanos.

Antropometría y estado nutricional

Los procedimientos (marcaje, delimitación y lugar de medición de los pliegues, circunferencias y diámetros bicondíleos) se realizaron teniendo en cuenta los lineamientos aprobados por la International Society for the Advancement of Kineanthropometry (ISAK). Un antropometrista entrenado y validado por la ISAK registró las mediciones. El peso corporal fue registrado con básculas digitales (Tanita mod. 682) y la talla con un estadímetro portátil (Seca mod. 208). Las demás mediciones fueron registradas con un antropómetro (Centurión Kit, Vancouver Canadá). La clasificación del estado nutricional de los participantes se realizó en base a los indicadores antropométricos talla para la edad (T/E), peso para la talla (P/T), peso para la edad (P/E) e índice de masa corporal [peso (kg)/ talla^2 (m^2)] para la edad (IMC/E). Para esto se empleó el paquete estadístico de cálculos antropométricos (EPIINFO 6.0), basado en las curvas de referencia y crecimiento estándar de niños americanos desarrollados por el Centro Nacional para Estadísticas en Salud (NCHS, por sus siglas en ingles) de los Estados Unidos de Norte América y adoptadas por la Organización Mundial de La Salud (OMS) como patrón internacional[18]. Los indicadores T/E, P/E, P/T e IMC/E ubicados entre las -1,9 y 1,9 desviaciones estándar (DE) fueron considerados como normales. El peso bajo (desnutrición aguda), talla baja (desmedro; desnutrición crónica) y la emaciación (desnutrición mixta) fueron definidos por los indicadores P/E, T/E y P/T ≤ 2 DE, mientras que el sobrepeso-obesidad fue definido cuando IMC/E ≥ 2 DE.

Los datos antropométricos de los participantes con diagnostico clínico de SD fueron adicionalmente analizados de acuerdo a los siguientes dos criterios: a) Las curvas para poblaciones con Síndrome de Down (2-18 años) para población estadounidense[19] y b) Las curvas de P/E para poblaciones con Síndrome de Down (3-15 años) emitidas por la Fundación Catalana de Síndrome de Down[11,20]. Para la evaluación del somatotipo[21] se tomaron adicionalmente otras medidas antropométricas: circunferencias de cintura, cadera, braquial (relajado y tensionado) y pantorrilla, anchos de fémur y humero, pliegues bicipital, tricipital, subescapular, supraespinal y de pierna. Las anteriores medidas antropométricas sirvieron para identificar los 3 componentes del somatotipo, siguiendo las ecuaciones y método descrito Sheldon y modificado por Heath y Carter[22] en el cual se suman los valores de los pliegues cutáneos o de las circunferencias o perímetros bicondilares (endomorfia y mesomorfia, respectivamente) corregidos por la talla o del índice ponderal (Talla/ peso; ectomorfia). Los valores obtenidos son graficados en la somatocarta[22]. Por último, las variables antropométricas de uno o de los dos padres fue determinada de la misma forma que a sus hijos, pidiéndoles no usar calzado y usar ropa ligera al momento de las mediciones. Las mediciones de los padres fueron: Peso, talla, circunferencia de cintura y circunferencia de cadera.

Factores socioeconómicos, culturales y alimentarios familiares

Con el fin de relacionar la obesidad y el sobrepeso de los participantes con factores ambientales que tradicionalmente se les ha relacionado con la génesis de este trastorno, se aplicaron instrumentos previamente validados y estandarizados en población mexicana, y abajo señalados:

a) Características socio-demográficas familiares: Ingreso familiar total y porcentaje del gasto en alimentos, pertenencia de vivienda, estado civil, edad del tutor, acceso a servicios médicos.
b) Inseguridad alimentaria familiar[23]. Este cuestionario fue diseñado para ser aplicado a mujeres del norte del país y fue construido a partir de la información recabada de 28 grupos focales ubicados en 8 municipios de Sonora y Sinaloa. Subsecuentemente fue validado frente a datos de ingreso neto familiar y características de alimentación familiar de 204 hogares. La escala permite ubicar en 4 niveles la experiencia en los hogares de inseguridad alimentaria (IA): Hogar seguro (S), inseguridad alimentaria leve (IL), moderada (IM) y severa (ISe). Para efecto de este estudio, se agruparon de forma binomial las escalas S + IL e IM + ISe.
c) Cuestionarios de conocimientos básicos de nutrición (CBN) y sobre la relación salud-nutrición (CSN)[24]. Según Sapp y Jensen, el conocimiento se refiere a las cualidades objetivas de un objeto [en este caso la aceptación (cualidad positiva) o rechazo (cualidad negativa) de algún alimento] que es reconocido por el individuo pero que su elección está influenciada por factores psicosociales (e.g. Actitud e intención) y motivacionales (e.g. presión y aceptación social). Estos cuestionarios validados y traducidos al español, han sido usados en diversos estudios epidemiológicos en personas adultas similares a la muestra aquí analizada, de varios países incluyendo a México[25]. Se definió un nivel "bueno" de conocimiento cuando se obtuvo un puntaje ≥ 75% de aciertos en cada cuestionario.

Análisis bioquímicos

Muestras de sangre periférica con y sin anticoagulante (EDTA) fueron obtenidos de cada participante en condición de reposo. Se evaluaron parámetros de citología hemática (hematocrito y hemoglobina), glucosa y lípidos [(triacilglicéridos, colesterol total y colesterol asociado a lipoproteínas de alta densidad (C-HDL)] por técnicas enzimático-colorimétricas comerciales. La variación intraensayo fue menor al 2,3%. Las dislipidemias fueron definidas cuando la concentración de triacilglicéridos, colesterol total o C-HDL era ≥ 150, ≥ 200 y < 40 mg/dl, respectivamente[26].

Tabla I
Características antropométricas de los participantes. Diferencias por condición de discapacidad intelectual (DI)

	SD	*EE*	*ODI*	*EE*	*p*
Edad (años)	16 ± 2	0.5	17 ± 5	0,7	0,690
Peso (kg)	60 ± 11	3.5	62 ± 16	2,2	0,753
Talla (cm)	**149 ± 7**	**2.2**	**161 ± 9**	**1,2**	**0,000**
IMC (kg/m^2)	27 ± 4	1.3	24 ± 6	0,8	0,095
Circunferencias (cm)					
Cintura	83 ± 8	2.7	79 ± 12	1,7	0,320
Cadera	97 ± 10	3.1	96 ± 12	1,6	0,840
Brazo (relajado)	29 ± 4	1.1	31 ± 20	0,6	0,404
Brazo (tensión)	30 ± 4	1.1	28 ± 5	0,7	0,363
Pantorrilla	33 ± 3	0.9	34 ± 5	0,7	0,83
Diámetros (cm)					
Fémur	9 ± 1	0.9	11 ± 8	0,7	0,830
Humero	6 ± 0	0.2	6 ± 1	0,1	0,693
Pliegues subcutáneos (mm)					
Bíceps	11 ± 4	1.3	12 ± 6	0,9	0,570
Tríceps	18 ± 7	2.2	17 ± 8	1,2	0,950
Subscapular	**23 ± 8**	**2.4**	**17 ± 9**	**1,2**	**0,045**
Supra espinal	17 ± 7	2.2	16 ± 8	1,1	0,780

Media ± DE; EE: Error estándar; SD: Síndrome de Down; ODI: Otras discapacidades intelectuales.

Análisis estadístico

Se utilizaron medidas descriptivas de tendencia central para la exploración inicial de los datos nominales (CI 95%). La comparación bivariada de variables paramétricas fueron analizadas por la prueba de t student para muestras independientes mientras que las no paramétricas por la prueba de Chi cuadrada (χ^2), a un nivel de significancia del 95% ($p < 0,05$). Se realizaron análisis de correlación de Spearman (variables ordinales) o Pearson (intervalos continuos) a $p < 0,05$ y $< 0,01$ y se determino el coeficiente de determinación (R^2) individual. Por último, se realizó un análisis de regresión lineal por el método de pasos sucesivos (stepwise) para modelar el efecto de las variables antropométricas de mayor peso estadístico con el IMC del participante con DI. La concordancia entre los tres criterios internacionales de corte para IMC y la consecuente determinación de la prevalencia de sobrepeso/obesidad de los participantes, se evaluó por kappa de Cohen. Todos los análisis estadísticos se realizaron en el programa SPSS (versión 15.0).

Resultados

Características de los participantes

De los 57 participantes el 16% tenían SD (n = 9), el resto otras formas de DI (n = 48). El 60% de toda la muestra fueron hombres. La edad promedio fue 17 ± 5 años sin diferencias entre sexos (p = 0,090).

Características de los tutores y familia

El 75% de los tutores entrevistados fueron madres con edad promedio de 44 ± 8 años, IMC = 30 ± 6 kg/m^2 (24% eutróficos, 42% sobrepeso y 34% obesidad), circunferencia de cintura de 91 ± 12 cm (51% en riesgo cardiovascular). 51, 67, 73, 70 y 40% de todos los tutores fueron originarios del estado de Chihuahua, vivían en casa propia, tenían acceso a servicios médicos, estaban casados y trabajaban, respectivamente al momento de la entrevista. El 61% de las familias sufría de algún grado de inseguridad alimentaria y sólo 6 y 42% de los padres poseían conocimientos básicos en nutrición (CBN) y su relación con la salud general (CSN).

Características antropométricas

En promedio, los hombres eran 7 cm más altos que las mujeres, siendo esta la única diferencia antropométrica estadísticamente significativa (p = 0,006) por sexo. La tabla I muestra las características antropométricas principales de los participantes por tipo de DI. Los participantes con SD eran 12 cm más pequeños y median 6 mm mas de pliegue subscapular que los participantes con otras formas de DI ($p < 0,05$). La endo-

Tabla II
Somatotipo de los sujetos con discapacidad intelectual (DI)

Grupo	*Endomorfia*	*Mesomorfia*	*Ectomorfia*
Hombres-SD	6,03 ± 1,54	6,09 ± 1,29	0,56 ± 0,75
Mujeres-SD	6,10 ± 1,77	6,14 ± 1,29	0,48 ± 0,66
Hombres-ODI	5,13 ± 1,96	4,38 ± 2,05	1,66 ± 1,29
Mujeres-ODI	5,59 ± 1,74	4,34 ± 2,61	1,62 ± 1,36

SD: Síndrome de Down; ODI: Otras discapacidades intelectuales (ODI).

morfia y mesomorfia fue mayor entre los jóvenes con SD que en el resto de jóvenes con DI (tabla II, fig. 1).

Estado nutricio

Mientras que el 48 y 39% de los hombres y mujeres tenían sobrepeso u obesidad en la muestra total (χ^2 = 0,35, p = 0,55), la proporción observada para personas con SD vs. otras DI fue del 70 (n = 7) y 44% (n = 21), respectivamente (χ^2 = 2,1, p = 0,15). La prevalencia de sobrepeso y obesidad en la submuestra de participantes con SD fue muy similar (Kappa de Cohen ≥ 0,61), cuando se utilizaron los puntos establecidos por la NCHS/CDC para jóvenes sanos, las tablas de la NCHS para síndrome de Down y las recomendadas por la Fundación Catalana de Síndrome de Down. Por último, 33% de los participantes con SD tenía desmedro mientras que esta proporción para las otras formas de DI era 19% (χ^2 = 0,58, p = 0,44).

Análisis bioquímicos

No hubo diferencias estadísticamente significativas por sexo (p ≥ 0,5) en el nivel (mg/dl) de glucosa (90 ± 27), triacilglicéridos (131 ± 118), colesterol total (168 ± 37) y C-HDL (46 ± 13) pero el nivel de hemoglobina (+1 g/dL) y hematocrito (+3%) fue mayor en hombres que en mujeres (p < 0,001). No hubo diferencias significativas en todos los parámetros bioquímicos entre sujetos con SD *vs.* otras formas de DI (p ≥ 0,6). 40% de los participantes presentaron alguna forma de dislipidemia, observándose un aumento de triacilglicéridos y colesterol y la disminución de C-HDL en 25, 14 y 25% de los casos, no habiendo diferencias significativas en sexo o forma de DI (p > 0,35).

Análisis de correlación y regresión lineal

El IMC del participante correlacionó fuertemente (p < 0,01) y en forma positiva con varios indicadores antropométricos y de adiposidad (r = 0,40 a 0,88), con el nivel plasmático de traciliglicéridos (r = 0,48) y de colesterol total (r = 0,44), asimismo con la edad del participante y la del tutor (r = 0,35; tabla III). Otras correlaciones negativas con significancia estadística (p < 0,05) incluyeron: el gasto destinado a la compra de alimentos con el pliegue subescapular del participante (r = -0,33) y con la circunferencia de cintura del tutor (r = -0,33), este último también correlacionó con el ingreso familiar total (r = -0,45). Sin embargo, el gasto destinado a alimentos (r = -0,26), que el tutor tra-

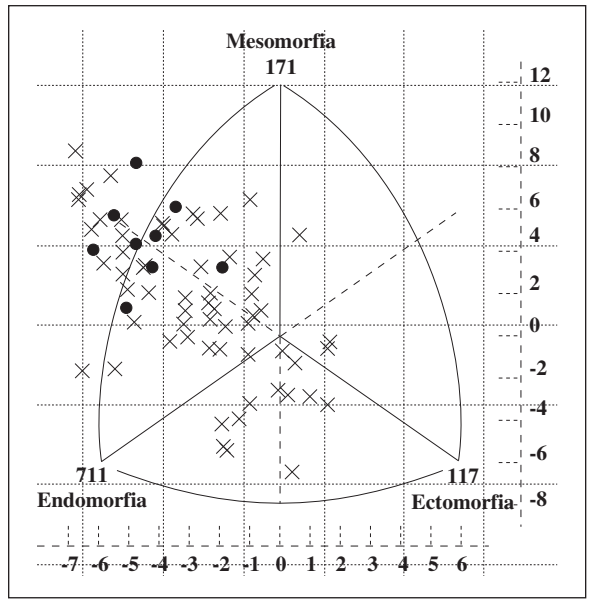


Fig. 1.—Distribución somatotípica de los sujetos con DI. Sujetos con síndrome de Down (puntos negros) u otra discapacidad intelectual (cruces).

Tabla III
*Índice de masa corporal (kg/m²) del participante y su correlación con factores antropométricos, bioquímicos y demográficos***

Variable	*Descripción*	*r**	*R²**
Antropométrica	Cintura (cm)	0,88	0,77
Antropométrica	Cadera (cm)	0,88	0,77
Antropométrica	Peso (kg)	0,88	0,77
Antropométrica	Circunferencia de brazo relajado (cm)	0,84	0,71
Antropométrica	Circunferencia de brazo tensionado (cm)	0,84	0,70
Antropométrica	Pliegue sub escapular (mm)	0,76	0,58
Antropométrica	Circunferencia de pantorrilla (mm)	0,76	0,58
Antropométrica	Pliegue supra espinal (mm)	0,75	0,56
Antropométrica	Pliegue tricipital (mm)	0,69	0,48
Antropométrica	Pliegue bicipital (mm)	0,63	0,40
Antropométrica	Plegue de Pierna (mm)	0,62	0,39
Antropométrica	Ancho de fémur (cm)	0,61	0,37
Antropométrica	Ancho de humero (cm)	0,40	0,16
Bioquímica	Triacilglicéridos (mg/dL)	0,48	0,23
Bioquímica	Colesterol total (mg/dL)	0,44	0,19
Demográfica	Edad tutor (años)	0,35	0,12
Demográfica	Edad participante (años)	0,35	0,12

r: Coeficiente de correlación; R^2: Coeficiente de determinación.
** Factores encontrados con significancia estadística p ≤ 0,01.

bajara (r = -0,21), la pertenencia de casa habitación (r = 0,23), el grado de inseguridad alimentaria familiar (r = -0,03) o el nivel de conocimientos básicos de nutrición del tutor (CBN, r = -0,26), no correlacionaron de forma significativa (p > 0,05) con el IMC del participante. Por último, el coeficiente de determinación individual (R^2) indicó que los cambios en el IMC del participante (como variable dependiente), podrían explicarse entre un 39 y 77% por el aumento del volumen corporal y deposito graso subcutáneo; siendo su relación con las dislipidemias (~20%) y edad del participante (12%) menor, pero igualmente significativa (p ≤ 0,01). Mediante el análisis de regresión lineal por el método de pasos sucesivos se pudo comprobar que la circunferencia de cadera por si sola explica el 81% de la varianza asociada al incremento del IMC (tabla IV) y las circunferencias de cintura y pantorrilla así como el pliegue subscapular contribuyen solo con un 8% adicional.

Tabla IV
*Variables antropométricas asociadas de manera independiente con las modificaciones en el índice de masa corporal (kg/m2)**

Variable	β	R^2	*p*
Constante	-15,701		
Circunferencia de cadera	0,186	0,81	0,000
Circunferencia de cintura	0,131	0,052	0,000
Circunferencia de pantorrilla	0,283	0,020	0,000
Pliegue subscapular	0,113	0,011	0,027

*Análisis de regresión lineal por el método de pasos sucesivos.
R^2: Coeficiente de determinación de la ecuación; β: Coeficiente para cada variable; p: Valor de α.
R^2 de la ecuación = 0,89.

Discusión

La presente investigación muestra que en jóvenes con Síndrome de Down u otra discapacidad intelectual, la obesidad de tipo endo-mosomorfico está asociada a diversos factores sociales y fisiológicos. Primeramente, aunque no de forma estadísticamente significativa (p ≥ 0,05), la tendencia de sobrepeso y obesidad fue más importante en hombres que en mujeres (48 *vs* 39%) y más en personas con SD que con otra forma de DI (70% *vs* 44%). En estos dos últimos el fenómeno fue concurrente al retardo en el crecimiento (33 y 19%). Cabe señalar que de acuerdo con la Encuesta Nacional de Nutrición del 2006, la prevalencia de sobrepeso y obesidad a nivel Nacional y para el estado de Chihuahua fue 33 y 32% para hombres y 36 y 34% para mujeres, respectivamente[27].

Una mayor prevalencia de sobrepeso y obesidad en personas con DI en relación a la prevalencia poblacional, ha sido reportada por otros autores. En el estudio reportado por Melville et al.[12] la prevalencia de sobrepeso y obesidad en mujeres y la de sobrepeso en hombres ingleses con SD fueron mayores que la del grupo control seleccionado por edad y sexo. Prasher et al.[28] estudiaron a 201 individuos ingleses con SD encontrando que el 31 y 22% de hombres y mujeres respectivamente tenían sobrepeso, mientras que la obesidad se presentó en el 47% de ambos sexos. Esto mismo fue reportado por Soler y Xandri[29] en 38 adultos (16-38 años) españoles. En población infantil, Pinheiro et al.[13] reportaron en 116 chilenos con SD de centros de apoyo Coanil (Fundación de ayuda al niño limitado) una alta prevalencia de obesidad en la muestra evaluada por los mismos estándares antropométricos utilizados en nuestro estudio. Lo mismo fue encontrado por Lopes et al.[14] en niños brasileños.

Cabe señalar, que en este estudio se evaluó a una población con edad intermedia a los estudios de referencia citados arriba, por lo que cualquier explicación comparativa se debe tomar con cautela. Sin embargo, resulta importante recordar que los riesgos asociados al sobrepeso u obesidad en personas con DI, y muy en particular en aquellos con SD, generalmente aumentan con la edad y los estragos aparecen a más temprana edad[30], provocando mayor demanda de servicios de cuidado especial[31] y/o participación en programas preventivos[32]. Si se considera por un momento que 1 de cada 4 participantes con o sin diagnóstico de sobrepeso y obesidad padecen de alguna forma de dislipidemia, fundamenta aun más la necesidad de atención especializada y oportuna para la población aquí estudiada.

Pinheiro et al.[13] y Lopes et al.[14] reportaron una baja concordancia en la prevalencia de sobrepeso y obesidad obtenidas con diferentes estándares de crecimiento. Estos estudios señalan que la distribución de P/E y T/E en las curvas de crecimiento para población sin SD[19] muestran un comportamiento más cercano a la curva Gaussiana; en cambio el IMC presenta un desplazamiento hacia el exceso de peso, de acuerdo a las tablas españolas para SD[11,20]. Estos autores concluyeron que la curva española es la que parece ser la más adecuada para observar déficit y excesos en cuanto a peso. En este estudio, la utilización de tres escalas para ubicar la distribución de IMC y con esto determinar la prevalencia de sobrepeso y obesidad en la población estudiada, fue similar (kappa ≥ 0,61). Es muy posible que esta aparentemente buena concordancia sea debida a la baja cantidad de participantes con SD de este estudio y al hecho de que la población sea de mayor edad.

Los factores socioculturales y familiares tienen gran influencia en la ocurrencia de sobrepeso y obesidad en poblaciones infantiles con y sin discapacidad intelectual[10]. Los cambios en la alimentación y el estilo de vida han favorecido la expresión de los genes que predisponen la obesidad, y a su vez han modificado los patrones de salud, en la población Mexicana. Sin embargo la "herencia familiar" no solo está circunscrita a los genes; en el seno familiar también se adquieren hábitos, costumbres y conductas que rigen de por vida los patrones de alimentación, estilo de vida y la probabilidad de padecer obesidad. Para el caso de las

personas con SD u otras formas de DI, varios estudios señalan que la no participación en programas escolares o la no asistencia a centros de cuidado especial y por consecuencia el estar más tiempo en casa, acelera la aparición de obesidad[33-35]. En el caso aquí estudiado, los participantes estaban adscritos a programas diurnos de actividad física y recreación proporcionados por centros especializados de atención para personas con DI.

En este estudio, la circunferencia de cintura del tutor, el nivel de conocimientos básicos de nutrición (CBN) y la relación salud-nutrición (CSN) del mismo se correlacionaron de manera negativa y débilmente, aunque de forma no significativa con el sobrepeso/obesidad en los jóvenes con DI. Aun así, el componente genético asociado sobre todo a los jóvenes con SD parece estar fuertemente influenciado por los factores socioculturales y conductuales de sus padres. Esto subraya la necesidad de incluir a los padres de niños y jóvenes con DI en todo programa dirigido ya sea para la prevención de la obesidad, como para incorporar estrategias de cambo conductual y de mejoramiento del estilo de vida.

La inequidad en el ingreso económico familiar y su relación con la presencia de sobrepeso y obesidad, o de bajo peso en niños, adolescentes[35] y adultos ha sido bien documentada. Sin embargo, la evidencia científica también fundamenta una estrecha relación entre la prevalencia de obesidad y la inseguridad alimentaria familiar en adultos, aunque en adolescentes y niños esta relación no es concluyente. En este estudio se encontró que el ingreso familiar, pero sobre todo el porcentaje que es destinado a la compra de alimentos (aunque no el grado de inseguridad alimentaria familiar), tenían una influencia leve y negativa en el IMC del participante ($p > 0,05$). Sin embargo, se encontraron correlaciones significativas ($p < 0,05$) entre el gasto destinado a la alimentación con otros factores de adiposidad del participante (e.g. pliegue subescapular) y el tutor (e.g. circunferencia de cintura). El IMC del tutor se correlacionó de forma inversa con el nivel de inseguridad alimentaria familiar (datos no mostrados). Por otra parte, el nivel de conocimientos básicos de nutrición y conocimientos de salud-nutrición fue muy pobre en el tutor, posiblemente influenciado por el igualmente bajo nivel de escolaridad del mismo (datos no mostrados). Lo anterior, aunado a la inseguridad alimentaria encontrada, podrían estar jugando un papel muy importante en la prevalencia de los desórdenes del crecimiento y desnutrición crónica (desmedro), pero no de la prevalencia de obesidad en los participantes. La relación de los factores socioeconómicos con la obesidad pareciera reproducirse en los padres pero no en los participantes, lo que confirma un factor de desregulación orgánica propia del participante con DI y muy en particular con aquel con SD.

Por último, la circunferencia de cadera, cintura, pantorrilla y el pliegue subescapular fueron los mejores parámetros antropométricos que se asociaron de manera independiente con los cambios en el IMC. La ecuación indica que el 89% de la varianza en el IMC fueron explicados por estas tres variables. Además, las asociaciones significativas entre el IMC con la concentración en plasma de triacilgliceroles y colesterol total puede significar el inicio temprano de campañas para la promoción del peso saludable; minimizando con ello el riesgo cardiovascular al que podrían estar sujetos este segmento poblacional, quienes de principio tienen un riesgo mayor de padecer enfermedades cardiovasculares derivadas de varios factores genéticos y ambientales.

Conclusión

Los factores genéticos y hábitos alimentarios de los participantes, aunados al escaso conocimiento nutricional y características socio-demográficas y culturales de los padres o tutores, estrechan su corresponsabilidad en la génesis de los distintos problemas nutricionales observados en este estudio. Dado a la mayor prevalencia de sobrepeso y obesidad entre las personas con SD u otras formas de DI, aunado a la particularidad de los determinantes de esta alta prevalencia, resulta indispensable el diseño de intervenciones que contemplen los diferentes aspectos socioeconómicos, educativos y culturales de los padres; con ello minimizar problemas de salud asociados a la discapacidad. Esto probablemente evitará inversiones cuantiosas tanto en programas educativos como en el gasto en salud de las familias. La compleja naturaleza que encierra el fenómeno alimentación-ingreso familiar-estado nutricio, encontrado entre los padres y sus hijos con DI, pone al padre o tutor en el centro de una problemática difícil de resolver sin ayuda especializada[29,31]. El conocimiento limitado que tienen las madres sobre la DI y su relación con la alimentación, constituye un factor estresante para las madres de este estudio. Esto a su vez pudiese estar contribuyendo a la construcción de imágenes y representaciones de inseguridad alimentaria propias de las madres aquí estudiadas. Así, este fenómeno merece ser explorado a mayor profundidad con muestras más grandes a la aquí realizada.

Agradecimiento

Los autores expresan su gratitud por el financiamiento otorgado por la Fundación Paso del Norte al proyecto *"Programa de Actividad Física y Educación Nutricional para Jóvenes de 12 a 18 años con Síndrome de Down"* del cual se derivo el trabajo que aquí se reporta. Adicionalmente se agradece a todos los estudiantes que colaboraron de forma directa o indirecta con las actividades del proyecto.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2028-2047
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Problemas nutricionales percibidos por los pediatras en niños españoles menores de 3 años

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Resumen

Introducción: **Los padres son los principales responsables de la educación nutricional de sus hijos y es labor del pediatra orientar y resolver problemas al respecto. En este estudio se pretende conocer la relevancia de las cuestiones nutricionales en la consulta del pediatra y los principales problemas nutricionales percibidos en los menores de 3 años.**

Métodos: **Estudio descriptivo, transversal en dos fases. La primera consistió en entrevistas y grupos de discusión con 30 pediatras seleccionados aleatoriamente en Madrid y Barcelona. Los resultados se utilizaron para diseñar el cuestionario online (76 preguntas relacionadas con la nutrición en niños de 0-3 años) de la siguiente fase, en la que participaron pediatras seleccionados de forma aleatoria y representativa del territorio nacional.**

Resultados: **De 258 pediatras seleccionados, completaron el cuestionario 151, que atendían a una media de 588 pacientes/mes. Los principales problemas nutricionales percibidos hasta los 12 meses fueron las deficiencias de hierro y vitaminas y la escasa ganancia de peso, y posteriormente la ingesta excesiva de carbohidratos y lípidos y el sobrepeso. Los padres fueron considerados los actores principales en la salud nutricional de sus hijos, pero su preocupación por esta cuestión se reduce significativamente ($p < 0,0001$) con la edad del niño. Los aspectos considerados más importantes para obtener unos buenos hábitos alimentarios fueron la alimentación adaptada a las necesidades del niño y respetar el tiempo de sueño. El porcentaje de pacientes que recibe recomendaciones de hábitos nutricionales varió del 88% (0-6 meses) al 61% (24-36 meses).**

Conclusiones: **A pesar de considerar la salud nutricional importante, la intervención educativa del pediatra al respecto no es óptima. Los problemas nutricionales percibidos fueron distintos según la edad.**

(*Nutr Hosp.* 2012;27:2028-2047)

DOI:10.3305/nh.2012.27.6.6026

Palabras clave: *Desnutrición. Trastornos de la nutrición del lactante. Trastornos de la nutrición del niño. Estado nutricional. Obesidad.*

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Recibido: 9-VI-2012.
1.ª Revisión: 26-VI-2012.
Aceptado: 7-VIII-2012.

NUTRITIONAL PROBLEMS PERCEIVED BY PEDIATRICIANS IN SPANISH CHILDREN YOUNGER THAN 3 YEARS

Abstract

Introduction: **Parents are most responsible for nutritional education of children, and pediatritians must advise and help them with their doubts. The purpose of this study was to know the relevance of nutritional topics in daily practice and the main nutritional problems perceived by pediatritians in children under 3 years of age.**

Methods: **Descriptive, cross-sectional study performed in 2 stages. First stage consisted on discussion meetings with 30 random-selected pediatritians from Madrid and Barcelona. Results were used to design the on-line questionnaire of the second stage (76 questions related to nutrition in children under 3 years). A random and representative sample of Spanish pediatritians was selected for this stage.**

Results: **One hundred and fifty one pediatritians, among 258 sampled, completed the questionnaire. They referred to see a mean of 588 patients/month. The main perceived nutritional problems in the first year of life were iron and vitamin deficiencies and poor weight gain. In the next months, excess in carbohydrates and lipid intake and overweight were the main problems perceived. Parents were considered the main actors regarding their children's nutritional health, but their concern in these questions significantly reduced with children's age ($p < 0,0001$). Factors considered to have the greatest relevance in the acquisition of good nutritional habits were to provide a diet adjusted for children's requirements and to observe the appropriate sleeping hours. The proportion of children who receive nutritional counseling varied from 88% (0-6 months) to 61% (24-36 months).**

Conclusions: **Despite of the relevance given by pediatritians, educational intervention regarding nutritional health is not ideal. Nutritional problems perceived by pediatritians varied with children's age.**

(*Nutr Hosp.* 2012;27:2028-2047)

DOI:10.3305/nh.2012.27.6.6026

Key words: *Malnutrition. Infant nutrition disorders. Child nutrition disorders. Nutritional status. Obesity.*

Introducción

Durante los 3 primeros años de vida del niño, el ritmo de crecimiento, los requerimientos energético-proteicos y de algunos micronutrientes y el patrón de ingesta alimentaria sufren cambios frecuentes y secuenciales. Los padres suelen ser los principales actores en la educación nutricional de sus hijos, siendo habitual que manifiesten dudas sobre la mejor forma de realizar esta tarea. En estas situaciones el pediatra es, hoy por hoy, la persona en quien recae la responsabilidad de una correcta orientación, vigilancia y resolución de dudas, temores y problemas a este respecto.

En el segundo semestre del primer año, la progresiva combinación de la leche materna o de fórmula con otro tipo de alimentos contribuirá a lograr una cobertura adecuada de los nutrientes necesarios para el crecimiento y desarrollo. Hacia los 12 meses de edad, el lactante ya debe recibir una variedad de alimentos distintos de la leche, a pesar de que ésta sigue siendo un alimento básico. Tras el periodo de lactante, el desarrollo del niño va estrechamente ligado al establecimiento del comportamiento alimentario, la velocidad de crecimiento disminuye y va adquiriendo habilidades progresivas para alcanzar la autoalimentación. En la etapa preescolar, y muy influenciado por el ejemplo de los adultos[1], se comienzan a adquirir preferencias, aversiones y hábitos que serán difíciles de modificar hasta etapas muy posteriores, por lo que el establecimiento de patrones saludables en esta edad es de crucial importancia[2-5]. Los malos hábitos adquiridos en este periodo pueden tener consecuencias y repercusiones en el medio y largo plazo, tal como se ha referido para la ferropenia[6] y el exceso de ingesta lipídica[7,8].

En nuestro medio, la adquisición desde edades tempranas de hábitos alimentarios y un estilo de vida saludables son aspectos insuficientemente considerados en la formación pediátrica general y posiblemente poco conocidos, por lo que resulta de interés determinar la percepción que sobre los mismos tienen los pediatras y la forma en que éstos manejan las recomendaciones sobre nutrición en su consulta diaria.

Objetivos

Con el presente estudio nos hemos propuesto conocer la relevancia de las cuestiones nutricionales en la consulta diaria de los pediatras, su opinión sobre cuáles son las principales deficiencias y excesos nutricionales en los niños menores de 3 años de edad y la importancia percibida de cada uno de los actores que condicionan las prácticas alimentarias y su rol, junto a las fuentes de información utilizadas para la recomendaciones nutricionales en la consulta.

Métodos

Se llevó a cabo un estudio descriptivo, transversal, realizado en dos fases. La primera fase (cualitativa) consistió en entrevistas personales y grupos de discusión con 30 pediatras seleccionados de forma aleatoria del total de pediatras de Madrid y Barcelona. Los resultados de esta fase fueron utilizados para diseñar el cuestionario a aplicar en la siguiente fase (cuantitativa), consistente en la recogida de datos a través de un cuestionario diseñado ad-hoc y administrado online. El cuestionario está recogido en el anexo I. Los participantes en esta segunda fase se seleccionaron a partir de una muestra aleatoria y representativa del territorio nacional de 240 centros de salud y 15 hospitales del total de centros de salud y hospitales que figuran en la base de datos oficial del Ministerio de Sanidad y Consumo. Dentro de los centros se seleccionaron aleatoriamente los pediatras a participar. Los criterios de inclusión utilizados fueron: haber superado el periodo de residencia, encontrarse en ejercicio activo (en centros públicos, privados o ambos) y con al menos un 40% de pacientes atendidos de forma habitual menores de 3 años. Los pediatras que aceptaron participar recibieron un correo electrónico con el enlace y las claves de acceso para poder completar el cuestionario alojado en la plataforma AXIS PHARMA MRO®.

El cuestionario contenía 76 preguntas (25 de ellas preguntas abiertas) en las que se interrogó a los participantes sobre la importancia en su actividad habitual de la nutrición y las alteraciones del estado nutricional en niños de 0 a 3 años, las fuentes de información sobre salud nutricional utilizadas en la práctica diaria, la importancia de los distintos actores (pediatra, padres, enfermeras, cuidadores, centros educativos, industria y organismos oficiales) y las recomendaciones sobre nutrición que se ofrecen habitualmente en la consulta.

El plazo concedido a los participantes para completar el cuestionario fue de 4 semanas. La recepción de los cuestionarios tuvo lugar entre el 30 de marzo y el 27 de abril de 2011, siendo volcados electrónicamente a una base datos informática diseñada específicamente para el estudio.

Para el análisis estadístico se utilizó el software XLSTAT Pro 2011. Se consideró para el estudio un margen de error de un 7,9% para un intervalo de confianza del 95%.

Todo el proceso de muestreo y recogida de datos se realizó conforme a la Ley Orgánica 15/1999 de Protección de Datos de Carácter Personal, así como de acuerdo al Código Internacional ICC/ESOMAR para la Práctica de la Investigación Social y de Mercados[9].

Resultados

De los 258 pediatras seleccionados, 151 completaron el cuestionario (fig. 1), lo que supone una tasa de respuesta del 62%. La distribución de la muestra según la zona geográfica fue: 25% de médicos de la zona sur (Andalucía y Extremadura), un 21% de la zona nordeste (Cataluña, Baleares y Aragón), un 22% de la zona centro (comunidad de Madrid, Castilla la Mancha y Castilla-León), un 18% del sudeste (Comunidad

Anexo I

Estudio sobre la Salud Nutricional en la población de 0 a 3 años

SECCIÓN 1: EPIDEMIOLOGÍA

1. Indique por favor el tipo de centro en el que trabaja usted (*)

☐ Centro de Salud Público
☐ Medicina Privada
☐ Ambos (público y privada)

2. Indique por favor los años de experiencia que tiene usted como pediatra tras haber completado la residencia (*)

Años de experiencia: .....

3. Indique el NÚMERO TOTAL de pacientes que atiende en 1 mes en su consulta (*)

N.º TOTAL de pacientes en 1 mes: .....

4. De estos pacientes que atiende en un mes, indique el % aproximado que tiene en cada uno de los siguientes tramos de edad (*) [La suma ha de ser 100]

% Entre 0-6 meses: .....

% Entre 6-12 meses: .....

% Entre 12-18 meses: .....

% Entre 18-24 meses: .....

% Entre 24-36 meses: .....

% Más de 36 meses: .....

5. Indique el % de consultas relacionadas con los siguientes motivos según el tramo de edad (*) [La suma de cada fila ha de ser 100]

	Revisión general	Enfermedades/ Patologías	Consultas/Consejos sobre nutrición	Otros
Entre 0-6 meses				
Entre 6-12 meses				
Entre 12-18 meses				
Entre 18-24 meses				
Entre 24-36 meses				

6. Del total de sus pacientes entre 0-6 meses que atiende en un 1 mes, qué % considera que se encuentra (*) [La suma ha de ser 100. Reparta el total de sus pacientes en este tramo de edad entre los distintos conceptos]:

- Incorrecto estado nutricional debido a DEFICIENCIAS: .....
- CORRECTO estado nutricional: .....
- Incorrecto estado nutricional debido a EXCESOS: .....
- No lo sé, tengo sospecha de problema nutricional, pero aun no he diagnosticado la causa: .....

7. Del total de sus pacientes entre 6-12 meses que atiende en un 1 mes, qué % considera que se encuentra (*) [La suma ha de ser 100. Reparta el total de sus pacientes en este tramo de edad entre los distintos conceptos]:

- Incorrecto estado nutricional debido a DEFICIENCIAS: .....
- CORRECTO estado nutricional: .....
- Incorrecto estado nutricional debido a EXCESOS: .....
- No lo sé, tengo sospecha de problema nutricional, pero aun no he diagnosticado la causa: .....

8. Del total de sus pacientes entre 12-18 meses que atiende en un 1 mes, qué % considera que se encuentra (*) [La suma ha de ser 100. Reparta el total de sus pacientes en este tramo de edad entre los distintos conceptos]:

- Incorrecto estado nutricional debido a DEFICIENCIAS: .....
- CORRECTO estado nutricional: .....
- Incorrecto estado nutricional debido a EXCESOS: .....
- No lo sé, tengo sospecha de problema nutricional, pero aun no he diagnosticado la causa: .....

9. Del total de sus pacientes entre 18-24 meses que atiende en un 1 mes, qué % considera que se encuentra (*) [La suma ha de ser 100. Reparta el total de sus pacientes en este tramo de edad entre los distintos conceptos]:

- Incorrecto estado nutricional debido a DEFICIENCIAS: .....
- CORRECTO estado nutricional: .....
- Incorrecto estado nutricional debido a EXCESOS: .....
- No lo sé, tengo sospecha de problema nutricional, pero aun no he diagnosticado la causa: .....

10. Del total de sus pacientes entre 24-36 meses que atiende en un 1 mes, qué % considera que se encuentra (*) [La suma ha de ser 100. Reparta el total de sus pacientes en este tramo de edad entre los distintos conceptos]:

- Incorrecto estado nutricional debido a DEFICIENCIAS: .....
- CORRECTO estado nutricional: .....
- Incorrecto estado nutricional debido a EXCESOS: .....
- No lo sé, tengo sospecha de problema nutricional, pero aun no he diagnosticado la causa: .....

11. Del total de sus pacientes entre 3-5 años que atiende en un 1 mes, qué % considera que se encuentra (*) [La suma ha de ser 100. Reparta el total de sus pacientes en este tramo de edad entre los distintos conceptos]:

- Incorrecto estado nutricional debido a DEFICIENCIAS: .....
- CORRECTO estado nutricional: .....
- Incorrecto estado nutricional debido a EXCESOS: .....
- No lo sé, tengo sospecha de problema nutricional, pero aun no he diagnosticado la causa: .....

▶ ▶ ▶

12. Indique el PROBLEMA/PATOLOGÍA PRINCIPAL que se encuentra usted en su consulta relacionado con la SALUD NUTRICIONAL en pacientes entre 0-6 meses y la posible causa de este problema (*)

Problema/patología: .....
Causa: .....

13. Indique el PROBLEMA/PATOLOGÍA PRINCIPAL que se encuentra usted en su consulta relacionado con la SALUD NUTRICIONAL en pacientes entre 6-12 meses y la posible causa de este problema (*)

Problema/patología: .....
Causa: .....

14. Indique el PROBLEMA/PATOLOGÍA PRINCIPAL que se encuentra usted en su consulta relacionado con la SALUD NUTRICIONAL en pacientes entre 12-18 meses y la posible causa de este problema (*)

Problema/patología: .....
Causa: .....

15. Indique el PROBLEMA/PATOLOGÍA PRINCIPAL que se encuentra usted en su consulta relacionado con la SALUD NUTRICIONAL en pacientes entre 18-24 meses y la posible causa de este problema (*)

Problema/patología: .....
Causa: .....

16. Indique el PROBLEMA/PATOLOGÍA PRINCIPAL que se encuentra usted en su consulta relacionado con la SALUD NUTRICIONAL en pacientes entre 24-36 meses y la posible causa de este problema (*)

Problema/patología: .....
Causa: .....

17. Puntúe del 1 al 10 según su grado de acuerdo con la siguiente afirmación: "Una nutrición adecuada en la etapa infantil (0-3 años) previene enfermedades y problemas en el futuro y asegura un correcto crecimiento" (*) [Siendo 10 = Totalmente de acuerdo y 1=Totalmente en desacuerdo]

Grado de acuerdo: .....

18. Indique cuál cree que será la patología que va a aparecer o a aumentar en un futuro como consecuencia de una mala alimentación en los primeros años de vida (*)

Patología: .....

19. Indique qué CARENCIAS EN NUTRIENTES (no alimentos) encuentra usted en su consulta en pacientes entre 0-6 meses y la posible causa. (*)

Carencias de nutrientes: .....
Causa de la carencia: .....

20. Indique qué CARENCIAS EN NUTRIENTES (no alimentos) encuentra usted en su consulta en pacientes entre 6-12 meses y la posible causa. (*)

Carencias de nutrientes: .....
Causa de la carencia: .....

21. Indique qué CARENCIAS EN NUTRIENTES (no alimentos) encuentra usted en su consulta en pacientes entre 12-18 meses y la posible causa. (*)

Carencias de nutrientes: .....
Causa de la carencia: .....

22. Indique qué CARENCIAS EN NUTRIENTES (no alimentos) encuentra usted en su consulta en pacientes entre 18-24 meses y la posible causa. (*)

Carencias de nutrientes: .....
Causa de la carencia: .....

23. Indique qué CARENCIAS EN NUTRIENTES (no alimentos) encuentra usted en su consulta en pacientes entre 24-36 meses y la posible causa. (*)

Carencias de nutrientes: .....
Causa de la carencia: .....

24. Indique qué EXCESOS EN NUTRIENTES (no alimentos) encuentra usted en su consulta en pacientes entre 0-6 meses y la posible causa. (*)

Excesos de nutrientes: .....
Causa de la carencia: .....

25. Indique qué EXCESOS EN NUTRIENTES (no alimentos) encuentra usted en su consulta en pacientes entre 6-12 meses y la posible causa. (*)

Excesos de nutrientes: .....
Causa de la carencia: .....

26. Indique qué EXCESOS EN NUTRIENTES (no alimentos) encuentra usted en su consulta en pacientes entre 12-18 meses y la posible causa. (*)

Excesos de nutrientes: .....
Causa de la carencia: .....

27. Indique qué EXCESOS EN NUTRIENTES (no alimentos) encuentra usted en su consulta en pacientes entre 18-24 meses y la posible causa. (*)

Excesos de nutrientes: .....
Causa de la carencia: .....

28. Indique qué EXCESOS EN NUTRIENTES (no alimentos) encuentra usted en su consulta en pacientes entre 24-36 meses y la posible causa. (*)

Excesos de nutrientes: .....
Causa de la carencia: .....

29. En un futuro cuál cree que será la tendencia en cuanto a problemas de malnutrición debido a DEFICIENCIAS (*)

☐ Aumentará ☐ Se mantendrá ☐ Disminuirá

30. En un futuro cuál cree que será la tendencia en cuanto a problemas de malnutrición debido a EXCESOS (*)

☐ Aumentará ☐ Se mantendrá ☐ Disminuirá

31. Puntúe del 1 al 10 las siguientes causas de malnutrición infantil según su relevancia (*) [Siendo 10 = Muy relevante para usted y 1 = Nada relevante]

- Malos hábitos nutricionales de los padres: .....
- Mayor uso de comidas preparadas: .....
- Poca dedicación de tiempo de los padres a los aspectos nutricionales: .....
- Inmigración: .....
- Bajo nivel económico: .....
- Más importancia de cantidad que la calidad: .....
- Falta de tiempo en las consultas de pediatría para hablar de temas nutricionales con los padres: .....
- Falta de medios en consultas de pediatría (materiales con pautas nutricionales, folletos para padres, ?): .....
- Poca regulación de las instituciones respecto a nutrición infantil (publicidad, alimentación guarderías, etiquetado de alimentos?): .....
- Otra causa de malnutrición: .....

32. En el caso que valorase "Otra causa de malnutrición" en la pregunta anterior indique a qué se refería:

.....
.....

▶ ▶ ▶

SECCIÓN 2: SALUD NUTRICIONAL-NIVEL DE CONOCIMIENTO

1. Valore del 1 al 10 los siguientes ítems según la importancia que les atribuya (*) [Siendo 10 = Muy importante y 1 = Nada importante]:

- Nivel de importancia de la Salud Nutricional dentro de la especialidad de pediatría: .....
- Importancia de la Salud Nutricional para usted en su consulta: .....
- Nivel de formación que tiene Ud. en cuanto a Salud Nutricional: .....
- Nivel de formación medio que tiene un residente de pediatría en cuanto a Salud Nutricional: .....
- Papel de la enfermera en su consulta en salud nutricional: .....

2. ¿Suele utilizar para su práctica clínica, alguna fuente de consulta y referencia relacionada con la nutrición infantil? (*)

☐ Sí

☐ No

3. Indique cuáles son las fuentes de consulta y referencia sobre nutrición infantil que utiliza en su consulta (*)

1: .....

2: .....

3: .....

4. Indique cuáles son los TRES principales canales de comunicación que utiliza para actualizarse en temas de Nutrición Infantil (*) [Seleccione tres opciones]

☐ Páginas web de las sociedades científicas nacionales

☐ Páginas web de las sociedades científicas internacionales

☐ Revistas de las sociedades científicas nacionales

☐ Revistas de las sociedades científicas internacionales

☐ Congresos

☐ Simposios

☐ Industria farmacéutica/alimentaria

☐ Otros ..... Indicar .....

.....

5. Indique cuáles son las principales necesidades de formación NO satisfechas en temas de Nutrición Infantil (*) [Puede marcar tantas opciones como sea necesario]

☐ Materiales para médicos
Indique temática .....

☐ Materiales para padres
Indique temática .....

☐ Cursos online para pediatras
Indique temática .....

☐ Cursos presenciales para pediatras
Indique temática .....

☐ Otros
Indique cuál y la temática .....

.....

6. Puntúe del 1 a 10 que cada uno de los siguientes temas sobre Salud Nutricional Infantil, según la importancia para su práctica clínica (*) [Siendo 10 = Muy importante y 1 = Nada importante]

- Alergias Alimentarias: .....
- Información de la composición de los alimentos: .....
- Alimentos funcionales: .....
- Asistencia a niños vegetarianos: .....
- Pautas dietéticas por edades: .....
- Suplementos nutricionales: .....
- Formación en Prevención: .....
- Formación en modificación de hábitos nutricionales: .....

SECCIÓN 3: ROLES

1. Puntúe del 1 al 10 la importancia que tiene cada uno de los siguientes actores dentro de la Salud Nutricional Infantil (0-3 años) (*) [Siendo 10 = Muy importante y 1 = Nada importante]

- Padres: .....
- Cuidadores (centros educativos y otros cuidadores de los niños): .....
- Pediatras: .....
- Enfermeras: .....
- Instituciones (estatales, científicas?): .....
- Industria alimentaria: .....
- Otros: .....

2. En el caso que valorase "Otros" en la pregunta anterior indique a qué se refería

.....

.....

3. Puntué del 1 al 10 la preocupación que usted considera que tienen los padres en la salud nutricional de sus hijos en los siguientes tramos de edad (*) [Siendo 10 = Muy preocupados y 1 = Nada preocupados]

	Nivel de preocupación
Entre 0-6 meses	.....
Entre 6-12 meses	.....
Entre 12-18 meses	.....
Entre 18-24 meses	.....
Entre 24-36 meses	.....

▶ ▶ ▶

4. Indique con qué frecuencia los padres le suelen consultar sobre los siguientes temas en su consulta en niños entre 0-6 meses (*)
[Marque una opción por fila]

	Rara vez/Nunca	Ocasionalmente	Frecuentemente/Regularmente
Mantenimiento de la lactancia materna	☐	☐	☐
Incorporación de leches de fórmula	☐	☐	☐
Cantidades de alimentos recomendada	☐	☐	☐
Introducción de alimentos	☐	☐	☐
Problemas de sobrepeso	☐	☐	☐
Problemas de bajo peso	☐	☐	☐
Pérdida de apetito del niño	☐	☐	☐
Dietas recomendadas	☐	☐	☐
Malnutrición: falta de nutrientes esenciales	☐	☐	☐
Calidad de alimentos	☐	☐	☐
Pautas y hábitos de nutrición	☐	☐	☐
Dietas equilibradas	☐	☐	☐
Otras	☐	☐	☐

5. Indique con qué frecuencia los padres le suelen consultar sobre los siguientes temas en su consulta en niños entre 6-12 meses (*)
[Marque una opción por fila]

	Rara vez/Nunca	Ocasionalmente	Frecuentemente/Regularmente
Mantenimiento de la lactancia materna	☐	☐	☐
Incorporación de leches de fórmula	☐	☐	☐
Cantidades de alimentos recomendada	☐	☐	☐
Introducción de alimentos	☐	☐	☐
Problemas de sobrepeso	☐	☐	☐
Problemas de bajo peso	☐	☐	☐
Pérdida de apetito del niño	☐	☐	☐
Dietas recomendadas	☐	☐	☐
Malnutrición: falta de nutrientes esenciales	☐	☐	☐
Calidad de alimentos	☐	☐	☐
Pautas y hábitos de nutrición	☐	☐	☐
Dietas equilibradas	☐	☐	☐
Otras	☐	☐	☐

6. Indique con qué frecuencia los padres le suelen consultar sobre los siguientes temas en su consulta en niños entre 12-18 meses (*)
[Marque una opción por fila]

	Rara vez/Nunca	Ocasionalmente	Frecuentemente/Regularmente
Mantenimiento de la lactancia materna	☐	☐	☐
Incorporación de leches de fórmula	☐	☐	☐
Cantidades de alimentos recomendada	☐	☐	☐
Introducción de alimentos	☐	☐	☐
Problemas de sobrepeso	☐	☐	☐
Problemas de bajo peso	☐	☐	☐
Pérdida de apetito del niño	☐	☐	☐
Dietas recomendadas	☐	☐	☐
Malnutrición: falta de nutrientes esenciales	☐	☐	☐
Calidad de alimentos	☐	☐	☐
Pautas y hábitos de nutrición	☐	☐	☐
Dietas equilibradas	☐	☐	☐
Otras	☐	☐	☐

▶ ▶ ▶

7. Indique con qué frecuencia los padres le suelen consultar sobre los siguientes temas en su consulta en niños entre 18-24 meses (*)
[Marque una opción por fila]

	Rara vez/Nunca	Ocasionalmente	Frecuentemente/Regularmente
Mantenimiento de la lactancia materna	☐	☐	☐
Incorporación de leches de fórmula	☐	☐	☐
Cantidades de alimentos recomendada	☐	☐	☐
Introducción de alimentos	☐	☐	☐
Problemas de sobrepeso	☐	☐	☐
Problemas de bajo peso	☐	☐	☐
Pérdida de apetito del niño	☐	☐	☐
Dietas recomendadas	☐	☐	☐
Malnutrición: falta de nutrientes esenciales	☐	☐	☐
Calidad de alimentos	☐	☐	☐
Pautas y hábitos de nutrición	☐	☐	☐
Dietas equilibradas	☐	☐	☐
Otras	☐	☐	☐

8. Indique con qué frecuencia los padres le suelen consultar sobre los siguientes temas en su consulta en niños entre 24-36 meses (*)
[Marque una opción por fila]

	Rara vez/Nunca	Ocasionalmente	Frecuentemente/Regularmente
Mantenimiento de la lactancia materna	☐	☐	☐
Incorporación de leches de fórmula	☐	☐	☐
Cantidades de alimentos recomendada	☐	☐	☐
Introducción de alimentos	☐	☐	☐
Problemas de sobrepeso	☐	☐	☐
Problemas de bajo peso	☐	☐	☐
Pérdida de apetito del niño	☐	☐	☐
Dietas recomendadas	☐	☐	☐
Malnutrición: falta de nutrientes esenciales	☐	☐	☐
Calidad de alimentos	☐	☐	☐
Pautas y hábitos de nutrición	☐	☐	☐
Dietas equilibradas	☐	☐	☐
Otras	☐	☐	☐

9. Indique cada cuanto tiempo suele realizar Ud. las revisiones sobre temas nutricionales en sus pacientes según el tramo de edad (*)
[Marque una opción por fila]

	1 vez al mes o más	Cada dos meses	Cada tres meses	Dos veces al año	Menor frecuencia que dos veces al año	Otra frecuencia: indique cuál
0-3 meses	☐	☐	☐	☐	☐	.....
3-6 meses	☐	☐	☐	☐	☐	.....
6-12 meses	☐	☐	☐	☐	☐	.....
12-18 meses	☐	☐	☐	☐	☐	.....
18-24 meses	☐	☐	☐	☐	☐	.....
24-36 meses	☐	☐	☐	☐	☐	.....

▶ ▶ ▶

10. Indique a qué pacientes suele valorar o medir su salud nutricional según el tramo de edad (*) [Marque una opción por fila]

	En ningún paciente	En aquellos pacientes en los que los padres presentan preguntas o inquietudes al respecto	En aquellos pacientes donde observo algún indicio de problema nutricional	En todos los pacientes
0-6 meses	☐	☐	☐	☐
6-12 meses	☐	☐	☐	☐
12-18 meses	☐	☐	☐	☐
18-24 meses	☐	☐	☐	☐
24-36 meses	☐	☐	☐	☐

11. Indique cuáles son las DOS principales herramientas que utiliza para valorar la salud nutricional infantil en sus pacientes (*) [Seleccione sólo dos opciones]:

☐ Antropométrica
☐ Analíticas
☐ Encuesta de hábitos nutricionales
☐ Otras Indique cuál .....

12. Indique en qué casos relacionados con la salud nutricional infantil Ud. suele pedir analíticas a sus pacientes (*) [Si no las utiliza introduzca ND]

1: .....
2: .....
3: .....

13. En su consulta diaria, ¿suele Ud. delegar todas o algunas de las funciones del seguimiento de la DIETÉTICA/ALIMENTACIÓN en enfermería? (*)

☐ Sí
☐ No

14. ¿Qué funciones delega principalmente en enfermería? (*)

1: .....
2: .....
3: .....

15. Puntúe del 1 al 10 la siguiente afirmación según la importancia que usted considere que tenga para su práctica clínica (*) [Siendo 10 = Muy importante y 1 = Nada importante. Si usted no sabe o no desea contestar indíquelo con el valor 0]

- Papel de la enfermera en el seguimiento de la nutrición infantil del niño: .....

16. Puntúe del 1 al 10 la siguiente afirmación según el nivel de formación que usted considere que tiene enfermería (*) [Siendo 10 = Muy bien formada y 1 = Ninguna formación. Si usted no sabe o no desea contestar indíquelo con el valor 0]

- Nivel de formación de enfermería en cuanto a Salud Nutricional Infantil: .....

SECCIÓN 4: OBJETIVOS NUTRICIONALES Y HÁBITOS NUTRICIONALES

1. Indique dentro de cada tramo de edad el % de estos pacientes en los que usted trabaja o recomienda hábitos nutricionales (*)

- Entre 0-6 meses: .....
- Entre 6-12 meses: .....
- Entre 12-18 meses: .....
- Entre 18-24 meses: .....
- Entre 24-36 meses: .....

2. ¿A través de que forma/medios trabaja o recomienda hábitos nutricionales infantiles en la consulta? (*) [Marque tantas opciones como sea necesario]

☐ Materiales proporcionados por la Industria Farmacéutica
☐ Materiales proporcionados por las Instituciones
☐ Información que preparo yo mismo
☐ Lo hago verbalmente
☐ Recomiendo Websites
☐ Otros Indicar cuáles .....
☐ No recomiendo hábitos nutricionales infantiles

3. Puntúe del 1 al 10 cada una de las siguientes pautas para obtener unos buenos hábitos dietéticos según cada tramo de edad (*)
[Siendo 10 = Muy importante y 1 = Nada importante. Si el ítem lo considera NO relevante para ese tramo concreto de edad introduzca el valor 0]

	Entre 0-6 meses	Entre 6-12 meses	Entre 12-18 meses	Entre 18-24 meses	Entre 24-36 meses
Alimentación variada	.....	.....	.....	.....	.....
Comida elaborada, no preparada	.....	.....	.....	.....	.....
Realización de 5 comidas al día	.....	.....	.....	.....	.....
Introducción de alimentos con cuchara	.....	.....	.....	.....	.....
Respetar las horas de sueño	.....	.....	.....	.....	.....
Ejercicio físico	.....	.....	.....	.....	.....
Enseñar al niño a que coma solo	.....	.....	.....	.....	.....
Proteínas de animales al menos 3 veces a la semana	.....	.....	.....	.....	.....
Dar 5 piezas de fruta y verdura al día	.....	.....	.....	.....	.....
Lactancia materna	.....	.....	.....	.....	.....
Leche adaptada hasta los 36 meses	.....	.....	.....	.....	.....
Alimentación adaptada a las necesidades del niño (diferente a la del adulto, en cantidad, o composición)	.....	.....	.....	.....	.....
Otros	.....	.....	.....	.....	.....

▶ ▶ ▶

4. Indique a qué se refería en "otros" en la pregunta anterior

.....

5. Puntúe de 1 a 10 los siguientes factores para establecer las recomendaciones nutricionales en el niño (*) [Siendo 10 = Muy importante y 1 = Nada importante]

- Edad del niño: .....
- Peso/talla: .....
- Recomendaciones nacionales: .....
- Recomendaciones internacionales: .....
- Patologías del niño: .....
- Otros: .....

6. Indique a qué se refería en "otros" en la pregunta anterior

.....

7. Puntúe de 1 a 10 las siguientes recomendaciones nutricionales en pacientes entre 0-6 meses (*) [Siendo 10 = Muy importante y 1 = Nada importante]

- Lactancia materna : .....
- Leche de fórmula: .....
- Combinar leche materna con leche de fórmula: .....
- Lactancia a demanda: .....
- Suplemento de vitamina D: .....
- Introducción de cereales: .....
- Introducción de verduras: .....
- Polivitamínicos: .....
- Otros: .....

8. Indique a qué se refería en "otros" en la pregunta anterior

.....

9. Puntúe de 1 a 10 las siguientes recomendaciones nutricionales en pacientes entre 6-12 meses (*) [Siendo 10 = Muy importante y 1 = Nada importante]

- Mantener la lactancia materna : .....
- Dar sólo leche de fórmula: .....
- Combinar leche materna con leche de fórmula: .....
- Introducción de cereales: .....
- Puré de fruta, verduras: .....
- Incorporación de alimentos ricos en hierro: .....
- Introducir los alimentos uno a uno: .....
- Suplementos de hierro: .....
- Introducción de alimentos ricos en proteínas: .....
- Alimentos con textura para iniciar la masticación: .....
- Otros: .....

10. Indique a qué se refería en "otros" en la pregunta anterior

.....

11. Puntúe de 1 a 10 las siguientes recomendaciones nutricionales en pacientes entre 12-18 meses (*) [Siendo 10 = Muy importante y 1 = Nada importante]

- Completar la introducción de alimentos: .....
- Crear hábitos saludables: .....
- Que el niño aprenda a comer solo: .....
- Eliminar el biberón: .....
- Alimentación variada: .....
- Introducción de leche de vaca: .....
- Introducción leche de crecimiento: .....
- Mantener leche de fórmula de continuación: .....
- Control de las cantidades ingeridas: .....
- Control de azúcares: .....
- Control de sal: .....
- Control de la cantidad de proteínas ingeridas: .....
- Otros: .....

12. Indique a qué se refería en "otros" en la pregunta anterior

.....

13. Puntúe de 1 a 10 las siguientes recomendaciones nutricionales en pacientes entre 18-24 meses (*) [Siendo 10 = Muy importante y 1 = Nada importante]

- Completar la introducción de alimentos: .....
- Crear hábitos saludables: .....
- Que el niño aprenda a comer solo: .....
- Eliminar el biberón: .....
- Alimentación variada: .....
- Introducción de leche de vaca: .....
- Introducción leche de crecimiento: .....
- Mantener leche de fórmula de continuación: .....
- Control de las cantidades ingeridas: .....
- Control de azúcares: .....
- Control de sal: .....
- Control de la cantidad de proteínas ingeridas: .....
- Otros: .....

14. Indique a qué se refería en "otros" en la pregunta anterior

.....

15. Puntúe de 1 a 10 las siguientes recomendaciones nutricionales en pacientes entre 24-36 meses (*) [Siendo 10 = Muy importante y 1 = Nada importante]

- Alimentación variada: .....
- Respetar las 5 comidas al día: .....
- Recomendar suplementos alimenticios: .....
- Introducción de leche de vaca: .....
- Introducción leche de crecimiento: .....
- Control de las cantidades ingeridas: .....
- Control de azúcares: .....
- Control de sal: .....
- Control de la cantidad de proteínas ingeridas: .....
- Otros: .....

16. Indique a qué se refería en "otros" en la pregunta anterior

.....

▶ ▶ ▶

17. Indique la media de edad en meses en que recomienda la introducción de los siguientes alimentos: (*) [Si no recomienda el alimento en una edad determinada ponga 99]

	Edad en meses
Leche de Inicio (si no es posible la lactancia materna)	.....
Leche de Continuación (si no es posible la lactancia materna)	.....
Leche de Crecimiento	.....
Leche de vaca	.....
Cereales sin gluten	.....
Cereales con gluten	.....
Fruta	.....
Verduras	.....
Carne de ave	.....
Carne de vacuno	.....
Carne de cerdo	.....
Pescado blanco	.....
Pescado azul	.....
Yogures	.....
Quesos y otros derivados lácteos	.....
Legumbres	.....
Huevos	.....
Azúcar	.....
Trozos de pan	.....
Golosinas	.....
Refrescos	.....
Bollería	.....

SECCIÓN 5: RECOMENDACIONES EN SALUD NUTRICIONAL

HTML Information Text

En las siguientes preguntas indique qué **recomendaciones** da en su consulta sobre salud nutricional infantil, los **materiales de apoyo utiliza** para dar estas recomendaciones y los que **necesitaría.** Indicando también el **rango de edad** a los cuáles realiza la recomendación.

Nota: Recuerde que los rangos de edad empleados en este estudio son:

– Entre 0-6 meses – Entre 6-12 meses – Entre 12-18 meses – Entre 18-24 meses – Entre 24-36 meses – Más de 36 meses

1. Mensaje N.º 1 sobre Salud Nutricional Infantil (*) [Si no proporciona ningún mensaje ponga ND]
- Mensaje: .....
- Material de apoyo que doy a este mensaje: .....
- Material de apoyo que necesitaría para este mensaje: .....
- Rango de edad (en meses) en el que realiza la recomendación: .....

2. Mensaje N.º 2 Salud Nutricional Infantil (*) [Si no proporciona ningún mensaje más ponga ND]
- Mensaje: .....
- Material de apoyo que doy a este mensaje: .....
- Material de apoyo que necesitaría para este mensaje: .....
- Rango de edad (en meses) en el que realiza la recomendación: .....

3. Mensaje N.º 3 Salud Nutricional Infantil (*) [Si no proporciona ningún mensaje más ponga ND]
- Mensaje: .....
- Material de apoyo que doy a este mensaje: .....
- Material de apoyo que necesitaría para este mensaje: .....
- Rango de edad (en meses) en el que realiza la recomendación: .....

4. Mensaje N.º 4 Salud Nutricional Infantil (*) [Si no proporciona ningún mensaje más ponga ND]
- Mensaje: .....
- Material de apoyo que doy a este mensaje: .....
- Material de apoyo que necesitaría para este mensaje: .....
- Rango de edad (en meses) en el que realiza la recomendación: .....

5. Mensaje Nº 5 Salud Nutricional Infantil (*) [Si no proporciona ningún mensaje más ponga ND]
- Mensaje: .....
- Material de apoyo que doy a este mensaje: .....
- Material de apoyo que necesitaría para este mensaje: .....
- Rango de edad (en meses) en el que realiza la recomendación: .....

Valenciana y Murcia) y un 14% de zona norte (Galicia, Asturias, Cantabria y País Vasco). Los encuestados refirieron atender una media de 588 pacientes al mes. La media de años de experiencia y ámbito de trabajo por zona geográfica se detalla en la figura 2.

Los participantes en el estudio estuvieron mayoritariamente de acuerdo en que una correcta nutrición entre los 0 y 3 años previene enfermedades y futuros problemas, asegurando un crecimiento adecuado (aseveración puntuada con 9,4 sobre 10, siendo 10 la máxima puntuación posible).

Importancia de las cuestiones nutricionales en la consulta diaria

Los niños de 0 a 12 meses y de 12 a 24 meses generan un número de consultas (espontáneas o programa-

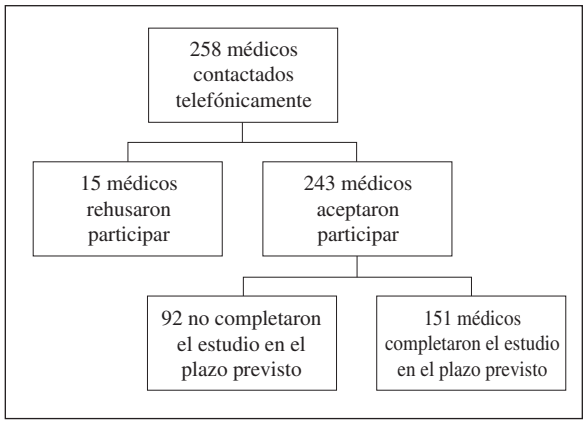


Fig. 1.—Resultado del estudio en relación al procedimiento de muestreo.

das) significativamente superior que los niños mayores de 24 meses (p = 0,004 y p < 0,0001 respectivamente, fig. 3). En un 17% de los casos el motivo de consulta es una preocupación de índole nutricional, según lo referido por los encuestados. Este porcentaje se reduce de forma significativa con el incremento de edad (p < 0,0001), pasando de un máximo de 22% para el tramo 0-6 meses de edad a un 11% para el de 24 a 36 meses (fig. 4).

La frecuencia de los controles nutricionales programados por parte del pediatra es también diferente según la edad del niño, siendo de media mensual para los de 0 a 3 meses, cada 2 ó 3 meses para 3 a 12 meses de edad y reduciéndose posteriormente a dos veces al año o menos para niños de 24-36 meses de edad. La frecuencia de estas revisiones es superior en niños que tienen proble-

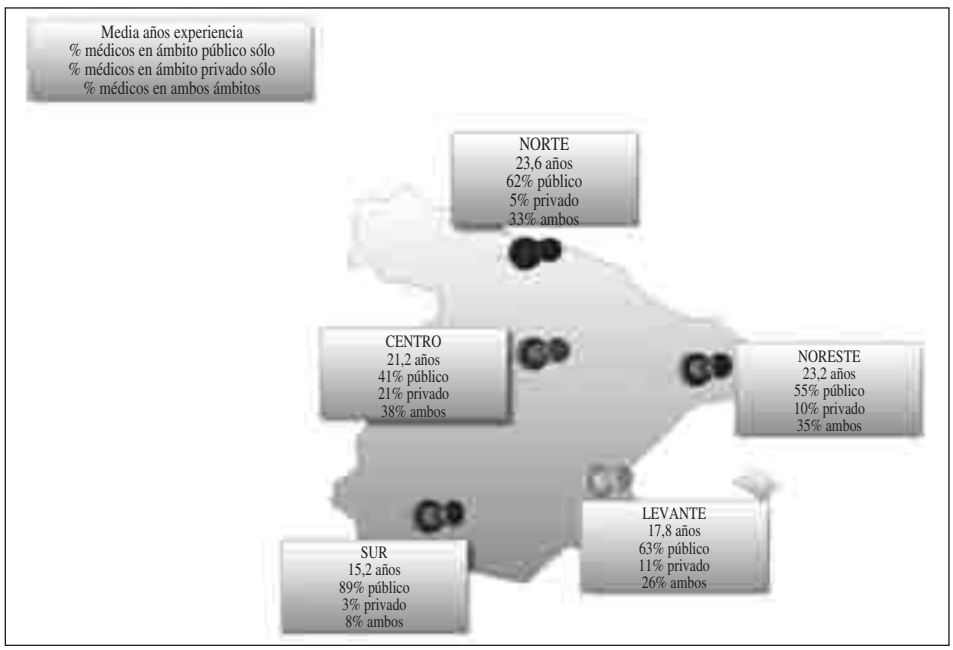


Fig. 2.—Media de años de experiencia y ámbito de trabajo de los médicos participantes por zona geográfica.

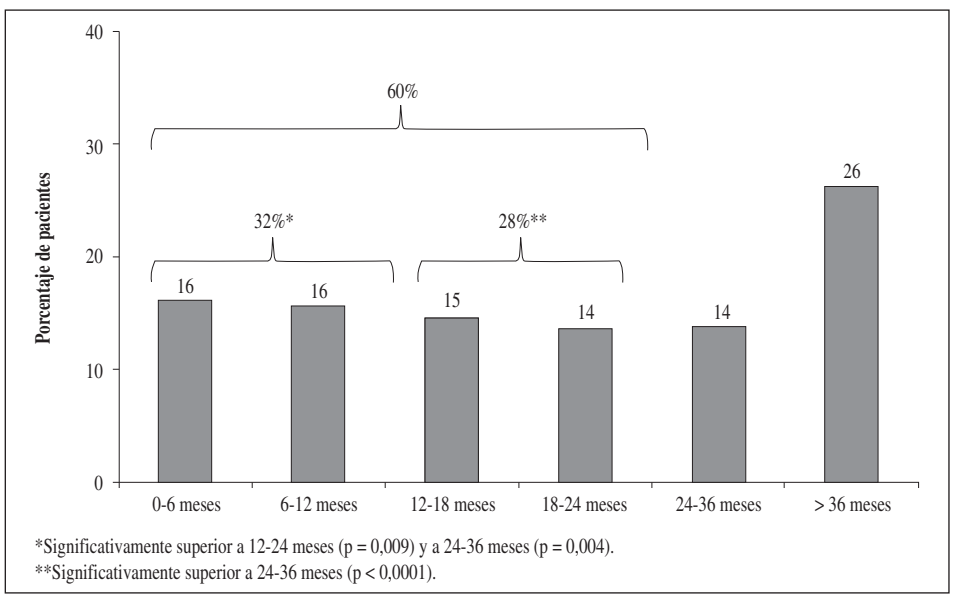


Fig. 3.—Porcentaje de pacientes atendidos en la consulta según tramo de edad.

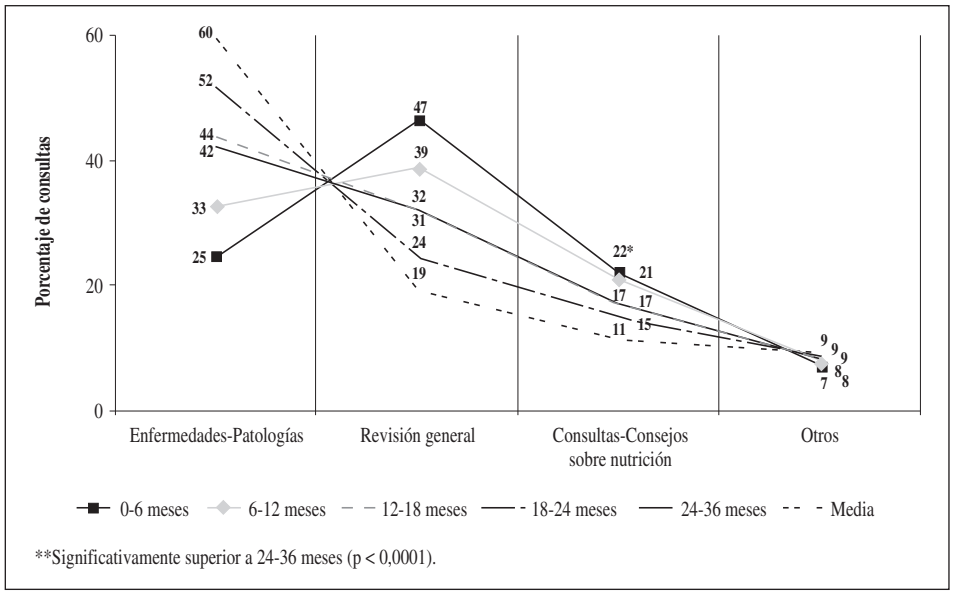


Fig. 4.—Porcentaje de consultas según temática por tramos de edad.

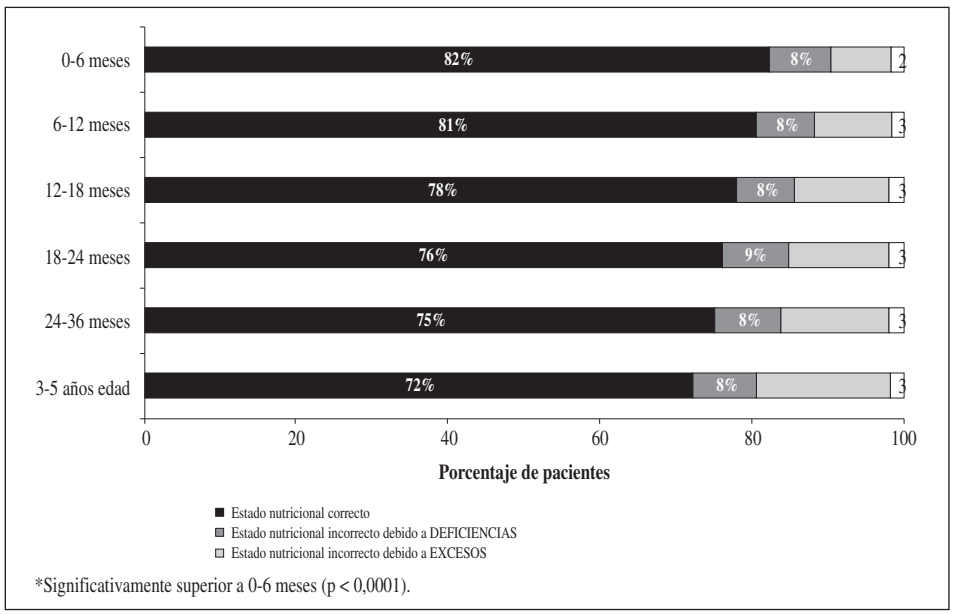


Fig. 5.—Porcentaje de pacientes según el estado nutricional por tramo de edad.

mas nutricionales o en aquéllos en los que los padres tienen consultas o preocupaciones al respecto.

Los pediatras participantes puntuaron con 8,8 puntos (en una escala del 1 al 10, siendo 10 la máxima puntuación posible) la relevancia de la salud nutricional en su consulta y con 8,8 puntos su relevancia en la especialidad de pediatría.

Desórdenes nutricionales en niños menores de 3 años

Las dos herramientas más utilizadas por los pediatras para establecer la salud nutricional son la antropometría (97%) y la encuesta de hábitos alimentarios (88%), según lo referido en este estudio.

Los pediatras encuestados consideran que la mayoría de los niños tiene un estado nutricional correcto. Su percepción es que las alteraciones del estado nutricional aumentan con la edad, siendo los problemas nutricionales por exceso proporcionalmente más importantes que la desnutrición. La prevalencia percibida de malnutrición por exceso fue mayor en el grupo de edad superior a 3 años (fig. 5).

Al ser preguntados de forma abierta sobre el principal problema relacionado con la salud nutricional encontrado en la consulta, las respuestas más frecuentes por grupos de edad fueron (tabla I):

- De 0 a 6 meses: la escasa ganancia de peso, mencionada por un 25% de los médicos encuestados, y relacionada por un 27% de ellos con la baja

Tabla I
Principal problema relacionado con la salud nutricional (ordenado de mayor a menor porcentaje)

Grupo de edad	*Respuesta*	*n (% pediatras)*
0-6 meses	Escasa ganancia ponderal	37 (25%)
	Otros	18 (12%)
	Intolerancias y alergias	15 (10%)
	Vómitos	13 (9%)
	Deficiencia o abandono de la lactancia	13 (9%)
	Déficit nutricional	11 (7%)
	Obesidad, exceso de peso	11 (7%)
	Cólico lactante	11 (7%)
	No aceptación de nuevos alimentos	7 (5%)
	Alimentación artificial	5 (3%)
	Ninguno	5 (3%)
	Problemas gastrointestinales	5 (3%)
6-12 meses	Falta de hierro	47 (31%)
	Escasa ganancia ponderal	31 (21%)
	Obesidad	23 (15%)
	Diarrea	20 (13%)
	Otros	17 (11%)
	Intolerancias y alergias	14 (9%)
	Incorporación de alimentos	13 (9%)
	Rechazo de alimentos	11 (7%)
	Malos hábitos	8 (5%)
	Estreñimiento	8 (5%)
	Gastroenteritis	5 (3%)
	Ninguno	3 (2%)
12-18 meses	Otros	30 (20%)
	Malnutrición	26 (17%)
	Sobrepeso, obesidad	22 (15%)
	Inapetencia del alimento	19 (13%)
	Escasa ganancia ponderal	18 (12%)
	Intolerancias y alergias	9 (6%)
	Ferropenia	8 (5%)
	Alteraciones digestivas	7 (5%)
	Diarrea	6 (4%)
	Estreñimiento	6 (4%)
18-24 meses	Otros	35 (23%)
	Sobrepeso	29 (19%)
	Malnutrición	26 (17%)
	Inapetencia	21 (15%)
	Escasa ganancia ponderal	16 (11%)
	Anemia, ferropenia	8 (6%)
	Diarrea	7 (5%)
	Anorexia	6 (4%)
24-36 meses	Otros	50 (33%)
	Sobrepeso	38 (25%)
	Alteraciones nutricionales	13 (9%)
	Anemia	11 (7%)
	Escasa ganancia ponderal	11 (7%)
	Diarrea o estreñimiento	11 (7%)
	Gastroenteritis	9 (6%)
	Inapetencia	8 (5%)

frecuencia de alimentación mediante lactancia materna.

- De 6 a 12 meses: la deficiencia de hierro (31%) y la escasa ganancia de peso (21%).
- De 12 a 18 meses: la desnutrición (17%) y la obesidad y el sobrepeso (15%).
- De 18 a 24 meses: la obesidad y el sobrepeso (19%) y la desnutrición (17%).
- De 24 a 36 meses: la obesidad y el sobrepeso (25%).

Sobre las carencias nutritivas, en pregunta abierta los participantes refirieron la deficiencia de hierro y de vitaminas como las de mayor prevalencia percibida en todos los tramos de edad de 0 a 3 años. En la figura 6 se detalla el porcentaje de médicos que perciben una deficiencia de hierro y de vitaminas según el tramo de edad. Este hecho fue puesto en relación con una escasa ingesta de alimentos ricos en hierro, el bajo consumo en frutas y la escasa exposición a la luz solar. Los datos detallados se presentan en la tabla II.

Respecto a las alteraciones nutricionales por exceso (tabla III), los pediatras participantes reportaron que el exceso en la ingesta de carbohidratos es el más prevalente hasta los 18 meses de edad y el exceso en la ingesta de lípidos el más presente a partir de esta edad (fig. 7). La sobrealimentación es la principal causa referida de estos excesos. El 77% consideró, en pregunta abierta, que la obesidad será en el futuro la principal consecuencia asociada a una nutrición incorrecta en los primeros años de vida.

Respecto a la evolución futura de los desórdenes nutricionales, el 89% de los pediatras consideró que aumentarán. En referencia a los desórdenes nutricionales por defecto, sólo el 19% de los encuestados cree que aumentarán, mientras que el resto de encuestados considera que se mantendrán igual (52%) o se reducirán (29%).

Participantes en la nutrición infantil y sus roles

Los encuestados consideran que los padres (con una puntuación de 9,5 sobre 10) son los actores principales en la salud nutricional de los niños entre 0 y 3 años, seguidos de los pediatras (8,8 sobre 10). Esta importancia del papel de los padres queda también reflejada en la percepción referida por los participantes de que las principales causas de malnutrición infantil son los malos hábitos nutricionales de los padres, la falta de tiempo de los padres para cuestiones nutricionales y, consecuentemente, el gran uso de comida preparada (fig. 8).

En opinión de los encuestados, la preocupación de los padres respecto a la nutrición se reduce de forma significativa ($p < 0,0001$) con la edad, siendo máxima en el tramo de 0 a 6 meses (9,4 sobre 10) y mínima en el tramo 24 a 36 meses (6,2 sobre 10). Los pediatras participantes en el estudio tienen la percepción de que los temas consultados por los padres son también diferentes según la edad, siendo los aspectos que originan mayor preocupación la introducción de la leche de fórmula y de nuevos alimentos, así como las recomendaciones sobre cantidades, para niños entre 0 y 12 meses de edad y la pérdida de apetito o la escasa ganancia de peso a partir de esa edad.

El 48% de los pediatras participantes consideró que, en la actualidad, las enfermeras pueden tener un

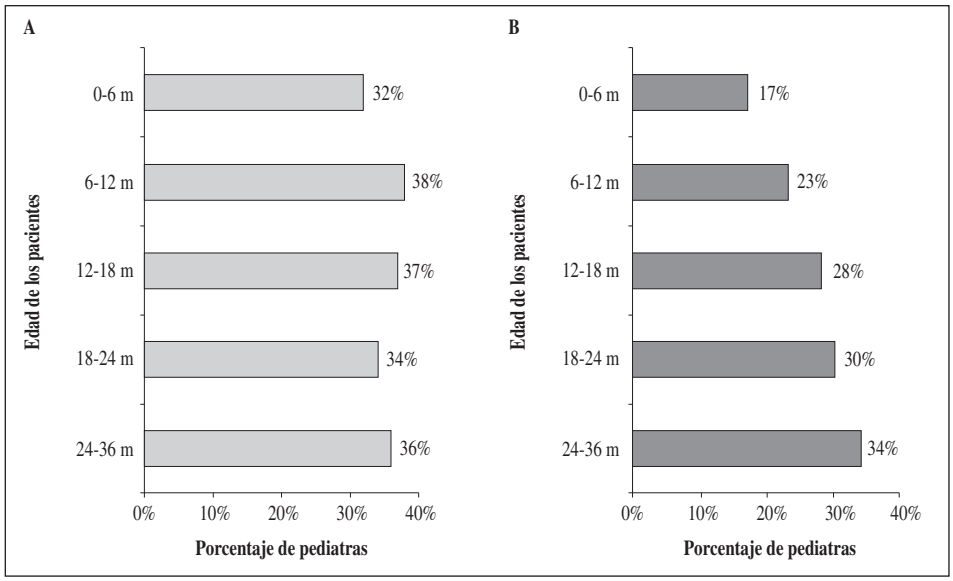


Fig. 6.—Deficiencia de A) hierro y B) vitaminas percibidas por los pediatras (n = 151).

Tabla II
Deficiencias de nutrientes más prevalentes para niños de 0 a 3 años según la opinión del pediatra

Tramos de edad	*Deficiencias*								
	Hierro	*Vit*	*Prot*	*Ninguna*	*CH*	*Fibra*	*Min*	*Calcio*	*Otras*
0-6 meses	32%	17%	5%	32%	2%	0-1%	3%	3%	6%
6-12 meses	38%	23%	8%	24%	4%	2%	3%	3%	15%
12-18 meses	37%	28%	14%	15%	2%	8%	7%	5%	9%
18-24 meses	34%	30%	14%	10%	3%	11%	7%	6%	14%
24-36 meses	36%	34%	12%	11%	2%	11%	7%	7%	15%

Vit: Vitaminas; Prot: Proteínas; CH: Carbohidratos; Min: Minerales.
Datos expresados como % de pediatras que las señaló. N = 151 pediatras.

Tabla III
Excesos de nutrientes más prevalentes para niños de 0 a 3 años según la percepción del pediatra

Tramos de edad	*Exceso*								
	CH	*Lip*	*Prot*	*Dvds. lácteos*	*Vit*	*Azúcares*	*Colesterol*	*Otros*	*Ninguno*
0-6 meses	19%	8%	6%	4%	14%	2%	0%	12%	46%
6-12 meses	30%	9%	11%	6%	0-1%	5%	0-1%	15%	34%
12-18 meses	33%	26%	12%	7%	0-1%	12%	3%	17%	16%
18-24 meses	32%	36%	15%	5%	0%	15%	5%	19%	11%
24-36 meses	32%	47%	11%	2%	0-1%	16%	9%	18%	10%

CH: Carbohidratos; Lip: Lípidos; Prot: Proteínas; Dvds.: Derivados; Vit: Vitaminas; Colest: Colesterol.
Datos expresados como % de pediatras que los señaló. N = 151 pediatras.

papel en las funciones de monitorización de la salud nutricional, siendo las tareas delegadas en este colectivo profesional la antropometría (46%), la información sobre alimentación y nutrición (39%), las pautas sobre la introducción de alimentos (33%), la educación sobre salud nutricional (24%), el control del peso (22%), el estudio de hábitos (15%), guías sobre lactancia (14%) y otros (6%).

Fuentes de información utilizadas por los pediatras en temas de salud nutricional

Para actualizarse respecto a salud nutricional, el 66% de los médicos entrevistados declaró usar guías clínicas de referencia, mayoritariamente materiales impresos y guías o protocolos científicos de las sociedades médicas; el 75% utiliza las webs de las socieda-

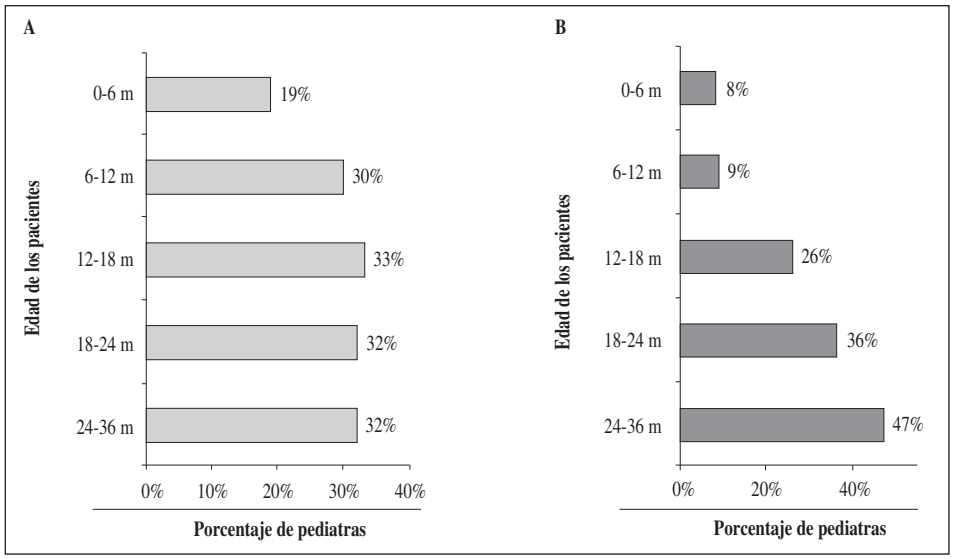


Fig. 7.—Exceso de A) carbohidratos y B) lípidos percibidos por los pediatras (n = 151).

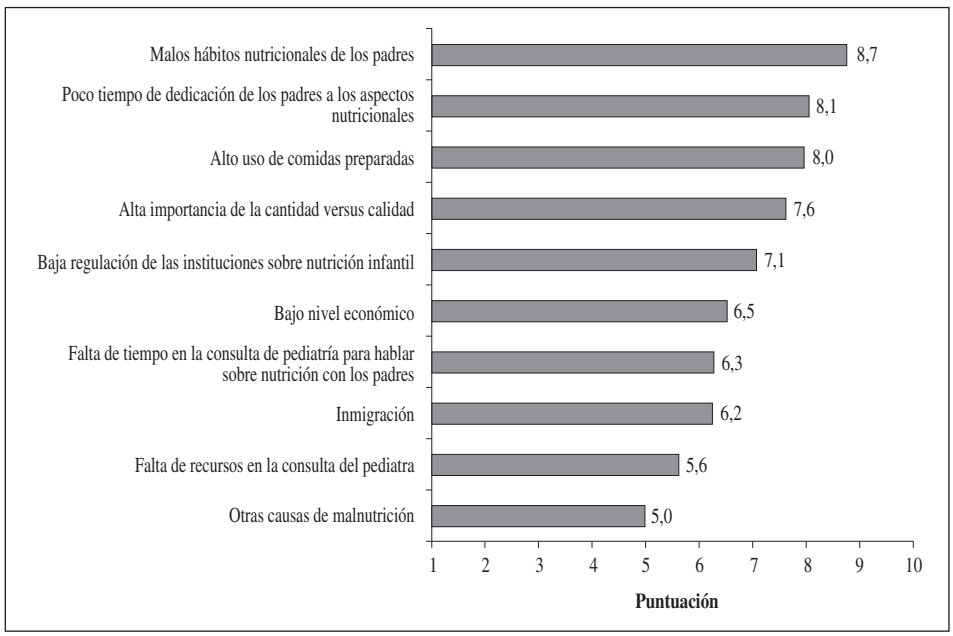


Fig. 8.—Causas principales de la malnutrición infantil.

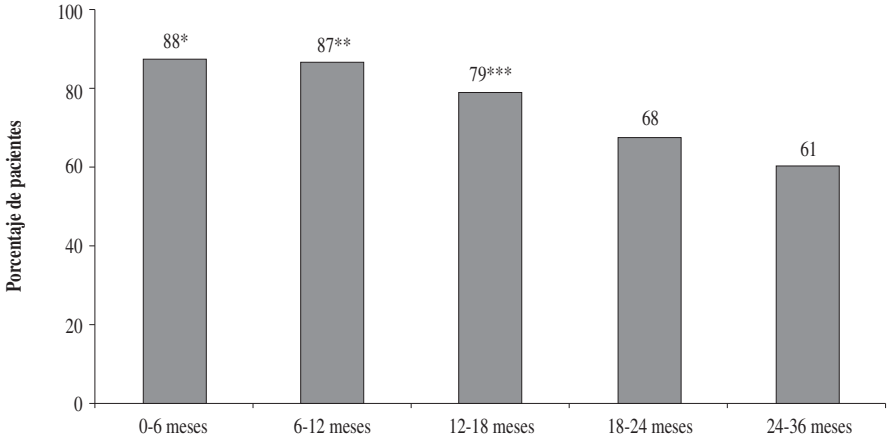
des médicas nacionales y el 68% sus revistas o publicaciones regulares. La principal necesidad transmitida por los pediatras entrevistados se refiere a materiales informativos para padres (71%) y material informativo (50%) y cursos online (63%) para profesionales.

Recomendaciones ofrecidas por el pediatra sobre salud nutricional

Los pediatras participantes realizan recomendaciones nutricionales a un porcentaje significativamente superior de pacientes de 0-6 meses ($p < 0,0001$), 6-12 meses ($p < 0,0001$) y 12-18 meses ($p=0,001$) que a pacientes a partir de 18 meses de edad (fig. 9). El 89% realiza estas recomendaciones de forma verbal y el 77% a través de materiales que han preparado ellos mismos. Los factores que más influyen en las recomendaciones nutricionales realizadas por el pediatra son la edad y la presencia de alguna patología de base.

En opinión de los participantes, los aspectos más importantes para obtener unos buenos hábitos alimentarios son, según el tramo de edad, los siguientes (tabla IV):

- En el grupo 0 a 6 meses: la promoción de lactancia materna, ofrecer alimentación adaptada a las necesidades del niño y respetar el tiempo de sueño.
- En el grupo 6 a 12 meses: ofrecer alimentación adaptada a las características del niño, respetar el tiempo de sueño y la introducción de comida de cuchara.



*Significativamente superior a 12-18 meses (p = 0,009); significativamente superior a 18-24 meses (p < 0,0001); significativamente superior a 24-36 meses (p < 0,0001).
**Significativamente superior a 12-18 meses (p = 0,016); significativamente superior a 18-24 meses (p < 0,0001); significativamente superior a 24 -36 meses (p < 0,0001).
***Significativamente superior a 18-24 meses (p = 0,001); significativamente superior a 24-36 meses (p < 0,0001).

Fig. 9.—Porcentaje de pacientes en los que el pediatra realiza recomendaciones de hábitos nutricionales por tramo de edad.

- En el grupo 12 a 18 meses: la introducción de una alimentación variada, respetar el tiempo de sueño, ofrecer una alimentación adaptada a las características del niño y la introducción de comida de cuchara.
- En el grupo 18 a 36 meses: la introducción de una alimentación variada, respetar el tiempo de sueño, asegurar 5 piezas de fruta y verduras al día, promover la autoalimentación y administrar proteínas animales al menos 3 veces por semana.

Discusión

Aunque son muchos los estudios publicados respecto a los problemas asociados a los desórdenes alimentarios en las edades tempranas y sus consecuencias[2,10-14], no se dispone de información sobre la percepción del pediatra respecto a las cuestiones y recomendaciones nutricionales en su consulta diaria. Éste es el primer estudio publicado en nuestro país respecto a la opinión de los pediatras en relación al estado nutricional y a las recomendaciones de ingesta en la población menor de 3 años.

Al diversificar la alimentación y progresar las habilidades y autonomía para su consumo, el niño va iniciando sus hábitos nutricionales, que se establecerán como definitivos durante estos primeros años y serán difíciles de modificar después[15-17]. Sólo por esta razón, esta etapa debe considerarse crucial como condicionante de la salud. A medida que el niño avanza en edad se reduce la frecuencia de visitas programadas dentro del control del niño sano y aumenta la proporción de consultas espontáneas motivadas por situaciones patológicas. Esto tiene como consecuencia lógica un menor número de oportunidades para tratar cuestiones nutricionales dentro de la consulta. El presente trabajo ha puesto de manifiesto que, a pesar de que los pediatras encuestados se mostraron conscientes de la importancia de la salud nutricional, su percepción es que a partir de los 2 años este aspecto sólo supone un pequeño porcentaje (11%) de las consultas. Esto señala un gran potencial de actuación, ya que esa relación más intensa con la familia y control más frecuente de los niños en las primeras etapas supone un momento en el que es más fácil reconocer factores familiares o sociales favorecedores de malas prácticas alimentarias y por tanto es un momento en el que el pediatra puede influir más en el inicio de hábitos de vida saludables[18,19]. Es más, la forma en que está organizado el trabajo en los centros de salud está pensada para ejercer estas actividades de forma constante a lo largo de la infancia y a veces mediante el desarrollo de programas específicos[20]; es decir, mediante actividades de supervisión, promoción de la salud y prevención de la enfermedad a las que "teóricamente" los profesionales de Atención Primaria debieran dedicar un 40% de su tiempo de consulta.

Además, desde la estimación de un porcentaje medio del 17% de las consultas motivadas por preocupaciones nutricionales en los primeros tres años, esta preocupación va disminuyendo desde el 22% en los primeros 6 meses hasta el 11% en el tercer año de vida. Por tanto, también la oportunidad de fomentar una nutrición adecuada y de iniciar a los niños en buenos hábitos de alimentación va siendo menor con el paso de los meses, especialmente a partir de los primeros dos años, cuando la mayoría de los pediatras participantes en el estudio reducen a dos o menos los controles anuales.

Resulta llamativo que el consejo nutricional por parte del pediatra no se haga en el 100% de los pacientes, ni siquiera en el caso de los lactantes; y que, si nos atenemos a la opinión de los pediatras encuestados,

Tabla IV

Aspectos más importantes para obtener buenos hábitos alimentarios (ordenados de mayor a menor valoración)

Grupo de edad	*Respuesta*	*n (% pediatras)*	*Valoración del 1 al 10*
3-6 meses	Lactancia materna	150 (99%)	9,8
	Alimentación adaptada a las necesidades del niño	112 (74%)	9,3
	Respetar las horas de sueño	137 (91%)	8,5
	Realización de 5 comidas al día	109 (72%)	6,9
	Comida elaborada, no preparada	94 (62%)	6,7
	Leche adaptada hasta los 36 meses	88 (58%)	6,7
	Introducción de alimentos con cuchara	99 (66%)	5,5
	Otros	12 (8%)	4,8
	Alimentación variada	89 (59%)	4,5
	Dar 5 piezas de fruta y verdura al día	66 (44%)	3,6
	Proteínas de animales al menos 3 veces a la semana	62 (41%)	3,6
	Ejercicio físico	66 (44%)	2,7
	Enseñar al niño a que coma solo	52 (34%)	2,2
6-12 meses	Alimentación adaptada a las necesidades del niño (diferente a la del adulto, en cantidad, o composición)	138 (91%)	9,2
	Respetar las horas de sueño	145 (96%)	9,0
	Introducción de alimentos con cuchara	146 (97%)	8,8
	Alimentación variada	141 (93%)	8,2
	Realización de 5 comidas al día	133 (88%)	8,2
	Comida elaborada, no preparada	134 (89%)	8,2
	Lactancia materna	145 (96%)	8,1
	Leche adaptada hasta los 36 meses	112 (74%)	7,9
	Proteínas de animales al menos 3 veces a la semana	135 (89%)	7,8
	Dar 5 piezas de fruta y verdura al día	116 (77%)	7,1
	Otros	11 (7%)	5,8
	Enseñar al niño a que coma solo	96 (64%)	5,1
	Ejercicio físico	90 (60%)	4,4
12-18 meses	Alimentación variada	146 (97%)	9,4
	Respetar las horas de sueño	143 (95%)	9,1
	Alimentación adaptada a las necesidades del niño (diferente a la del adulto, en cantidad, o composición)	144 (95%)	9,1
	Introducción de alimentos con cuchara	135 (89%)	9,0
	Proteínas de animales al menos 3 veces a la semana	144 (95%)	8,7
	Dar 5 piezas de fruta y verdura al día	141 (93%)	8,7
	Realización de 5 comidas al día	138 (91%)	8,4
	Comida elaborada, no preparada	143 (95%)	8,3
	Leche adaptada hasta los 36 meses	120 (79%)	8,1
	Enseñar al niño a que coma solo	136 (90%)	7,8
	Ejercicio físico	125 (83%)	6,7
	Otros	13 (9%)	6,2
	Lactancia materna	114 (75%)	5,9
18-24 meses	Alimentación variada	146 (97%)	9,6
	Respetar las horas de sueño	144 (95%)	9,1
	Dar 5 piezas de fruta y verdura al día	142 (94%)	9,0
	Enseñar al niño a que coma solo	145 (96%)	8,9
	Proteínas de animales al menos 3 veces a la semana	144 (95%)	8,9
	Introducción de alimentos con cuchara	128 (85%)	8,8
	Alimentación adaptada a las necesidades del niño (diferente a la del adulto, en cantidad, o composición)	145 (96%)	8,5
	Realización de 5 comidas al día	138 (91%)	8,5
	Comida elaborada, no preparada	143 (95%)	8,3
	Ejercicio físico	132 (87%)	7,7
	Leche adaptada hasta los 36 meses	123 (81%)	7,5
	Otros	12 (8%)	6,2
	Lactancia materna	91 (60%)	4,1
24-36 meses	Alimentación variada	146 (97%)	9,7
	Enseñar al niño a que coma solo	144 (95%)	9,5
	Dar 5 piezas de fruta y verdura al día	144 (95%)	9,3
	Respetar las horas de sueño	144 (95%)	9,2
	Proteínas de animales al menos 3 veces a la semana	146 (97%)	9,0
	Ejercicio físico	138 (91%)	8,7
	Introducción de alimentos con cuchara	128 (85%)	8,6
	Realización de 5 comidas al día	137 (91%)	8,4
	Comida elaborada, no preparada	143 (95%)	8,3
	Alimentación adaptada a las necesidades del niño (diferente a la del adulto, en cantidad, o composición)	145 (96%)	8,1
	Otros	11 (7%)	7,5
	Leche adaptada hasta los 36 meses	125 (83%)	7,0
	Lactancia materna	71 (47%)	3,2

este porcentaje se reduzca de forma importante en niños de 24-36 meses, entre los que un 39% no recibe ningún consejo nutricional. Esta distancia entre la preocupación manifestada y la realidad de la práctica clínica sólo cabría entenderla como una declaración de la excesiva dedicación a actividades asistenciales no programadas, solicitadas espontáneamente por la familia y con una escasa intervención de tipo educativo, tal como ya ha sido referido[21], y que representa, además, una pérdida de efectividad en la función preventiva del pediatra y la introducción de un importante factor de variabilidad en el desarrollo del ejercicio profesional.

Es interesante comprobar que los pediatras consideran el exceso de peso como principal problema de salud nutricional ya a partir del año y que reconocen su relación con las prácticas alimentarias incorrectas y de inicio precoz. El aumento en la tasa de sobrepeso y obesidad observado en las últimas décadas se ha relacionado con el mantenimiento de malos hábitos alimentarios y de estilo de vida desde edades tempranas[19,22], tendencia que no parece haber mejorado en épocas recientes.

Algunos autores han relacionado la excesiva ganancia de peso con la ingesta inadecuada de determinados nutrientes, especialmente de energía y de proteínas, desde etapas iniciales e incluso con la calidad de la nutrición intraútero[23,24].

Los pediatras encuestados percibieron la escasa ganancia ponderal como uno de los principales problemas nutricionales en el primer año de vida, mientras que a partir de los 18 meses el sobrepeso y la obesidad pasan a ocupar el primer lugar. Durante el primer año de vida las características de la alimentación del lactante, su ritmo de crecimiento y la frecuencia de controles nutricionales, son muy diferentes a las de los niños mayores de esta edad. Esto podría influir en la percepción de los pediatras encuestados sobre las ingestas y requerimientos nutricionales en los diferentes grupos de edad, aunque este estudio no permite aclarar este punto. En ese sentido, algunos estudios han relacionado la nutrición en los primeros meses de vida y la cantidad de ingesta proteica con el exceso de ganancia de peso en edades posteriores[23,25].

A la vista de la presente encuesta, cabe preguntarse si los pediatras disponen de suficiente información sobre tal relación y la importancia de su intervención nutricional temprana. En esto también puede influir el hecho de que algunos trabajos muestran que en el niño en edad escolar, en el adolescente y en el adulto el seguimiento de una dieta hiperproteica pudiera prevenir el aumento de peso. En el mismo sentido, es destacable que en el presente estudio el exceso de ingesta proteica no sea percibido como un desorden importante, mientras que el excesivo consumo de lípidos y carbohidratos sí sea referido como un problema.

La opinión respecto a la deficiencia de hierro se corresponde con las observaciones clínicas y estudios epidemiológicos[26], que señalan la ferropenia como la alteración nutricional más prevalente a nivel mundial. Respecto a la deficiencia de vitaminas expresada de forma general, puede estar relacionada más concretamente con el déficit de vitamina D, muy extensamente comentado en la bibliografía reciente y que puede haber generado una mayor preocupación en el pediatra en los últimos años[27].

Los actores principales en la nutrición infantil, según los encuestados, son los padres y los propios pediatras. Esto coincide con lo señalado en los principales documentos sobre intervención educativa en la infancia para la prevención de enfermedades relacionadas con la nutrición, en las que se señala que el esfuerzo principal debería realizarse de forma integrada en el ámbito familiar desde edades tempranas[28]. En este sentido, los pediatras parecen defender la idea de desarrollar la educación familiar en la consulta, favoreciendo hábitos saludables y modificando prácticas erróneas. Igualmente, sería importante hacer los consejos individualizados y adaptados a cada familia, teniendo presente, además, que los hábitos alimentarios se desarrollan con el tiempo y los mensajes tendrán que adecuarse a cada momento[24].

Aunque esta tarea educativa no compete exclusivamente al pediatra, en él recae la labor de transmisión de mensajes con base científica contrastada que constituyan una auténtica educación para la salud. Es significativo que tres de cada cuatro pediatras encuestados utilicen internet y las páginas web institucionales de las sociedades profesionales como fuentes principales de información, tanto en lo que se refiere a la actualización de sus conocimientos sobre nutrición como al uso de recursos disponibles on-line para entregar a los padres. Esto pudiera interpretarse como una demanda real de los profesionales, que estaría mostrando un amplio campo de trabajo al que debiera prestarse mayor atención. De hecho, la mayoría de las consultas pediátricas están ahora informatizadas y el acceso inmediato a la información que se pueda precisar en un momento dado está desplazando a la consulta de revistas y publicaciones regulares en papel[29]. En el caso de las familias, una información nutricional que se oriente hacia el aprendizaje de unos hábitos alimentarios saludables, apoyándose en conocimientos científicos y que tenga como objetivo la promoción de la salud del individuo y de la comunidad debe considerarse como un objetivo deseable[30,31]. No puede olvidarse que la mayoría de la población accede regularmente a internet; además, 8 de cada 10 usuarios lo hacen para consultar información sobre problemas de salud, y entre ellos más de la mitad en busca de consejos dietéticos y de información nutricional[32,33]. Dentro de este marco, el pediatra general debería liderar estas acciones y reclamar un protagonismo principal, ya que la responsabilidad en este tema es suya más que del pediatra especialista en nutrición. Lógicamente, esto pasa por una adecuada formación del profesional médico, que incluya el mantenimiento y puesta al día de los conocimientos a través de las diversas herramientas disponibles actualmente.

La participación de otros actores en el proceso educativo familiar merece una consideración especial, sobre todo en lo referente al personal de enfermería.

La formación pediátrica específica, reglada, controlada y reconocida del personal enfermero es una obligación relacionada con la exigencia de calidad asistencial, tanto en el ámbito hospitalario como en el centro de salud[34]. En el medio ambulatorio recae sobre estos profesionales gran parte del programa de vacunaciones y del desarrollo del programa del niño sano, que integra contenidos conjuntos pediatra/profesional de enfermería de gran responsabilidad dentro de las actividades preventivas y de educación para la salud. Su relación con los padres es regular y a veces de gran poder de influencia. Sin embargo, su preparación es variable, constituyendo un colectivo sumamente heterogéneo en sus conocimientos, y su preparación técnica sigue siendo a veces casual, poco uniforme y deficiente[35]. Al tema de la participación de los pediatras en el desarrollo de la enfermería pediátrica debería dársele la mayor importancia. El colectivo enfermero tendría que demandar el reconocimiento de este campo profesional, la estabilidad en su dedicación y el valor de sus funciones dentro del sistema asistencial; pero reclamar, además, una formación más competente, continuada y del mayor nivel posible.

En suma, este trabajo muestra que a pesar de considerar la salud nutricional como un aspecto importante de su trabajo, la intervención educativa por parte del pediatra en este tema es insuficiente, lejos de ser universal, individualizada y constante a largo plazo, tal como señalan las actuales recomendaciones. Además, para los encuestados el exceso de peso es percibido como el principal problema relacionado con las prácticas alimentarias. En opinión de los profesionales los padres son la vía natural para intervenir en el inicio y consolidación de unos hábitos de alimentación saludables.

Agradecimientos

Este estudio ha sido financiado por Almiron/Danone Baby Nutrition.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2048-2054
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Traducción y validación de la versión en español de la escala EAT-10 (Eating Assessment Tool-10) para el despistaje de la disfagia

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Resumen

Introducción: **El Eating Assessment Tool-10 (EAT-10) es un instrumento analógico verbal, unidimensional y autoadministrado, para el despistaje de la disfagia.**

Objetivos: **Traducir y adaptar al español la escala EAT-10, y evaluar sus propiedades psicométricas, fiabilidad y validez.**

Métodos: **Tras la traducción, traducción inversa y aprobación por los investigadores de la versión española de la escala (EAT-10 ES), se realizó un estudio prospectivo en pacientes con diagnóstico de disfagia (DD), pacientes no diagnosticados con riesgo de disfagia (RD) y pacientes sin riesgo de disfagia (SRD), procedentes de tres escenarios clínicos: una unidad de soporte nutricional hospitalaria (USN), una residencia geriátrica (RG) y un centro de atención primaria (CAP), que respondieron a la EAT-10 ES durante una única visita. Pacientes e investigadores respondieron a un cuestionario de comprensión del instrumento.**

Resultados: **El estudio incluyó 65 pacientes (75±9,1 años de edad; 52,3% mujeres). El tiempo medio de administración fue de 3,8 ± 1,7 minutos. El 95,4% de los pacientes consideró comprensibles todos los ítems de la escala y el 72,3% consideró fácil la asignación de puntuaciones. El coeficiente de consistencia interna alfa de Cronbach fue 0,87. La correlación entre las puntuaciones de cada ítem y el total de la escala fue elevada (p < 0,001). Las puntuaciones EAT-10 ES medias fueron 15 ± 8,9 (D), 6,7 ± 7,7 (RD) y 2 ± 3,1 (SRD), y significativamente más altas en pacientes varones, pacientes con diagnostico previo de disfagia y procedentes de la USN (p < 0,001).**

Conclusión: **La escala EAT-10 ES ha probado su fiabilidad, validez y consistencia interna. Es un instrumento fácil de comprender y rápido de completar, por lo que se considera útil para el despistaje de la disfagia en la práctica clínica.**

(*Nutr Hosp.* 2012;27:2048-2054)

DOI:10.3305/nh.2012.27.6.6100

Palabras clave: *Disfagia. Deglución. Trastornos de la deglución. Despistaje. Validez. Fiabilidad. Eating Assessment Tool-10.*

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Recibido: 6-VIII-2012.
Aceptado: 11-IX-2012.

TRANSLATION AND VALIDATION OF THE SPANISH VERSION OF THE EAT-10 (EATING ASSESSMENT TOOL-10) FOR THE SCREENING OF DYSPHAGIA

Abstract

Rationale: **The Eating Assessment Tool-10 (EAT-10) is a self-administered, analogical, direct-scoring screening tool for dysphagia.**

Objective: **To translate and adapt the EAT-10 into Spanish, and to evaluate its psychometric properties.**

Methods: **After the translation and back-translation process of the EAT-10 ES, a prospective study was performed in adult patients with preserved cognitive and functional abilities. Patients in 3 clinical situations, diagnosed with dysphagia (DD), patients at risk of dysphagia (RD), and patients not at risk of dysphagia (SRD) were recruited from 3 settings: a hospital Nutritional Support Unit (USN), a nursing home (RG) and primary care centre (CAP). Patients completed the EAT-10 ES during a single visit. Both patients and researchers completed a specific questionnaire regarding EAT-10 ES' comprehension.**

Results: **65 patients were included (age 75 ± 9.1 y), 52.3% women. Mean time of administration was 3.8 ± 1.7 minutes. 95.4% of patients considered that all tool items were comprehensible and 72.3% found it easy to assign scores. EAT-10 ES' internal consistency, Cronbach's Alpha coefficient was 0.87. A high correlation was observed between all tool items and global scores (p < 0.001). Mean score for patients in group DD was 15 ± 8.9 points, 6.7 ± 7.7 points in group RD, and 2 ± 3.1 points in group SRD. Male patients, previously diagnosed of dysphagia or patients from the NSU showed significantly higher scores on the EAT-10 ES (p < 0.001).**

Conclusion: **EAT-10 ES has proven to be reliable, valid and to have internal consistency. Is it an easy-to-understand tool that can be completed quickly, making it useful for the screening of dysphagia in routine clinical practice.**

(*Nutr Hosp.* 2012;27:2048-2054)

DOI:10.3305/nh.2012.27.6.6100

Key words: *Dysphagia. Deglutition. Deglutition disorders. Screening. Validity. Reliability. Eating Assessment Tool-10.*

Abreviaturas:

ASDS: Acute Stroke Dysphagia Screen.

AVC: Accidente Vascular Cerebral.

CAP: Centro de Atención Primaria.

DD: Diagnóstico previo de Disfagia.

EAT-10: Eating Assessment Tool-10.

EAT-10 ES: Versión española del Eating Assessment Tool-10.

GSS: Gugging Swallowing Screen.

MMAN: Modified Mann Assessment of Swallowing Ability.

RD: Riesgo de Disfagia.

RG: Residencia Geriátrica.

SRD: Sin Riesgo de Disfagia.

SWAL-QOL: Swallow Quality of Life.

TOR-BSST: Toronto Bedside Swallowing Screening Test.

USN: Unidad de Soporte Nutricional.

Introducción

El concepto de disfagia, o dificultad para deglutir, comprende las alteraciones conductuales, sensoriales y motoras que ocurren durante la deglución, incluyendo el estado de consciencia previo al acto de comer, el reconocimiento visual de los alimentos y las respuestas fisiológicas al olor y la presencia de alimentos[1]. Se trata de una patología con una morbi-mortalidad elevada y con importantes implicaciones sociales, emocionales y socioeconómicas[2].

Los trastornos de la deglución pueden afectar a sujetos de cualquier edad, como consecuencia de anomalías congénitas, lesiones de estructuras anatómicas o patologías clínicas diversas, y pueden aparecer de forma aguda, por ejemplo tras un accidente vascular cerebral (AVC) , o bien de forma insidiosa y progresiva, como en caso de un tumor faríngeo o de ciertas enfermedades neurológicas[3-8].

La prevalencia de disfagia en la población anciana es elevada y varía según la patología subyacente. Se estima que el 55% de los sujetos que han sufrido un AVC presentan disfagia, y es aun más prevalente en pacientes con otras patologías neurológicas, como la enfermedad de Parkinson, con una prevalencia estimada del 84%[9,10]. Los trastornos de la deglución afectan también a más del 50% de los pacientes con procesos neoplásicos de cabeza y cuello, a los que causa una importante merma de la calidad de vida[11]. La edad es además un factor independiente asociada a una mayor prevalencia de disfagia, con cifras que varían entre el 11,4% en ancianos en la comunidad y el 65% en pacientes institucionalizados[12-14].

La presencia de disfagia se asocia significativamente a la aparición de dos grupos de complicaciones clínicamente relevantes: una reducción en la eficacia de la deglución que a puede cursar con malnutrición y/o deshidratación, y una reducción en la seguridad de la deglución que puede cursar con aspiración y neumonía por aspiración[15]. Por ello, se observa que en pacientes con disfagia son frecuentes los episodios recurrentes de neumonía y la pérdida de peso no explicable por otras razones.[9] Asimismo, presentan riesgo aumentado de sufrir ansiedad o depresión, y más del 40% se han observado crisis de pánico o ansiedad durante las comidas[16].

Diversos signos y síntomas pueden orientar hacia la presencia de disfagia. Los pacientes con disfagia pueden tener dificultades para controlar y retener los alimentos y la saliva en la boca. Después de tragar pueden tener necesidad de toser o aclararse la garganta, presentar cambios en la calidad vocal, con voz húmeda o gorjeo, y mayor cantidad de mucosidad.[9] El paciente puede ser muy consciente de su problema o ignorar completamente su dificultad deglutoria. En el caso de la disfagia orofaríngea el paciente suele describir el problema con gran precisión, mientras que en el caso de disfagia esofágica tiende a hacerlo de forma imprecisa[17,18]. Esta variabilidad de los pacientes para percibir y describir los signos y síntomas asociados a la disfagia, constituye una de las razones de su infra-diagnóstico. Por ello, diversos estudios concluyen en la necesidad de hacer un cribado sistemático de los pacientes ancianos en cualquier ámbito asistencial, y en pacientes con patologías de riesgo[18,19].

Para el despistaje la disfagia se han desarrollado diversos instrumentos que han sido validados para patologías específicas, como el *Swallow Quality of Life* (SWAL-QOL)[20], pero debido a sus limitaciones de extensión y tiempo, ninguno de ellos se ha implementado de forma rutinaria en la práctica clínica, por lo que disponer de una herramienta sencilla y universal que permita descartar la presencia de disfagia sigue siendo una necesidad aún no cubierta. El despistaje de la disfagia entraña la identificación de signos y síntomas que permitan determinar el riesgo de disfagia del sujeto. Como cualquier método de cribado, éste debería ser sencillo, eficaz, coste-efectivo y seguro, y permitir identificar claramente a los pacientes en riesgo para, posteriormente, poder implementar métodos válidos que permitan establecer el diagnóstico de confirmación, bien sean clínicos o instrumentales[14,18,19].

La herramienta *Eating-Assessment Tool-10* (EAT-10) es un instrumento analógico verbal, unidimensional, autoadministrado y de puntuación directa para la evaluación de síntomas específicos de disfagia, que ha mostrado una consistencia interna y reproductibilidad excelentes, y cuya validez y fiabilidad han sido probadas en una amplia cohorte de pacientes con trastornos de la deglución debidos a diversas causas, tanto para el establecimiento inicial de la gravedad del síntoma como para la valoración del tratamiento de la disfagia en una gran variedad de situaciones clínicas. La versión original de la escala en inglés se puede administrar en menos de 2 minutos y la puntuación total se obtiene con facilidad, sin que sea necesario referirse a subescalas ni utilizar fórmulas complejas para su cálculo[2].

La sencillez y rapidez de administración de esta nueva escala de despistaje en inglés, motivó su traduc-

ción y validación al idioma español, con la finalidad de dotar a la comunidad clínica castellanohablante de un instrumento útil para el diagnóstico y el manejo de los pacientes con disfagia.

Objetivos

Los objetivos de este estudio fueron:

- Evaluar las propiedades psicométricas de la versión española de la escala EAT-10 (EAT-10 ES) en relación a la idoneidad de exposición del objetivo y las instrucciones, adecuación y comprensibilidad de las preguntas, idoneidad del sistema de respuesta y puntuación, presencia de sesgos y factibilidad de administración.
- Validar la escala EAT-10 ES a partir de análisis de factibilidad, en términos de tiempo de administración y porcentaje de omisión de respuesta, consistencia interna y validez del instrumento.

Métodos

Descripción del instrumento

La EAT-10 es una escala de autoevaluación analógica verbal, unidimensional y de puntuación directa para evaluar síntomas específicos de disfagia. La validez y fiabilidad de la versión original han sido previamente demostradas y publicadas. Se trata de un cuestionario de 10 preguntas diseñado por un grupo multidisciplinar de expertos en el que intervinieron digestólogos, otorrinolaringólogos, especialistas en patologías del habla y nutricionistas. El paciente debe responder a cada pregunta de forma subjetiva en una escala de cinco puntos (0-4 puntos), en la que cero (0) indica la ausencia del problema y cuatro (4) indica que considera que se trata de un problema serio. Su administración es rápida y el instrumento no contiene subescalas, escalas analógicas visuales ni fórmulas para el cálculo de la puntuación final, por lo que el clínico sólo debe sumar las puntuaciones obtenidas en cada ítem. Las puntuaciones más altas indican mayor percepción de disfagia y, a pesar de que la ausencia de campos específicos impide la clasificación de la patología en sus subcategorías social, emocional y funcional, esta limitación queda compensada por su simplicidad y facilidad de administración y puntuación, y por su utilidad en sujetos con trastornos deglutorios muy diversos[2].

Traducción y adaptación del instrumento

Tras la obtención de los permisos necesarios y la evaluación de la factibilidad de la traducción al español del instrumento por parte de un grupo bilingüe de expertos, la primera fase del estudio consistió en un proceso de traducción al español, traducción inversa al inglés y adaptación al contexto español hasta que los investigadores aprobaron su administración a pacientes.

Sujetos

Se incluyeron 65 sujetos castellanohablantes de ambos sexos, mayores de 18 años, primando el reclutamiento de ancianos debido a la mayor prevalencia de disfagia en este grupo de edad, que supiesen leer y escribir y no presentaran ninguna alteración significativa de las funciones cognitivas que pudiese dificultar la comprensión del contenido y el sentido de las preguntas. Se reclutaron pacientes de tres escenarios clínicos: una consulta de una unidad de soporte nutricional hospitalaria (USN), una residencia geriátrica (RG) y una consulta de atención primaria (CAP), y en tres situaciones clínicas diferentes: pacientes con diagnóstico previo documentado de disfagia (DD), pacientes no diagnosticados y con riesgo de disfagia debido a la edad, los antecedentes patológicos o la enfermedad actual (CRD), y pacientes sin riesgo de disfagia (SRD). Fueron excluidos del estudio los sujetos analfabetos, sujetos con deterioro cognitivo de cualquier grado según el Cuestionario portátil del estado mental de Pfeiffer y sujetos con una puntuación > 4 en la Escala de deterioro global de Reisberg.

Procedimiento

La evaluación psicométrica del instrumento se realizó a partir de una encuesta ad-hoc de utilidad subjetiva y comprensión con dos formularios separados, uno formal dirigido al paciente y otro en el que el investigador destacó las dificultades que habían tenido los pacientes al rellenar el cuestionario. Se redactaron unas instrucciones con el objetivo de homogeneizar las respuestas de los evaluadores a las dudas que pudieran plantearles los pacientes durante la encuesta, que respondieron después de la administración de la escala. La encuesta evaluó el grado de adecuación de la escala en relación a la idoneidad de exposición del objetivo y las instrucciones, la adecuación de las preguntas, la corrección, comprensión y extensión del enunciado, la idoneidad de los sistemas de respuesta y puntuación, la presencia de sesgos de respuesta, y la duración de la administración del instrumento.

Análisis

La validación de la escala EAT-10 ES incluyó una evaluación de su factibilidad en cuanto al tiempo medio de administración y al porcentaje de respuestas omitidas. La consistencia interna del instrumento se evaluó mediante el coeficiente alfa de Cronbach y un análisis de correlación ítem-total para el que se utilizó

Tabla I
Características demográficas, situación clínica y procedencia de los pacientes

	Muestra	*Edad*		
	N (%)	*Edad media (± DT)*	*Mínima*	*Máxima*
Total	63/65	75 (±9,1)	52	98
Sexo				
Mujeres	34 (52,3%)	77,3 (±10,3)	52	98
Varones	31 (47,7%)	72,3 (±7)	59	88
Disfagia (DD)	20 (30,8%)	71,8 (±11,4)	52	98
Riesgo de disfagia (RD)	21 (32,3%)	76,1 (±6,7)	65	87
Sin riesgo de disfagia (SRD)	24 (36,9%)	76,6 (±8,9)	59	90
USN	22 (33,8%)	68,9 (±7,1)	52	81
Residencia geriátrica	20 (30,8%)	80,4 (±9,9)	58	98
CAP	23 (35,4%)	75,7 (±7,1)	59	87

el coeficiente de correlación de Spearman. Para evaluar la validez del cuestionario las puntuaciones obtenidas se compararon según edad, sexo y situación clínica, y ésta última se analizó manteniendo los tres grupos de estudio (SRD, RD y DD), así como agrupando los pacientes de los grupo CRD y DD frente a los pacientes del grupo SRD. Para las comparaciones de puntuaciones según sexo o situación clínica se utilizó un análisis de varianza, mientras que para las comparaciones según edad se utilizó el coeficiente de correlación de Pearson.

Tabla II
Diagnósticos previos más frecuentes según la situación clínica

	N	*%*
Con diagnóstico de disfagia	20	
Enfermedad del sistema circulatorio	11	55%
Neoplasia	7	35%
Con riesgo de disfagia	21	
Enfermedad del aparato digestivo	10	47,6%
Anciano frágil	8	38,1%
Sin riesgo de disfagia	24	
Enfermedad del aparato locomotor y tejido conectivo	9	37,5%
Enfermedad del sistema circulatorio	8	33,3%

Resultados

Características socio-demográficas y clínicas de los pacientes

Se incluyeron 65 pacientes, con una edad media de 75 ± 9,1 años y de los cuales un 52% eran mujeres. Un 22% de los pacientes tenían entre 71 y 75 años de edad, seguidos del grupo de 81-85 años (17%) y de 66-70 años (17%) Las características demográficas de la muestra y su distribución según situación clínica y procedencia se muestran en la tabla I.

Las patologías más frecuentemente observadas fueron las del sistema circulatorio (37%), sistema locomotor y tejido conectivo (25%), endocrinas, metabólicas e inmunitarias (25%) y neoplasias (23%). Los diagnósticos previos más frecuentemente observados por situación clínica se muestran en la tabla II.

Adecuación de la escala EAT-10 ES

Respecto a la evaluación de las propiedades psicométricas de la escala, un 78,1% de los investigadores y un 89,2% de los pacientes consideraron que el objetivo de la escala se expone con claridad. El 68,7% de los pacientes consideró que las instrucciones para responder a cada pregunta eran suficientemente claras y el 71,9% manifestó le había quedado claro qué debía hacer con los resultados del test. Sin embargo, un 62,5% de los investigadores reportó que los pacientes habían requerido alguna aclaración en alguna de las preguntas.

En relación a la adecuación de las preguntas, sólo un 4,8% de los pacientes solicitó alguna aclaración de vocabulario, siendo las más frecuentes las de la palabra "estresante" del ítem 10 y la expresión "alimentos sólidos y los líquidos" de los ítems 3 y 4. Pacientes e investigadores consideraron que la escala no contiene ninguna pregunta que el paciente rechace responder. Más del 80% de los pacientes consideraron que estas preguntas pueden ayudarle a él o a su médico a saber si tiene dificultad para tragar.

Respecto a la idoneidad del sistema de respuesta y puntuación de la escala, un 72,3% de los pacientes declaró no tener dificultad para asignar puntuaciones a cada pregunta, sin embargo un 60,6% hubiese preferido que las preguntas las hubiese formulado un médico o profesional de la salud.

Tabla III
Correlación entre las puntuaciones de ítems y la puntuación total de la escala EAT-10 ES

Ítem de la EAT-10 ES	*Correlación*	*Valor de p*
EAT1-Mi problema para tragar me ha llevado a perder peso	0,7295	< 0,0001
EAT2-Mi problema para tragar interfiere con mi capacidad de comer fuera de casa	0,7618	< 0,00
EAT3-Tragar líquidos me supone un esfuerzo extra	0,7182	< 0,0001
EAT4-Tragar sólidos me supone un esfuerzo extra	0,7836	< 0,0001
EAT5-Tragar pastillas me supone un esfuerzo extra	0,6044	< 0,0001
EAT6-Tragar es doloroso	0,4173	0,0015
EAT7-El placer de comer se ve afectado por mi problema para tragar	0,6719	< 0,0001
EAT8-Cuando trago, la comida se pega en mi garganta	0,5774	< 0,0001
EAT9-Toso cuando como	0,5893	< 0,0001
EAT10-Tragar es estresante	0,5570	< 0,0001

Los investigadores no observaron sesgos destacables de tendencia central: tendencia del paciente a escoger las puntuaciones centrales de la escala (3,1%), deseabilidad social, referido a la tendencia a responder lo que el paciente considera socialmente aceptable (1,6%) y/o sesgo de aprendizaje, la tendencia observada del paciente a repetir la misma puntuación asignada en la primera pregunta al resto de preguntas (0%) . Un 84,4% de los pacientes consideró adecuado el tiempo empleado en responder el test, y 7 de los 8 pacientes que no lo consideraron adecuado precisaron alguna aclaración sobre cómo responder a las preguntas tras leer las instrucciones.

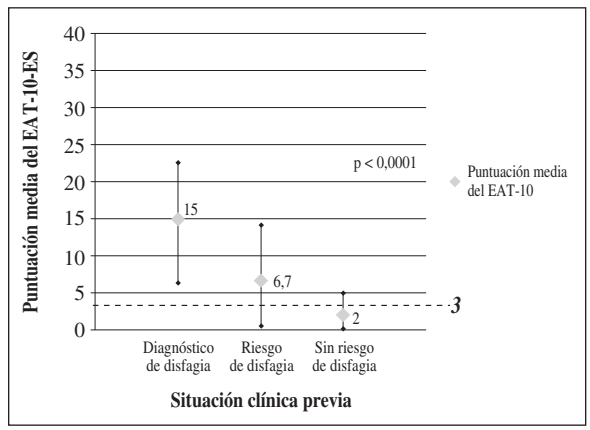


Fig. 1.—Puntuación media de la escala EAT-10 ES de acuerdo a la situación clínica.

Validación de la escala EAT-10 ES

Para la validación de la escala EAT-10 ES se tuvo en consideración su factibilidad, consistencia interna y validez.

El tiempo medio de respuesta al cuestionario, un aspecto clave para poder considerar que el mismo es factible, fue de 3,8 ± 1,7 minutos, con un rango entre 1,4 y 9,6 minutos. Todos los pacientes incluidos en el estudio, respondieron a la totalidad de preguntas de la EAT-10 ES.

El coeficiente Alpha de Cronbach de consistencia interna de la escala EAT-10 fue de 0,878, superior al mínimo establecido de 0,7. Al calcular la correlación excluyendo cada una de las dimensiones de la escala no se observaron incrementos significativos del coeficiente, con valores comprendidos en un rango de 0,858 a 0,878, lo que corrobora la idoneidad de los ítems evaluados.

La puntuación media del test para todos los pacientes fue 7,5 puntos y la puntuación más frecuentemente observada fue de 0 puntos. Se observaron puntuaciones más altas en la EAT-10 ES en varones, en pacientes con diagnóstico y riesgo de disfagia, y en aquellos procedentes de la USN. La escala EAT-10 ES mostró una correlación moderada con la edad (CC de Spearman de 0,37). En la tabla III se presentan las correlaciones entre las puntuaciones de cada una de las preguntas y la puntuación total, que fueron altas y confirmaron la adecuación de las diferentes preguntas que componen la escala.

En el análisis de grupos por situación clínica, la puntuación media del grupo DD (15 ± 8,9 puntos) fue significativamente más alta que la del grupo RD (6,7 ± 7,7 puntos) y a su vez significativamente más alta que la puntuación media del grupo SRD (2 ± 3,1 puntos) (fig. 1). Las puntuaciones medias por género, presencia o no de riesgo de disfagia y escenario clínico se muestran en la tabla IV.

Discusión

Los resultados presentados confirman las propiedades psicométricas, la fiabilidad y la validez de la versión en español de la escala EAT-10 ES y confirman que es una herramienta útil para el despistaje de la disfagia en pacientes con nivel cognitivo conservado.

La EAT-10 ES es un método de cribado simple y breve. Ello contrasta con otros instrumentos diseñados y validados previamente para la evaluación de los trastornos de la deglución, como la SWAL-QOL, una

Tabla IV
Puntuación media de la escala EAT-10 ES de acuerdo al género, el riesgo de disfagia y el escenario clínico

	N	*Puntuación media (± DE)*	*Valor de p*
Género			p = 0,03
Mujeres	34	5,4 (±7,6)	
Varones	31	9,8 (±9,2)	
Riesgo de disfagia			p < 0,001
No	24	2 (±3,1)	
Si (diagnosticado o no)	41	10,8 (±9,2)	
Escenario clínico			p < 0,001
Unidad de Soporte Nutricional	22	15,6 (±8,1)	
Residencia Geriátrica	20	5,9 (±7,1)	
Centro de Atención Primaria	23	1,3 (±1,6)	

escala de 43 preguntas que evalúa la calidad de vida y la evolución de pacientes con disfagia orofaríngea, cuyo empleo no se ha extendido en la práctica clínica rutinaria entre otras razones por su extensión y porque su objetivo difiere del de una herramienta puramente de cribado.[21] Otras herramientas de aparición y validación reciente, aunque de gran utilidad en algunos escenarios clínicos, han sido desarrolladas o validadas en pacientes con patologías específicas. Tal es el caso del "*Toronto Bedside Swallowing Screening Test*" (TOR-BSST)[22], el "*Modified Mann Assessment of Swallowing Ability*" (MMAN)[23] y el "*Acute Stroke Dysphagia Screen*" (ASDS)[24] o el "*Gugging Swallowing Screen*" (GSS)[25], todos validados y/o desarrollados en pacientes con ictus, bien agudos o en rehabilitación.

Además de cribar la presencia de disfagia sin importar la patología que la origina, la EAT-10 ES tiene la ventaja de mostrarse fiable cuando es auto-administrado o en presencia del médico. Tanto el MMAN como el ASDS requieren personal sanitario para su administración, y el TOR-BSST requiere además que este personal esté entrenado en la administración de la herramienta de despistaje. Por último, el *Dewsbury Feeding and Swallowing Screen*[26], es una herramienta diseñada para ser utilizada en cualquier escenario clínico y en una gran variedad de patologías, pero por requerir de la observación directa del personal de enfermería, estos deben entrenarse con un pack contentivo de 2 manuales y un DVD, y administrar líquidos y sólidos al paciente durante su primera visita y en presencia de alguna condición que sugiera previamente riesgo de disfagia.

La evaluación de las propiedades psicométricas de la escala EAT-10 ES mediante la encuesta de comprensión mostró la claridad de exposición del objetivo de la escala, tanto para los pacientes como para los investigadores. El vocabulario empleado en los enunciados de la EAT-10 ES es correcto, comprensible y su extensión adecuada. Debido al porcentaje de pacientes que solicitaron alguna aclaración sobre las instrucciones generales de la herramienta, parece oportuno asegurarse de su comprensión antes de iniciar la administración de los ítems específicos, puesto que la brevedad en su administración lo permite.

Son todos estos aspectos los que dan la utilidad a la escala EAT-10 ES: aplicabilidad en menos de 5 minutos, con el paciente solo o en presencia de algún personal implicado en el cuidado del paciente, fácil de entender y de obtener resultados que permitan descartar la presencia de disfagia o la necesidad de una valoración radiológica posterior que complemente la valoración clínica, aporte datos sobre la fisiopatología del proceso deglutorio en ese paciente y permita identificar las estrategias terapéuticas de éstos pacientes. Además, se trata de una herramienta útil tanto en medio hospitalario como en el ámbito residencial de personas ancianas, y también en Atención Primaria. Como única limitación debemos considerar que no es una herramienta adecuada para el despistaje de la disfagia en pacientes con deterioro cognitivo, ya que se requiere de la colaboración del paciente y de que éste pueda comunicar los síntomas sobre los que se le interroga.

La disfagia es un síntoma frecuentemente no diagnosticado a pesar de su alta prevalencia y de su impacto clínico[27]. Los pacientes ancianos con disfagia o signos basales de trastornos deglutorios tienen un riesgo significativamente más alto de presentar desnutrición, infecciones del tracto respiratorio inferior[19] y una tasa más elevada de mortalidad a un año, que los pacientes sin disfagia[15]. Esto hace imperativa la necesidad de implementar una herramienta de cribado sencillo que permita evaluar la presencia de disfagia en cualquier escenario clínico en la que se tenga acceso a los pacientes mayores de 60 años, sin importar el motivo de consulta, su patología de base o asociadas y sin consumir excesivo tiempo del personal, en un sistema que cada vez más demanda eficiencia en el uso de sus recursos.

Contribuciones a la autoría

Rosa Burgos, Hegoi Segurola, Cleofé Pérez, Krysmarú Araujo y Núria Barcons desarrollaron la idea del estudio y estuvieron involucrados en su diseño. Rosa Burgos, Hegoi Segurola y Cleofé Pérez supervisaron por completo el desarrollo del mismo. Belén Sarto, Ana Romagosa, Carolina Puiggrós, Concepción Vázquez y Guillermo Cárdenas participaron en el diseño del protocolo y como investigadores colaboradores llevaron a cabo la investigación y contribuyeron en el análisis de los datos. Todos los autores contribuyeron y revisaron la versión final del artículo.

Financiación

Este estudio ha contado con el soporte técnico y económico de Nestle Health Science.

Declaración de conflicto de intereses

Todos los autores excepto N. Barcons y K. Araujo declaran la independencia del órgano promotor y financiador en el análisis de resultados y la elaboración de las conclusiones y niegan conflictos de intereses con las organizaciones mencionadas. N. Barcons y K. Araujo son personal del Departamento Médico de Nestlé Health Science y centraron su participación en el diseño del estudio y la revisión del manuscrito final.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2055-2065
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Un juego de cartas durante los recreos escolares mejora los hábitos alimentarios en adolescentes

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Resumen

Introducción: **Los hábitos alimentarios de la población española son un problema cada vez más preocupante en la actualidad y, en especial, durante la adolescencia.**

Objetivos: **Mejorar los hábitos alimentarios saludables (desayuno, ingestas de fruta y agua, consumo de refrescos, bollería-golosinas y fritos) en adolescentes.**

Métodos: **La intervención se llevó a cabo durante 3 meses, con alumnos de entre 12 y 16 años, mediante una propuesta educativa a través de un juego de cartas (construido ad hoc), denominado "Fighting for my health", y que se desarrolló en los recreos escolares. Éste se complementó con la metodología del compromiso saludable, caracterizado fundamentalmente por el trabajo colaborativo entre escuela y familia y por el fomento de la responsabilidad del alumnado hacia su salud. Se contó con 2 grupos (experimental y control), cada uno de ellos con un número total de 48 adolescentes.**

Resultados: **Tras la puesta en práctica de la intervención se lograron mejoras significativas en 5 de los 6 hábitos trabajados (la excepción fue el consumo de fritos) en el grupo experimental. Entre ellas sobresale especialmente la diferencia altamente significativa ($p \leq 0{,}001$) obtenida en el Desayuno y la Fruta, entre pretest y postest y entre pretest y retest. Sin embargo, en el grupo control no se produjeron diferencias significativas en ninguno de ellos.**

Conclusión: **Una intervención escolar realizada desde el departamento de Educación Física, mediante compromisos saludables a través de juego de cartas, mejora los hábitos alimentarios en adolescentes.**

(*Nutr Hosp.* 2012;27:2055-2065)

DOI:10.3305/nh.2012.27.6.6071

Palabras clave: *Hábitos alimentarios. Adolescentes. Intervención educativa. Educación física.*

A SCHOOL BREAKS CARD GAME IMPROVES EATING HABITS IN ADOLESCENTS

Abstract

Introduction: **Feeding habits among the Spanish population are currently an increasing and concerning problem, especially during adolescence.**

Objectives: **To improve feeding habits (breakfast, consumption of fruit and water, soft drinks, pastries, sweets and fried food) in adolescents.**

Methods: **The intervention was conducted for 3 months in students from 12 to 16 years old, through an educational proposal based on a card game (built ad hoc) called "Fighting for my health", which was developed during the school breaks. This game was supplemented with the methodology of a healthy commitment, based mainly on the cooperative work between schools and families and the promotion of the responsibility among students about their health. Two groups were included (intervention and control), each one with a total number of 48 adolescents.**

Results: **After the intervention, significant improvements were achieved in 5 of the 6 habits addressed (the exception was consumption of fried food) in the intervention group. Among them, it is necessary to highlight the significant difference ($p \leq 0.001$) obtained in breakfast and consumption of fruit between pretest and posttest and between pretest and retest. However, in the control group there were no significant differences in any of them.**

Conclusion: **A school-based intervention conducted from the Department of Physical Education, through healthy commitments using a card game, improved the feeding habits in adolescents.**

(*Nutr Hosp.* 2012;27:2055-2065)

DOI:10.3305/nh.2012.27.6.6071

Key words: *Eating habits. Adolescents. Educational intervention. Physical intervention.*

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Recibido: 12-VI-2012.
1.ª Revisión: 20-VII-2012.
Aceptado: 7-VIII-2012.

Abreviaturas

E.F.: Educación Física.
E.S.O.: Educación Secundaria Obligatoria.

Introducción

Existe una gran preocupación por el establecimiento de hábitos de vida saludables en la población, en especial en grupos vulnerables de edad como la adolescencia[1-3]. Estudios recientes[4] encuentran que hasta un 72% de la población española necesita cambios en su alimentación. La prevalencia de sobrepeso es del 34,2% y la de obesidad del 13,6%[5].

No obstante, el ámbito escolar posee un gran potencial y, por tanto, una enorme responsabilidad para evitar esta situación. De hecho, la idoneidad de los centros educativos, así como el impacto que pueden suponer los programas de Educación Física (E.F.) sobre la promoción de actividad física y la salud, es una cuestión ampliamente reconocida[6-8].

Sin embargo, apenas existen referencias en la literatura científica nacional de intervenciones con la finalidad de promover la adquisición y/o mejora de hábitos alimentarios en la adolescencia. Y las diversas iniciativas institucionales existentes no acaban de concretarse en acciones que realmente ayuden a promocionar la salud de los educandos[9].

Por tanto, urge seguir invirtiendo en investigación para diseñar propuestas de intervención que actúen sobre los malos hábitos de alimentación[10], dado que es un factor determinante en la obesidad[11]. Al mismo tiempo, además de seguir investigando en torno a esta temática no será menos importante también difundir los hallazgos de las investigaciones[12]. De este modo, el resto de profesionales tendrán la posibilidad de contar con valiosas referencias (de actuaciones llevadas a la práctica y debidamente evaluadas) a la hora de diseñar sus propias intervenciones.

No puede obviarse, además, que los adolescentes actuales distan mucho de sentirse atraídos por aquellas actividades y estrategias metodológicas que no hace mucho tiempo resultaban significativas al alumnado de esa misma etapa educativa. Circunstancia que exige modificaciones, tanto de tipo estructural (sistemas educativos) como en las propias prácticas escolares, para no caer en un anacronismo pedagógico[13]. Por tanto, los profesionales de la Educación Física (E.F.) deben apostar por programas de intervención alternativos y más significativos para el alumnado. De hecho, muchos de los enfoques y planteamientos que se llevan a cabo no están en consonancia ni con las necesidades de los niños y jóvenes ni con las características de la sociedad actual[14]. Y para ello resulta evidente la importancia de saber conectar con aquello con que le es significativo al alumnado, conocer su lenguaje para hacerse entender y adecuar los métodos y estrategias de intervención a las nuevas realidades[15]. En este sentido, en la actualidad los juegos de cartas, como "Magic: The Gathering" o "Yu-Gi-Oh!", poseen un elevado atractivo entre gran parte de la población adolescente, circunstancia que se ha aprovechado para construir la propuesta que ha dado lugar al presente trabajo.

En un intento de dar respuesta a las demandas planteadas, el objetivo del presente estudio ha sido evaluar los efectos de una propuesta educativa de compromisos saludables, mediante el juego de cartas "Fighting for my health" (construido *ad hoc)*, realizada durante los recreos escolares, orientada a la promoción de hábitos alimentarios en adolescentes.

Metodología de investigación

Sujetos y contexto

En este trabajo participaron 48 alumnos de Educación Secundaria Obligatoria (E.S.O.), de un total de 197 que componían los 8 grupos de dicha etapa educativa. Estos 48 sujetos han sido valorados, por tanto, como un solo grupo (grupo experimental). Se ha contado también con un grupo control, compuesto por el mismo número de alumnos que el grupo experimental (48) y en la misma proporción con respecto a cada uno de los 8 grupos. Todos ellos pertenecen a un centro educativo ubicado en una zona periférica de la ciudad de Granada, acogiendo alumnos de clase media-baja. El centro es de tipo dos, con doble línea por curso, y abarca los niveles educativos que van desde educación infantil hasta el final de la E.S.O. Tras informar a la dirección del centro y a las familias se obtuvo su permiso y autorización.

Diseño de investigación

Se empleó un diseño cuasiexperimental con dos grupos (experimental y control), con medidas pretest (justo antes de la implementación de la propuesta), postest (tras los 3 meses de duración de la intervención) y retest (tres meses después de finalizada la intervención) en ambos grupos, para poder establecer las comparaciones pertinentes.

Variables del estudio

La variable independiente la conformó la puesta en práctica del juego de cartas "Fighting for my health" (ver Anexo), a través de una liga interna durante los recreos, con una duración de 3 meses, y la variable dependiente estuvo configurada por los hábitos alimentarios saludables en los adolescentes (desayuno, fruta, agua, refrescos, bollería-golosinas y fritos).

Tabla I
Sistema de competición de "Fighting for my health"

Fase	*Distribución*	*Objetivo*
I	8 grupos de 6 jugadores	Quedar entre los 3 primeros (formarían la 1.ª división). El resto constituirían la 2.ª división
II	4 grupos de 6 jugadores (1ª división)	Clasificarse entre los 2 primeros de cada grupo (para poder jugar por el título y evitar la lucha por el descenso)
	4 grupos de 6 jugadores (2ª división)	Clasificarse entre los 2 primeros de cada grupo (para poder jugar por el ascenso y evitar ser los últimos clasificados)
III	1 grupo de 8 jugadores	Lograr el título (o quedar entre los 3 primeros)
	4 grupos de 4 jugadores	Evitar el descenso (el último de cada grupo)
	1 grupo de 8 jugadores	Lograr el ascenso (los 4 primeros)
	4 grupos de 4 jugadores	Evitar ser los últimos clasificados

Variable independiente: programa de intervención

La intervención consistió en la puesta en práctica de un juego de cartas basado en el desarrollo de hábitos saludables de vida y actividad físico-deportiva (construido *ad hoc)*, denominado "Fighting for my health" (ver Anexo). Este formó parte de la liga interna que suele desarrollarse cada año en el centro, aprovechando el tiempo de recreo de cada jornada escolar. Al igual que el resto de actividades, fue totalmente voluntaria y sin carácter excluyente, por lo que los alumnos podían apuntarse a todas aquellas actividades que formaban parte de dicha liga (fútbol, baloncesto, voleibol y el juego de cartas "Fighting for my health"). El hecho de plantear la actividad como parte integrante de la liga interna fue un incentivo importante, pues iba a contar con las mismas recompensas que en el resto de competiciones deportivas (trofeos y material deportivo para los 3 primeros clasificados). El sistema de competición constó de 3 fases (tabla I).

Durante todo el tiempo que duró la liga interna cualquier jugador tenía la opción de aumentar sus posibilidades de éxito en los enfrentamientos (partidas) con otros compañeros si decidía mejorar o adquirir algún hábito de alimentación saludable (relacionado con el desayuno, la ingesta de fruta y agua) o, por el contrario, eliminar o reducir algún otro que tuvieran y fuera poco saludable (excesiva ingesta de bollería o golosinas, de fritos y consumo de refrescos). Para ello, la dinámica del juego de cartas se complementó con la metodología de "el compromiso saludable" [16]. Tras determinar junto al profesor de E.F. cuál iba a ser su compromiso de alimentación saludable (hasta un máximo de 2) que, en el caso de cumplir, le otorgaría unos beneficios especiales en los diferentes enfrentamientos, los alumnos debían designar a una persona significativa en su vida (padre, madre, tutor...) que sería la encargada de realizar el seguimiento del compromiso y de verificar su cumplimiento.

Variable dependiente

Los hábitos de alimentación saludable que se llevaron a cabo, y que determinaron la variable dependiente, no fueron imposiciones del profesor, sino que surgieron a partir del análisis conjunto del alumno y el profesor, junto al visto bueno de las familias, siguiendo los principios de actuación de Pérez López (2009)[16]. Como referencia para cada uno de los compromisos de alimentación saludable que asumió el alumnado se partió de la propuesta de Pérez López y Delgado (en prensa)[17].

El seguimiento de los diferentes compromisos lo coordinaron los 2 profesores de E.F. en E.S.O. del centro que, además, fueron los responsables del correcto funcionamiento de la competición mediante el juego de cartas en los recreos. Tras los 3 meses que duró la competición se solicitó a todos los implicados (alumnos y personas que colaboraron en el seguimiento) una valoración final, tanto de la actividad como del beneficio o no que le hubiera podido reportar al alumno en cuestión, a través de un informe escrito. Y a los 3 meses siguientes al término de la liga interna, en los que no se incidió de manera intencionada, se revisó el grado de consolidación de cada uno de los compromisos, a través de un nuevo informe por parte de quienes colaboraron en esta iniciativa.

Todo el proceso estuvo constantemente asesorado y supervisado por profesores expertos en la materia de la Facultad de Ciencias de la Actividad Física y el Deporte de Granada.

Análisis de los datos

Con respecto a la evaluación de la propuesta se realizó, por un lado, una evaluación cuantitativa, en la que se comprobró la existencia o no de diferencias significativas entre las 3 medidas realizadas (pretest, postest y retest), para lo que se aplicó la prueba de Friedman para "K muestras relacionadas" y, posteriormente, en aquellas variables donde se hubiera determinado significatividad se realizó la comparación por pares, para "2 muestras relacionadas" (Wilcoxon). Además, se realizó la estadística descriptiva de los porcentajes del grado de cumplimiento de cada uno de los hábitos en los diferentes momentos de evaluación, así como de la media y desviación típica con respecto a la valoración

Tabla II
Distribución del número de alumnos por compromiso (grupo experimental)

Compromisos a adquirir o aumentar		
Desayuno	*Fruta*	*Agua*
26	21	8
Compromisos a reducir		
Refrescos	*Bollería-Golosinas*	*Fritos*
7	6	4

de los participantes sobre el planteamiento y sus logros. El análisis se realizó a través del paquete estadístico SPSS 15.0.

Además, todo ello se complementó con el análisis cualitativo (mediante el programa NVivo 8) de las valoraciones que realizaron al término de la intervención tanto los alumnos como el resto de personas implicadas en el proceso (familiares). A través de un informe debían significar aquellos aspectos más positivos y negativos del programa, así como el grado de satisfacción con el planteamiento llevado a cabo y los logros alcanzados. La escala de medición de las respuestas fue de cinco puntos, siendo sus extremos "Muy satisfecho" (5) y "Muy insatisfecho" (1). Circunstancia que determinará que en la exposición de los resultados se haga referencia a cada uno de ellos como A-1, A-2, etc. (cuando se trate de opiniones del alumnado) y F-1, F-2,... (en el caso de los familiares). El análisis de la información se ha realizado siguiendo las pautas marcadas por Strauss y Corbin (2002)[18] en la Teoría Fundamentada.

Resultados

Antes de reseñar aquellos resultados más relevantes con relación al desarrollo de hábitos alimentarios saludables, cabe destacar el alto índice de participación en esta nueva iniciativa. De hecho, cerca de 1 de cada 4 alumnos de E.S.O. (un 24,36%) se apuntó voluntariamente a la liga interna de "Fighting for my health", lo que supuso que fuera la segunda actividad más solicitada después del fútbol (39,6%), y por delante del voleibol (22,3%) y del baloncesto (14,2%). El porcentaje de muerte experimental fue 0.

El número total de compromisos adquiridos por los 48 alumnos (grupo experimental) fue de 72 (tabla II). Los hábitos más demandados fueron los relacionados con el "Desayuno" y la "Fruta". Entre ambos abarcan cerca de 2 tercios del total de compromisos desarrollados (65,3%), seguidos ya de lejos por el de una adecuada hidratación ("Agua"), con 8 alumnos (11,1%), y por el de la reducción del consumo de refrescos, con 7 alumnos (9,7%).

Tras la puesta en práctica de la intervención se lograron mejoras significativas en 5 de los 6 hábitos trabajados (la excepción fue el consumo de fritos) en el grupo experimental (tabla III). Entre ellas sobresale especialmente la diferencia altamente significativa ($p \leq 0,001$) obtenida en el Desayuno y la Fruta, entre pretest y postest y entre pretest y retest. Sin embargo, en el grupo control no se produjeron diferencias significativas en ninguno de ellos.

Con respecto al Desayuno, el porcentaje de alumnos (tabla IV) que no desayunaba en el grupo experimental se redujo en un 34,6% (entre quienes decidieron mejorar dicho hábito). Es más, los alumnos que al término de la intervención desayunaban adecuadamente (de los 26 que adquirieron este compromiso) se situó en el 73,1%, de los cuales el 57,7% aún mantenía dicho hábito a los 3 meses (en el retest).

En este sentido, destaca el hecho de que en el postest (en el grupo experimental) el porcentaje de quienes "No" tomaban fruta o agua, o sí consumían "Diariamente" fritos, bollería o golosinas, o refrescos pasó a ser inexistente (entre los alumnos que se propusieron los citados compromisos), cuando en el pretest dicho porcentaje oscilaba entre el 25% (en el mejor de los casos, el de los fritos) y el 87,5% (en la variable con peor resultado antes de la intervención, el agua). Mientras tanto, en el grupo control la modificación de los hábitos apenas resultó relevante pues, en general, los porcentajes obtenidos en el pretest se mantuvieron en el postest y el retest.

Del total de compromisos desarrollados (72), en 45 de ellos (un 62,5%) se consiguió el máximo nivel de

Tabla III
Grado de significatividad de los hábitos donde se produjeron diferencias significativas tras la intervención (grupo experimental)

Compromiso	*Valor de significación*		
	Pretest-Postest	*Postest-Retest*	*Pretest-Retest*
Desayuno	$p \leq 0,001$	$p \leq 0,05$	$p \leq 0,001$
Fruta	$p \leq 0,001$	$p \leq 0,05$	$p \leq 0,001$
Agua	$p \leq 0,01$	NS	$p \leq 0,05$
Bollería-Golosinas	$p \leq 0,05$	NS	$p \leq 0,05$
Refrescos	$p \leq 0.05$	NS	$p \leq 0,05$

NS: No significativo.

Tabla IV

Nivel de partida y grado de cumplimiento de los hábitos valorados en el grupo control, experimental global y experimental parcial (con los alumnos que se comprometieron a mejorarlos)

Compromisos	*Grado de cumplimiento*	*Pretest (%)*		*Postest (%)*		*Retest (%)*		*G. E. (parcial)*		
		G.C	*G.E*	*G.C*	*G.E*	*G.C*	*G.E*	*% Pre*	*% Pos*	*% Rest*
Desayuno	No	14,6	25	10,4	8,3	12,5	10,4	42,3	7,7	11,5
	Insuficientemente	62,5	64,6	72,9	47,9	70,8	52,1	57,7	19,2	30,8
	Sí	22,9	10,4	16,7	43,8	16,7	37,5	–	73,1	57,7
Fruta	No	25	39,6	25	14,6	25	18,8	52,4	–	4,8
	Insuficientemente	66,7	56,3	68,8	58,3	72,9	60,4	47,6	42,9	52,4
	Sí	8,3	4,2	6,3	27,1	2,1	20,8	–	57,1	42,8
Agua	No	37,5	33,3	31,3	20,8	27,1	20,8	87,5	–	12,5
	Insuficientemente	33,3	43,8	43,8	45,8	50	50	12,5	25	25
	Sí	29,2	22,9	25	33,3	22,9	29,2	–	75	62,5
Fritos	Diariamente	4,2	6,3	2,1	4,2	2,1	6,3	25	–	–
	Habitualmente	54,2	62,5	56,3	47,9	54,2	41,7	75	50	50
	Ocasionalmente	41,7	31,3	41,7	47,9	43,8	52,1	–	50	50
Bollería y golosinas	Diariamente	14,6	20,8	8,3	10,4	4,2	6,3	50	–	–
	Habitualmente	47,9	35,4	54,2	47,9	58,3	50	50	33,3	50
	Ocasionalmente	37,5	43,8	37,5	41,7	37,5	43,8	–	66,7	50
Refrescos	Diariamente	29,2	20,8	25	25	27,1	29,2	71,4	–	14,3
	Habitualmente	45,8	60,4	54,2	45,8	50	43,8	28,6	57,1	57,1
	Ocasionalmente	25	18,8	20,8	29,2	22,9	27,1	–	42,9	28,6

Desayuno: Sí (Zumo o fruta, productos lácteos y alimentos energéticos: cereales, tostadas… —al menos 2 de ellos—), Insuficiente (Solamente un alimento de los anteriores), No (No desayuna); Fruta: Sí (4-5 piezas diarias), Insuficiente (1-3 piezas diarias), No (Menos de 1 pieza diaria); Agua: Sí (6-8 vasos al día), Insuficiente (3-5 vasos diarios), No (2 ó menos vasos al día); Fritos, Bollería y golosinas y Refrescos: Diariamente (6-7 días a la semana), Habitualmente (2-5 días a la semana), Ocasionalmente (1 vez a la semana, o menos).

cumplimiento (según las referencias de Pérez-López y Delgado, en prensa). Sin embargo, 23 (31,9%) no cumplieron al completo las expectativas iniciales, aunque sí lograron mejorar los registros iniciales del pretest. Y en 4 casos (3 relacionados con el desayuno y 1 con la ingesta de fruta), es decir, en el 5,6%, no se alcanzó ningún tipo de mejora.

Otro dato revelador del efecto de la metodología utilizada es el porcentaje de consolidación obtenido a los 3 meses de haber finalizado la intervención. Éste se situó en el 51,4%, es decir, que algo más de 1 de cada 2 alumnos seguían manteniendo los valores alcanzados en el postest, mientras que el 33,3% no lo logró, pero sí seguían por encima del nivel de partida en el pretest. Y el 15,3% no mostró ninguna mejora con respecto a la referencia obtenida 6 meses antes.

La mejora expuesta hasta el momento se corrobora aún más a raíz de las valoraciones realizadas por los alumnos (del grupo experimental) y sus familias (o personas cercanas a los sujetos que colaboraron realizando el seguimiento), con relación tanto al planteamiento como al logro alcanzado con él (tabla V). En este sentido sobresale la alta valoración de unos y otros del planteamiento que sostiene esta propuesta, pues en ambos casos se supera el valor de 4 ("Satisfecho"), llegando a situarse cerca del 5 ("Muy satisfecho") en aquellos que lo experimentaron de forma directa (con un al 4,71). A tenor de los comentarios realizados del alumnado, dicha valoración estuvo motivada porque les pareció un planteamiento muy atractivo y significativo para ellos: "Nunca imaginé que en el colegio fueran a organizar una competición de cartas. Si el profe quería llamar nuestra atención lo ha conseguido de verdad" (A-3), "Cuando le comentaba a mis amigos que en el colegio estaba participando en una competición del estilo de Yu-Gi-OH y que además estaba mejorando mi salud no se lo creían" (A- 11).

Tabla V

Grado de satisfacción del alumnado y familias con el planteamiento de la intervención y con los logros alcanzados (grupo experimental)

		Media (desviación típica)
Planteamiento	Alumnado	4,71 (0,46)
	Familias	4,58 (0,54)
Logros	Alumnado	4,23 (0,59)
	Familias	4,54 (0,58)

La opinión de los alumnos se ratifica con la del resto de agentes implicados con comentarios como: "Debo reconocer que cuando mi hijo me comentó lo que había planteado el profesor de E.F. no me atrajo mucho la idea, pues no entendía qué tenía que ver con la asignatura ni con la salud, pero al final lo he visto tan motivado que no cabe duda de que ha sido un éxito" (F-16) o "Ha sido un

planteamiento muy diferente a lo que conocemos pero muy atractivo para ellos, por lo que me contaba mi hijo" (F-27). El hecho de haber contado con las familias para lograr un objetivo tan valioso en la actualidad, como es el desarrollo de hábitos saludables, ha sido otro de los motivos de la alta valoración de éstos: "Tanto mi marido como yo estamos encantados de haber colaborado con usted en algo tan importante para nuestro hijo como es su salud" (F-5) o "Esta forma de implicarnos en la formación de nuestros hijos me ha parecido una gran idea. Le animo tanto a usted como al centro a seguir adelante con iniciativas de este tipo" (F-41).

Con respecto a los logros alcanzados, tanto unos como otros, también muestran un alto grado de satisfacción. Entre el alumnado, tras el análisis realizado, el aspecto más repetido es la sensación de haber conseguido algo importante para su salud pasándoselo muy bien: "Lo mejor ha sido mejorar mi salud de una manera divertida. Estaba tan metida en la competición que en todo momento he estado muy animada para cumplir mis compromisos" (A-9) o "Nunca hubiera imaginado que podía tener mejor salud gracias a un juego de cartas. Sabes que este tipo de juegos me encantan por lo que para mí ha sido un trimestre que no olvidaré" (A-30). Por parte de las familias, lo más relevante es el haber conseguido algo que muchos de ellos habían intentado sin mucho éxito: "Es sorprendente como con esta iniciativa usted ha logrado algo que llevo intentando desde hace tiempo, que mi hijo tome más fruta, y sin obligarle. Enhorabuena!" (F-45) o "Es una pena que esta iniciativa no se le haya ocurrido antes. Llevo mucho tiempo explicándole a mi hijo lo importante que es desayunar correctamente, sin conseguir nada. Muchas gracias, y no deje de tener nunca tanta implicación con la salud de sus alumnos" (F-23).

Discusión

Una intervención escolar basada en un juego de cartas realizado durante los recreos, que implica al alumnado de E.S.O. a adquirir compromisos saludables en hábitos alimenticios produce una mejora en la conducta de desayunar y del consumo de fruta y agua, así como una reducción de refrescos, bollería-golosinas y fritos.

Estos resultados son difíciles de cotejar dada la escasez de intervenciones publicadas en la literatura científica con el objetivo de promover hábitos alimentarios en adolescentes[17,19-22].

Con respecto a la metodología, salvo el primero de ellos, el resto difieren considerablemente con el trabajo aquí expuesto. Tanto Martínez et al. (2009)[21] como Puig et al. (2006)[22] llevaron a cabo un programa de educación nutricional a través de talleres, mientras que Espejo et al. (2009)[19] y Herrero y Fillat (2010)[20] aplicaron un programa de educación nutricional dentro del horario escolar, en tutoría y otras asignaturas, a lo que los primeros añadieron una charla trimestral con padres sobre los temas tratados en clase. Sin embargo, Pérez López y Delgado (en prensa)[17] es el único en el que se utilizó la misma metodología (el "Compromiso saludable"), aunque sin el apoyo de ningún material en concreto (como en esta ocasión sucedió con el juego de cartas).

Algo similar ocurre tanto en los instrumentos utilizados para su evaluación como en las personas que certificaron los resultados de los alumnos implicados. De hecho, se produce una considerable diferencia entre las cuatro últimas intervenciones, donde se utilizó fundamentalmente un test o encuesta sobre frecuencia de alimentos cumplimentadas por el propio alumnado, y la de Pérez López y Delgado (en prensa)[17]. En ella, al igual que en esta ocasión, se utilizó como instrumento de registro del cumplimiento o no de los hábitos un informe realizado por un familiar, o persona significativa en la vida del alumnado, responsabilizada del seguimiento del proceso de adquisición de hábitos.

En cuanto a los resultados obtenidos, los alimentos en los que se produjeron diferencias significativas en el trabajo de Martínez et al. (2009)[21], y que también han sido evaluados en éste, fueron: la ingesta de frutas y el desayuno, así como en la reducción de bollería industrial y golosinas. Espejo et al. (2009)[19] destacan igualmente el descenso en la frecuencia de ingesta de bollería en su estudio, junto al consumo de refrescos. Mientras tanto, Herrero y Fillat (2010)[20] tras la intervención observaron 2 resultados similares a los obtenidos en la presente propuesta: por un lado una mejora significativa en el desayuno (en el grupo de intervención) y, por otro, la inexistencia de este hecho en el grupo control. Dicha mejora significativa en el desayuno fue también uno de los resultados más relevantes en el trabajo de Puig et al. (2006)[22].

Por último, Pérez López y Delgado (en prensa)[17] también lograron mejoras altamente significativas tanto en el desayuno como en la ingesta de fruta, así como muy significativas en el consumo de agua, aunque no con el mismo grado de afianzamiento en el retest ($p \leq 0,05$ frente $p \leq 0,01$, a favor de la intervención de Pérez López y delgado, en prensa[17]). Igualmente, en ambos trabajos se produjo una mejora significativa en la reducción del consumo de bollería y refrescos. Pero en aquella ocasión no contaron con un grupo control, como sí ha sucedido aquí, para poder establecer una comparación más real.

Iturbe y Perales (2002)[23] también llevaron a cabo un programa de intervención dietética con adolescentes, pero en su caso no valoraron la adquisición o mejora de ningún hábito en concreto sino la evolución individual de la dieta de éstos en general. La valoración la realizaron a través de la opinión subjetiva de los alumnos participantes a los 8 meses de la finalización del programa. Éste consistió en un bloque inicial teórico en el que explicaban los conceptos básicos de alimentación, dietética y nutrición, un taller con propuestas de dietas equilibradas y una última actuación, con las familias, en la que se les explicó también las cuestiones teóricas y se les pidió su apoyo para poner en práctica las mejoras dietéticas que éstas decidieran llevar a cabo.

Junto a los trabajos anteriores, cabe reseñar igualmente otros 2 que coinciden en el objetivo con el actual (promoción de hábitos de alimentación saludables), aunque no en la población en la que se intervino, pues fue con alumnos de Primaria. En el trabajo de Ruiz Santana et al. (2009)[24] la actuación se basó en una sesión a través de un material educacional (minipirámide de "consulta") y explicación del mismo, junto a una segunda sesión de recordatorio. Gracias a ello obtuvieron una mejora significativa en la ingesta de frutas y en la reducción de dulces, como sucediera también en el trabajo aquí expuesto, aunque con la diferencia de que en esta ocasión la mejora en el consumo de fruta ha llegado a ser altamente significativa. Dicha valoración la realizaron mediante encuesta, a la semana siguiente a la primera sesión. Sin embargo, Ruiz Santana et al. (2009)[24] no obtuvieron esos mismos resultados en la tercera encuesta (a los 2 meses de la segunda sesión), mientras que en el trabajo actual sí se mantuvieron en el retest los resultados obtenidos en el postest.

Por otro lado, Calleja et al. (2011)[25] intervinieron para modificar los hábitos alimentarios solamente en el almuerzo. Su actuación consistió en charlas formativas al profesorado y los padres, sobre la importancia de una correcta alimentación, y en la entrega del almuerzo a los alumnos durante dos semanas (incluyendo lácteos, fruta y bocadillo tradicional). Tras la intervención se produjo un incremento del 9,2% de individuos que almorzaban y una modificación en algunos de los alimentos consumidos, pero sin llegar a ser significativa en el caso de la fruta y sí en el de la bollería, aunque en sentido negativo, lo que supone notables diferencias con los resultados aquí presentados.

Conclusiones

En conclusión, es viable la realización de un programa de intervención escolar basado en el juego de cartas "Fighting for my health" en los recreos escolares dado el alto grado de adherencia, e idóneo dado que consigue mejorar significativamente los hábitos alimenticios del desayuno y el consumo de fruta y agua, así como una reducción del consumo de bollería y golosinas, lo que avala la propuesta (metodología y material curricular) aquí presentada en el alumnado adolescente.

Anexo

"Fighting for my health": Guía de juego[1]

En el juego se enfrentarán 2 jugadores, utilizando diversas cartas de personaje y mágicas (de salud y enfermedad), con el objetivo de lograr 5.000 puntos de vida. Esta circunstancia representaría haber alcanzado el nivel máximo de salud y, con ello, la inmortalidad. Los puntos se consiguen a través de duelos.

Para empezar a jugar

Lo que necesitas para comenzar un duelo es simplemente un mazo de 40 cartas y 10 fichas de puntuación (4 de 1.000, 1 de 500, 4 de 100 y 1 de 50) que marcarán tu progresión en puntos de vida, a lo que habría que añadir una última ficha que determinará el posible carácter negativo de dichos puntos. A partir de aquí ya solo quedará barajar las cartas de tu mazo y jugarte a "piedra-papel-tijera" a quién pertenece el primer turno de juego.

Tipos de cartas

Cada mazo de cartas se compone de 20 cartas de personaje y 20 cartas mágicas (10 de salud y otras 10 de enfermedad).

Cartas de personaje

Los personajes de "Fighting for my health" se dividen en 4 razas diferentes, cada una de las cuales con una característica definitoria que determinará su perfil básico, teniendo como referencia un estilo de vida saludable. Cada raza posee unos atributos específicos, los cuales se concretan a su vez en una habilidad principal. Y, por último, todo ello puede ser desarrollado en distinto nivel (entre 1 y 3, donde el 3 representa el máximo nivel de partida).

Cada carta de personaje incluye, además de la información señalada anteriormente, la imagen del personaje[2] y la descripción básica de algún aspecto relevante de su vida (fig. 1).

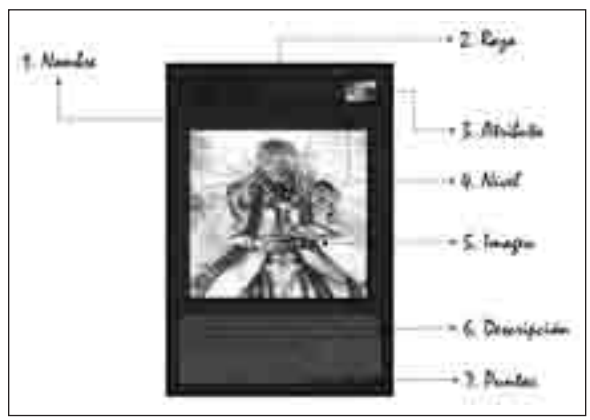


Fig. 1.—Descripción de las cartas de personaje.

[1] En la redacción de esta guía de juego se utiliza habitualmente la segunda persona del singular porque es el formato habitual de este tipo de documentos.

[2] La imagen que ilustra la carta de personaje ha sido tomada de: http://www.taointegral.net/el-arte-de-la-meditacion. Y la de la carta mágica de: http://www.flickr.com/photos/fleurdelis1993/4564452343.

Tabla VI
Razas y aspectos de identificación de los diferentes personajes

Raza	*Característica definitoria*	*Perfil de estilo de vida*	*Color de identificación*
Dioses	Responsables	Saludables	Azul
Héroes	Voluntariosos	Activos	Verde
Humanos	Perezosos	Sedentarios	Marrón
Demonios	Irresponsables	Insanos	Rojo

1. Nombre

En este apartado aparece el nombre del personaje en cuestión. Éste no es algo casual o irrelevante, sino que significa que dicho personaje es el primogénito de su estirpe y, por tanto, el único descendiente a quien se le reserva el honor de recibir las más valiosas enseñanzas de su padre, por lo que representa un enorme orgullo y responsabilidad.

2. Raza

Las 4 razas existentes (tabla VI) se identifican con un color distinto. Todas ellas, además, tienen una característica definitoria que determina el perfil de estilo de vida de dicha raza.

3. Atributo

Existen 4 atributos diferentes (mentales, físicos, instrumentales y sociales) dependiendo de la raza de cada personaje (Dioses, Héroes, Humanos y Demonios, respectivamente) que configuran la personalidad de cada uno de ellos y determinan su habilidad principal.

4. Nivel

Representa el grado de dominio alcanzado por el personaje en el atributo predominante dentro de su raza, pudiendo oscilar entre 1 (el nivel más bajo, y representado por una estrella) y 3 (el más alto, e identificado con tres estrellas). De modo excepcional, y gracias a la activación de una de las cartas mágicas, los Dioses y Demonios pueden alcanzar el nivel 5 en su raza.

5. Imagen

Muestra a cada uno de los personajes tal y como son en la actualidad, lo que te permitirá hacerte una idea bastante ajustada de la fisonomía de éstos.

6. Descripción

En ella se señalan algunos de los aspectos más relevantes de la vida de cada personaje. De esta forma podrás conocer parte de su historia, así como la razón de ser de su raza y nivel.

7. Puntos

Este apartado se divide en puntos de ataque (ATK) y puntos de defensa (DEF). Los primeros representan los puntos que ese personaje tiene para atacar la salud de los demás (como consecuencia de sus malos hábitos de vida), mientras que los segundos se refieren a la defensa que cada personaje tiene de su salud (gracias a los hábitos saludables de vida y actividad físico-deportiva que lo caracterizan).

Estos puntos son los que se utilizarán en los enfrentamientos directos entre personajes, que cada jugador tiene la posibilidad de llevar a cabo en su turno, como se explicará más adelante.

Cartas mágicas

Las cartas mágicas se componen de diferentes apartados, tal y como se presenta en la figura 2:



Fig. 2.—Descripción de las cartas mágicas.

1. Tipo de carta mágica

Las cartas mágicas se dividen en:

- Cartas de salud: Son aquellas que favorecen el desarrollo de hábitos saludables de vida y actividad físico-deportiva. Y, por tanto, potencian fundamentalmente las acciones de los Dioses y Héroes. El color que las identifica es el blanco.

- Cartas de enfermedad: Son aquellas que dificultan o impiden el desarrollo de hábitos saludables de vida y actividad físico-deportiva. Y, por tanto, la mayor parte de ellas potencian las acciones de los Demonios y Humanos. El color que las identifica es el negro.

2. Contenido de la carta

En este apartado se señala el contenido al que hace referencia la carta (con relación a diversos aspectos básicos para lograr, o impedir, un estilo de vida saludable), el cual condicionará el efecto de la misma, en función de su importancia o peculiaridad.

3. Imagen alusiva

Se trata de una imagen que representa el contenido de la carta.

4. Descripción del beneficio o perjuicio sobre la salud

En esta ocasión, como su propio nombre indica, se describe el beneficio (en el caso de las cartas de salud) o perjuicio (en el de las de enfermedad) que el contenido de esa carta tiene sobre la salud.

5. Efecto de la carta

Por último, en las cartas mágicas se señala el efecto que esa carta provoca en los personajes de un jugador, en los del rival o en la dinámica del juego. Además, en algunas de ellas se incluye la palabra "Volteo", lo que significará que no será necesario que dicha carta se active mediante una carta de personaje, sino que se podrá girar (y con ello activar) en cualquier momento para hacer efectivo su efecto.

Dinámica de juego

Una vez barajadas las cartas, y decidido quién comienza el duelo, cada jugador cogerá 7 cartas de su montón (mazo), y colocará las que crea conveniente sobre la mesa antes del primer turno de juego. En cada turno (que irá alternándose) podrás, y no necesariamente en este orden:

1. Robar, colocar cartas en la mesa, modificar el estado de éstas (por ejemplo, de boca abajo girada a boca arriba) y/o devolver cartas de la mesa a la mano.
2. Elegir 1 acción entre: atacar la salud de una de las cartas de tu rival, prevenir una enfermedad (ataque) o comparar la salud de uno de tus personajes con la de uno de los del rival.
3. Activar un máximo de 2 cartas mágicas, una a partir de una carta de personaje (para lo que ésta deberá estar girada boca abajo en la zona de juego al menos desde el turno anterior) y otra por volteo.

Y el jugador al que no le pertenece el turno tendrá la posibilidad de:

1. Bloquear la activación de una carta mágica cuando ésta se realice mediante una carta de personaje.
2. Activar una carta mágica por volteo para afrontar con mayores garantías un enfrentamiento directo.

En la tabla VII se recogen los aspectos a tener en cuenta en cada una de las acciones anteriores, así como las consecuencias del resultado que se produzca en ellas.

Todo jugador tiene la opción de aumentar sus posibilidades de éxito en los enfrentamientos con otros compañeros si decide mejorar o adquirir algún hábito saludable (relacionado con el desayuno, la ingesta de fruta o el consumo de agua) o, por el contrario, reducir algún otro que tenga y sea poco saludable (excesiva ingesta de fritos, bollería-golosinas o de refrescos). Para ello deberá reunirse previamente con el profesor de E.F. y determinar cuál será su compromiso (hasta un máximo de 2), y establecer una estrategia de actuación concreta que, en el caso de cumplir, le otorgará unos beneficios especiales en los diferentes enfrentamientos (bloquear el efecto de una carta de enfermedad, mejorar la defensa de los héroes en 500 puntos…). Al mismo tiempo determinarán qué persona significativa en su vida (padre, madre, tutor, entrenador...) le llevará a cabo el seguimiento, pues ella será quien verifique semanalmente (mediante un informe que recibirá el profesor de E.F.) el grado de cumplimiento, o no, del compromiso adquirido. En el caso de no cumplir el compromiso acordado el jugador en cuestión se verá penalizado con la imposibilidad de utilizar a sus personajes de nivel 3.

Tipos de victoria

Existen diferentes formas de ganar un Duelo, teniendo más valor unas que otras (en orden descendente):

1. *Victoria por inmortalidad*: Se trata de la victoria de mayor mérito en "Fighting for my health", lográndose cuando un jugador alcanza los 5.000 puntos de vida.
2. *Victoria inversa*: Se produce cuando uno de los jugadores reduce la puntuación de su rival hasta los -5.000 puntos de vida.

Tabla VII
Posibles acciones de enfrentamiento directo, pasos a seguir y consecuencias

Acción a realizar	*Valores a comparar*	*Resultado*	*Consecuencia*
Ataque	Tu ATK con la DEF de la carta que elijas de las que tu rival tiene boca abajo (en vertical)	Ganas	1. Pierdes la diferencia en puntos de vida. 2. Tu carta irá al montón o al cementerio (si la diferencia es de al menos 500 puntos).
		Empatáis	1. Ambos perderéis 100 puntos de vida.
		Pierdes	1. Tu carta irá al cementerio. 2. Él sumará la diferencia en puntos de vida.
Prevención	Mi DEF con el ATK de la carta que elijas de las que tu rival tenga boca arriba	Ganas	1. Tú sumarás la diferencia en puntos de vida. 2. Su carta irá al montón o al cementerio (si la diferencia es de al menos 500 puntos).
		Empatáis	1. Ambos perderéis 100 puntos de vida.
Comparación	Mi DEF con la DEF de la carta que tu rival elija de las que tiene boca abajo (en vertical)	Ganas	1. Tú sumarás la diferencia en puntos de vida. 2. Su carta irá al montón o al cementerio (si la diferencia es de al menos 500 puntos).
		Empatáis	1. No pasa nada.
		Pierdes	1. Tu carta irá al montón. 2. Él sumará la diferencia en puntos de vida.
Bloqueo	Mi DEF o ATK (de una de las cartas en la mano) con el ATK o DEF de la carta que tu rival tenga boca abajo girada	Ganas	1. Su carta de personaje irá al cementerio.
		Empatáis	1. Él no podrá activar la carta mágica en ese turno.
		Pierdes	1. Él sumará la diferencia en puntos de vida. 2. Tu carta irá al cementerio.

3. *Victoria incompleta*: Se obtiene cuando tu rival se queda sin cartas con las que continuar el Duelo.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2066-2071
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Actitud de enfermería ante el dolor infantil y su relación con la formación continua

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Resumen

Introducción: **Generalmente, la actitud se ha definido como la fuerza integradora fundamental en el desarrollo de la personalidad y que da consistencia a la conducta del individuo.**

Objetivo: **Determinar la actitud del personal de enfermería, ante el dolor en la infancia.**

Material: **El universo estuvo constituido por 121 enfermeros(as) que laboran en los servicios pediátricos del nivel secundario de salud en la provincia de Cienfuegos (Cuba).**

Método: **Se realizó un estudio observacional y descriptivo en los servicios de atención pediátrica; se les presentó un cuestionario para identificar la actitud que tienen hacia el niño con dolor y se relacionó dicha actitud con las variables de experiencia laboral y formación continuada. El análisis se efectuó valorando las diferencias entre las frecuencias de las respuestas de los distintos grupos de participantes, para lo que se utilizó la prueba de Chi cuadrado. La comparación de medias se efectuó con la prueba t de Anova para grupos independientes. Se consideró significación estadística una $p < 0,05$.**

Resultados: **Dentro de los principales resultados, se destaca que el 71.1% de los participantes tiene una actitud desfavorable hacia el dolor, lo que se relaciona significativamente con la capacitación.**

Conclusiones: **En la medida en que se incrementan las acciones capacitantes, la actitud ante el dolor se hace más favorable.**

(*Nutr Hosp.* 2012;27:2066-2071)

DOI:10.3305/nh.2012.27.6.6029

Palabras clave: *Dolor en la infancia. Actitud de la enfermera.*

NURSE'S ATTITUDES TO PAIN IN CHILDREN AND THEIR RELATION TO CONTINUING

Abstract

Introduction: **Broadly speaking, attitude can be defined as one of the basic elements in personality development, which shapes a person's behavior.**

Objetive: **To determine the attitude of nursing professionals to pain in children.**

Material: **The universe of subjects consisted of 121 male and female nurses who worked in pediatric services at secondary-level health facilities in the province of Cienfuegos (Cuba).**

Method: **A descriptive observational study was performed in the pediatric services of these health centers. The subjects were given a questionnaire to identify their attitude towards pain in children. This attitude was related to the variables, work experience and continuing education. The differences between response frequencies of the groups of participants were analyzed by means of the chi square test. Mean values were compared by using the Anova t-test for independent groups. The value regarded as statistically significant was $p < 0.05$.**

Results: The results obtained showed that 71.1% of the participants have a negative attitude towards pediatric pain, and that this attitude is significantly related to their training.

Conclusions: **As nurses received more training, their attitude towards pain in children was found to be more tolerant and positive.**

(*Nutr Hosp.* 2012;27:2066-2071)

DOI:10.3305/nh.2012.27.6.6029

Key words: *Pain in children. Nurse's attitude.*

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Recibido: 28-VI-2012.
Aceptado: 7-VIII-2012.

Introducción

Generalmente, la actitud se ha definido como la fuerza integradora fundamental en el desarrollo de la personalidad y que da consistencia a la conducta del individuo[1,2]. Otros autores la definen como la evaluación general que las personas realizan sobre lo favorable o desfavorable que resultan los objetos y las personas de su entorno[3,4]. Etimológicamente, actitud significa disposición de ánimo de algún modo manifestado. Es una capacidad que emana de los seres humanos para pensar, sentir y actuar ante determinadas circunstancias; incluye componentes afectivos, pues le da carácter emocional y cognitivo y está relacionado con los conocimientos que se poseen del objeto de la actitud y conativos. Es lo que el sujeto hace, su conducta y, en fin, su forma de actuar[5,6].

La definición de actitud desde el punto de vista psicológico refiere que constituye formas organizadas de pensar, sentir y actuar ante los objetos, fenómenos, personas y grupos. Se forman a lo largo de la vida, son producto del proceso de socialización por el que atraviesa toda persona y el resultado del aprendizaje y de la experiencia, así como del incesante intercambio social que lleva cabo el individuo durante el proceso de su transformación de la realidad objetiva[7,8,9,10].

El análisis de los modelos y teorías de enfermería permite acercarse a la teoría desarrollada por Ernestine Wiedenbasch, basada en una vasta experiencia práctica y educativa que demuestra el efecto ejercido por los pensamientos y sentimientos de las enfermeras en el resultado de sus acciones. Esta autora afirma que en la filosofía de cada enfermera, su actitud ante la vida y la realidad que emana de sus creencias y de su código de conducta, reside en su motivación para actuar y el principio que guía sus pensamientos sobre sus actos y decisiones[11,12].

Es oportuno destacar que la actitud que asuma el personal de enfermería en la prevención del dolor en la infancia será un elemento decisivo en la transición hacia una fase superior en la medicina preventiva, que permita rebasar los actuales métodos de trabajo y formar nuevos protocolos de acción; estos orientan el trabajo e influyen favorablemente en los cambios de la escala de valores y en la actitud que predomina en la sociedad[13,14,15,16].

La ejecución adecuada de los procedimientos con los niños es uno de los retos que los profesionales de enfermería deben afrontar a lo largo de su desempeño profesional en el ámbito de la pediatría. Supone, a menudo, una experiencia difícil y dolorosa, tanto para el niño, como para la familia y la enfermera. Los procedimientos son necesarios y no hay manera de evitarlos; alguien debe hacerlo y muchas veces será la enfermera la encargada de ello, por lo que son exigibles conocimientos amplios de estrategias y comunicación que minimicen las molestias y favorezcan el éxito de la técnica.

Las técnicas usadas para desarrollar los procedimientos pueden influir de manera significativa en las reacciones al dolor. En diferentes estudios realizado por Heaton, se ha demostrado que la venopunción causa menos dolor que la lanceta del talón, por lo que es el método más deseable en la obtención de las muestras de sangre de los neonatos, cuando lo efectúan profesionales de la salud debidamente capacitados. Los catéteres venosos centrales insertados por vía percutánea son los preferidos, porque requieren menos intentos para la inserción de cada dispositivo, en comparación con los intravenosos periféricos[6].

Los profesionales de la salud involucrados en la atención sanitaria de la infancia tienen la responsabilidad de tratar de asegurar los cambios en la práctica clínica basándose en los ensayos clínicos publicados. No se pueden evitar todos los procedimientos dolorosos, pero sí minimizar el dolor y la angustia después de los mismos. No hay razón alguna para llevarlos a cabo, sin una adecuada sedación y analgesia; y es que importante recordar que todos los niños, desde la etapa de recién nacido hasta la adolescencia, sienten el dolor y la ansiedad, por lo que deben ser tratados de forma adecuada. La lactancia materna es una forma de terapia no farmacológica en los bebés. Esta forma de alimentación proporciona numerosas ventajas para la madre y el niño. La lactancia materna se ha establecido como un método eficaz en la prevención del cáncer de mama y obesidad. El contenido de la leche humana está adaptada perfectamente a las necesidades del bebé, incluso con diferentes compuestos en el día y en la noche[17,18,19,20,21].

Hoy se constata la necesidad de cambiar la actitud y la percepción del dolor en la infancia, de modo que sea posible adquirir una visión holística, compleja, integral, ética y responsable sobre su atención y prevención en la infancia. Actualmente existe consenso a la hora de reconocer la necesidad imperiosa de insistir en su prevención, por lo que resulta necesario buscar estrategias y alternativas en la capacitación profesional. Es preciso implementar intervenciones educativas de una máxima complejidad en los conocimientos, habilidades y valores relacionados con esta delicada cuestión. Las terapias no farmacológicas como forma de minimizar el dolor es una alternativa eficaz.

Este estudio se está realizando en varios países de Europa y de Iberoamérica y está coordinado por el Grupo de Investigación CTS 367 del Plan Andaluz de Investigación (PAI) de la Junta de Andalucía (España).

Objetivo

Determinar la actitud del personal de enfermería ante el dolor en la infancia.

Diseño metodológico

Se realizó un estudio observacional y descriptivo en los servicios de atención pediátrica. El universo estuvo constituido por el personal de enfermería que allí

labora, con N = 121; se le presentó un cuestionario para identificar la actitud del personal de enfermería hacia el niño con dolor, esto es, favorable o desfavorable. Una vez identificada la actitud, se relacionó con las variables de experiencia laboral y formación continuada. El análisis se llevó a cabo evaluando las diferencias entre las frecuencias de las respuestas de los distintos grupos de participantes, para lo que se utilizó la prueba de Chi cuadrado. La comparación de medias se efectuó con la prueba t de Anova para grupos independientes. Se consideró significación estadística una $p < 0,05$.

Procedimiento técnico

Una de las técnicas de evaluación de actitudes es la basada en el uso de cuestionarios de respuesta cerrada, como las escalas Likert. Las encuestas tipo Likert son las más empleadas a la hora de obtener información rápida, pues son más fáciles de evaluar.

Pasos en la elaboración de la escala

Contempla un proceso sistemático de juicios y procedimientos estadísticos. En los juicios se incluye la definición de los ítems; entre los procedimientos estadísticos básicos está la medida de la validez de contenido y de la fiabilidad. Teniendo en cuenta estos requisitos, se presentan de forma resumida los pasos seguidos para la elaboración de la escala de actitudes del personal de enfermería, ante el dolor del niño.

1. Definición de la actitud

Con el fin de delimitar la actitud que se quiere evaluar, debe elegirse el objeto de la misma y enmarcarlo en apartados o categorías que contribuyan a especificar el objeto de medida. En esta investigación, el objeto es el dolor del niño y las categorías son las que aparecen representadas al final de esta sección. Se eligieron 5 apartados, en función del interés de los contenidos seleccionados para el estudio del problema. En la definición de los apartados participaron profesionales dedicados durante más de 15 años a la salud infantil, profesores de Enfermería Infantil y otros profesionales vinculados a la atención del niño.

En esta fase se definen claramente las características de cada categoría y el número dedicado a cada apartado. Al principio fue conveniente incluir un mayor número de ítems en cada apartado, puesto que en la fase de validación algunos fueron excluidos. Conviene señalar que las distintas cuestiones de cada categoría tienen relación entre ellas.

Así pues, es importante especificar las características de los contenidos de cada apartado mediante el acuerdo de los miembros del equipo que elaboró la escala. En el estudio se estableció que las categorías de la escala sobre la actitud del personal de enfermería ante el dolor infantil contemplaran los aspectos siguientes:

- *Categoría 1 (C1).*El dolor en la infancia como problema de salud.
- *C2.* El dolor en la infancia y su relación con la recuperación de la salud. La atención de enfermería en la prevención del dolor.
- *C3.* Las diferentes escalas para medir el dolor y su utilidad en la práctica asistencial.
- *C4.* La prevención y el tratamiento del dolor.
- *C5.* El tratamiento no farmacológico del dolor.

2. Elección de los enunciados de cada cuestión

Los enunciados de los ítems se presentan en primera persona y reflejan la opinión personal o la disposición a actuar. Se formularon en un lenguaje directo. Antes de definir las preguntas, se pidió a los encuestados que hicieran comentarios sobre sus experiencias respecto al objeto de la actitud. Se utilizaron frases extraídas de las ideas remarcadas por las enfermeras y se recurrió también a la información que proporcionan los trabajos de investigación y la literatura existente sobre el tema del dolor en la infancia.

3. Redacción y presentación de los enunciados

Las actitudes tienen la función de expresar la valoración que una persona hace de los resultados de sus acciones. La formulación de los ítems contempló otro requisito, el de marcar la posición favorable, desfavorable o indiferentes hacia los resultados de una determinada conducta.

Se produjo un equilibrio entre el número de enunciados que se presentan como favorables y los que remarcan la posición desfavorable. En todos los ítems se pidió que mostraran su grado de acuerdo, indiferencia o desacuerdo con las propuestas. La graduación se presentó con cinco posiciones que solicitaron mostrar la conformidad entre los extremos "totalmente de acuerdo" y "totalmente en desacuerdo". Las intermedias fueron "de acuerdo", "indiferente" y "en desacuerdo".

El número aproximado de ítems del cuestionario inicial sobre la actitud ante el dolor del niño fue de 30. Una vez formulados los ítems de cada categoría, se distribuyó al azar en la escala. Los enunciados de cada apartado no se presentaron juntos, sino intercalados con los de otras categorías, para reconocer la consistencia de las respuestas a lo largo de la escala. También se distribuyeron al azar los ítems que marcan las posiciones favorable y desfavorable.

4. Búsqueda de la validez de contenido de los ítems y de la fiabilidad

Los ítems han de estar correlacionados entre sí y deben ser instrumentos estables de medición (han de

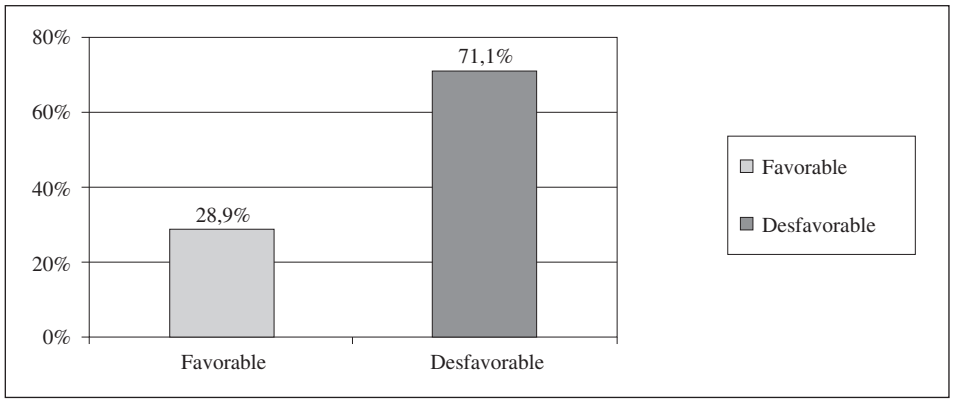


Fig. 1.—Actitud del personal de enfermería ante el dolor infantil.

ser utilizados con distintas muestras de profesionales de enfermería y en situaciones análogas). Para determinar la validez, o sea, para saber si el cuestionario mide la actitud hacia la atención del dolor del niño, se parte del supuesto de que si todos los ítems tienen correlaciones positivas con los demás, expresan la misma actitud. En este caso, el poder discriminativo de los enunciados se estableció mediante las pruebas de correlación ítem-total (o índice de homogeneidad). Los ítems definitivos son los que obtuvieron un valor de correlación situado por encima de 0,20.

Para medir la fiabilidad se optó por la aplicación del coeficiente alpha de Cronbach, para el que se estableció un valor superior a 0,80.

5. Presentación del cuestionario definitivo

Se le aplicó a 121 enfermeros(as) que representa la totalidad de la población estudiada, en su puesto de trabajo. Para determinar la actitud, se estableció una puntuación mayor o igual a 80 puntos, para la de carácter favorable, y con valores inferiores a 80 puntos, para la actitud desfavorable.

El análisis de los resultados se realizó mediante las diferencias entre las frecuencias de las respuestas de los distintos grupos de participantes y se utilizó la prueba de Chi cuadrado. La comparación de medias se efectuó con la prueba t de Anova para grupos independientes. Se consideró significación estadística una $p < 0,05$. Los resultados se presentan en las tablas.

Resultados (fig. 1)

El 71,01% del personal de enfermería estudiado presenta actitudes desfavorables hacia el niño con dolor y solamente el 28,9% manifiesta una actitud favorable.

Al analizar la actitud del personal de enfermería en relación con la experiencia laboral encontramos que el mayor porcentaje de enfermeros(as) con una actitud desfavorable presentan una experiencia laboral entre 5-10 años. A destacar que no existieron diferencias significativas con respecto a los demás grupos (fig. 2).

Al caracterizar la actitud del personal de enfermería respecto a la formación continuada se pudo constatar que el 52% de los enfermeros(as) no han recibido ninguna capacitación en el postgrado con temáticas rela-

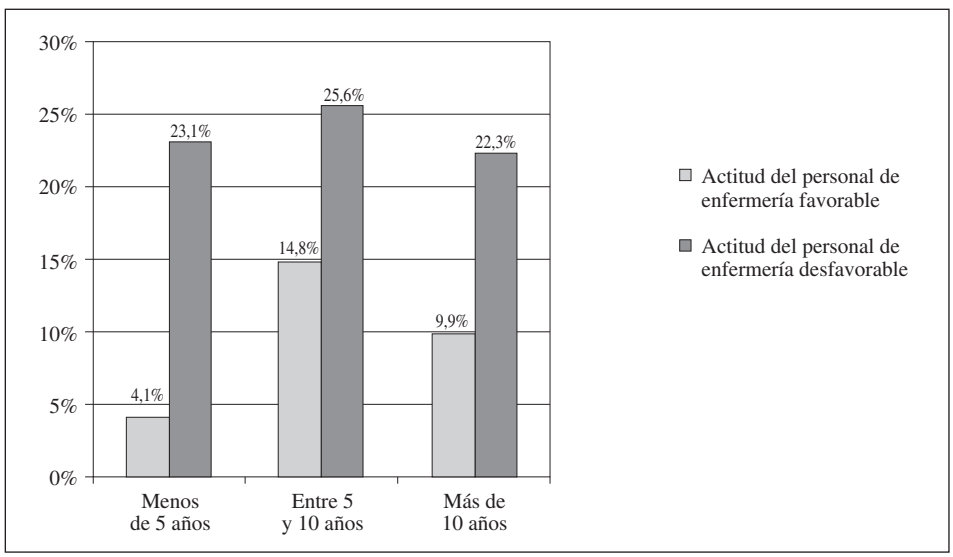


Fig. 2.—Relación de la actitud del personal de enfermería ante el dolor infantil y la experiencia laboral.

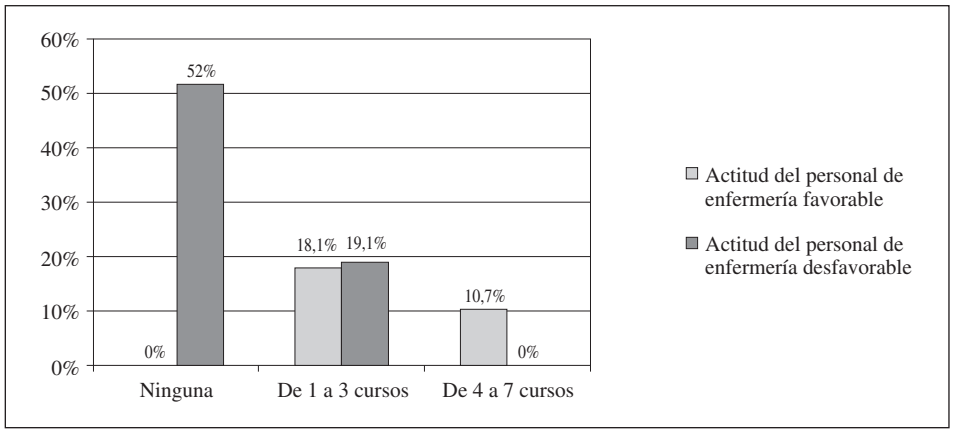


Fig. 3.—Relación de la actitud del personal de enfermería ante el dolor infantil y la formación continuada en los últimos cinco años.

cionadas con el dolor y son las que mayoritariamente muestran actitudes desfavorables. Las actitudes favorables se evidencian en quienes han recibido capacitación (18,1% y 10,7%, respectivamente); a mayor número de cursos recibidos, mejor es la actitud. Esta diferencia fue estadísticamente significativa con un valor de $p < 0,05$ (fig. III).

Discusión

El dolor es una experiencia humana universal. De hecho, es el motivo más frecuente en la demanda de cuidados sanitarios, así como la primera señal de múltiples patologías. Hasta hace poco tiempo, se ha visto el dolor de los niños como un síntoma de la enfermedad o trauma, y no como un problema que requiere evaluación y tratamiento. El nuevo enfoque depende, en gran medida, de la actitud del personal de enfermería que, a su vez, se ve relacionado con los conocimientos básicos que posee, con su apreciación subjetiva, con la afectación emocional y con la percepción. Todos estos factores están sujetos al contexto social y cultural en donde desempeñan su labor los profesionales sanitarios.

En el estudio realizado (fig. 1) se evidencia un porcentaje elevado de enfermero(as) con actitudes desfavorables, aspecto que debe hacer reflexionar acerca del modo de la actuación profesional. Al revisar la literatura, estudios realizados por Collao afirman que la evolución positiva de un niño y su estadía en el hospital, se acorta en función de la actitud que la enfermera tenga hacia su dolor[22].

Otros trabajos de Twycross destacan que existen factores que inciden en que las enfermeras no siempre perciban el dolor de sus pacientes, lo que se asocia invariablemente con la valoración que el profesional haga del dolor[23].

Por otra parte, *Jacobs* concluye que no hay evidencia en los registros clínicos de que las enfermeras desarrollen herramientas apropiadas para valorar el dolor y evalúen las respuestas de los niños hacia las estrategias de manejo, lo que representa también una actitud desfavorable[24].

De un modo general, los resultados de este estudio son similares a los de otros autores mencionados anteriormente. Se puede afirmar que es responsabilidad de todos los que día a día protegen la salud infantil prevenir y aminorar el dolor. Para ello, hay que adoptar las medidas adecuadas, por las que se logre que los enfermero(as) tengan una actitud más favorable en el manejo del dolor. Ello debe ser el centro de la práctica de enfermería.

Un aspecto explorado en este estudio (fig. 2) fue la relación entre la actitud del personal de enfermería y la experiencia laboral en los servicios pediátricos. No se observaron diferencias significativas entre esas variables, por lo que este resultado no difiere del estudio realizado por Salantera. Aunque éste no midiera la actitud, sino el conocimiento, concluyó que, cuando se trata sólo de conocimientos acerca del manejo del dolor, no existen diferencias, ni por edad, ni por experiencia laboral[25].

Los resultados de este estudio y los comentarios anteriores ponen de manifiesto que la actitud favorable no precisa de tiempo en el desempeño para manifestarse y que está dada por la capacidad que emana de los seres humanos para pensar, sentir y actuar ante determinadas circunstancias y se forman a lo largo de la vida.

La (fig. III) expresa la relación que tiene la formación continuada con la actitud del personal de enfermería. En este caso, asociada a la atención del dolor a la infancia, donde las enfermera(os) que no han recibido capacitación o cursos de superación profesional presentan una actitud desfavorable, lo que demostró una diferencia significativa entre ambas variables.

Estudios anteriores, como los realizados por Twycross, aún cuando no relaciona la actitud frente al dolor, concluye que, derivado de la inadecuada educación recibida por las enfermeras pediátricas, tanto en el pregrado como en el postgrado, los niños continúan sufriendo innecesariamente durante su hospitalización. De lo que se deriva que las enfermeras no dan prioridad al manejo del dolor tanto como a otras actividades de su quehacer profesional. Así pues, los currículos de pregrado deben evaluarse y ajustarse introduciendo conte-

nidos que permitan el conocimiento y el manejo adecuado del dolor, sobre todo en las asignaturas de pediatría y las otras que se relacionen con ella.

En esta investigación se pone de manifiesto que las personas que no han recibido capacitación durante su vida laboral en la temática del dolor, son las que mayoritariamente muestran actitudes desfavorables frente al niño que lo padece. Se pudo constatar que el modo de actuación del personal de enfermería está en estrecha relación con su capacitación; este aspecto es imprescindible para alcanzar un desempeño profesional de calidad y garantizar una atención integral al dolor en la infancia.

En la medida en que la superación profesional avance, tendrá lugar un cambio en la actitud de los profesionales de enfermería, en nuestro caso, en lo relacionado con la atención al dolor en la infancia. De ahí, la importancia de las acciones capacitantes.

Conclusiones

La revisión de la literatura pone de manifiesto que la atención al dolor no ha sido debidamente tratada en la formación inicial y posgraduada de enfermería.

Al identificar la actitud del personal de enfermería hacia el dolor del niño, se evidenció que es necesario un cambio en el actuar de enfermería con la perspectiva de transformar la realidad objetiva. Existe un porcentaje elevado de enfermeros(a) con actitudes desfavorables en este sentido.

Se pudo constatar que la posición favorable de la actitud está en estrecha relación con la capacitación. En la medida en que el profesional de enfermería recibe nuevas acciones capacitantes, su actitud ante el dolor cambia y, con ello, su modo de actuación profesional.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2072-2078
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Phase angle as a nutritional evaluation tool in all stages of chronic liver disease

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Abstract

Introduction: **Malnutrition is commonly and frequently under-diagnosed in clinical settings in patients with chronic liver disease(CLD) due to the limitations of nutritional evaluation methods in this population. We hypothesized that the bioelectrical impedance analysis derived phase angle (BIA-derived PhA) might be considered as a nutritional indicator in CLD since it represents either cell death or malnutrition characterized by changes in cellular membrane integrity.**

Objective: **The aim of this study was to evaluate the BIA-derived PhA as a nutritional evaluation tool in all stages of CLD, including chronic hepatitis, liver cirrhosis and hepatocellular carcinoma (HCC). Liver-related death and survival were evaluated.**

Methods: **A total of 66 patients were enrolled in a cross-sectional study. For the nutritional diagnosis, mid-arm circumference (MAC), triceps skinfold thickness (TST), mid-arm muscle circumference (MAMC) and Subject Global Assessment (SGA) were evaluated. Biochemical and clinical evaluations were performed.**

Results: **Our results showed that PhA was higher in well-nourished patients, according to SGA and in the patients without hepatic encephalopathy. PhA correlated significantly with MAMC, MAC and albumin and was inversely correlated with age. No correlation was found between PhA values and the Child-Pugh score and ascites. PhA was strongly associated with survival and PhA ≤ 5.18° with relative risk increase of 2.5 for death.**

Conclusions: **We conclude that the BIA-derived PhA is a relevant nutritional evaluation tool in chronic hepatitis, liver cirrhosis and HCC and the role of PhA in the prediction of survival in CLD should be examined further in a controlled study.**

(*Nutr Hosp.* 2012;27:2072-2078)

DOI:10.3305/nh.2012.27.6.6015

Key words: *Phase angle. Subject global assessment. Chronic liver diseases. Nutritional status. Anthropometry.*

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Recibido: 1-III-2012.
1.ª Revisión: 20-VI-2012.
Aceptado: 11-IX-2012.

ÁNGULO DE FASE COMO UNA HERRAMIENTA PARA EVALUAR EL ESTADO NUTRICIONAL EN TODAS LAS ETAPAS DE LA ENFERMEDAD HEPÁTICA CRÓNICA

Resumen

Introducción: **La malnutrición es común y frecuentemente subdiagnosticada en el ámbito clínico en pacientes con enfermedad hepática crónica (EPC), ya que las limitaciones de los métodos de evaluación nutricional en esta población. La hipótesis de que el análisis de impedancia bioeléctrica derivada del ángulo de fase (AF) puede ser considerado como un indicador nutricional en la EPC, ya que representa tanto la muerte celular o la desnutrición se caracteriza por los cambios en la integridad de la membrana celular.**

Objetivos: **El objetivo de este estudio fue evaluar la AF como un instrumento de evaluación nutricional en todas las etapas de la EPC, incluyendo hepatitis crónica, cirrosis hepática y carcinoma hepatocelular (CHC).**

Métodos: **Se evaluó la muerte relacionada con el hígado y la supervivencia. Un total de 66 pacientes fueron incluidos en un estudio de corte transversal. Para el diagnóstico nutricional, circunferencia del brazo (CB), el pliegue del tríceps (PT), circunferencia del brazo muscular (CBM) y la valoración global subjetiva (VGS) fueron evaluados. Evaluaciones bioquímicas y clínicas se llevaron a cabo.**

Resultados: **Nuestros resultados mostraron que la AF fue mayor en los pacientes bien nutridos, de acuerdo con VGS y en los pacientes sin encefalopatía hepática. El AF se correlacionó significativamente con la CBM, CB y la albúmina y se correlaciona inversamente con la edad. No se encontró correlación entre los valores de la AF y la puntuación de Child-Pugh y la ascitis. La AF está fuertemente asociada con la supervivencia y la AF ≤ 5,18 ° con el aumento de riesgo relativo de 2,5 para la muerte.**

Conclusiones: **Llegamos a la conclusión de que la AF es una herramienta relevante la evaluación nutricional en la hepatitis crónica, cirrosis hepática y carcinoma hepatocelular y el papel de la AF en la predicción de la supervivencia de la EPC debe seguir siendo examinado en estudios controlados.**

(*Nutr Hosp.* 2012;27:2072-2078)

DOI:10.3305/nh.2012.27.6.6015

Palabras clave: *Ángulo de fase. Valoración global subjetiva. Enfermedades crónicas del hígado. Estado nutricional. Antropometría.*

Abbreviations

CLD: Chronic liver disease.
BIA: Bioelectrical impedance analysis.
PhA: Phase angle.
HCC: Hepatocellular carcinoma.
MAC: Mid-arm circumference.
TST: Triceps skinfold thickness.
MAMC: Mid-arm muscle circumference.
SGA: Subject Global Assessment.
PTA: Prothrombin time activity.
BCM: Body cell mass.
R: Resistance.
Xc: Reactance.
PCR: Polymerase chain reaction.
CT: Computed tomography.
RM: Scan and/or magnetic resonance imaging.
HIV: Human immunodeficiency virus.
CI: Confidence interval.

Introduction

Patients with chronic liver disease (CLD) carry a risk of specific life threatening complications and comorbidities. The nutritional status has been proposed as a prognostic factor in cirrhotic patients and was originally suggested as a prognostic factor for cirrhosis by Child and Turcotte.[1-3] Malnutrition is highly prevalent among patients with CLD, occurring early in the natural history of the disease and accompanying functional hepatic deterioration, thereby contributing to overall mortality and complications rate.[4-6] Although the course of CLD varies according to several factors, the need for a nutritional evaluation tool is highlighted in order to manage the patient's response to therapy, thus reducing the complications of the treatment.[7,8]

Traditionally, assessment of nutritional status has included measures of anthropometry and Subject Global Assessment (SGA). Anthropometric measurements are one of the most useful indices of nutritional evaluation in patients with CLD[6] and MAMC is considered the most sensitive marker of body cell mass (BCM).[9] Hasse et al.[10] have shown there is some benefit in using SGA to evaluate adult liver-transplant candidates, however, it remains controversial whether or not SGA underestimates the nutritional status in patients with liver cirrhosis.[11] Therefore, the lack of a valid and reliable tool to measure nutritional status in these patients is still a challenge as CLD affects most of the traditional tools of nutritional evaluation.

The bioelectrical impedance analysis (BIA) is a promising nutritional assessment tool that incorporates both functional and morphological evaluation. BIA is a simple, non-invasive, and reproducible technique that measures body composition.[12] BIA uses body resistance (R) and reactance (Xc) to a flow of alternating electrical current to determine impedance. Resistance is inversely proportional to the amount of body water and electrolyte. Reactance is related to the capacitance properties of the cell membrane since the applied current will charge cell membranes, and variations can occur depending on its integrity, function and composition.[13] Phase angle (PhA) is obtained from the direct measurements of R and Xc and is calculated as the arctangent of the ratio of Xc to R.[14] PhA can be interpreted as an indicator of fluid distribution or electric resistance and cellular membranes capacitance of the human body. Theoretically, PhA might be considered as a nutritional indicator, since malnutrition is characterized by alterations in fluid balance and changes in cellular membrane integrity.[15] Lower PhA appears to be consistent with low Xc or with cell death or a breakdown in the selective permeability of the cell membrane and thus it may be a predictive factor for survival.[16]

Findings from other studies indicate that PhA is a good prognostic indicator. It has been suggested that PhA represents the body cell mass and indicates nutritional status, with significant prognostic power, in HIV-infected patients,[17] and further in patients with liver cirrhosis,[18] in peritoneal dialysis patients,[19] in cancer patients,[20-23] in amyotrophic lateral sclerosis,[24] in advanced cancer,[25] in hepatitis C infection following antiviral therapy,[26] in preoperative patients[27] and hospitalized patients.[28]

The role of PhA for nutritional evaluation in all stages of CLD still remains to be investigated inasmuch as it has been previously studied only in liver cirrhosis.[18] Our hypothesis is that PhA might be considered as an indicator of nutritional status in CLD. To clarify this issue, the objective of the present study was to evaluate the association between BIA derived PhA and traditional methods of nutritional evaluation considering all stages of CLD, including chronic hepatitis, liver cirrhosis and hepatocellular carcinoma (HCC).

Methods and materials

Subjects

In the cross-sectional phase of the present study, data were collected from January 2009 to December 2010 at the University Hospital of the Federal University of Rio de Janeiro, Rio de Janeiro, Brazil. Patients with age ≥ 18 years with chronic hepatitis, liver cirrhosis and HCC were eligible for enrolment in the study.

The diagnosis of hepatitis was based on polymerase chain reaction (PCR). The diagnosis of liver cirrhosis was based on clinical manifestations and laboratorial test, as well as on ultrasonographic imaging and histological evaluation whenever necessary. The diagnosis of HCC was based on computed tomography (CT), scan and/or magnetic resonance imaging (RM) finding and serum alpha-fetoprotein. The degree of ascites and hepatic encephalopathy were based on ultrasound data or on clinical evaluation, respectively.

The number of liver-related deaths was recorded during the observation period. The Kaplan-Meier method was used to calculate survival.

Exclusion criteria comprised patients with cardiac pacemaker, amputated limbs, aneurysm clip, metal implants, chronic renal failure, hemodialysis, active alcohol abuse or history of respiratory or cardiovascular disease, co-infection with human immunodeficiency virus (HIV) and unwillingness to participate in the study.

The study protocol was approved by the Research Ethics Committee of the University Hospital of the Federal University of Rio de Janeiro, protocol 068/01, and it conforms to the provisions of the Declaration of Helsinki. An informed written consent was requested from all subjects before they enrolled in the study.

Clinical variables were recorded during the study by the same investigator. The laboratory data collected included albumin, bilirubin and prothrombin time which were measured by previously established standard laboratory methods. Laboratory data and degree of ascites and hepatic encephalopathy were used to calculate the Child-Pugh score. The patients were then stratified as A, B, or C in accordance with the Child-Pugh classification criteria.[2]

The patients selected for the study underwent baseline nutritional evaluations which included anthropometry, BIA and SGA, conducted at the same time by the same trained nutritionist.

Phase angle

BIA measurements were taken on the right side of the body using a tetrapolar BIA-101 impedance analyzer (RJL Systems Inc., Clinton Township, MI, USA), at 800 mA and a single frequency of 50 KHz. The measurements were taken in the morning after each participant had fasted for at least 8 hours and with an empty bladder. All impedance measurements were conducted while the participants were lying supine on bed, with legs apart and arms not touching the torso. The four electrodes were placed separately. Two on the dorsal surface of the right wrist, medially between the distal prominences of the radius and the ulna and on the dorsal surface of the right ankle, between the medial and lateral malleoli; two on the dorsal surface of the right hand and foot at the third metacarpophalangeal and metatarsophalangeal joints, respectively. R and Xc were directly measured in ohms (W). The PhA was calculated using the following equation:

PhA = arc-tangent reactance/resistance x 180°/p

Anthropometry

Anthropometric parameters like mid-arm circumference (MAC) and triceps skinfold thickness (TST) were measured with a tape and a Lange skinfold caliper, respectively. TST was measured to the nearest 0.1 mm with calipers at the triceps. Measurements were taken midway between the tip of acromion and olecranion process on the non-dominant arm, being the patient in a relaxed position. To minimize practical variability, the average of three consecutive measurements for TST was recorded. The mid-arm muscle circumference (MAMC) was calculated by the formula MAMC (cm) = MAC – [P x TSF (cm)][29]. For the nutritional diagnosis, the anthropometric parameter was compared with Frisancho's reference standard.[29]

Subjective global assessment

SGA was performed using a standard questionnaire as proposed by Hasse et al. adapted to liver disease[10]. On the basis of the patient history, physical appearance and existing clinical conditions focused on nutritional aspects, the patients were classified as not, moderately or severely malnourished. For the purpose of this article, malnutrition was defined as either moderately or severely malnourished.

Statistical analysis

The Statistical Package for Social Science software version 17.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analysis. Data were expressed as median and range. For the Kaplan-Meier survival analysis, PhA measurements were categorized into two equal and mutually exclusive groups with a median PhA score of 5.18° as the cut-off. The influence of possible risk factors on patient survival was analyzed by Cox multivariate regression. Kruskal-Wallis one-way analysis of variance, Mann–Whitney *U* test and Spearman's correlation test (*r*) were used in the statistical analysis. Significance level was defined as $P < 0.05$.

Results

A total of 66 patients with CLD who met the inclusion and exclusion criteria were enrolled. The median age was 59 years (range 41-79). There were 34 male patients (57.6%). The etiology of the CLD was as follows: 60.8% chronic hepatitis C infection, 24.0% chronic hepatitis B infection and 15.2% alcohol-related. According to liver disease severity, there were 14 patients in the chronic hepatitis group, 8 in the cirrhosis Child-Pugh A group, 11 in the Child-Pugh B group, 14 in the child-Pugh C group and 19 in the HCC group. In the HCC group, 15 patients were Child-Pugh A and 4 were Child-Pugh B.

All patients in the cross-sectional sample were followed for at least 17 months.

Table I
Descriptive statistics for bioelectrical parameters by chronic liver disease stage

CLD stages	*PhA (degrees)**	*Resistance (Ω)**	*Reactance (Ω)**
Chronic hepatitis (n = 14)	5.6 (4.0-6.9)	512 (401-612)	49 (32-58)
Cirrhosis child A (n = 8)	5.4 (1.9-6.4)	524 (338-646)	56 (11-63)
Cirrhosis child B (n = 11)	4.6(4.1-6.7)	502 (396-712)	54 (28-69)
Cirrhosis child C (n = 14)	4.4 (3.2-7.4)	495.5 (386-589)	41 (22-63)
H < CC (n = 19)	4.8 (2.9-6.7)	494 (360-710)	39 (26-69)
P-value**	0.36	0.55	0.15

*Values are expressed as median (minimum-maximum).
**Differences between groups were tested with Kruskal-Wallis at 5% probability.
Note: BIA: Bioelectrical impedance; CLD: Chronic liver disease; PhA: Phase angle; HCC: Hepatocellular carcinoma.

The parameters of BIA distribution in chronic hepatitis, liver cirrhosis and HCC are shown in table I. There were no statistically significant differences with respect to PhA, R and Xc median values between chronic hepatitis, liver cirrhosis and HCC ($P = 0.36$, $P = 0.55$ and $P = 0.15$, respectively).

The median (range) of PhA regarding all the patients was 5.18° (range 1.86-8.40).

The median PhA was 5.31° (range 3.45-7.42) in well-nourished patients being significantly higher than malnourished patients (4.35°, range 1.86-6.73) ($P = 0.005$), according to SGA results.

Correlation coefficients between PhA and age, liver function test and anthropometry parameters in CLD patients are shown in Table 2. PhA correlated significantly with MAMC ($r = 0.29$, $P = 0.015$), MAC ($r = 0.29$, $P = 0.023$) and albumin ($r = 0.27$, $P = 0.036$). The PhA was correlated inversely and significantly with age ($r = - 0.48$, $P < 0.001$). The median age was 63.5 years (range 43-79) and 55.0 years (range 41-68) for the below median and above median PhA groups respectively ($P = 0.015$). There was no significant difference in PhA values between the sexes ($P = 0.59$).

A comparison of phase angle between the groups with presence or absence of hepatic encephalopathy and ascites has shown that the median of PhA was 4.17° (range 3.19-7.42) in patients with hepatic encephalopathy being significantly lower than in patients without hepatic encephalopathy (5.04°, range 1.86-6.89) ($P = 0.003$).

The median PhA was 4.62° (range 1.86-7.42) in patients with ascites and 5.03° (range 2.94-6.89) in patients without ascites with lower values of PhA in patients with ascites, but the results have not shown statistical significance, only a strong tendency ($P = 0.05$). With respect to hepatocellular function evaluated according to the Child-Pugh score, no statistically significant correlation was found between PhA, R and Xc values and Child-Pugh score ($P = 0.17$, $P = 0.29$ and $P = 0.16$, respectively).

During the study period, there were 37 patients who died and 25 were censored (reached the end of their follow-up period without experiencing death). PhA was strongly associated with survival ($P = 0.013$). The survival curves were stratified by median (fig. 1). Patients with PhA lower or equal than 5.18° (n = 38) had a median survival time of 62 months (95% confidence interval [CI]: 55.5-68.5) while those with PhA > 5.18° (n = 21) had a median survival time of 122 months (95% CI: 67-177). The difference was statistically significant ($P = 0.01$).

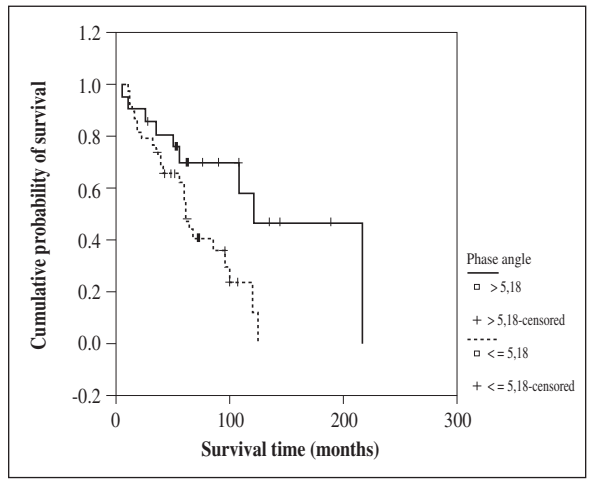


Fig. 1.—Survival time stratified by median phase angle (PhA) categories of ≤ 5.18° (dashed line) or > 5.18° (solid line). Vertical lines indicate censored patients, i.e., those who reached the end of their follow-up without experiencing death.

In a multivariate Cox regression analysis, after adjusting for age, PhA ≤ 5.18° was found to be associated with a hazard ratio increase of 2.5 for death (95% CI: 1.85-6.01) ($P = 0.032$).

The median phase angle of patients who died within the observation period was significantly lower than the median phase angle of patients who survived (median 4.55° compared to 5.28°, $P = 0.01$).

Discussion

This study adds a growing body of evidence on the clinical applications of BIA derived phase angle beyond its use in body composition equations.

Table II
Correlation coefficients between phase angle and age, liver functions test and anthropometry parameters in CLD patients

Variables	*PhA (r)*	*p-value*
Age	-0.48	< 0.001
Albumin	0.27	0.036
Bilirubin	0.033	0.80
MAC	0.290	0.023
MAMC	0.29	0.015
TST	0.21	0.10

r = Spearman correlation coefficient.
Note: CLD: Chronic liver disease; PhA: Phase angle; MAC: Mid-arm circumference; MAMC: Mid-arm muscle circumference; TST: Triceps skinfold thickness.

The inverse relationship between age and PhA observed in the current study supports results of a previous study on healthy subjects.[30] It has been speculated that the decrease in PhA values correlating with increasing age could be an indicator of a reduction in skeletal muscle mass and general health in the elderly.[31,32] At the same time, there was no statistically significant difference with respect to PhA and sex, a finding that is similar to the results obtained by Baumgartner et al.[13] and Selberg and Selberg[18], but not to those obtained from other studies on healthy adults.[30,33]

In the present study, the median of R, Xc and PhA was lower than the values described by Selberg and Selberg[18] in healthy control subjects. In addition, our results of PhA values found in chronic hepatitis, cirrhosis Child A, B, C and HCC were lower than the population reference values described by Barbosa et al.[34] that ranged between 7.90° and 5.64°.

PhA and Xc are directly reflecting the intra/extra cellular masses proportion (ECM/BCM) and malnutrition is characterized by both increased ECM and decreased BCM, so changes of the ECM to BCM ratio are probably associated with changes in PhA.[35]

PhA is also related with the BIA estimated extracellular water (ECW), and intracellular water (ICW) ratio and wasting diseases are reported to be associated with intracellular dehydration.[15] In fact, results of other studies support the idea that markedly loss of body protein, which occurs in critically ill patients, is triggered and maintained by cell shrinkage secondary to cellular dehydration.[15,36,37,38] Previous studies have demonstrated that the decrease of intracellular water (ICW) and the increase of the extracellular water (ECW) are indicators of the catabolic reaction of the sepsis.[36,38] Finn et al.[36] demonstrated that such patients lose approximately 15% to 20% of protein and potassium in about 21 days of illness and the cellular volume also decreases around 15% to 20%.

It has been suggested that PhA values reflect quantities of intact cell membranes and BCM. In this study, according to the diagnosis of a traditional method of nutritional assessment, significantly higher PhA was found in well-nourished patients and correlated with MAMC and MAC, in agreement with findings from a previous concept that states that PhA represents a simple muscle index.[18]

Besides, our results that PhA was related to albumin, an important parameter of liver function, is in agreement with findings from other studies on liver cirrhosis.[18]

This study found lower PhA in hepatic encephalopathy, suggesting a relation between a decrease in BCM, malnutrition and hepatic encephalopathy. The loss of BCM has been described in the advanced stages of liver cirrhosis[5], and the protein-restricted diets usually prescribed for cirrhotic patients in order to treat or prevent hepatic encephalopathy may deplete the muscle mass compartment without resulting in an improvement of hepatic encephalopathy.[39]

Moreover, patients with malnutrition suffered more frequently from hepatic encephalopathy,[40,41] supporting an experimental study that suggested that low energy intake and malnutrition may facilitate the development of hepatic encephalopathy.[42]

Patients with ascites showed a tendency towards lowered values of PhA ($p = 0.05$). It is likely that the lack of statistical significance is due to the small number of patients with ascites ($n = 25$). These findings support observations from clinical practice where there is greater degree of malnutrition in patients with ascites. Sorrentino et al.[43] observed in their study that liver-cirrhosis patients with ascites are malnourished despite numerically adequate calorie-intake.

PhA was not associated with chronic hepatitis, liver cirrhosis and HCC. In patients with liver cirrhosis and HCC, PhA did not correlate with the Child-Pugh score, although there is a tendency towards reduced PhA values with the concurrent worsening of the liver cirrhosis. The findings of our study do support the previous study[18] that demonstrated that PhA is not simply associated with the stage of liver cirrhosis, as assessed using the Child-Pugh score.

Considering all stages of CLD, our results show, after controlling for age, that patients with PhA equal or less than 5.18° had shorter survival. A similar study conducted in 57 cirrhotic patients demonstrated that patients with PhA equal or less than 5.4° had shorter survival than patients with higher PhA.[18] In the present study, it is possible to point the role of PhA as a potential predictor of survival in CLD after controlling for age. Nonetheless, it is still necessary to conduct studies with larger sample sizes that assess the prognostic role of PhA, considering all stages of CLD.

Moreover, the median PhA of the patients who died was significantly lower than that of the patients who survived, with median less than 18.5°, thereby reinforcing the findings of low survival rates in patients with lower PhA that are associated with cell death or decrease in cellular integrity.

Findings from other studies have previously demonstrated that low BIA derived PhA values may indicate

worse prognosis in many clinical situations.[17-25,27,28] Gupta et al.[20-22] found that PhA values above 5.0°, 5.6° and 5.3° were associated with improved survival in patients with advanced pancreatic cancer, breast cancer and stage IIIB and IV non-small cell lung cancer, respectively. In addition, PhA lower than 6.0° has been shown to be an adverse predictor of survival in peritoneal dialysis patients.[19] In the present study our median PhA value was similar to the results obtained in pancreatic cancer[20] and in patients suffering from cirrhosis.[18]

In conclusion, our results are consistent with the hypothesis of the present study and concur for the relevance of BIA derived PhA as an indicator of nutritional status in patients with CLD. BIA-derived PhA may become a useful surrogate tool for the nutritional evaluation and could help clinical practitioners aiming to attest malnutrition diagnosis in CLD. Nevertheless, it is necessary to define further the threshold values for PhA as a nutritional evaluation tool in CLD and evaluate the role of PhA in the prediction of survival in chronic hepatitis, liver cirrhosis and HCC patients in a controlled study.

Acknowledgments

This study was financed by a grant provided by the Brazilian programs, CAPES (Coordination for the Improvement of Higher Education Personnel) and CNPQ (National Counsel of Technological and Scientific Development). We thank the whole team of the Hepatology Service, University Hospital of the Federal University of Rio de Janeiro, RJ, Brazil.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2079-2088
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

How to reduce avoidable admissions due to acute diabetes complications? Interrelation between primary and specialized attention in a diabetes unit

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Abstract

Introduction: **Type 2 Diabetes Mellitus is a serious health problem. In the year 2030 it will affect 366 million people around the world.**

Objective: **Evaluate the effectiveness of a mixed intervention and reducing the amount and seriousness of acute complications in diabetics from our Health Area.**

Materials and method: **Protocols of action as well as information documents were produced. Diabetes Unit coordinated educational activities in the different support levels of the Area VII of Murcia. Information talks were provided for the people in charge of the Diabetes Unit in every Care Center and Service of the Health Area. Personalized training was provided for patients treated in the differet Care levels. The study comprised three stages. Information leaflets were spread and talks offered to the patient regarding in house handling of hypo and hyper glycemia.**

Results: **A reduction of 39% of the emergencies due to acute non complicated diabetes was achieved, as well as a reduction of 47.6% of hospital admissions. There was a reduction of 67.8% of the amount of total hospital stays for the group of patients under 35 years who were admitted into the hospital due to type 1 or 2 diabetes mellitus that didn't show any complications (GRD295).**

Conclusions: **There was a reduction of more than thirty percent in the emergencies due to acute decompensations in the disease and a significant reduction in the avoidable hospital stays in the young adult, thus improving the patients' life quality and reducing the social cost of the diabetic patient.**

(*Nutr Hosp.* 2012;27:2079-2088)

DOI:10.3305/nh.2012.27.6.6151

Key words: *Diabetes. Hospital stay. Avoidable admissions. Emergencies.*

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Recibido: 4-IX-2012.
Aceptado: 11-IX-2012.

¿CÓMO REDUCIR LOS INGRESOS EVITABLES POR COMPLICACIONES AGUDAS DE LA DIABETES? INTERRELACIÓN ENTRE ATENCIÓN PRIMARIA Y ESPECIALIZADA EN UNA UNIDAD DE DIABETES

Resumen

Introducción: **La diabetes mellitus tipo2 es un problema de salud grave. En el año 2030 afectará a 366 millones de personas en todo el mundo.**

Objetivo: **Evaluar la eficacia de una intervención mixta y reducir la cantidad y gravedad de las complicaciones agudas de la diabetes en nuestra Área de Salud.**

Material y método: **Se diseñaron protocolos de actuación y documentos de información. La Unidad de Diabetes coordinó las actividades educativas en los diferentes niveles de soporte de la VII Zona de Murcia. Se realizaron charlas de información para los responsables de la Unidad de Diabetes en cada Centro de Atención y Servicio del Área de Salud. Se dio formación personalizada a los pacientes tratados en los distintos niveles de atención. El estudio constó de tres etapas. Se entregaron folletos informativos y charlas al paciente con respecto a la manipulación domiciliaria de hipo e hiperglucemia.**

Resultados: **Se logró una reducción del 39% de las emergencias debidas a diabetes aguda no complicada, así como una reducción del 39% de las emergencias debidas a diabetes aguda no complicada, así como una reducción del 47,6% de los ingresos hospitalarios. Hubo una reducción del 67,8% de la estancia hospitalaria total para el grupo de pacientes menores de 35 años que fueron ingresados en el hospital debido a diabetes tipo 1 o 2 que no mostraron ningún tipo de complicaciones (GRD295).**

Conclusiones: **Se observó una reducción de más del treinta por ciento en los casos de urgencias por descompensaciones agudas de la enfermedad y una reducción significativa en las estancias hospitalarias evitables en el adulto joven, mejorando así la calidad de vida de los pacientes y reduciendo el costo social del paciente diabético.**

(*Nutr Hosp.* 2012;27:2079-2088)

DOI:10.3305/nh.2012.27.6.6151

Palabras clave: *Diabetes. Estancia hospitalaria. Ingresos evitables. Urgencias.*

Abbreviations

DM: Diabetes Mellitus.
DM1: Type 1 Diabetes Mellitus.
DM2: Type 2 Diabetes Mellitus.
DU: Diabetes Unit.
PC: Primary Care.
CIE.9.MC: International Classification of Diseases, Ninth Revision, Clinical Modification.
CMBD: Minimum Data Set Database.
HGRS: Reina Sofía University Hospital.
DEP: Diabetes Education Program.
IC: Interactive consultation.
CT: Traditional consultation.
A1C: Glycated hemoglobin.
GRD: Groups related to the Diagnosis.

Introduction

Diabetes Mellitus(DM) is a multiple ethiology disease. Its main feature is chronic hyperglycemia with carbohydrates, fats and proteins methabolic disorders due to a deficient secretion of insulin caused by destruction of beta cells of the istels of Langherhans in the pancreas and the subsequent absence of the hormone or its action (due to the increase in peripheric resistence to insulin due to a variety of causes, some of them unknown) or both.[1]

Type 1 Diabetes Mellitus(DM1) comprises most of the cases that are produced by the destruction of the beta cells. DM1 pathogenesis includes a genetic disposition to the disease, as well as triggering factors of environmental nature that can activate mechanisms leading to a gradual loss of the beta cells. Type 2 Diabetes Mellitus(DM2) is the most common type of diabetes, being its main feature a certain degree of insulin hyposecretion and higher contribution to insulin resistance. Most of the patients suffering from DM2 are obese, what worsens insulin resistance. Abdominal obesity is a bigger problem than peripheric obesity.

The mainstays of DM treatment are diabetologic education, diet, exercise, self-control and medication. There are very few health conditions that require such a level of understanding from the patient and its relatives as DM does. This is due to the fact that since the moment of its clinic appearance, the patient becomes the role leader in a drama that is going to accompany him through his whole life.

The education of the diabetic patient must be gradual and continuous, aiming to accomplish the active incorporation of the patient and his relatives to the treatment. He must know about diabetic requirements and individual planning regarding his meals; benefits and harms of physical activity; interaction between diet and physical activity and pharmacological treatment; how to react in an emergency; insulin administration; self-monitoring glycemia methods, the different types of oral hypoglycemiant and its ways of administration to generate a real conscience of the problem enabling him to achieve the changes in his life style that may help him get a better attention of his health condition.[2]

Diabetologic education is composed of three stages:

- *Initial education.* After diagnosis. It enables the patient to carry out immediate attention, which is doubtlessly important in the case of DM1. Information is aimed to diagnosis, basic features of the syndrom, self control of glucose in blood and urin, diet, administration of insulin or oral compounds and severe complications. This is the right moment to convey the relatives the need for them to take part in the treatment. Planning of the educational and therapeutic program is done by the health team and the patient in a joint way, which will lead to a higher level of responsibility.
- *Deep education.* After the first 3 or 4 weeks, the patient is ready to stretch and deepen his knowledge about diabetes. After the impact of finding out he has a chronic disease for the rest of his life has been overcome, he can realize the difficulties that prevent him from complying with the adequate treatement, which on the other hand stimulates his motivation to learn.
- *Continuous education.* The philosophy behind any diabetologic education program must include continuous training of the patient and the health professionals, as a way of updating (by incorporating the new concepts) and checking the fundamental available information.

There are different ways of training and educating the diabetic patient. *Individual education* has the advantage of providing answers to personal concerns and benefiting from the doctor-patient relationship. It is traditionally appreciated and highly regarded in the health-disease couple. Its disadvantages are that it does not encourage the team work spirit, it is time consuming and more expensive, and it requires better pedagogical training on the side of the educator. *Group education* can reach more patients and promotes interaction and support between them mediated by the professional. It is a very useful way of putting pedagogical methods into practice and a wonderful socialization tool. Among its disadvantages, it is impossible to assist strictly personal and individual needs. Combination of different forms produce sucessfull results in the teaching process. Education must be enjoyable and simple, with a clear and comprehensible language, devoid of extremely technical terms.

Because of its high prevalence and also to the fact of it being a direct cause of death, disability and high public health expenses, diabetes constitutes a priority area of intervention in the health plans of the Autonomous Regions and the Ministry of Public Health and Social Policy in Spain.

In order to deal with the magnitude of this problem called "Diabetes" in a comprehensive fashion, our Diabetes Unit(DU) was created in 2007 in the context of the new Single Management of the Area VII Murcia East. It is coordinated by Endocrinology and composed by Nurses Educators in Diabetes, Nutritionists, Surgeon, Diabetic Foot Nurse, Podiatrist, Ophthalmologist, Psychiatrist, Neurologist, Vascular Radiologist, Anesthetists, Pneumologist, Nephrologist, Cardiologist, Emergency Doctor, Rehabilitator, ten Primary Care(PC) Doctors and ten PC Nurses, whom in turn coordinate the rest of the health professionals in their respective PC Centers and all the Specialized Services of the Reina Sofía University Hospital(HGRS) of Murcia that are related to the assistance to the diabetic patient.

Our general goals are the decrease in mortality and morbidity in the diabetic population. The intermediate goals are the decrease in incidence of acute and chronic diabetic complications.

At the beginning, we observed a high number of cases in the Emergency Service as well as a high number of diabetes related hospital admissions, these both being indirect signs of these complications in diabetic patients. A cycle of improvement in the Area was started, materializing in the *"Protocol of reduction of avoidable admissions due to short term complications in diabetic patients"*, which in turn was contemplated in our Managing Contract from 2007 to 2010. This protocol was developed under the coordination of the DU in our 10 PC centers and Emergency, and Specialized Services of the Hospital, both in ambulatory assistance and hospitalization.

Our general goal consisted in evaluating the effectiveness of a mixed intervention, with educational, self-evaluation and feedback components, in order to reduce the amount and seriousness of acute complications, indicated by emergency assistance cases and avoidable hospital admissionss, in diabetic patients from our Health Area.

The specific goals were:

1. Quantifying avoidable admissions in the Hospital Emergency Service, associated to severe diabetic complications, before and after improvement intervention.
2. Quantifying avoidable admissions due to severe complications of diabetes, before and after improvement intervention.
3. Reducing the number of assistance cases in the Hospital Emergency Service due to severe diabetes complications.
4. Reducing the number of admissions to the Hospital associated to severe diabetes complications.
5. Reducing Public Health expenses owing to avoidable admissions due to severe diabetes complications.
6. Improving inter-professional communication regarding diabetes matters in our Health Area.

Starting point

DM nowadays constitutes a serious Public Health issue all around the world, with a high morbimortality rate, both in developed and developing countries. In 2000 there were 175 millions of diabetics in the world, of which 80 or 90% corresponded to DM2. It is calculated that in 2010 there would be 239 millions and 300 millions in 2025. That justifies defining it as a "global pandemic".

The main goals of diabetes education are providing diabetologic information and knowledge and training to be capable of acquiring the necessary skills and habits. It aims to generate in the patient a real conscience of his problem that enables him to achieve changes in his life style, so as to have a better assistance of his health condition. DM is an example of the need for a therapeutic education process that, along with clinical cares, guarantees the effectiveness in the treatment. At the end of the last century, diabetology accepted the idea that an effective treatment of diabetes requires education and training of the patient.

In Europe, Prof. JPh Assal stood out in what regards teaching actions and their effectiveness to achieve goals and the study of different pedagogical strategies to identify its advantages and disadvantages in the field of health.[3] American groups were developed in a more pragmatic line, highlighting the need to change behaviors and improving acceptance of treatment.[4]

The National Diabetes Program has been developed in Cuba for the last 25 years. It carried out a continuous training of the health personnel and it started on the primary health level, where more than 85% of the people with DM received assistance.[5] It focused on declaring education as the primary function, establishing courses of basic information and publishing information brochures. They desing a Diabetes Education Program(DEP) that was later extended to all the services of the health system and several countries in the region received support to develop their programs. A better quality in PC services was achieved.

Also in Cuba, to evaluate the effect of a 10 year long interactive consultation treatment on the understanding and acceptance of treatment, as well as clinical, biochemical and therapeutical changes achieved in group of patients with DM1, García studied 40 people with DM1 and not more than five years of diagnosis assigned to interactive consultation (IC). Results were compared to those obtained in a control group, with identical general and clinical variables at the beginning of the study that continued with the education process through traditional consultation (CT). Participants in IC showed better results in all the analyzed parameters compared to those in CT.[6]

In the United States 6.3% of the population has DM. In Utah, medical care and training by a clinic doctor trained as "diabetes educator" showed that total cholesterol, low density lipoproteins, glycated hemoglobin (A1C) and triglycerides diminished significantly.[7]

Other observational one year long study proved that systematic efforts aiming to educate the diabetic patient were needed to improve the clinical, economical and human aspects of this disease.[8]

Small groups training with the interactive participation method enables the participants to exchange experiences, learn from the others and reinforce positive criteria and feelings regarding daily care. It turns out to be more effective as compared to the results obtained in traditional educational interventions, just as other authors from different fields of therapeutic education have reported subsequently.[9] In another study results of diabetologic education carried out in groups were compared to those carried out individually. It proved that both were equally effective in achieving glycemic control, although results of the latter were slightly better. However the group education is considered superior from the point of view of the cost-profit analysis.[10]

There have also been some studies comparing diabetic education effectiveness when carried out through the use of telemedicine technologies as when it is done in personal meetings. With both of them good results regarding metabolic control can be achieved and both methods are well accepted by patients. Therefore it is generally considered that telemedicine can be successfully employed as an education tool for diabetic patients.[11]

The link between primary and secondary health assistance has to be dispensed as a comprehensive assistance of the patient. Being a chronic non transmissible disease and given its prevalence and incidence, DM is one example of it. Improving and strengthening this link is extremely important in order to carry out a comprehensive treatment of these patients.[12] As with other chronic and non transmissible diseases the educational and prevention battle is won in the arena of primary health assistance where more than 80% of the population receives assistance.

Material and methods

Study design

The members of the DU created the protocol and the agreed information documents, and coordinated the sequence of educational activities in the different assistential levels of the Area VII Murcia East: in the 10 PC Centers and Emergency Services, in the Hospital Services involved, particularly in the Short Stay Unit and the Internal Medicine Service and the Emergency Service. The protocol was spread through talks given by the coordinators of the DU in each center and service of the Health Area, addressed to both doctors and nurses, and through individual diabetologic education for the diabetic patients assisted in the different assistential levels (fig. 1).

The tools employed for its dissemination were, on one hand, an action protocol for the health professional, based on the current guides of clinical practice in diabetes[13] and aiming to prevent, solve and refer in a coordinated way the acute diabetologic emergencies

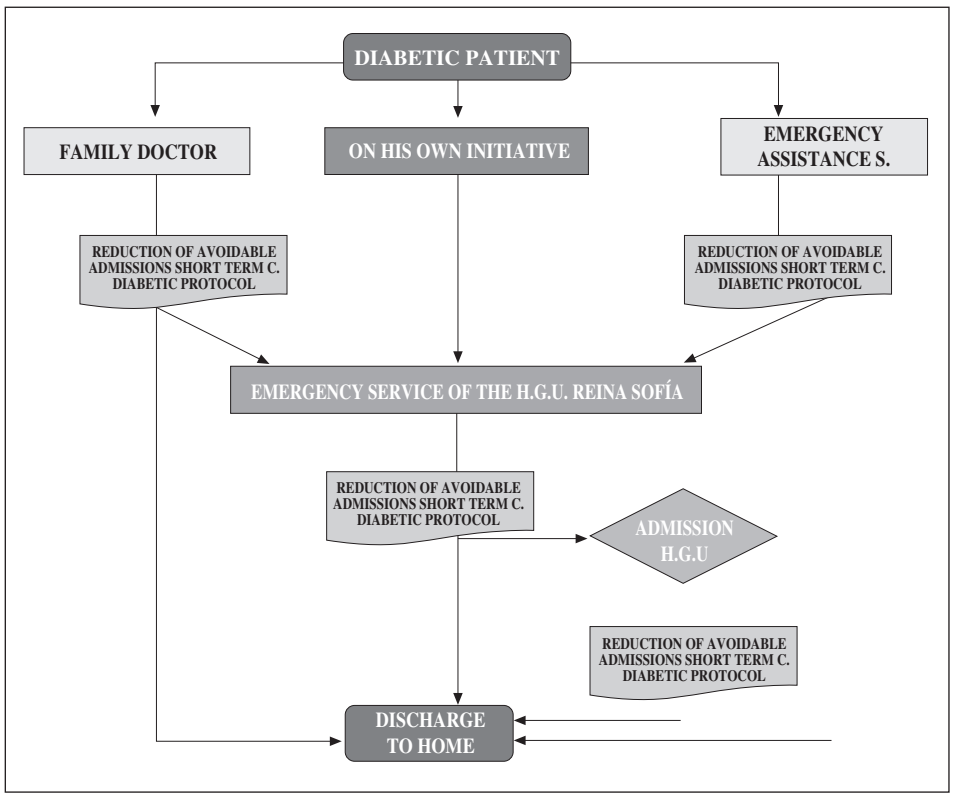


Fig. 1.—Sequence of interactions in the "Protocol of reduction of avoidable admissions due to short term complications in diabetic patients".

(hypoglycemia and hyperglycemia) in the Health Area. The main idea was that non complicated emergencies would be assisted in the PC Center while complicated emergencies would be assisted in Emergency Service of the Hospital. Specific hospital admission critera due to acute diabetes decompensation were established. On the other hand, information brochures teaching the patient how to handle at home mild hypoglycemia and hyperglycemia were supplied as tools for the diabetologic education of the patient.

The study was carried out in three stages:

- *First Stage or pre-intervention period (year 2007):* Observational, descriptive and retrospective study, in which information regarding all the diabetic patients assisted in Emergencies or admitted for the evaluation previous to the intervention were collected.
- *Second Stage or intervention period (year 2008):* Creation and dissemination of the protocol, through talks given at the PC Centers and the Hospital Services by the professionals in charge of the DUs, as well as distribution of information material regarding how to handle severe diabetes complications in the PC Centers, Emergency Centers and hospitalization. The trained health professionals, in turn, provided their patients with therapeutic Education regarding how to handle severe diabetes complications.
- *Third Stage or post-intervention stage (years 2009 and 2010):* Collection of information through analysis of the document environment of the Area and statistical comparative analysis of the results, with subsequent dissemination of them.

Statistical analysis

As search strategy, for both assisted emergencies and hospital admissions related to diabetes, a series of codes were selected from the International Classification of Diseases, Ninth Revision, Clinical Modification(CIE.9.MC).[14] Codes comprehended between the 250.00 up to the 250.93 were employed for the diagnosis related to "diabetes" or "hyperglycemia", and the ones between the 251.00 up to the 251.99 were added for the diagnosis related to "hypoglycemia".

The CIE.9.MC codes related to assisted emergencies due to diabetes were used along with the Minimum Data Set Database (CMBD) of the Emergency Service of the HGRS.[15] In the case of admissions related to diabetes, the Groups related to the Diagnosis database (GRD) v.21 was used.[16] For estimation of health expenses the database GRD-State regulation-Year 2007 was applied.[17,18]

Among all the CIE codes related to diabetes, only the codes related to "severe diabetes decompensations: hyperglycemia and hypoglycemia" were regarded as avoidable assistances in the Emergency Service:

- 251.2: Non-specified Hypoglycemia.
- 250.00: DM without mention of complication type 2 or unspecified non decompensated.
- 251.1: Other specified hypoglycemias.

Similarly, only the GRDs related to "severe diabetes complications having a low specific weight (lower than 1)" were regarded as avoidable hospital admissions:

- 294: Patients over 35 years old, admitted due to DM1 or DM2, non complicated(weight GRD v21: 0,9828)
- 295: Patients under 36 years old, admitted due to DM1 or DM2, non complicated(weight GRD v21: 0,841)

The following were the indicators to be measured:

- Number of avoidable admissions in the Emergency Service of the Hospital by codes: 251.2, 250.00, and 251.1.
- Number of hospital admissions/discharges, total stays, average stay and specific weight by GRDs: 294 and 295.

Results

Avoidable diabetologic emergencies

Three years after establishing the protocol(from 2007 to 2010), a reduction of 39% in emergencies due to severe diabetes decompensations non complicated or avoidable was observed(codes 250.0, 251.1 and 251.2). The reduction of 52.2% in the code 250.00, that comprehends simple hyperglycemic decompensations, was the most marked. The second most marked reduction was that of 33.7% in the codes 251.1 and 251.2 that comprehend non complicated hypoglycemias (table I, fig. 2).

Avoidable admissions due to severe diabetes decompensations

For the GRD 295, our action protocol implied, after three years of operation (from 2007 up to 2010), a reduction of 47.6 % both in the number of avoidable admissions/discharges. Also in the specific weight for GRD 295 (-16% and -16.4% between 2007-2008, -33% and -26.4% between 2008-2009, and -1.6% and -0.8% between 2009-2010, respectively).

We also achieved a 67.8% reduction in the number of total hospital avoidable stays for GRD 295 (-17% between 2007-2008, -39% between 2008-2009, -26.3% between 2009-2010), reaching 1.59 days reduction in the average stay for GRD 295 between 2007-2010, which means 2,55 days less of stay than the country's average (5, 10 days) (table II, fig. 3a).

Table I
Avoidable diabetologic emergencies

Code and diagnosis	*May-Dec 2007*	*May-Dec 2008*	*Jan-Jun 2008*	*Jan-Jun 2009*	*Jan-Jun 2010*	*Total*
			Observed values			
250.00: DM without mention of complication type 2 or unspecified non decompensated	23	10	6	9	11	59
251.1: Other specified hypoglycemias	15	6	13	9	6	49
251.2: Non-specified Hypoglycemia	74	65	62	50	52	302
Total	**112**	**81**	**80**	**68**	**69**	**410**
			Expected values			
250.00: DM without mention of complication type 2 or unspecified non decompensated	16.1	11.7	11.5	9.9	9.8	59
251.1: Other specified hypoglycemias	13.4	9.7	9.6	8.2	8.1	49
251.2: Non-specified Hypoglycemia	82.5	59.7	58.9	50.8	50.1	302
Total	**112**	**81**	**80**	**68**	**69**	**410**
Real significance	**p = 0.2006 (NS)**					

DM: Diabetes Mellitus; NS = Statistically non significant for the Chi-Square Test.

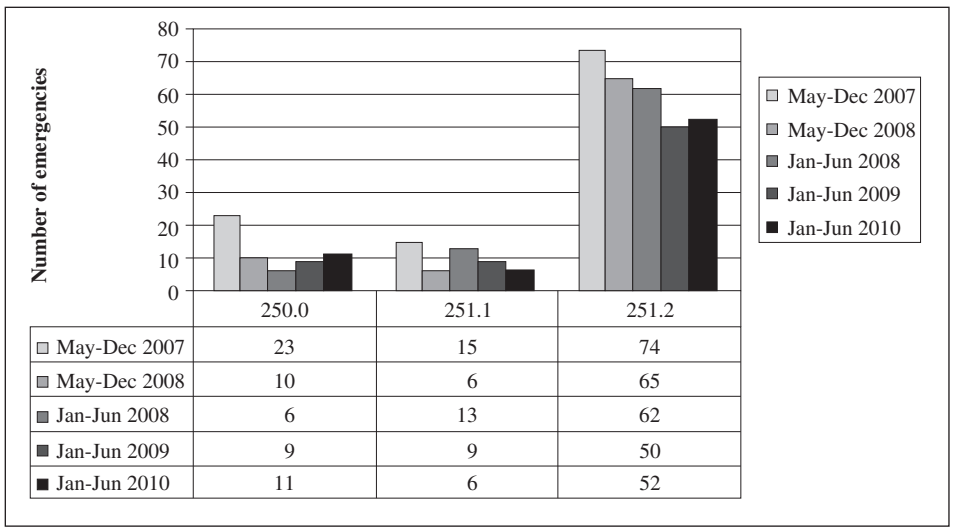


Fig. 2.—Avoidable diabetologic emergencies.

All of this implied a saving of 36,920 euros per year (1,846.05 euros per case).[18]

Similarly, for the GRD 294 our protocol implied a reduction of 27% and 28% in the number of avoidable stays/discharges between 2007 and 2010, and in the specific weight for GRD 294 (-23/-22% between 2007-2008, -4/-6% between 2008-2009, and 0/2% between 2009-2010, respectively).

We also achieved a 23.4% reduction in the number of avoidable total hospital stay with GRD 294 (-7% between 2007-2008, -12% between 2008-2009, -5% between 2009-2010), reaching 0.62 days less of average hospital stay than the country's average (6.51 days) (table II, fig. 3b).

Therefore, the result of our intervention in the GRD 294 implied a saving of 71,924 euros per year (2,766.34 euros per case).[18]

Considering the total expenses resulting from admissions due to severe diabetes complications in GRDs 294 and 295, our protocol implied a saving of 108,844 euros per year, which adds up a total saving of 326,532 euros in 3 years (2007-2010).

Discussion

Current prevalence in the Region of Murcia, according to DINO study,[19] is of around 11% of the general population over 19 years old. Therefore, with the available prevalence data, in our health area, with a total population of 200,662, it is estimated that there are 15,000 diabetic patients over 18 years old.

Table II
Patients admitted due to DM1 for type 2, non complicated

A. Patients under 36 years old admitted due to DM1 or DM2, non complicated					
		Observed values			
*GRD 295 weight v.21**	*Number of discharges*	*Total stay (days)*	*Average stay (days)*	*Weights sum*	*Total*
0.841 Jan-Jun 2007	21	87	4.14	17.66	129.8
0.841 Jan-Jun 2008	18	73	4.06	14.77	109.83
0.841 Jan-Jun 2009	12	38	3.17	9.85	63.02
0.841 Jan-Jun 2010	11	28	2.55	9.25	50.8
Total	**62**	**226**	**13.92**	**51.53**	**302.65**
		Expected values			
0.841 Jan-Jun 2007	26.6	96.9	6.0	22.1	129.8
0.841 Jan-Jun 2008	22.5	82.0	5.1	18.7	109.83
0.841Jan-Jun 2009	12.9	47.1	2.9	10.7	63.02
0.841 Jan-Jun 2010	10.4	37.9	2.3	51.5	50.8
Total	**62**	**226**	**13.92**	**51.53**	**302.65**
Real Significance	**P = 0.0000**				
B. Patients over 36 years old admitted due to DM1 or DM2, non complicated					
		Observed values			
*GRD 294 weight v.21**	*Number of discharges*	*Total stay (days)*	*Average stay (days)*	*Weights sum*	*Total*
0.9828 Jan-Jun 2007	48	269	5.6	47.17	369.77
0.9828 Jan-Jun 2008	37	252	6.63	36.57	332.20
0.9828 Jan-Jun 2009	35	218	6.23	33.68	292.91
0.9828 Jan-Jun 2010	35	206	5.89	34.40	281.29
Total	**155.00**	**945**	**24.35**	**151.82**	**1276.17**
		Expected values			
0.9828 Jan-Jun 2007	44.91	273.81	7.06	43.99	369.77
0.9828 Jan-Jun 2008	40.35	245.99	6.34	39.52	332.20
0.9828 Jan-Jun 2009	35.58	216.90	5.59	34.85	292.91
0.9828 Jan-Jun 2010	34.16	208.29	5.37	33.46	281.29
Total	**155.00**	**945.00**	**24.35**	**151.82**	**1276.17**
Real Significance	**P = 0.9950 (NS)**				

*Highly significant for the Chi-Square Test
NS = Statistically non significant for the Chi-Square Test.

In 2007, there were 350 cases of assistance due to diabetes in the Emergency Service of the HGRS because of diabetes decompensation, of which 153 cases (44%) required hospital admission. This entails a high number of admissions related to diabetes, above the country's average.

Comprehensive assistance to the diabetic patient has not only proved capable of reducing the rate of chronic complications, but also of hospital admissions due to severe complications and average stay adjusted by GRD.[20-22]

Achieving this goal requires making the most of the available health resources, and rationalizing them, as well as an effective and efficient coordination between the different health levels, through multidisciplinary DUs, that must follow certain preventive, healing and rehabilitation aspects of the disease.

The approach, through education programs at an interdisciplinary level, applicable to the whole health area and in all its assistential levels, is similar to other designs, just as showed by international studies that have proved that the DU improve the patient control.[23-28]

PC has a strategic role in the assistance to the diabetic patience, given the high prevalence, chronicity and socio-sanitary implication of this disease, particularly in the case of patients with DM2, since the nature of the cares they require make this assistance level the most suitable for them. At the same time, the Specialized Assistance levels plays a primary role in ensuring an adequate assistance to the diabetic patient in his complications, particulary the more unstable patients, as is the case with DM1, and always in coordination with the PC in order to achieve a permanent assistance.

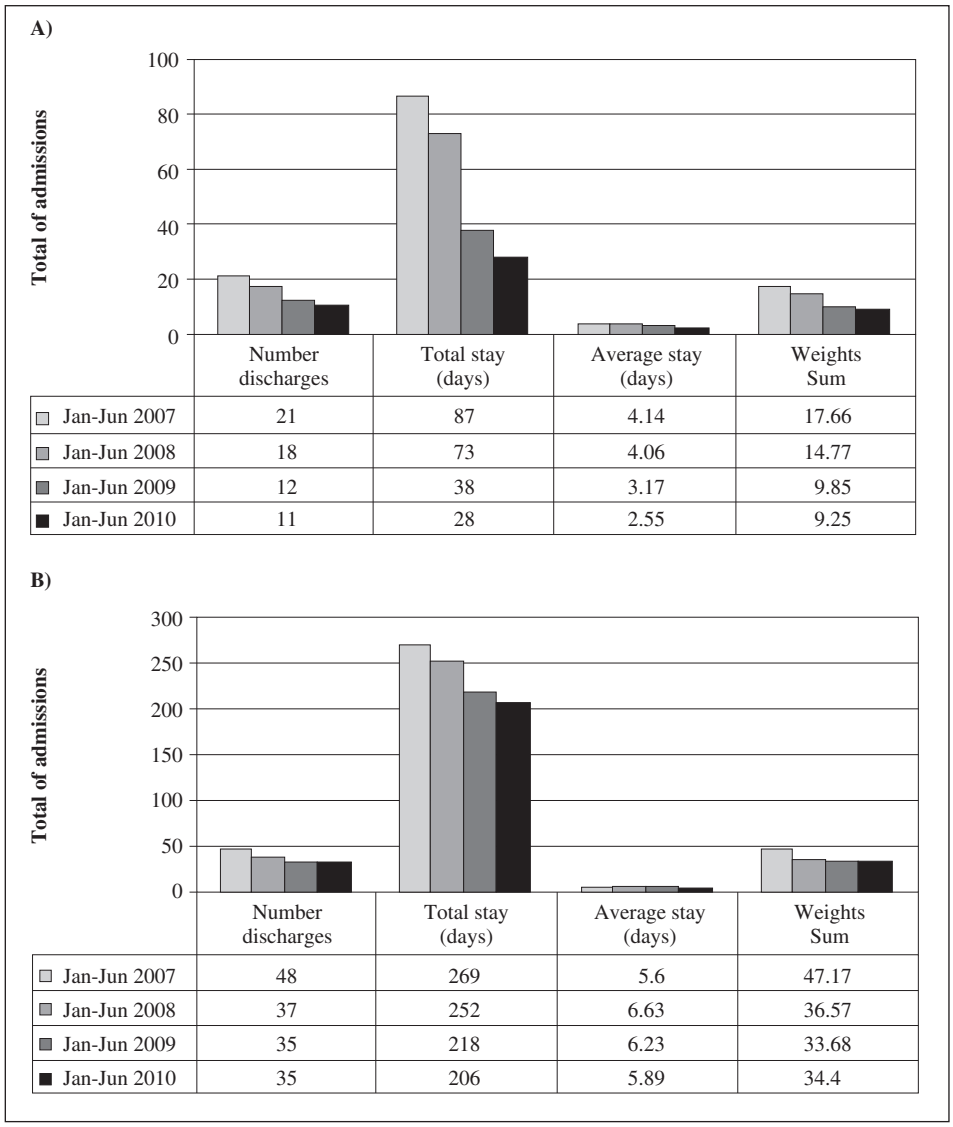


Fig. 3.—Admissions related to diabetes (a) in patients under 36 years old (GRD 295) and (b) in patients over 36 years old (GRD 294).

Most of the authors likewise consider indispensable that the diabetic patient takes active part in his own care and relate the lack of self-care with the higher number of assistances due to diabetologic emergencies.[29] In order to achieve a suitable level of self-care in the diabetic patient it is essential, to provide him with the therapeutic education that may work as a mainstay of the comprehensive health assistance, that at a structural level is represented by the figure of Nursing Specialized in Diabetologic Education, which after being incorporated to the health plans has achieved an improvement in the diabetes control.[30] For this reason, our DU was created with two hospital nurses specialized in Diabetologic Education, but also, and no less important, with ten PC nurses responsible of Diabetologic Education who in turn coordinate the other nurses at their center or service. In this sense, it is proved that assistance carried out by the PC Nurse improves the patient's satisfaction and the efficiency in the diabetes global care. Approaching the issue of Diabetologic Education addressed to the community that depends on health center has proved to be effective in reducing the number of emergencies related to diabetes.

Even so, there are some authors that have shown an increase in severe hypoglycemia cases after implementation of the DEPs aiming to achieve the current and growingly ambitious goals of glycemic control, particularly in adult diabetics.[31] However, in our work we have been able to reduce both the emergencies related to hyperglycemia (53,2%) and the emergencies related to hypoglycemia (33,7%) in just three years. This difference is explained by the existence of the DUs in our area, which consider PC and Diabetologic Therapeutic Education as the strong point of our assistance, allowing a comprehensive and multidisciplinary assistance of the diabetic patient, in all the stages of his life and his disease.

As to the contents of this education, hypoglycemia is regarded as the main restricting factor to achieve an

optimum diabetes control, both because it is the most common severe complication in the hypoglycemiant treatment and because of its negative repercussion in patients' quality of life.[32] Therefore, we believe that any intervention in diabetes must include a reduction of hypoglycemia among its goals, both in the number of emergency assistance and in the severity and amount of admissions due to that cause, as we have presented in our study with the 27% reduction in the avoidable admissions because of GRD 294, of which around one third are patients with DM2 that enter the hospital with a secondary diagnosis of "adverse effect of insulin and anti-diabetic agents".

Apart from the individual education, other of our strong points has been the fact of carrying out talks on diabetologic survival education addressed to groups of patients that had been previously assisted due to glycemia decompensation, in emergency service, ambulatory service or hospital admissions. This way of carrying out diabetologic education in groups has proved to be efficient in preventing acute and chronic diabetic complications.[33]

Our results are of a high socio-sanitary relevance given the great economic repercussion of diabetes, because of its prevalence, and the complications and restrictions that it entails. In our study a total saving has been estimated of 326,532 euros in 3 years (2007-2010) with the reduction of avoidable admissions due to diabetes. This expenses reduction due to admissions related to severe diabetes complications has been achieved by other authors, through establishment of protocols of therapeutic education in diabetes, including the use of telephone assistance and telemedicine as actual advances in the means of communication between the health professional and the patient.[34] Besides, other models of diabetologic education employing informatic systems to encourage decisions related to diabetes, both for patients and health professionals, have proved to be effective in reducing avoidable emergencies and admissions due to diabetes.[35]

Conclusions

A DEP must be focused in the person, not in the disease, and it must be based on the principles of interactive participation and group support to the decision making process of each individual. It has been proved that those programs are effective in increasing understanding of the disease, developing skills necessary to cope with the treatment and changing behaviors.

The interactive work of the PC and the DU enables, through the use of educational protocols of action, a reduction of more than a third of the number of emergencies related to severe decompensation of the disease and a significant reduction of the yearly hospital admissions of the young adults, improving life quality and reducing the social cost associated to the diabetic patient, as well as the reduction of sanitary expenses resulting from avoidable admissions.

This interactive work improved interprofessional communication regarding diabetes in the Health Area VII of Murcia East.

Acknowledgements

The cooperation of the Collaborative Group of the Diabetes Unit of the Reina Sofía University Hospital (Murcia, Spain), and of Dr. M Palacín Solís (Ph.D. Analysis and Group Leadership) is gratefully acknowledged.

The members of the Collaborative Group of the Diabetes Unit of the Reina Sofía University Hospital (Murcia, Spain) are:

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2089-2092
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Should ascitis volume and anthropometric measurements be estimated in hospitalized alcoholic cirrotics?

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Abstract

Introduction: **Ascitis and undernutrition are frequent complications of cirrhosis, however ascitis volume and anthropometric assessment are not routinely documented or considered in prognostic evaluation . In a homogeneous cohort followed during two years these variables were scrutinized, aiming to ascertain relevance for long-term outcome.**

Methods: **Population (N = 25, all males with alcoholic cirrhosis) was recruited among patients hospitalized for uncomplicated ascitis. Exclusion criteria were refractory or tense ascitis, cancer, spontaneous bacterial peritonitis, bleeding varices and critical illness. Measurements included ultrasonographically estimated ascitis volume, dry body mass index/BMI , upper arm anthropometrics, hematologic counts and liver function tests.**

Results: **Population (age 48.3 ± 11.3 years, BMI 21.1± 3.5 kg/m², serum albumin 2.5 ± 0.8 g/dL) was mostly in the Child-Pugh C category (77.8%) but clinically stable. During the follow-up period of 22.6 ±3.8 months, additional hospitalizations numbered 1.7 ± 1.0 and more than one quarter succumbed . Admission ascitis volume corresponded to 7.1 ± 3.6 L and dry BMI to 18.3 ± 3.5 kg/m². Child Pugh index was relevant for both mortality and rehospitalization. Nevertheless, similar matches for mortality were documented with ascitis volume and dry BMI, and arm circumference below the 5th percentile was highly significantly associated with rehospitalization.**

Conclusions: **A greater association than hitherto acknowledged, between ascitis volume and anthropometric measurements from one side, and long-term rehospitalization and mortality from the other, was demonstrated in male stable alcoholic cirrhotics. Further studies with alcoholic and other modalities of cirrhosis including women are recommended.**

(*Nutr Hosp.* 2012;27:2089-2092)

DOI:10.3305/nh.2012.27.6.6123

Key words: *Alcoholic cirrhosis. Ascitis. Malnutrition. Dry body mass. Ascitis volume. Anthropometric assessment. Rehospitalization. Mortality.*

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Recibido: 20-VIII-2012.
Aceptado: 13-X-2012.

¿ES CONVENIENTE ESTIMAR EL VOLUMEN ASCÍTICO Y LAS MEDIDAS ANTROPOMÉTRICAS EN PACIENTES HOSPITALIZADOS CIRRÓTICOS?

Resumen

Introducción: **Ascitis y desnutrición son complicaciones frecuentes de la cirrosis, pero el volumen ascítico y la evaluación antropométrica no son como rutina documentadas o consideradas para la evaluación del pronóstico. En un coorte homogéneo de pacientes acompañados por dos años estas variables fueron escrutinadas, con el objetivo de determinar su relevância para los resultados clínicos de largo plazo.**

Métodos: **La población (N = 25, todos hombres con cirrosis alcohólica) fue recrutada entre pacientes hospitalizados por ascitis no complicada. Los critérios de exclusión fueron ascitis tensa o refractária, peritonitis bacteriana espontánea, varices sangrantes y enfermedad crítica. Los métodos involucraron volumen ascítico estimado ultrasonograficamente, el índice seco de masa corporal/IMC seco, antropometria del brazo, recuentos hematológicos y pruebas de función hepática.**

Resultados: **La población (edad 48,3 ± 11,3 años, IMC 21,1 ± 3,5 kg/m², albumina sérica 2,5 ± 0,8 g/dL) encontrabase predominantemente en la categoria Child-Pugh C (77,8%) , pero clinicamente estable. En el período de seguimiente de 22,6 ± 3,8 meses hubo 1,7 ± 1,0 hospitalizaciones adicionales por paciente, y mas de una cuarta parte sucumbió. El volumen ascítico de admisión fue de 7,1 ± 3,6 L y el IMC seco de 18,3 ± 3,5 kg/m². El indice de Child-Pugh fue relevante tanto para mortalidad como para rehospitalización. Asociaciones similares para mortalidad fueron demonstradas para volumen ascítico y para IMC seco, y la circunferencia del brazo abajo del 5º percentil fue un indicador muy significativo para rehospitalización.**

Conclusiones: **Una asociación mas importante que lo hasta ahora publicado ocurrió entre volumen ascítico y antropometria de una parte, y mortalidad asimismo rehospitalización de otra parte, en pacientes masculinos cirróticos alcohólicos estables. Estúdios adicionales con cirrosis alcohólica y de otras modalidades incluyendo mujeres son recomendados.**

(*Nutr Hosp.* 2012;27:2089-2092)

DOI:10.3305/nh.2012.27.6.6123

Palabras clave: *Cirrhosis alcohólica. Ascitis. Desnutrición. Masa corporal magra. Volumen ascítico. Medidas antropométricas. Rehospitalización. Mortalidad.*

Introduction

Malnutrition has been emphasized in liver cirrhosis for decades, with prevalence as high as 75%.[1-5] Ascitis is not uncommon either, especially in late disease.[6,7] With few exceptions, modern therapeutic protocols have not substantially touched the main liver damage.[8] Nevertheless, the alluded to complications typically respond to nutritional support and diuretic administration. In this sense they are prone to be overlooked within the larger context of the disease.

Earlier protocols highlighted association between both undernutrition[3,4] and ascitis[4,6,7] with mortality. Indeed, in the absence of severe portal hypertension the two complications tend to be related.[2] In contrast to some recommendations,[9,10] prognostic indices such as Child Pugh and MELD (Model for End-Stage Liver Disease)[11] do not consider these variables.

Given the prognostic relevance of ascitis and malnutrition particularly in alcoholic cirrhosis,[12,13] a prospective pilot study was conducted. The aim was to analyze mortality and rehospitalization during a two-year period, in a homogeneous male cohort followed in an academic setting.

Material and methods

The study was approved by the institutional Ethical Committee, and all patients gave written informed consent.

Population (N = 25, all males), with clinically diagnosed alcoholic cirrhosis confirmed by imaging methods, was consecutively recruited among patients hospitalized for ascitis treatment. Exclusion criteria were refractory or tense ascitis, cancer, alcoholic hepatitis, spontaneous bacterial peritonitis, bleeding varices, critical illness or admission to the intensive care unit .

Patients were seen by a multidisciplinary team including dietitian, surgeon and gastroenterologist, along with other specialists whenever required. Diet, diuretics and other prescriptions were in agreement with accepted protocols, and abstinence was a therapeutic priority.[7,8]

Measurements included nutritional status (arm circumference, triceps skinfold, body mass index/BMI, plasma proteins) liver function tests, lipid fractions and hematologic counts. Dietary intake and also Child-Pugh and MELD indices were calculated.

Exploratory paracentesis was not routine, ascitic fluid analysis being conducted when any clinical or biochemical sign of infection was present. Ascitis was clinically evaluated at admission[14] and the volume sonographically defined.[15] On the basis of ascitis volume, corrected (dry) BMI was estimated.

Values are presented as mean ± SEM. Student's "t" test was selected for continuous variables, if necessary employing logarithmic conversion. Pearson correlation coefficient (r) was calculated for targeted measurements, and positive findings were confirmed by multivariate analysis.

A significance level of 5% was established, and Graph Pad Prism 4.0 software (Graph Pad, San Diego, CA, USA) was utilized for all calculations.

Table I
Demographic findings, prognostic indices and general outcome

Age (years)	48.3 ± 11.3
Gender	100% males
Child-Pugh (%)	22.2% B, 77.8% C
MELD (points)	28.9 ± 8.6
Follow up (months)	22.6 ± 3.8
Mortality (%)	27.8% (5/18)
Rehospitalizations (episodes/patient)	1.7 ± 1.0

Results

All patients agree to the protocol however exclusion criteria were identified in seven , therefore the effective cohort encompassed 18 cases. General features of these patients are depicted in table I.

Dietary intake during admission was excellent (2,815 ± 279 kcal and 130 ± 12 g protein/day) however prehospitalization dietary recall could not be performed. Most were in the Child-Pugh C category, and mortality was comparably elevated within the observation period, despite adequate follow-up.

Biochemical profile was consistent with the advanced cirrhosis status. Serum albumin was severely depressed, anemia was common and systemic inflammation was confirmed, but without peritonitis or sepsis. Uncorrected BMI was acceptable but not triceps skinfold and arm circumference. Skinfold below the 5th percentile was not as common (16.7%, 3/18) as arm circumference (77.8%, 14/18), indicating predominant muscle wasting.

Mean ascitis volume reached 7.1 ± 3.6 liters, and when dry BMI was computed also this anthropometric measurement was below the normal range, confirming both visceral and somatic malnutrition (table II).

A few results were relevant for survival, namely number of hospital admissions which was quite obvious, and classic Child-Pugh index. Low platelet count is a known marker of liver fibrosis and of portal hypertension and did not surprise. A negative impact for low BMI (dry weight) as well as of massive ascitis was evident . MELD did not reach significance.

As concerns rehospitalizations Child-Pugh C index appeared again, but a particularly good match was noticed for arm circumference below the 5th percentile (table III).

Ascitis volume, dry BMI and arm circumference correlated with themselves as well as with other nutri-

Table II
Biochemical, anthropometric and ascitis volume results

Total bilirubin (mg/dL)	4.2 ± 4.8
Prothrombin time (s)	36.4 ± 14.8
International normalized ratio	3.6 ± 1.5
C-reactive protein (mg/dL)	13.2 ±16.7
Platelets (X 1,000/mm^3)	169 ± 101
White blood cell count/mm^3	7,759 ± 4,304
Serum albumin (g/dL)	2.5 ± 0.8
Hemoglobin (g/dL)	9.7 ± 3.1
Arm circumference (cm)	23. 9 ± 3.4
Tríceps skinfold (mm)	8.2 ± 7.9
BMI (standard) (kg/m^2)	21.1± 3.5
Ascitis volume (L)	7.1 ± 3.6
BMI (dry weight) kg/m^2	18.3 ± 3.5

tional and metabolic markers, but not with Child-Pugh, MELD or other tests. Such profile reinforces the contribution of body protein consumption to the unfavorable clinical course, independently from traditional prognostic signals (table IV).

Discussion

Currently the main chronic liver derangement worldwide as well as the principal predisposing condition for liver cirrhosis, cancer and transplantation is nonalcoholic fatty liver disease, a condition associated with overweight and metabolic syndrome.[16] Even statistics of viral and alcoholic cirrhosis are influenced by the widespread obesity epidemic, and obesity has been shown to be an independent predictor of clinical decompensation, including ascitis, in cirrhosis of all etiologies.[17]

Yet malnutrition is a classic feature of liver cirrhosis which depends on degree of liver damage , hypermetabolism, renal compromise and other complications, but also on such iatrogenic causes as repeated paracenteses, lactulose-related diarrhea, degree of protein restriction, and other interventions. In nonabstinent alcoholics, the substance addiction itself may be a precipitant of systemic inflammation and muscle wasting.[1,8,18]

Developing countries understandably exhibit higher proportions of body protein consumption than industrialized ones, due to the synergy between primary and secondary malnutrition.[1,5,12] Yet in Child-Pugh C patients, such as the majority of the currently documented cases, cachexia risk seems to be universal.[2,5,19]

In most centers anthropometric assessment along with dry weight are not calculated and ascitis classification is qualitative, as adopted by the International Ascites Club.[20] The advent of ascitis has been associated with up to 50% mortality within two years.[21] Prognosis of malnutrition is less precise, in spite of ample evidence for a deleterious impact,[1,3-5,12,22] one of the reasons being lack of consensus on which malnutrition indices are most useful for this population.[8,22,23]

Body mass index, upper arm anthropometrics, subjective global assessment, biochemical markers, dietary intake and complex body composition techniques have all been investigated, but with rather conflicting results. Admittedly liver dysfunction, and especially peripheral and peritoneal fluid accumulation, tend to interfere with most of these indices.[8,22,23]

Large population studies exist but participants are often heterogenous, including both stable and critically ill cases. The interference of obese cirrhotics on mean nutritional results, as already alluded to, may be conspicuous in certain environments. Moreover, independent and meaningful end-points such as number of hospitalizations and long-term mortality are not often selected. To the best of our knowledge, this is the first long-term observation with stable alcoholic cirrhosis and uncomplicated ascitis, focusing the role of anthropometric findings.

Current results endorse the association of ascitis volume and dry body mass index with mortality in the

Table III
Outcome differences

Mortality	*Yes*	*No*	*Significance*
Ascitis volume(L)	6.4 ± 2.8	8.9 ± 3.2	P = 0.041
BMI (dry weight) (kg/m^2)	18.9 ± 3.6	15.4 ± 1.6	P = 0.047
Rehospitalization(/patient)	1.3 ± 0.8	2.8 ± 1.0	P = 0.011
Child Pugh classification	69.2% C (9/13)	100% C (5/5)	P = 0.045
MELD (points)	28.3 ± 8.3	29.4 ± 9.4	P = 0.481
Platelet count (X 1,000/mm^3)	194 ± 101	103 ± 57	P = 0.048
Rehospitalization	*Yes*	*No*	*Significance*
Arm circumference < 5th	100% (13/13)	0%(0/5)	P < 0.001
Child Pugh C	84.6% (11/13)	40.0%(3/5)	P = 0.037

Obs: Arm circumference < 5th percentile.

Table IV
Correlations of ascitis volume, dry BMI and arm circumference

Variable	*"r" correlation index*	*Significance*
Ascitis volume		
Arm circumference	**0.631**	**P = 0.006**
Tríceps skinfold	0.505	P = 0.037
HDL cholesterol	**0.504**	**P = 0.037**
Dry BMI		
Arm circumference	**0.608**	**P = 0.008**
Triceps skinfold	0.578	P = 0.010
Arm circumference < 5th percentile		
Hemoglobin	**0.483**	**P = 0.048**

Obs: Values in bold were confirmed by multivariate analysis.

ensuing two years. Depressed arm circumference shoud be underscored as well, because of robust correlation with these primary markers, and notably with rehospitalizations. Some of these measurements have been addressed in other protocols, but targeting different populations and outcomes.[1,3,4,23]

The lack of end-stage liver disease may explain why MELD failed. The same reason justifies the lack of liver transplantaion in this series. Child-Pugh classification retained its prognostic interest, although correlation was not better than with the highlighted measurements. Given the fact that this was a pilot protocol, additional investigations will be necessary to confirm present findings.

Conclusions

A greater association than hitherto acknowledged, between ascitis volume and anthropometric measurements from one side, and long-term rehospitalization and mortality from the other, was demonstrated in stable hospitalized alcoholic cirrhotics. Paracentesis was not necessary for volume estimation. Further studies with alcoholic and other modalities of cirrhosis are recommended.

Acknowledgments

We are indebted to the staff and the administration of Academic Hospital Lauro Wanderley for providing technical conditions and supporting the costs of this protocol. The authors have no conflict of interest to declare.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2093-2101
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

One-year effectiveness of two hypocaloric diets with different protein/carbohydrate ratios in weight loss and insulin resistance

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Abstract

Background: **The maintenance of weight loss may be influenced by the distribution of macronutrients in the diet and insulin sensitivity.**

Objective: **The objective of the study was to evaluate the long-term effect of two hypocaloric diets with different protein/carbohydrate ratios in overweight and obese individuals either with insulin resistance (IR) or without insulin resistance (IS).**

Design: **Prospective, randomized, clinical intervention study. Forty patients were classified as IR/IS after a 75 g oral glucose tolerance test and then randomized to a diet with either 40% carbohydrate/30% protein/30% fat (diet A) or 55% carbohydrate/15% protein/30% fat (diet B).**

Results: **After one year of follow-up there was no difference in weight loss between diets A and B in each group, but the IS group maintained weight loss better than the IR group [-5.7 (3.9) *vs.* -0.6 (4.1); P = 0.04]. No differences were found in either Homeostasis Model Assessment (HOMA) or other metabolic glucose parameters except lower insulin at 120 minutes with diet A [21.40 (8.30) *vs.* 71.40 (17.11); P = 0.02].**

Conclusions: **The hypocaloric diets with different protein/carbohydrate ratios produced similar changes in weight. Insulin resistance may play a negative role in maintaining weight loss.**

(*Nutr Hosp.* 2012;27:2093-2101)

DOI:10.3305/nh.2012.27.6.6133

Key words: *Insulin resistance. Carbohydrates. Proteins. Diet.*

EFECTIVIDAD A UN AÑO DE DOS DIETAS HIPOCALÓRICAS CON DIFERENTE PROPORCIÓN DE PROTEÍNAS Y CARBOHIDRATOS EN LA PÉRDIDA DE PESO Y EN LA RESISTENCIA A LA INSULINA

Resumen

Introducción: **El mantenimiento de la pérdida de peso puede estar influido por la distribución de macronutrientes en la dieta y la sensibilidad a la insulina.**

Objetivo: **El objetivo del estudio fue evaluar el efecto a largo plazo de dos dietas hipocalóricas con diferente distribución de proteínas y carbohidratos (HCO) en individuos con sobrepeso y obesos ya fuese con resistencia a la insulina (IR) o sin resistencia a la insulina (IS).**

Metodología: **Estudio prospectivo, aleatorizado, de intervención clínica. Cuarenta pacientes fueron clasificados como IR / IS después de una prueba de tolerancia oral de 75 g de glucosa y luego asignados al azar a una dieta con 40% de HCO/ 30% proteína /30% grasa (dieta A) o el 55% HCO /15% proteína /30% grasa (dieta B).**

Resultados: **Tras un año de seguimiento, no se observaron diferencias en la pérdida de peso entre las dietas A y B en cada grupo, pero el grupo IS mantuvo la pérdida de peso mejor que el grupo IR [-5,7 (3,9) *vs* -0,6 (4,1), p = 0,04]. No se encontraron diferencias en ninguno en el Homeostasis Model Assessment (HOMA) u otros parámetros metabólicos de glucosa excepto en una insulina inferior a los 120 minutos con la dieta A [21,40 (8,30) *vs* 71,40 (17,11), p = 0,02].**

Conclusiones: **Las dietas hipocalóricas con diferentes proporciones de proteínas y carbohidratos produjeron cambios similares en el peso. La resistencia a la insulina puede jugar un papel negativo en el mantenimiento de la pérdida de peso.**

(*Nutr Hosp.* 2012;27:2093-2101)

DOI:10.3305/nh.2012.27.6.6133

Palabras clave: *Resistencia a la insulina. Hidratos de carbono. Proteínas. Dieta.*

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Recibido: 22-VIII-2012.
Aceptado: 11-X-2012.

Introduction

During the last few decades the prevalence of obesity has surged in an epidemic-like manner in both developed and developing countries.[1] Several metabolic disturbances such as dyslipidemia, diabetes, and hypertension, which are associated with increased visceral fat mass and insulin resistance, have increased in parallel. Lifestyle changes are the cornerstone of therapy for obesity, and research has been focused on which macronutrient distribution could be more beneficial for weight loss and help improve these metabolic conditions.

Nowadays there is revived interest in high-protein diets for weight loss. The protein content in these diets can vary from 25% to 45%.[2,3] Many studies in the literature indicate that high-protein diets achieve better weight loss results than high-carbohydrate diets in periods of less than 6 months.[3,4] Increasing the dietary protein content is usually accompanied by a reduction in carbohydrates. In fact, the terms high-protein and low-carbohydrate are often used indistinctly.

A recent trial comparing several hypocaloric diets with different ratios of fat, protein, and carbohydrates (20/15/65, 40/15/45, 20/25/55, 40/25/35) did not find significant differences between them in weight loss, hunger sensations or compliance;[5] a previous meta-analysis had shown that low-carbohydrate diets were not associated with a greater weight loss after 6 months of follow up.[6] Nevertheless, some authors have hypothesized that insulin resistance could influence weight loss associated with a hypocaloric diet: the trial by Cornier et al. described greater weight loss with a low-carbohydrate diet in insulin-resistant women and a high-carbohydrate diet in insulin-sensitive women.[7] A new randomized trial was conducted to test this hypothesis in which patients with and without insulin resistance received diets with different carbohydrate/ protein/fat ratios (40/30/30 or 55/15/30) for 16 weeks, and similar results regarding weight, body composition, and metabolic parameters were found.[8] Thus, we tried to evaluate the long-term effects on weight loss and insulin resistance of two hypocaloric diets with different protein/carbohydrate ratios in obese people either with insulin resistance (IR) or without insulin resistance (IS). After previously publishing the results of the first 16 weeks of this trial, we now report the results after 1 year of follow-up.

Methods

A prospective, randomized, clinical intervention study was designed to evaluate the effectiveness of different energy-restricted diets with different macronutrient compositions over a period of 1 year.

Subjects

A total of 40 obese or overweight patients (body mass index (BMI) between 28 to 35 kg/m^2; aged between 18 to 70 years old) were enrolled in the trial at the Complejo Asistencial Universitario de León, Spain. The study protocol was approved by the Ethics and Clinical Investigation Committee of the hospital (November 2005), and each participant gave informed consent. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. The exclusion criteria were participation in a weight loss treatment in the 6 months prior to the trial, any severe psychiatric illness, pregnancy, diabetes (fasting plasma glucose > 126 mg/dL or > 200 mg/dL at 120 min after an oral 75 g glucose tolerance test (OGTT), previous bariatric surgery, and eating disorders.

Procedure

The patients were placed in either the insulin resistance (IR) or the insulin sensitive (IS) group after a 75-g OGTT and Homeostasis Model Assessment (HOMA) index. The latter was calculated as the product of the fasting plasma glucose level (mmol/L) and the fasting plasma insulin level (mU/mL) divided by 22.5. We established a diagnosis of IR when the HOMA index was ≥ 3.8 or the fasting plasma insulin value was ≥ 15 mU/l.[9]

Daily energy requirements were estimated using the resting metabolic rate calculated by the Harris-Benedict equation,[10] and an activity factor of 1.5 was added in order to estimate the total caloric requirement.[11] The daily caloric intake for weight loss was calculated as the total caloric requirement minus 1,000 kcal. The subjects were free living and were asked to maintain their usual patterns of activity.

The patients were randomized to follow either a 40% carbohydrate/30% protein/30% fat diet (diet A) or a 55% carbohydrate/15% protein/30% fat diet (diet B). Random allocation to each dietary group was performed by the main investigator (MDBP) by using the Web site Randomization.com (http://www.randomization.com) upon the request of the study dietitian (ACF) after the eligibility of a participant was confirmed and assignment to either of the insulin resistance or insulin sensitivity groups had been performed. The dietitian was responsible for providing individual counseling and written material to the participants on the initial visit, and then the patients were instructed to record their food intake in a daily food diary and to discuss it with the dietitian on each visit at every 2 weeks for 16 weeks at the beginning of the trial and on each 3 monthly visit for 1 year. The medical assessments were blinded to the type of diet being followed.

At baseline, a physical examination including anthropometric measurements (weight, height, BMI, waist and hip circumference) and blood pressure was performed, and a 72-h dietary recall was performed. Body weight was measured to the nearest 0.5 kg and then taken using calibrated digital scales at the same

time of day on each subsequent visit. The subjects wore street clothing, removed their shoes, and voided their bladder before being weighed. On each visit, waist and hip circumferences were measured to the nearest 0.5 cm using a spring-loaded tape measure. Waist circumference was measured at the level of the umbilicus and hip circumference at the level of the greater trochanters.[12] Body composition was evaluated by means of a tetrapolar, single-frequency bioelectrical impedance analyzer (BIA) (Holtain BC Analyzer, UK) and a segmental hand-to-hand BIA unit (Omron BF 300, Tanita Corp., Kyoto, Japan). The patients were evaluated every 2 weeks for 16 weeks during the first follow-up period and every 3 months for 1 year during the second follow-up period. The examinations included anthropometric measurements, body composition and dietary recalls and were performed by the same dietitian. Baseline and final assessments in the first and second period also included a 75-g OGTT and blood samples for total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol triglycerides, liver and kidney function tests, TSH, iron, ferritin, and C-reactive protein. The blood samples were collected via venipuncture by a nurse after an overnight fast. The analyses were performed by the Clinical Biochemistry Department at the Complejo Asistencial Universitario de León.

Dietary intake

The patients provieded prospective serial assessment of nutritional intake over 3 days, including a weekend day, written food records at the baseline visit, and 24-h dietary recall the rest of the visits. The subjects were instructed by a dietitian to provide as much information on the food and drinks consumed (e.g., volume, ingredients, type of oil, brand name, etc.) as possible. The records were reviewed by the dietitian and analyzed using a computer-based data evaluation system with Dietsource 2.0 software (Novartis Consumer Health-Cath Soft, 1997-2003).

Statistical analyses

Ene 2.0 software (http://www.e-biometria.com/ene-ctm/index.htm) was used to calculate the sample size required to detect a difference of 3-4 kg with a power of β 0.80 and a significance of α 0.05, following the methods of McLaughlin[11] and Cornier.[7]

Changes in body weight, the primary outcome analyzed, were calculated as the body weight after the first and the second periods of being on the hypocaloric diet minus the weight at the baseline visit and expressed as absolute change in kilograms or as a percentage change from baseline. The descriptive data are presented as the mean ± SD. The analysis was performed on an intention-to-treat basis, with the last observation carried forward in case of withdrawal. The significance tests are two-sided, with the significance set at $P < 0.05$. A Shapiro-Wilks' test was performed to check whether or not the quantitative data were normally distributed. Pearson's chi-square and independent-sample T-tests (or the Mann-Whitney test if normality could not be assumed) were used to compare

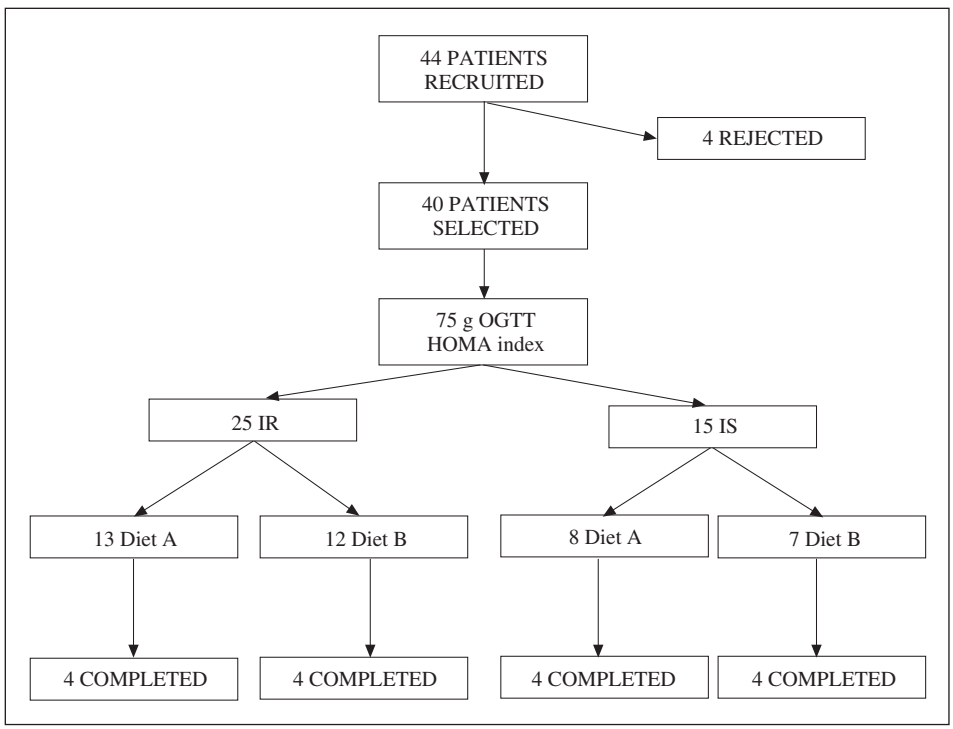


Fig. 1.—Flow chart of the study.

Table I
Baseline characteristics of the sample

	IR		*IS*	
	A *Mean (SD)*	*B* *Mean (SD)*	*A* *Mean (SD)*	*B* *Mean (SD)*
Age (years)	35.85 (12.42)	42.17 (15.08)	47.25 (11.76)	40.57 (14.55)
Sex (female/male)	7/6	9/3	7/1	4/3
Weight (kg)	90.78 (15.72)	88.09 (11.46)	85.38 (8.44)	85.56 (8.80)
BMI (kg/m^2)	31.18 (2.71)	32.02 (2.01)	32.99 (2.45)	31.44 (2.21)
Waist circumference (cm)	102.58 (7.82)	106.25 (8.87)	105.75 (6.27)*	98,50 (4.91)*
Waist-hip circumference (cm)	0.94 (0.06)	0.92 (0.05)	114.00 (4.44)	110.14 (4.45)
Fat mass (%)	31.39 (7.72)	35.91 (7.32)	31.86 (2.28)	26.91 (3.18)
Systolic blood pressure (mmHg)	123.78 (16.98)	120.00 (16.43)	126.67 (20.82)	132.50 (16.66)
Diastolic blood pressure (mmHg)	77,33 (14.67)	74.17 (9.17)	83.33 (10.41)	82.50 (15.41)
Glucose (mg/dL)	86.77 (10.46)	80.25 (26.46)	84.63 (11.40)	80.71 (6.90)
Insulin (μU/mL)	20.41 (5.45)	36.72 (49.64)	9.51 (2.26)	9.19 (3.26)
HOMA index	4.39 (0.99)	4.90 (3.06)	2.01 (0.52)	1.78 (0.50)
AST (U/L)	25.15 (10.20)	23.25 (13.35)	22.63 (11.04)	20.86 (11.73)
ALT (U/L)	39.77 (30.34)	35.50 (31.84)	30.25 (26.50)	22.14 (14.24)
Total cholesterol (mg/dL)	190.00 (36.83)	198.00 (30.73)	224.38 (38.98)	210.29 (35.30)
HDL-cholesterol (mg/dL)	47.38 (14.52)	50.58 (11.56)	59.88 (21.26)	57.14 (19.28)
LDL-cholesterol (mg/dL)	113.28 (28.81)	115.65 (28.56)	125.86 (22.77)	125.23 (28.67)
Triglycerides (mg/dL)	150.85 (91.71)	150.50 (62.46)	161.88 (122.41)	139.57 (59.26)
C-protein reactive (mg/dL)	3.47 (5.32)	4.14 (2.84)	4.00 (1.32)	2.03 (0.76)

*P = 0.026; **P = 0.004.

baseline characteristics and weight loss between the groups (IR *vs.* IS, diet A *vs.* B). Repeated measures ANOVA was performed to detect changes in HOMA, glucose, insulin and lipid profiles and also to detect any differences in dietary composition.

Results

The trial included 40 patients: 25 were insulin resistant (IR) and 15 were insulin sensitive (IS). Diet A was randomly assigned to 21 patients (13 IR, 8 IS) and diet B to 19 patients (12 IR, 7 IS). The allocation of patients is shown in figure 1. Their general characteristics are summarized in table I.

Weight loss and body composition

No differences were found between the groups in weight loss during the first 16 weeks, as described previously.[8] When compared to the first visit, no significant differences in the weight loss percentage were found between IR and IS at 6 months [-5.6% (8.7) *vs.* -5.5% (5.1); P = 0.964], but after 12 months of follow-up IS maintained weight loss better than IR [-5.7 (3.9) *vs.* -0.6 (4.1); P= 0.04]. No differences were found between diets A and B at 6 months [-4.3% (85.4) *vs.* -7.1% (9.3); P = 0.368] or 12 months [-2.2% (5.6) *vs.* -3.5% (3.4); P = 0.630] in the overall group. The change in weight did not differ according to diet in either of the IR or IS groups at any visit (table III).

No significant differences in BMI, fat mass, waist circumference, or waist-to-hip ratio were found on any visit according to insulin resistance/sensitivity or diet in the overall group or in each of the four groups.

Diet

The usual dietary intake of the four groups is reported in table II; there were no significant differences between the groups. When both diets were compared, the patients on diet A ate a lower percentage of carbohydrates at 3 [40.1 (12.6)% *vs.* 53.4 (7.4)%; P = 0.04] and 12 months [39.5 (9.0)% *vs.* 51.0 (9.9)%; P = 0.04], a higher proportion of saturated fat at 3 months [11.6 (4.0)% *vs.* 6.0 (2.8)%; P = 0.04], and a higher proportion of monounsaturated fat at 3 [18.0 (7.0)% *vs.* 13.5 (3.2)%; P = 0.046] and 12 months [16.7 (4.2)% *vs.* 9.8 (6.0)%; P = 0.03]. The differences between IR and IS according to the type of diet are reported in table IV.

Table II
Baseline nutrient intake

	Insulin resistant				*Insulin sensitive*			
	A		*B*		*A*		*B*	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Kcal	1,912	682.52	2,250	1,165.69	1,688	657.94	1,615	566.69
Carbohydrate (%)	42.85	9.15	45.90	10.06	42.25	9.39	40.43	14.32
Protein (%)	22.15	3.98	18.36	4.01	21.50	2.56	20.14	1.86
Total fat (%)	34.92	9.84	34.79	9.54	36.38	8.47	39.43	12.92
Saturated fat (%)	9.65	4.73	9.43	4.40	10.83	3.44	9.37	5.00
Monounsaturated fat (%)	16.27	4.55	15.45	3.92	14.80	4.50	18.60	6.08
Polyunsaturated fat (%)	2.98	1.29	3.30	1	3.44	0.96	4.35	2.09
Cholesterol (mg)	413.58	219.15	428.58	346	373.65	118.48	469.76	354.08
Fiber (g)	17.49	8.04	19.07	6.38	16.03	7.31	16.93	7.01

$P > 0.05$.

Table III
Weight loss and anthropometric changes

	IR		*IS*	
	A *Mean (SD)*	*B* *Mean (SD)*	*A* *Mean (SD)*	*B* *Mean (SD)*
Weight loss (%)				
3 months	-7.76 (5.87)	-10.37 (7.55)	-11.12 (3.07)	-9.19 (1.53)
6 months	-10.25 (4.88)	-10.53 (10.67)	-12.14 (3.29)	-9.63 (2.51)
9 months	-7.82 (7.44)	-10.81 (11.48)	-12.38 (4.90)	-7.53 (2.71)
12 months	-6.87 (3.29)	-7.38 (1.96)	10.57 (5.51)	-8.55 (0.83)
BMI (kg/m²)				
3 months	30 (2.78)	29.77 (3.18)	30.12 (2.58)	28.80 (2.05)
6 months	28.93 (2.19)	29.77 (3.93)	29.55 (0.90)	28.52 (2.68)
9 months	29.82 (3.06)	28.82 (3.60)	29.95 (3.27)	29.22 (2.71)
12 months	29.26 (2.63)	29.84 (2.18)	30.52 (2.90)	29.98 (2.63)
WHR				
3 months	0.92 (0.06)	0.95 (0.08)	0.91 (0.04)*	0.88 (0.01)*
6 months	0.92 (0.05)	0.92 (0.08)	0.91 (0.05)	0.95 (0.08)
9 months	0.95 (0.06)	0.95 (0.09)	0.90 (0.05)	0.91 (0.04)
12 months	0.93 (0.05)	0.94 (0.11)	0.92 (0.09)	0.93 (0.04)
Fat mass (%)				
3 months	29.40 (9.46)	37.32 (8.01)	38.18 (3.28)	33.53 (7.51)
6 months	27.61 (8.77)	37.19 (8.17)	37.22 (4.22)	33.03 (9.14)
9 months	27.44 (10.16)	34.80 (8.32)	38.33 (3.26)	34.20 (8.76)
12 months	31.18 (10.67)	39.08 (5.57)	39.38 (4.46)**	30.95 (14.21)**

* $P = 0.046$; ** $P = 0.033$.

Glucose metabolism

In the IR group, no differences were found between the levels of fasting plasma glucose, fasting insulin or the HOMA index either before the diet or at any point during follow-up; after 12 months, insulin at 120 minutes after the OGTT was lower with diet A [21.40 (8.30) *vs.* 71.40 (17.11); $P = 0.02$].

Table IV
Changes in dietary intake

	IR		*IS*	
	A Mean (SD)	*B* Mean (SD)	*A* Mean (SD)	*B* Mean (SD)
Energy (kcal)				
3 months	2,176.79 (766.73)	1,665.99 (345.62)	1,668.86 (587.99)	1,813.93 (409.68)
6 months	2,006.51 (777.74)*	1,562.67 (328.86)*	1,389.12 (376.62)	2,315.75 (889.22)
9 months	2,350.53 (547.55)	1,637.52 (398.67)	1,561.03 (177.14)	1,761.70 (677.04)
12 months	1,911.18 (409.35)	1,161.95 (302.49)	1,486.83 (301.58)	1,592.85 (408.50)
CHO (%)				
3 months	40.89 (12.77)	51.38 (8.05)	38.60 (13.58)	57.50 (3.79)
6 months	47.88 (8.92)	50.86 (11.36)	44.80 (15.14)	47 (10.74)
9 months	42.29 (7.95)	52.20 (12.03)	47.75 (6.18)	45.75 (2.06)
12 months	41.75 (11.18)	50.50 (12.66)	37.25 (7.23)	52.00 (2.83)
Protein (%)				
3 months	19.89 (6.79)*	18 (2.51)*	19.20 (3.11)	18.75 (1.71)
6 months	19.25 (5.20)	19.14 (5.79)	20 (6.04)	17 (2.94)
9 months	20.71 (2.56)	16.00 (1.58)	18.25 (4.79)	19.75 (3.20)
12 months	22.25 (2.63)	23.00 (6.78)	22.25 (2.99)	16 (0.00)
Fat (%)				
3 months	39.22 (12.74)*	30.63 (7.48)*	41.80 (13.66)*	24.25 (3.77)*
6 months	32.88 (13.13)	30 (11.25)	35.40 (13.67)	35.75 (10.14)
9 months	37 (9.76)	31.80 (12.83)	34 (8.29)*	34.50 (4.20)*
12 months	36 (13.49)	26.05 (14.82)	40.50 (8.50)	31.50 (2.12)
SFA (%)				
3 months	11.10 (5.24)	7.83 (3.48)	12.43 (8.98)	5.80 (2.40)
6 months	8.28 (5.60)	9.59 (4.43)	8.72 (3.43)	9.32 (4.27)
9 months	9.89 (4.60)	7.25 (3.75)	8.58 (3.92)	9.95 (3.59)
12 months	7.80 (4.52)	5.31 (3.28)	9.69 (3.82)	7.45 (0.07)
MUFA (%)				
3 months	18.17 (6.19)	14.35 (3.65)	17.62 (19.19)	11.75 (1.19)
6 months	14.07 (5.25)	13.15 (3.64)	14.40 (4.33)	14.43 (2.43)
9 months	16.09 (3.94)	14.08 (5.38)	16.68 (3.30)**	16.03 (0.39)**
12 months	15.25 (4.05)	6.87 (4.90)	18.20 (4.36)	15.80 (0.99)
PUFA (%)				
3 months	3.49 (1.04)	2.44 (0.73)	3.61 (1.76)	2.09 (0.48)
6 months	3.77 (2.46)	2.32 (0.68)	3.11 (0.98)	3.49 (1.23)
9 months	3.69 (1.11)	2.40 (1.17)	3.43 (0.62)	3.15 (1.34)
12 months	3.55 (1.44)	3.24 (2.86)	4.31 (0.24)**	3,75 (1.23)**
Cholesterol (mg)				
3 months	413.58 (219.15)	428.58 (346.00)	460.76 (270.53)*	342.18 (88.18)*
6 months	449.98 (247.72)	284.59 (166.80)	265.4 (218.62)	395.50 (160.17)
9 months	383.69 (204.14)	258.19 (153.51)	365.03 (238.24)*	325.80 (104.27)*
12 months	361.05 (150.69)	100.75 (143.01)	400.75 (115.17)*	437.10 (469.66)*
Fibre (g)				
3 months	16.74 (7.30)	18.20 (3.78)	11.70 (6.15)	22.60 (6.22)
6 months	20.14 (11.26)	14.66 (6.39)	11.52 (7.97)	25.38 (5.86)
9 months	22.89 (6.79)	17.76 (6.42)	20.65 (9.33)	23.40 (12.56)
12 months	15.65 (6.50)	19 (6.82)	15.53 (8.69)	19.85 (5.30)

* $p < 0.05$; ** $p < 0.005$.

Table V
Laboratory parameters at the end of the study

	Diet		*Glucose sensitivity*	
	A *Mean (SD)*	*B* *Mean (SD)*	*A* *Mean (SD)*	*B* *Mean (SD)*
Glucose (mg/dL)	81.00 (7.32)	91.00 (16.52)	86.50 (11.67)	80.00 (11.14)
Insulin (μU/mL)	6.10 (4.27)	14.32 (4.03)	11.79 (4.20)	2.95 (2.64)
HOMA index	1.24 (0.85)	3.33 (1.58)	2.59 (1.33)	0.63 (0.61)
AST (U/L)	19.50 (5.47)	18.33 (8.50)	17.83 (6.24)	21.67 (6.02)
ALT (U/L)	16.33 (5.85)*	27.33 (22.23)*	23.00 (15.70)	14.00 (2.00)
C-protein reactive (mg/dL)	2.07 (0.88)	2.70 (0.71)	2.52 (0.88)	1.73 (0.60)
Total cholesterol (mg/dL)	206.67 (54.84)	216.67 (25.01)	197.83 (31.13)	234.33 (67.01)
HDL-cholesterol (mg/dL)	54.67 (12.71)	48.67 (16.17)	48.83 (14.86)**	60.33 (4.04)**
LDL-cholesterol (mg/dL)	134.17 (46.94)	140.47 (39.08)	127.03 (29.93)	154.73 (63.80)
Triglycerides (mg/dL)	89.17 (41.22)	137.67 (8.74)	109.83 (42.29)	96.33 (44.97)

*P = 0.009; ** P = 0.030.

Other laboratory parameters

In the IR group, no differences were found in the lipid profiles between the diets. Among the patients with IR, similar levels were found in the liver function test, BUN, creatinine, and inflammatory parameters (ferritin, CRP). The differences at the end between the IR and IS groups and between the two types of diet are reported in table V.

Discussion

Weight loss is dependent on the existence of an energy deficit between intake and expenditure, which can be achieved by increasing energy expenditure through physical activity or reducing caloric intake. Both cases are conditioned by environmental, social, and genetic factors that could influence their efficacy. Over the past few decades various diets have been designed to reduce weight in an easy way. The present study describes the long-term results of following two hypocaloric diets with different protein/carbohydrate ratios and supports the theory that the macronutrient composition of a diet does not influence weight loss, body composition or improvements in insulin resistance. Nevertheless, IR was associated with poor weight loss after a period of 1 year, and the carbohydrate-rich (55% of the total calories) diet showed higher insulin levels after the OGTT.

Some data in the literature suggest that higher protein contents in the diet can contribute to weight loss. First, high-protein diets may be related to higher levels of thermogenesis, which can increase energy efficiency during weight loss and help to avoid weight regain.[12] Second, the replacement of some dietary carbohydrates by protein (up to 25% of calorie intake *vs.* 12% in controls) in an *ad libitum* fat-reduced diet has been associated with a lower energy intake and thus with greater weight loss.[13] A study by Dumesnil et al. also reported favorable changes in hunger/satiety with a high-protein diet (30%) compared to a balanced diet (16%, according to the American Heart Association), but no significant differences were found in the loss of body weight.[14] Third, dietary protein can enhance body composition by reducing fat mass and increasing lean body mass. Laymen et al. found that a higher protein/carbohydrate ratio produced a better ratio of fat-to-lean mass loss. Weight loss was similar for both diets as they were both isocaloric.[15] In studies that compared a low-carbohydrate diet with *ad libitum* energy intake or a low-fat diet, the decrease in fat mass was also significantly greater in the high-protein group.[6,16]

Despite the theoretical advantages of increasing the protein content of a diet, the results of several trials are consistent with our results regarding the lack of efficacy of increasing the composition of this macronutrient over the long term, although some studies showed better weight loss after 6 months of follow-up.[4,18] Delbridge et al., using the same protein/carbohydrate ratio as in our study, did not find any differences in weight-loss maintenance. Both groups of diet, kept the weight off over 12 months, but the authors did not study the influence of IR on weight loss.[17] This trial did not find any differences in fat loss between the diets after 1 year of dietary counseling, and neither did we. The differences between studies have several possible explanations. The amount of protein given varies between the studies and is difficult to standardize what a high-protein diet actually is, especially when the usual recommended quantity of protein (0.8 g/kg) is far from the actual intake in developed countries. Important differences were also found in the diets used as the control (e.g. balanced or low fat). One of the advan-

tages of our study was the free-living setting, where no food was provided to the patients; they had to buy and process it according to recommendations by themselves. This could also have been a disadvantage since it is very difficult to quantify compliance with the diet. However, the clinical setting varies between studies, with some of them being performed in a controlled environment. Over the ensuing months the patients changed the scheduled diet and both groups eventually consumed a diet containing a similar macronutrient composition. This result, which is consistent with that observed by Dansinger et al.,[18] shows that it is difficult to maintain dietary changes over the long time in free-living situations, which could definitively influence the outcome.

One of the most relevant results of this study was the fact that patients in the IS group maintained their weight loss better than patients in the IR group, independently of the diet. IR is related to disturbances in lipid oxidation and to other metabolic abnormalities that could make weight loss difficult. Nevertheless, some studies have shown that glycemic status does not play a role in weight loss,[19] and others showed that insulin sensitivity did not affect weight loss in obese or overweight patients treated with hypocaloric diets,[11,20,21] as noted in our initial study.[8] Our results might have been influenced by the loss of patients during follow-up, which was largest in the IR group. The insulin peak after OGTT was higher among patients who received the carbohydrate-rich diet, but this macronutrient distribution was not associated with adverse outcomes related to glucose (either glucose levels or HOMA) or lipid metabolism. Several studies have shown evidence of the cardiovascular benefits of energy-restricted high-protein diets through reducing the amount of triglycerides and increasing HDL-cholesterol.[4] In McLaughlin's study,[22] several cardiovascular disease risk factors (day-long insulin concentrations, lipid and lipoprotein concentrations and cellular adhesion molecules) significantly improved in the subjects who followed the 40% carbohydrate diet, without showing any difference in weight loss. In our study, when comparing the IS group with the IR group, a significant increase was found in triglycerides in the IS group but there were no significant changes in total cholesterol, LDL-cholesterol, or HDL-cholesterol, as found when diets A and B were compared.

Our study has several limitations that should be discussed before any conclusion is reached. The sample size required in order to find significant differences in weight was calculated following the methods of previous studies,[7,9] but the number of subjects per group was small and we could not reach statistical significance in the secondary end-points. Furthermore, only a few patients in each group attended each visit, probably those who were more motivated to lose weight. Attrition rates were high, although similar to other studies on this topic, reflecting the difficulty of maintaining long-term diets.[18,23] Also, the study was only carried out in one center, so these results cannot be generalized. Dietary intake was assessed using a 24-h dietary recall method, which probably only gave limited or biased information about the real intake. Another limitation of the trial was that energy expenditure was not measured, therefore the influence of macronutrients on this parameter or on food thermogenesis could not be quantified.

In conclusion, after 1 year of follow-up, the hypocaloric diets with different protein/carbohydrate ratios resulted in similar changes to body weight and metabolic parameters, and insulin resistance was associated with a lower weight loss independently of macronutrient distribution. Dietary changes are difficult to maintain in free-living conditions over the long term, and this imposes limits on sustained weight control.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2102-2108
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

La estimulación prenatal; resultados relevantes en el periparto

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Resumen

Durante el proceso gestacional, el estrés prolongado y las preocupaciones que genera este período pueden alterar el desarrollo y la función del hemisferio derecho; de ahí la importancia que se atribuye a los distintos programas de estimulación temprana dirigido a las mujeres gestantes.

Objetivos: **Determinar los resultados perinatales en el momento del parto de las mujeres que recibieron el programa de estimulación prenatal.**

Material: **Se realizó un estudio experimental en cinco áreas de salud del municipio de Cienfuegos (Cuba) para identificar los resultados perinatales en el momento del parto y de las mujeres que recibieron el programa de estimulación prenatal.**

Metodología: **Se efectuó una muestra intencional de la totalidad del universo, correspondiente a una n = 200 embarazadas, entre las 20 y las 28 semanas de gestación. Las variables estudiadas fueron la duración del trabajo del parto, el peso del recién nacido, el apgar al nacimiento, el tipo de parto y la opinión que las mujeres estudiadas tenían sobre el programa.**

Resultados: **En el 36% de la población estudiada, el trabajo del parto fue menor de 6 horas. En el 67,5%, el recién nacido tuvo un peso comprendido entre 2.500 y 3.000 gramos y para el 96,5% de los hijos de las madres estimuladas, el apgar al nacer fue evaluado entre 8 y 9. En el 68,5% de las mujeres que recibieron el programa de estimulación, su parto fue eutócico y el 96% de las mujeres participantes está satisfecha con el programa recibido. Conclusiones. Se ha demostrado que estos nuevos programas de estimulación prenatal son bien aceptadas por la embarazada.**

(*Nutr Hosp.* 2012;27:2102-2108)

DOI:10.3305/nh.2012.27.6.6019

Palabras clave: *Estimulación prenatal. Trabajo de parto.*

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Recibido: 1-III-2012.
1.ª Revisión: 22-VI-2012.
Aceptado: 11-IX-2012.

PRENATAL STIMULATION. RESULTS IN THE PERIPARTUM PERIOD

Abstract

During pregnancy, the prolonged stress and worry felt by mothers can alter the development and function of the right brain hemisphere. For this reason, importance is given to prenatal stimulation programs for pregnant women.

Objectives: **To determine the perinatal results in the moment of childbirth in mothers who had participated in prenatal stimulation programs. Material. An experimental study was conducted in five health districts in the town of Cienfuegos (Cuba) with a view to identifying the perinatal results at the moment of childbirth in women that had participated in prenatal stimulation programs.**

Methodology: **The study consisted of an intentional sampling of all of the subjects (n = 200 women who were 20-28 weeks pregnant). The variables studied were the following: duration of labor, baby's birth weight, Apgar score at birth, type of childbirth, and opinion of the subjects about the prenatal stimulation program.**

Results: **Of the population sample, 36% of the subjects gave birth in less than six hours; 67.5% had babies weighing 2,500-3,000 grams; and 96.5% had babies whose Apgar scores were between 8 and 9. Finally, 68.5% of the subjects had natural childbirths and 96% were satisfied with the prenatal stimulation program. Conclusions. The results obtained showed that these new prenatal stimulation programs were well received by the subjects in this study.**

(*Nutr Hosp.* 2012;27:2102-2108)

DOI:10.3305/nh.2012.27.6.6019

Key words: *Prenatal stimulation. Labor.*

Introducción

Buscar asistencia podría haber aparecido en los primeros miembros del género Homo y posiblemente se remonte a unos 5 millones de años, cuando nuestros antepasados iniciaron la marcha bípeda. Varios investigadores concluyen que la asistencia al parto es una costumbre casi universal[1]. Es indispensable que durante el parto esté presente una persona de mucha confianza de la parturienta, preferiblemente su pareja. Esto forma parte de la herencia instintiva, cualidad de los hombres necesaria para poder sobrevivir en la naturaleza y que la diferencia de otros mamíferos; si no se satisface este apego pre y post natal, el hijo difícilmente sobrevive[2].

La evolución del embarazo delimita tres períodos, coincidentes con cada trimestre de gestación, en donde diferentes situaciones, como el stress, el desconocimiento relacionado con el embarazo y los eventos del parto, constatan un aumento de la dependencia, la pasividad y la introversión, lo que persistirá hasta algunas semanas después del parto. La percepción del embarazo, de los movimientos fetales y de la proximidad del parto representa el núcleo de cada uno de estos períodos. Durante el trabajo del parto la parturienta debe recurrir a sus propios recursos (posturales, emocionales) que la ayuden a pasar las poderosas contracciones del reflejo de expulsión del bebé. Las endorfinas que se generan son los mejores calmantes y una mujer que se sienta segura y firme puede producirlas en abundancia, lo que la dota de un estado emocional altamente positivo, que le ayudará en el período expulsivo[3].

Durante el proceso gestacional, el estrés prolongado, la falta de amor y todas las preocupaciones propias del período alteran el desarrollo y la función del hemisferio derecho. Éste se estimula con la música de forma positiva en el nivel cerebral; de ahí, la importancia que se le atribuyen a los distintos programas de estimulación temprana dirigidos a gestantes y niños discapacitados[4].

En el contexto latinoamericano, las estrategias en el ámbito materno-infantil centran su trabajo en la atención a la maternidad y a la paternidad responsables. Tienen por objeto preparar a la pareja para el momento del parto. No se conocen en este contexto los resultados que pueden tener sobre los eventos del periparto las acciones organizadas, cargadas de afectividad y en donde la comunicación madre-hijo tiene un papel determinante. Igualmente la lactancia materna tiene beneficios para el bebé y para su madre. Se ha comprobado que es un método eficaz para la prevención del cáncer de mama, previene la obesidad materna y del niño, e influye sobre el peso y la morbilidad[5,6,7,8,9].

Por ello, el objetivo del presente estudio es determinar cómo influye la estimulación prenatal en los resultados perinatales centrados en el parto. Este trabajo está dirigido y coordinado por el Grupo de Investigación CTS 367 del Plan Andaluz de Investigación (PAI) de la Junta de Andalucía (España) para llevarlo a cabo en países de Iberoamérica.

Objetivo

Determinar los resultados perinatales en el momento del parto en mujeres que recibieron el programa de estimulación prenatal.

Material y método

Se realizó un estudio experimental con un solo grupo de control en la atención primaria de salud en las áreas I, II, III, IV y V, de Cienfuegos (Cuba) durante el período de abril de 2010 a noviembre de 2011. El universo estuvo constituido por embarazadas entre 20- 28 semanas de gestación (SG) N = 348. Se realizó un muestreo intencional del 57% del total del universo n = 200.

Variables a utilizar: Se estudiaron variables para caracterizar la población objeto del estudio**,** como Edad, Estado Civil, Paridad y Nivel profesional. Después del parto se estudiaron variables relacionadas con el trabajo del parto, el tipo de parto, la duración del trabajo del parto, el test de Apgar, el peso del recién nacido y, por último, la opinión de las gestantes sobre el programa de estimulación prenatal recibido.

Criterios de inclusión: Embarazadas entre 20 y 28 semanas de gestación.

Criterios de exclusión: Se excluyeron en nuestro estudio a las gestantes con embarazo gemelar, gestantes con riesgo de nacimiento pretérmino, pacientes con alteraciones mentales y aquellas que abandonaron el programa.

Técnicas y procedimientos

Entrenamiento de los facilitadores (enfermeras de las áreas de salud, vinculadas a la atención de la embarazada).

Entrega del programa a cada facilitador, que viene estructurado por temas.

a) Comunicación madre-hijo.
b) Estímulos afectivos para el niño.
c) Estímulos auditivos.
d) Estímulos táctiles activantes.
e) Estímulos táctiles sedantes.
f) Estímulos vestibulares.
g) Estímulos visuales.

Cada tema tiene una duración de 50 minutos y se aplicó con una frecuencia de dos veces por semana.

Al concluir el tema N°. 7 se efectuó una encuesta para determinar la opinión de la gestante relacionada con el programa de estimulación prenatal.

Obtención de la información: La información se obtuvo mediante la historia clínica del paciente, después de haber finalizado el evento del parto y por el departamento de estadística, y que se registró en un for-

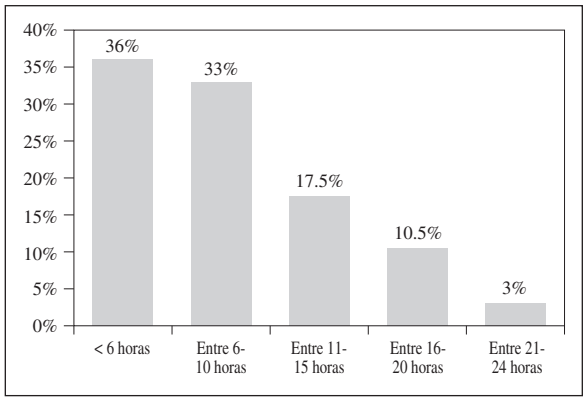


Fig. 1.—Duración del trabajo de parto en gestantes que recibieron estimulación prenatal.

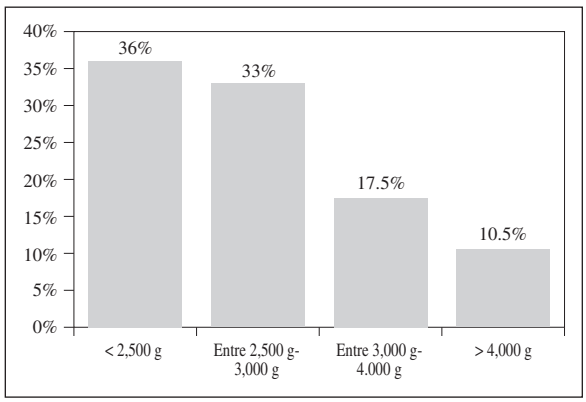


Fig. 2.—Peso al nacimiento de los recién nacidos estimulados intraútero.

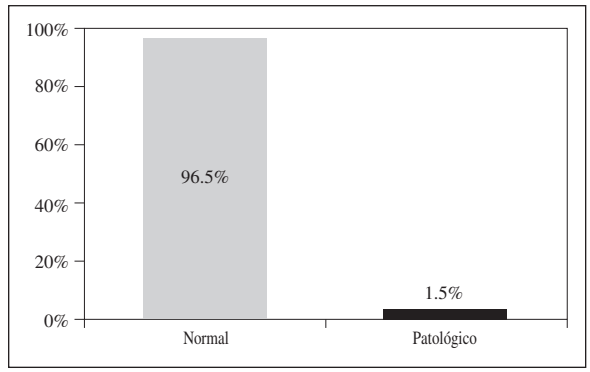


Fig. 3.—Apgar al nacimiento de los recién nacidos estimulados intraútero.

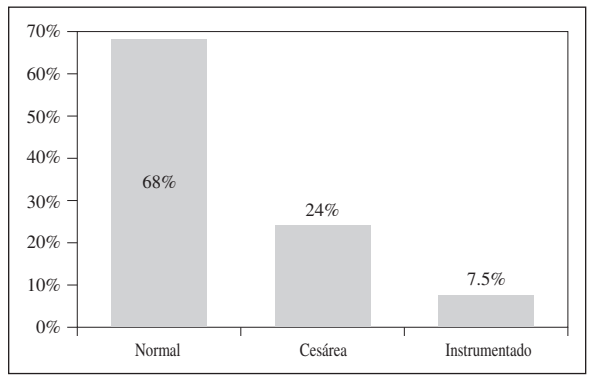


Fig. 4.—Tipo de parto en gestantes que recibieron estimulación prenatal.

mulario confeccionado al efecto. La opinión sobre el programa se midió por un instrumento de evaluación.

Procesamiento estadístico: Los métodos estadísticos utilizados fueron los siguientes:

- Distribución de frecuencias empíricas con cálculo de medidas descriptivas.
- Correlaciones bivariadas no paramétricas.

Resultados

En la figura 1 se observa la duración del trabajo de parto en las pacientes que recibieron el programa de estimulación prenatal y se constata que las mujeres estimuladas en mayor porcentaje su trabajo de parto tuvo una duración menor de 6 horas, seguidas del grupo cuya duración estuvo entre 6 y 10 horas.

Se aprecia que en el 67,5% las madres estimuladas el peso de sus hijos se sitúan en el rango de los 2.500 y los 3.000 gramos (fig. 2).

El apgar al nacimiento según refleja la tabla III se consideró normal en el 96,5% de las mujeres estudiadas (fig. 3).

Al analizar el tipo de parto según refleja la figura 4 se observa que el 68 % de las mujeres que recibieron la estimulación en la etapa prenatal su parto fue eutócico.

La tabla I nos muestra la correlación entre las variables tipo de parto, apgar del recién nacido y peso al nacimiento, donde puede observarse que el apgar promedio fue normal en todos los casos independientemente del peso y del tipo de parto.

Al analizar en la tabla II la opinión de las gestantes en relación al programa de estimulación que le fue impartido, se observa que existe un criterio bueno en el 96% de las mismas. Por otra parte con ayuda de medidas de tendencia central como la mediana y la moda, que muestran resultados coincidentes, se puede concluir que la evaluación promedio otorgada es buena.

En la tabla III se refleja que existe correlación estadística entre las variables: tipo de parto y opinión de las gestantes estimuladas con el programa de estimulación prenatal, para ello se calcularon los coeficientes no paramétricos de kendall y Spearman.

Discusión

La tabla I muestra la duración del trabajo del parto. Se puede afirmar que el 69% de las mujeres que recibieron estimulación prenatal tuvieron trabajos de parto de hasta 10 horas. La literatura especializada plantea que la duración del trabajo del parto es mayor en la nulípara que en la multípara. Se demora más en la nulí-

Tabla I
Correlación no paramétrica entre el tipo de parto- apgar del recién nacido y peso al nacimiento
*[*Correlation is significant at the 0.05 level (2-tailed)]*

			Tipo de parto	*Apgar Recién nacido*	*Peso al nacer*
Kendall					
	Tipo de parto	Correlación Coeficiente	1,000	-0,020	-0,154*
		Sig. (2- tailed)		0,772	0,020
		N	200	200	200
	Apgar R/N	Correlación Coeficiente	-0,020	1,000	0,015
		Sig. (2- tailed)	0,772		0,778
		N	200	200	200
	Peso al nacer	Correlación Coeficiente	-0,154*	0,019	1,000
		Sig. (2- tailed)	0,020	0,778	
		N	200	200	200
Spermam					
	Tipo de parto	Correlación Coeficiente	1,000	-0,21	-0,164*
		Sig. (2- tailed)		0,773	0,021
		N	200	200	200
	Apgar R/N	Correlación Coeficiente	-0,021	1,000	0,020
		Sig. (2- tailed)	0,773		0,779
		N	200	200	200
	Peso al nacer	Correlación Coeficiente	-0,164*	0,020	1,000
		Sig. (2- tailed)	0,021	0,779	
		N	200	200	200

Tabla II
Opinión de las gestantes relacionado con el programa de estimulación prenatal

		Frequency	*Percent*	*Valid percent*	*Cumulative percent*
Valid	Bueno	192	96	96	96
	Regular	8	4	4	100
	Total	200	100	100	

Fuente: Formulario.

para teniendo en cuenta que fisiológicamente en las primeras comienzan las modificaciones por el orificio cervical interno, mientras que el externo ofrece mayor resistencia, es decir primero ocurre el borramiento y luego la dilatación.

Estudios realizados en torno a la estimulación demuestran su efectividad y que se aceleran los procesos fisiológicos, coincidiendo los resultados de este estudio con lo planteado por la literatura. Utilizar la estimulación como mecanismo para la relajación durante el trabajo del parto constituye la base de todas las técnicas de educación en esta etapa. La tensión durante ese trabajo es una respuesta natural a las contracciones del útero. Sin embargo, produce agotamiento, disminuye el oxígeno, reduce el umbral del dolor y prolonga el trabajo del parto. En ese momento, es la adrenalina la hormona que acompaña al síndrome de temor, tensión y dolor e inhibe el efecto de la oxitocina que provoca las contracciones uterinas[10].

Con la aplicación de la estimulación prenatal, la gestante durante el parto se comporta de forma más relajada, lo que favorece la síntesis de oxitocina, llamada también la hormona del amor, y que se libera antes, durante y después del trabajo del parto. Existen investigaciones que demuestran un mejor comportamiento maternal con la síntesis de oxitocina en este periodo.

Tabla III
Relación entre el tipo de parto y la opinión relacionada con el programa. Correlación no paramétrica

			Tipo de parto	
Kendall's tau_b	Tipo de parto	Correlation coefficient	1,000	0,243**
		Sig. (2-tailed)		0,000
		N	200	200
	Opinión de las gestantes	Correlation coefficient	0,243**	1,000
		Sig. (2-tailed)	0,000	
		N	200	200
Spearman's rho	Tipo de parto	Correlation coefficient	1,000	0,250**
		Sig. (2-tailed)		0,000
		N	200	200
	Opinión de las gestantes	Correlation coefficient	0,250**	1,000
		Sig. (2-tailed)	0,000	
		N	200	200

**Correlation is significant at the 0,01 level (2-tailed).

Esta investigación pone de manifiesto que el grado de preparación que logra la embarazada en la etapa prenatal con la utilización de la estimulación intrautero y la relajación, se relaciona de forma significativa con la duración del trabajo del parto.

Al analizar los resultados de la tabla II se constata que un buen estado nutricional de la madre durante el embarazo influye positivamente en el peso de su hijo. Es obvio que una de las premisas que permiten garantizar una adecuada nutrición es la estabilidad emocional, en relación con los procesos adaptativos del embarazo, además de todos los factores sociales, culturales y económicos que intervienen en la nutrición del individuo.

Diversos factores influyen en el estado nutricional y en la alimentación diaria. Se describen aquellos determinantes del consumo alimenticio (hambre, apetito y costumbres) de cada embarazada, aunque existen otros que disminuyen el apetito, lo que se relaciona con las preocupaciones, temores y los problemas o dificultades que se presenten a lo largo del proceso gestacional[11].

La literatura plantea que con el uso de estimulantes emocionales positivos (estimulación prenatal) se favorecen las situaciones que propician la tranquilidad, la alegría, el entusiasmo y la estimulación del ego, lo que influye favorablemente en el estado nutricional de la gestante. De esta forma, la embarazada logra una adecuada ganancia de peso, por lo que se obtendrán recién nacidos con buen peso al nacimiento. Una correcta nutrición y una adecuada estimulación sensorial favorecen el desarrollo de las células cerebrales[12].

Existen dos tendencias sobre el desarrollo cerebral del feto, una biologista, que define el aspecto hereditario y genético, y la otra ambientalista, que cree en el papel fundamental que juega el medio ambiente en el desarrollo fetal. Las dos tienen bases bastantes firmes e interesantes, pero se puede concluir que, garantizando un medio enriquecido durante todo el proceso gestacional, se logrará un adecuado desarrollo fetal[13].

Al analizar los resultados del apgar al nacimiento, que aparecen referidos en la tabla III, se aprecia que los resultados fueron muy favorables en el grupo de mujeres estimuladas. Investigaciones recientes refieren que la estimulación prenatal, como disciplina psicoterapeuta, propicia al feto las condiciones idóneas para el desarrollo intraútero; así se fortalecen sus sistemas nervioso y muscular, mediante las interconexiones neuronales, lo que favorece un apgar con puntuación normal en el momento de nacer[14].

Algunos estudios reflejan que la musicoterapia con recién nacidos prematuros es muy favorable para su desarrollo, pues se observa una mejora de la frecuencia cardiaca y del nivel de oxígeno, así como mayor relajación y un sueño más tranquilo. Esto hace suponer que tendría el mismo efecto en la etapa prenatal[15]. Los resultados de este estudio coinciden con otras investigaciones que confirman un buen apgar al nacimiento en niños que fueron estimulados con anterioridad[16].

En la figura 4 se pone de manifiesto que un mayor número de mujeres estimuladas tuvieron un parto eutócico. Estos resultados coinciden con lo que afirma la literatura internacional. Se considera como una vía facilitadora de todos los procesos fisiológicos, lo que explica que las pacientes que asisten a cursos de estimulación en la etapa prenatal, con ejercicios y técnicas de relajación, suelen estar mejor preparadas para el trabajo del parto.

El proceso de trabajo del parto y el parto inminente producen una ansiedad normal, que no es más que una anticipación de los acontecimientos que tendrán lugar; por tanto, la mayoría de las mujeres lo sobrelleva mejor cuando se las prepara durante la gestación y se les explica cómo transcurrirá el trabajo del parto[17].

Las correlaciones no paramétricas de Kendall y Spearman que aparecen reflejadas en la tabla I coinciden en mostrar medidas inversas significativas sólo en el caso de las variables peso y tipo de parto, para un 0,05% de significación estadística. Estos resultados

son los esperados y coinciden con lo descrito por otros autores. Los fetos cuyos pesos no superan los 3.500 gramos, generalmente nacen por vía fisiológica, lo que no ocurre con aquellos cuyos pesos están por encima de ese valor.

Cabe destacar que la estimulación afecta a una adecuada oxigenación y una mejora de la nutrición fetal; estas condiciones favorecen el peso fetal y éste, a su vez, se convierte en un factor que, en algún momento, puede condicionar la vía del parto o el uso de algún tipo de instrumento[18,19,20].

Otra variable estudiada fue la opinión de las gestantes sobre el programa recibido, lo que se recoge en la tabla II. Es habitual que las mujeres embarazadas y sus familias se interesen por aprender los cuidados de la maternidad, pues consideran que estos conocimientos forman parte de sus derechos. Resulta interesante constatar, de acuerdo con la bibliografía consultada, que todos los programas de estimulación han sido aceptados por las gestantes, las parejas o la familia[21,22,23].

Los programas de estimulación prenatal son diseñados como una alternativa durante el embarazo. Si la madre está feliz, la estimulación es el instrumento adecuado para fomentar esa actitud. Por el contrario, si está preocupada, o si el embarazo no ha sido deseado, las sesiones pueden convertirse en una opción que favorezca el cambio de parecer de la gestante, con relación con su embarazo[24].

La literatura plantea que las características del aprendizaje del adulto difieren del resto de las personas. En el adulto, las experiencias previas sirven como fuente de aprendizaje para el grupo; en el caso de las gestantes, las experiencias vividas por ellas o por algún familiar relacionado con el proceso gestacional o el trabajo de parto, servirá como un nuevo recurso para el profesor y para el resto de las mujeres del grupo[25].

Los grupos son convenientes porque el intercambio de experiencias entre las mujeres que tienen preocupaciones similares proporciona apoyo y aliento. Por otra parte, son motivadores, ya que en ellos se comparten recursos y se produce un proceso de socialización entre las personas que comparten intereses comunes. Las sesiones deben comenzar y terminar en un tiempo determinado, pues las embarazadas necesitan sentir que han aprendido y que el tiempo dedicado no ha sido en vano.

En este sentido, los resultados obtenidos son similares a los descritos por la bibliografía consultada, en donde se indica que es conveniente que las enfermeras dediquen más tiempo al entrenamiento de las pacientes embarazadas en el uso de programas que incluyan la estimulación prenatal.

En la tabla III se recoge la correlación estadística entre las variables tipo de parto y opinión de las gestantes estimuladas con el programa de estimulación prenatal. Esta correlación pone de manifiesto que, en la medida en que la mujer tiene un parto eutócico, su opinión sobre el programa es mejor, lo que hace suponer que las mujeres que recibieron la estimulación prenatal en nuestro medio, esperaban, tras la aplicación del programa, una vía del parto más natural.

Todos los estudios consultados confirman que la participación de la futura madre y de su pareja en todas las fases del ciclo reproductivo beneficia, no sólo a ellos mismos, por ser las personas que reciben los cuidados y la educación, sino también a las enfermeras que los administran. Una mujer preocupada y con buenos conocimientos sigue un régimen más saludable durante su embarazo. La mujer bien preparada y el compañero que desea participar pueden adaptarse en forma positiva a las tensiones del trabajo del parto, al enriquecer su relación y favorecer su maduración psicológica[26].

En ese sentido, es importante que, tras recibir el programa de estimulación prenatal, la gestante lo ponga en marcha desde los inicios del trabajo del parto y pueda dar a conocer al equipo de salud que se trata de una mujer preparada para afrontar ese momento.

Las gestantes que reciben algún método en particular, con frecuencia tienen que afrontar la presión del personal, al intentar usar las técnicas empleadas durante el embarazo. En ocasiones, se obliga a la mujer a seguir conductas prescritas por el médico, al considerar que es lo mejor en ese caso, aunque todo indique que ello no es necesario y no se le da importancia a las técnicas aprendidas por ella.

No obstante, los seguidores de la estimulación prenatal como método integral para la preparación del parto reportan desde hace tiempo que las parejas experimentan más satisfacción y los recién nacidos se encuentran menos deprimidos, al usar estos métodos.

Conclusiones

- Se ha puesto de manifiesto que la estimulación prenatal, sustentada en acciones organizadas, cargadas de afecto y con énfasis en la comunicación madre-hijo influye positivamente en los eventos del periparto, tales como duración del trabajo de parto y tipo de parto, lo que denota que la manera en cómo los padres interactúan con los bebés antes de nacer tiene un impacto positivo en el periparto y en el desarrollo posterior del niño.
- Los programas de estimulación prenatal tienen buena aceptación por la embarazada y su aplicabilidad demuestra que con las técnicas de estimulación prenatal se enseña a los padres a proveer un ambiente seguro y amoroso que motive a los niños a aprender ya desde antes de su nacimiento.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2109-2115
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Nootropic and hypophagic effects following long term intake of almonds *(Prunus amygdalus)* in rats

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Abstract

Introduction: **Over a period of time researchers have become more interested in finding out the potential of various foods to maintain the general health and to treat diseases. Almonds are a very good source of many nutrients which may help to sharpen the memory and to reduce cardiovascular risk factors.**

Objective: **The present study was conducted to evaluate the nootropic effects of almonds. Effect of oral intake of almond was also monitored on food intake and plasma cholesterol levels.**

Methods: **Rats were given almond paste orally with the help of feeding tube for 28 days. Memory function in rats was assessed by Elevated Plus Maze (EPM) and Radial Arm Maze (RAM). Brain tryptophan, 5-HT and 5-HIAA were estimated at the end of the treatment by HPLC-EC method.**

Results: **A significant improvement in learning and memory of almond treated rats compared to controls was observed. Almond treated rats also exhibited a significant decrease in food intake and plasma cholesterol levels while the change in growth rate (in terms of percentage) remained comparable between the two groups. Analysis of brain tryptophan (TRP) monoamines exhibited enhanced TRP levels and serotonergic turnover in rat brain following oral intake of almonds.**

Conclusion: **The findings show that almonds possess significant hypophagic and nootropic effects. Results are discussed in context of enhanced 5-HT metabolism following almond administration.**

(*Nutr Hosp.* 2012;27:2109-2115)

DOI:10.3305/nh.2012.27.6.6140

Key words: *5-HT turnover. Almond. Cholesterol. Hypophagic action. Nootropic substance.*

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Recibido: 29-VIII-2012.
Aceptado: 11-IX-2012.

EFECTOS NOOTRÓFICOS E HIPOFÁGICOS DEL CONSUMO PROLONGADO DE ALMENDRAS *(PRUNUS AMYGDALUS)* EN RATAS

Resumen

Introducción: **De un tiempo a esta parte, los investigadores se han interesado cada vez más en encontrar el potencial de diversos alimentos para mantener la salud en general y tratar la enfermedad. Las almendras son una muy buen fuente de muchos nutrientes que pueden ayudar a agudizar la memoria y reducir los factores de riesgo cardiovascular.**

Objetivo: **Este estudio se realizó para evaluar los efectos nootróficos de la almendra. También se monitoreó el efecto de la ingestión oral de almendra sobre el consumo de alimentos y las concentraciones plasmáticas de colesterol.**

Métodos: **Se suministró a las ratas pasta de almendra por vía oral con la ayuda de una sonda de alimentación durante 28 días. Se evaluó la función de memoria de las ratas mediante Elevated Plus Maze (EPM) y Radial Arm Maze (RAM). Se estimaron el triptófano cerebral, la 5-HT y el 5-HIAA al final del tratamiento mediante un método de HPLC-EC.**

Resultados: **Se observó una mejoría significativa en el aprendizaje y la memoria en las ratas tratadas con almendra en comparación con los controles. Las ratas tratadas con almendra también mostraron una reducción significativa del consumo de alimentos y de las concentraciones plasmáticas de colesterol, mientras que el cambio en la tasa de crecimiento (en términos de porcentaje) siguió siendo comparable entre ambos grupos. El análisis de las monomaninas y de triptófano cerebral mostró unas concentraciones superiores de triptófano y del recambio serotoninérgico del cerebro de la rata tras el consumo de almendras.**

Conclusión: **los hallazgos sugieren que las almendras poseen unos efectos hipofágicos y nootróficos significativos. Los resultados se debaten en el contexto del metabolismo mejorado de la 5-HT tras la administración de almendras.**

(*Nutr Hosp.* 2012;27:2109-2115)

DOI:10.3305/nh.2012.27.6.6140

Palabras clave: *Recambio de 5-HT. Almendra. Colesterol. Acción hipofágica. Sustancia nootrófica.*

Abbreviations

5-HIAA: 5-hydroxy indole acetic acid.
5-HT: 5-hydroxy tryptamine.
CVD: Cardiovascular disease.
EPM: Elevated plus maze.
HPLC-EC: High performance liquid chromatography with electrochemical detection.
PUFAs: Polyunsaturated fatty acids.
RAM: Radial arm maze.
TRP: Tryptophan.

Introduction

Diet plays an influential role in the maintenance of general health as well as in the prevention and treatment of diseases. Memory loss[1] and obesity[2] are two of the prevalent diseases throughout the world. With the passage of time there is increased trend to maintain general health through diet. Various foods including tree nuts have been shown to affect central nervous system,[3] enhance learning, memory and intelligence.[4] Memory formation is the complex process and involves various neurotransmitters and neuronal pathways.[5] It is well established that serotonergic system has an important role in memory function.[6] Tryptophan (TRP), the precursor of serotonin (5-hydroxy tryptamine; 5HT) and an essential amino acid, has also been shown to increase learning and memory.[7,8] Source of TRP is dietary only and increased brain TRP availability has been revealed to increase brain serotonin synthesis.[9]

Obesity and being overweight are linked to reduce quality of life, greater morbidity[10] and mortality.[11] Elevated cholesterol as a result of obesity is one of the risk factor for cardiovascular diseases (CVD).[12] Nuts are high-fat, energy rich foods (e.g. pecan 70%, macadamia nut 66%, Brazil nut 65%, walnut 60%, almonds 55%),[13] so it is logical that frequent consumption of nuts may lead to increased cholesterol and weight gain and, consequently, increase the risk of cardiovascular disease and many chronic diseases. But prior studies did not show any adverse effect of nut consumption on energy balance or body weight. [14] In fact, a growing body of evidence indicates that eating nuts on the regular basis may be linked to decreased weight gain as well as cholesterol levels in various human populations. [15-17]

Nuts are energy-dense and nutrients loaded foods. Walnuts and almonds both have been used as a nootropic substance from time immemorial. To experimentally show this we previously analyzed the walnut.[18] The findings tempted us to investigate the effects of almonds on learning and memory functions. These nuts contain a wide variety of bioactive compounds that seem to have constructive effects on human health.[19] According to US department of Agriculture Nutrient Database, almonds have a high protein content (21.22 g/100 g of raw almond) and the TRP content of this nut is about 214 mg/100 g of almond. These nuts provide 5.75 kcal/g of energy and are low in saturated fat (< 8% of total fats) but rich in unsaturated fats (92% of total fats), mainly of which are monounsaturated (66.15%). Almonds are one of the most important source of plant protein, and good source of dietary fiber, minerals, antioxidants, vitamins and numerous bioactive substances, such as phytosterols and flavonoids. These nutrients may possess health benefits by producing synergistic effects and/or interactions with each other. Hence this study was intended to investigate the neurochemical pathways involved in the enhancement of memory by these nutritious nuts. The study was further aimed to examine food intake, body weight and plasma cholesterol levels following long term administration of almonds in rats.

Material and methods

Animals

The Animal Care Ethical Committee of the University had approved this investigation. Locally bred male Albino Wistar rats with mean weight 200 g were used for the experiment. Animals were caged individually in plastic cages with cubes of standard rodent diet and tap water *ad libitum* for 3 days before starting the experiment. Body weight and food intake of all rats were monitored during the experimental period.

Experimental protocol

Shelled almonds of best quality were purchased from the local super market which were then peeled, finely crushed and refrigerated in air tight bottle. 80 mg[20] finely crushed almond was prepared as suspension in deionized water which was then orally administered to the rats.

In the beginning of experiment animals were divided into two groups, control and test. Rats were given standard rodent diet and water throughout the experiment. Fresh almond suspension was prepared daily. Body weight and food intake of all rats were monitored. Control rats (n = 6) were given deionized water and test rats (n = 6) were given almond suspension orally with the help of feeding tube. This treatment was continued for 28 days.

Food intake and body weight were monitored till almond administration. After 28 days of administration, memory test was performed and rats were decapitated. Brain and plasma samples of both groups were stored at -70°C. Tests were conducted in a noise-free environment between 9:00-13:00 hrs. Memory assessment by RAM was carried out after performing EPM test.

Memory function test by Elevated Plus Maze (EPM)

EPM was used as a behavioral model to evaluate memory in rats. The apparatus constructed of Perspex plastic with 4 arms of 50 × 10 cm area. The two enclosed arms had side walls of 40 cm high. The open and closed arms were connected with a central square (5 × 5 cm) to give the apparatus a plus sign appearance. The whole maze was raised 60 cm above the floor. The maze was placed in the same position throughout the test in laboratory where extra maze cues were there to facilitate learning. The procedure and technique was same as reported earlier by Haider et al.[18] Briefly, the test comprised of three days, first day was training session while the next two days were considered as test sessions. In the training session each rat was placed in the central square and allowed to explore the EPM for 10 min and then returned to the home cages. During test sessions cut off time was 5 min and time spent in open arm was recorded. A significant decrease in time spent in open arm on subsequent EPM exposure was taken as an index of successful memory retention. This is based on the idea that during repeating testing on EPM rat acquires information about the spatial environment and avoids the elevated and open arms of the maze and prefers to stay in the closed arms where it could be safe on the maze. Total time spent in the open arm measured on the first day served as an index of learning and acquisition, whereas on the 2nd day it served as an index of retention of learned task (memory) and on the 3rd day further served as the index of consolidation of memory. Memory was measured by the degree to which the rat remembers and avoids the elevated and unenclosed arms of the maze and prefers to stay in the closed arms.

Memory function test by Radial Arm Maze (RAM)

Spatial working memory testing using eight arm radial maze task was also conducted as described by Neese et al.[21] with slight modifications.[22] The maze utilized in this research study consisted of a central platform, 32 cm in diameter, with 8 arms of equal length (58 cm) and width (12 cm) extending radially. Each arm had side walls of 38 cm high. The apparatus was mounted on a table so that it was 58 cm off the ground. Rats were freely allowed to visit all arms to get the food reward, which was placed near the end of one of the arm in a small plastic receptacle, this was habituation phase for 20 min. After 24 hrs, training was performed, during this phase all arms were blocked except one which was baited with food at small intervals in order to attract the rat to the end of the arm. Once the rat reached the end of the arm, the rat was returned to the central platform and the arm was rebaited in order to continue the training procedure. The training was continued for 15 min. At the end of 15 min food rewards were only placed at the end of the arm to train the rat to run to end of the arm to receive the reward. The test session was performed after 24 hrs of training, during which the same arm was again baited with food and rest of the arms were also unblocked, rats had free access to all arms. The total cut off time was 5 min and the time elapsed before the rat entered the baited arm was recorded. Throughout the experiment, care had to be taken that the relative position of maze with respect to any object serving as visual cues in laboratory was not changed. To motivate the performance, rats were food-restricted to 50% for 1 week before subjecting them to the RAM test but had free access to water.

Plasma cholesterol estimation

Plasma cholesterol was estimated by standard laboratory method.

HPLC-EC analysis

At the end of the experiment animals were decapitated using guillotine. Brain was removed immediately and stored at -70°C for the determination of TRP, 5-HT and 5-HIAA by HPLC-EC as described earlier.[23] A 5-II Shim-Pack octadecylsilane separation column of 4.0 mm internal diameter and 150mm length was used. Separation was achieved by a mobile phase containing methanol (14%), octyl sodium sulfate (0.023%) and ethylenediaminetetraaceticacid (0.0035%) in 0.1 M phosphate buffer at pH 2.9, on Schimadzu LEC 6A detector at an operating potential of 0.8 volts for biogenic amines and 1.0 volts for TRP.

Statistical analysis

The behavioral and neurochemical data were analyzed by Student's *t*-test. *P* values < 0.05 were considered significant.

Results

Food intake and body weight

Weekly growth rate and food intake of rats following the administration of almond for 4 weeks are shown in figures 1 and 2 respectively. Test groups exhibited no differences in growth rate during the course of the study. However, there were differences in food intake, with the test group eating significantly less than the control group. Caloric intake data during the 4 weeks is summarized in table I.

Memory testing

The memory function for control and test groups following long term intake of almond measured by

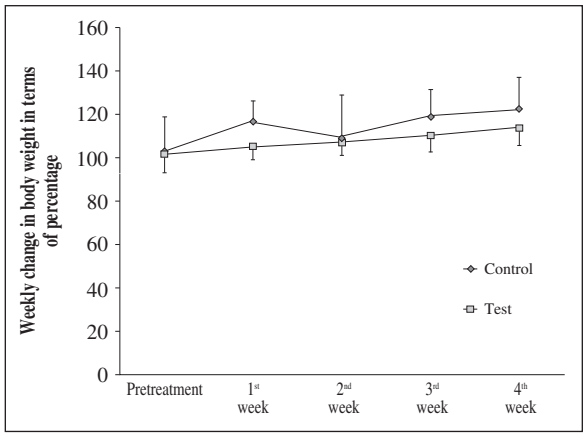


Fig. 1.—Effects of oral intake of almond for 28 days on weekly change in body weight in terms of percentage. Values are mean ± SD (n = 6) non significant difference by Student's t-test with respect to controls.

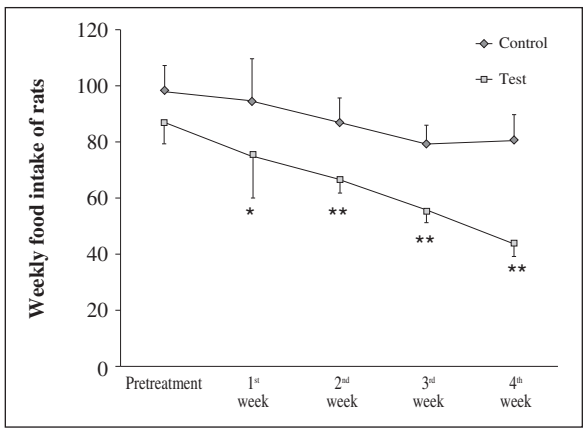


*Fig. 2.—Effects of oral intake of almond for 28 days on weekly change in food intake. Values are mean ± SD (n = 6) significant differences by Student's t-test *p < 0.05 and **p < 0.01 with respect to controls.*

EPM (fig. 3) as time spent in open arm in terms of percentage. Data analyzed by Student's *t*-test did not reveal significant difference on the first day, however, there was significant decrease in % time spent in open arm on subsequent exposure on 2nd day ($P < 0.01$) and 3rd day ($P < 0.01$) following almond administration in rats. This observed fact taken as successful memory retention, since repeated testing on the EPM provides

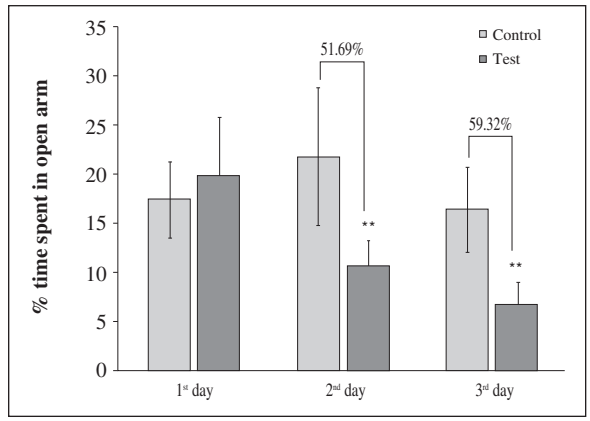


*Fig. 3.—Effects of oral intake of almond for 28 days on memory function in rats assessed by Elevated Plus Maze. 1st day is training session while 2nd and 3rd days are test sessions. Values are mean ± SD (n = 6) significant differences by Student's t-test **p < 0.01 with respect to controls. The decrease in % time spent in open arm between the control and test groups is expressed in terms of percentage.*

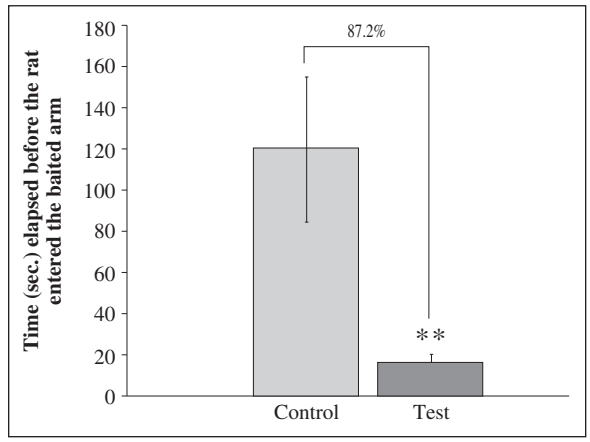


*Fig. 4.—Effects of oral intake of almond for 28 days on memory function in rats assessed by Radial Arm Maze. Values are mean ± SD (n = 6) significant differences by Student's t-test **p < 0.01 with respect to controls. The decrease in time elapsed before the rat entered the baited arm between the control and test groups is expressed in terms of percentage.*

an index of acquisition and retention as the rat learned where it could be safe on the maze.

Spatial working memory was also observed during RAM testing following almond administration for 4 weeks (fig. 4). When data was analyzed by Student's

Table I
Effects of almond administration on weekly caloric intake of rats

	Control (kcal)	*Test (kcal)*	*% decrease*
Pretreatment	440.29 ± 40.05	388.62 ± 42.74	11.7%
1st week	423.89 ± 68.07	338.37 ± 68.88	20.17%
2nd week	389.82 ± 37.05	298.05 ± 21.36 **	23.54%
3rd week	354.78 ± 30.17	248.88 ± 18.9 **	29.84%
4th week	359.79 ± 42.6	196.68 ± 20.74 **	45.33%

Values are mean ± SD (n = 6) significant differences by Student's t-test **p < 0.01 with respect to controls. % decrease is the difference between control and test group during the week in terms of percentage.

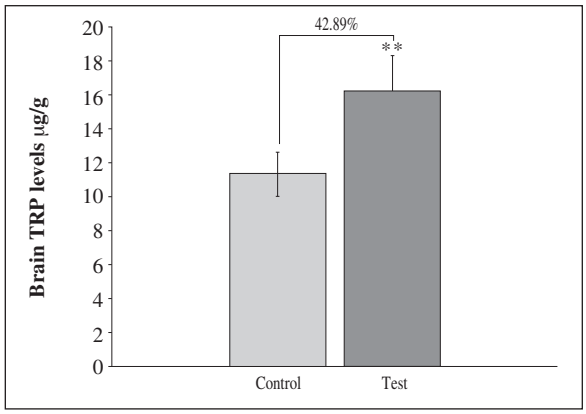


*Fig. 5.—Effects of oral intake of almond for 28 days on brain tryptophan levels. Values are mean ± SD (n = 6) significant differences by Student's t-test**p < 0.01 with respect to controls. The increase in brain TRP (µg/g) between the control and test groups is expressed in terms of percentage.*

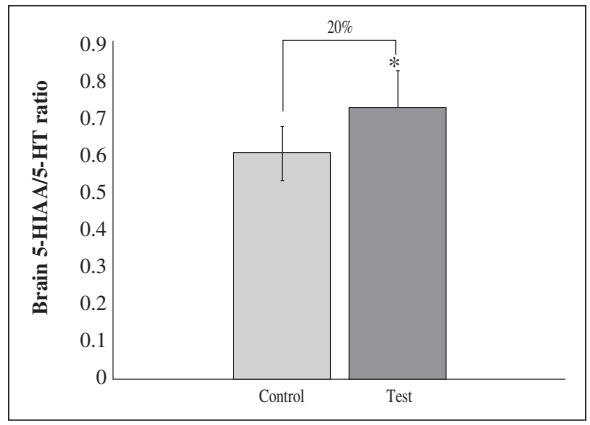


*Fig. 6.—Effects of oral intake of almond for 28 days on brain5-HT turnover (5-HIAA/5-HT). Values are mean ± SD (n = 6) significant differences by Student's t-test *p < 0.05 with respect to controls. The increase in brain 5-HT turnover between the control and test groups is expressed in terms of percentage.*

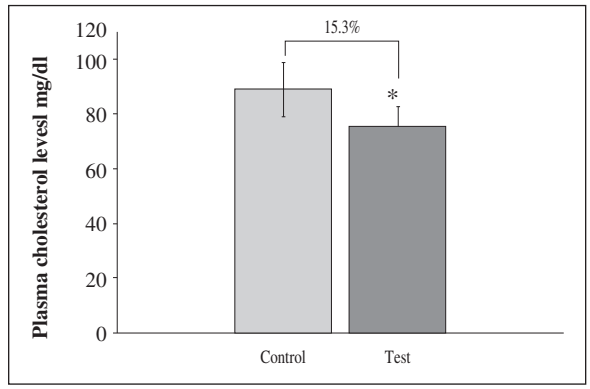


*Fig. 7.—Effects of oral intake of almond for 28 days on plasma cholesterol levels. Values are mean ± SD (n = 6) significant differences by Student's t-test *p < 0.05 with respect to controls. The decrease in plasma cholesterol level between the control and test groups is expressed in terms of percentage.*

t-test, a significant increase ($P < 0.01$) in memory function was observed as the time elapsed before the rat entered into baited arm was revealed significantly lower in test group than the control group.

Brain tryptophan and neurochemical estimations

Total brain TRP (µg/g of whole brain) and 5-HT turn over (5-HIAA/5-HT ratio) were measured following 4 weeks administration of almond. The levels of TRP ($P < 0.01$, fig. 5) and 5-HT turn over ($P < 0.05$, fig. 6) both were increased significantly in the whole brain after long term intake of almond. This shows that intake of almond increased the overall brain 5-HT metabolism.

Plasma cholesterol estimation

Plasma cholesterol levels for both groups were also estimated after decapitation and shown in figure 7. Student's *t*-test revealed significant reduction ($P < 0.05$) in plasma cholesterol in test group by ~ 15% when compared with the control group.

Discussion

The finding of primary interest in the present experiment is that the long term administration of almond produces enhancing effect on memory function. This improved memory retention was evident from the gradual and significant decrease in time spent in open arm on subsequent exposures to EPM (fig. 3). Results of RAM also emphasized the same assumption as there was significant decrease in time elapsed before the rat entered the baited arm (fig. 4). Long term intake of almond was also showed to significantly increase whole brain serotonin metabolism. This can be explainable in terms of increased brain TRP concentration and 5-HT turnover in almond treated rats (fig. 5 and 6).

Memory function in rats was assessed by EPM and RAM. Both paradigms are widely used for the screening of nootropic substances.[20,22,24,25] The present study showed that almond has an augmenting effect on memory retention in rats. The results are in agreement with the previously reported studies. It has been demonstrated that administration of almond improved scopolamine induced amnesia in rats.[26] Central serotonin is considered as one of the neurotransmitter involved in regulation of cognitive functions. A decrease in the serotonin is believed to be involved in the occurrence of amnesia in impaired cognitive diseases.[27,28] On the other hand it has been reported that increased brain 5-HT improves cognitive performance.[7,29] In the present work almond administration for 4 weeks increased brain 5-HT turnover. This increased turnover was associated with an increase in the level of its precursor, TRP. The 5-HT biosynthetic enzyme, TRP hydroxylase exists in unsaturated state with its substrate. Therefore, the rate of 5-

HT synthesis depends upon the brain concentration of its precursor. Increased 5-HT turnover are often taken as a measure of increased 5-HIAA levels and ultimately increased 5-HT release. An increased brain 5-HT turnover exhibited by almond-treated rats indicates an increased release of 5-HT in these rats and hence greater availability of 5-HT towards its respective receptors. Almond is rich in TRP, which is an essential amino acid, because it cannot be synthesized in vivo and must be obtained from diet. It has been shown that increased dietary availability of TRP increases 5-HT metabolism and enhances cognitive performance.[9] Therefore, in the current study long term administration of almond increased brain 5-HT metabolism by elevating TRP concentration and 5-HT turnover in the brain and ultimately improved memory in rats.

The plausible active constituents of almond are polyunsaturated fatty acids (PUFAs) and choline that could be involved in memory enhancement in the present study. Dietary PUFAs [α linolenic acid; 18:3 (n-3) and linoleic acid; 12:2 (n-6)] are the main essential fatty acids that serve as precursor for fatty acids component of neuronal membrane. These fatty acids are important for the structural integrity of cell membranes and for neurotransmission, signaling and modulation of enzymatic activity.[31] The PUFAs have shown to be involved in serotonin neurotransmission[32] and in increased memory function.[33] In addition to serotonin, acetylcholine is also considered as an important neurotransmitter involved in the regulation of cognitive function.[34] Studies have revealed that consumption of essential fatty acids can effectively modulate cholinergic system.[35] Acetylcholine is synthesized from substrates choline and acetyl CoA by the enzymatic action of choline acetyltransferase. Studies have indicated that increased dietary choline supplementation increases the synthesis of acetylcholine and facilitates memory function. Cohen and Wurtman[36] showed that dietary intake of choline at increasing doses elevated serum choline, brain choline and brain acetylcholine concentrations in rats. Recently, a study examined the effect of dietary choline intake on memory in nondemented individuals and it was found that individuals with higher choline intake performed better on the memory tests.[37] Although we did not estimate the choline and acetylcholine concentrations in the present study but from these evidences it can be suggested that in addition to TRP, important biological constituents of almond such as PUFAs and choline may also be involved in memory improving effects of almond following its long term administration in rats.

Since almonds are high in fats (55%)[13] and energy dense food therefore consumers regard them as fattening foods. In the present study body weight and food intake were also measured during the course of the treatment and at the end plasma cholesterol levels were estimated in both control and test groups. After long term almond administration the body weight remained unaffected (fig. 1) while the food intake and plasma cholesterol levels were significantly decreased (table I, fig. 2 and fig. 7). The suppression in food intake in test animals may be attributed to observe increased serotonin metabolism. Several lines of evidence demonstrate that serotonergic system is recruited to reduce meal size.[38,39] Serotonin modulating drugs such as 5-HT reuptake inhibitor/5-HT releaser fenfluramine has been used for the management of obesity.[40] It is possible that regular intake of almonds may satisfy the appetite quickly and may decrease the food intake and ultimately decrease the plasma cholesterol level by limiting the intake of other energy-dense food.[41] Hence, despite the fact that almond is rich in fats but this fatty food was not shown to exert adverse effects on body weight and plasma lipid profile[16,17] as observed in the present study.

High level of cholesterol is one of the prominent risk factor for CVD. Several lines of evidence indicate that the type of fat is more important in decreasing CVD risk than the total amount of fat in the diet.[42,43] According to the food composition database published by the US Department of Agriculture, 100 g of almonds contain 50.6 g of fats, majority of which are unsaturated fats.[44] Unsaturated fatty acids have consistently shown to reduce total, LDL cholesterol.[45] Animal studies have repeatedly performed to determine the mechanisms behind these effects and it is revealed that dietary unsaturated fatty acids enhance hepatic receptor-dependent clearance of LDL and concomitantly reduce LDL cholesterol production.[46] Almonds provide a dietary source of unsaturated fatty acids which may help to reduce total cholesterol as found in the current study and may be helpful in the management of CVD.

Conclusion

In conclusion, we tested the nootropic effects of almond in male rats. The results revealed that long term almond intake enhances activity and performance in spatial memory test. Present results also indicate that almond intake increases serotonin metabolism which might be involved in memory enhancing and appetite decreasing effects. So these findings demonstrate that long term intake of almond may have beneficial effects on learning and memory processes and therefore emphasize on the use of almond as a supplement in learning and memory deficits. Almond administration also decreases food intake and total cholesterol levels. This cholesterol lowering effect may be attributed to the presence of unsaturated fatty acid content of these nuts. Therefore current findings also suggest that almond supplementation may be beneficial not only in improving memory function but also in reducing obesity and CVD risk factors.

Acknowledgement

The authors are thankful to the University of Karachi, Pakistan for funding this project.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2116-2121
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Planificación alimenticia en personas mayores: aspectos nutricionales y económicos

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Resumen

La malnutrición en personas mayores es uno de los grandes síndromes, asociado a mayor prevalencia de enfermedades crónicas y aumento la morbilidad, estancia hospitalaria y mortalidad. Por otro lado, la malnutrición en el 4º mundo se asocia a otro factor de riesgo de gran importancia, la precaria situación económica. El objetivo del estudio fue elaborar un menú equilibrado para ancianos, ajustando su precio al gasto medio que esta población dedica a su alimentación. Teniendo en cuanta el Gasto del hogar 2010 del Instituto Nacional de Estadística, se estableció que el precio medio de cada menú debía ser inferior a 5,57 € al día. Se elaboraron dos menús tipos, ambos adaptados a esta población y a la dieta mediterránea. La valoración económica fue de 5,02 € y de 5,06 €, respectivamente. Debido a la prevalencia de malnutrición en esta población, es necesario poder planificar adecuadamente su alimentación, tanto a nivel nutricional como económico.

(*Nutr Hosp.* 2012;27:2116-2121)

DOI:10.3305/nh.2012.27.6.6090

Palabras clave: *Malnutrición. Ancianos. Tercera edad. Menús económicos. Cuarto mundo.*

MEAL PLANNING IN THE ELDERLY: NUTRITIONAL AND ECONOMIC ASPECTS

Abstract

Malnutrition in elderly people is one of the major syndromes associated to greater prevalence of chronic diseases and increased morbidity, hospital staying, and mortality. On the other hand, malnutrition in the fourth world is associated to another important risk factor, which is the poor economic status. The aim of this study was to elaborate a balanced menu for the elderly adjusting its price to the mean expense that this population dedicates to its feeding needs. Taking into account the Household expense for 2010 of the National Institute of Statistics, we established that the average price for each menu ought to be less than 5.57 € per day. Two type menus were elaborated, both adapted to this population and to the Mediterranean diet. The economic assessment was 5.02 € and 5.06 €, respectively. Given the prevalence of malnutrition in this population, it is essential being able to appropriately plan their feeding needs, at both the nutritional and economic levels.

(*Nutr Hosp.* 2012;27:2116-2121)

DOI:10.3305/nh.2012.27.6.6090

Key words: *Malnutrition. Elderly. Seniors. Economic meals. Fourth world.*

Abreviaturas

PVP: Precio de Venta al Público.
DT: Desviación Típica.
AGP: Ácidos Grasos Poliinsaturados.
AGS: Ácidos Grasos Saturados.
AGM: Ácidos Grasos Monoinsaturados.
B6: Vitamina B6.
INE: Instituto Nacional de Estadística.
CDR: Cantidad Diaria Recomendada.
IDR: Ingesta Diarias Recomendadas.

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Recibido: 19-VI-2012.
1.ª Revisión: 21-VIII-2012.
Aceptado: 24-VIII-2012.

Introducción

La esperanza de vida en España ha aumentado en los últimos años, debido los avances médicos y científicos que permiten un mejor tratamiento de las enfermedades[1,2]. En el año 2010 el 17% de la población española era mayor de 65 años, situando nuestro país en el cuarto a nivel mundial con mayor envejecimiento poblacional[3]. Sin embargo, el hecho de vivir más no es necesariamente un indicativo de una mejor calidad de vida. Durante la última etapa de la vida convivimos con enfermedades crónicas que afectan negativamente a

nuestra calidad de vida, y muchas están relacionadas con el estado nutricional[4]. Las personas mayores tienen unos requerimientos energéticos menores que los adultos más jóvenes debido a una disminución del gasto metabólico basal, cambios en la composición corporal y a una menor actividad física, entre otros factores. Esto conlleva un mayor riesgo de sufrir malnutrición por una menor ingesta, así como una mayor probabilidad de sufrir sobrepeso u obesidad por ingerir más calorías de las realmente necesarias, que muchas veces no incluyen los nutrientes adecuados, produciéndose igualmente carencias de algunos micronutrientes[5]. La malnutrición, está asociada a mayor prevalencia de enfermedades crónicas, al aumento de la morbimortalidad y la estancia hospitalaria.

Además hay que considerar que no sólo las enfermedades tienen influencia sobre la esperanza de vida, sino que la posición socioeconómica tiene un impacto en ella, así como en la calidad de vida[6,7]. Según datos recientes, en España hay una relación directamente proporcional entre el poder adquisitivo y la esperanza de vida de una persona. Más de la mitad de los ancianos refiere tener dificultades para llegar a fin de mes por unos ingresos económicos bajos, con una media de 641 €, y más de la mitad de la población entre 300 y 600 €. Esto conlleva una mayor dificultad para adquirir ciertos productos alimenticios que les permitan una alimentación adecuada a sus necesidades[8]. Por todo ello, se considera indispensable trabajar en la elaboración de menús adaptados a las necesidades nutricionales de los ancianos, pero teniendo en cuenta el aspecto económico de los mismos, de manera que sean factibles a la hora de ser llevados a la práctica.

Objetivos

El objetivo principal del estudio fue elaborar un menú equilibrado para ancianos, teniendo en cuenta el precio del mismo, de manera que se adecuara al gasto medio que esta población dedica a su alimentación. Pretendiendo demostrar que se puede hacer una buena alimentación con un precio ajustado.

Metodología

Se elaboraron dos menús de una semana, uno de otoño-invierno y otro de primavera-verano. Ambos, se plantearon como saludables y específicos para la población anciana, por ello, debían cumplir las recomendaciones nutricionales específicas (2.000 kilocalorías, 50-60 % de hidratos de carbono, 15-18% de proteínas, 30-35% de lípidos, 30 g/día de fibra, < 300 mg/día de colesterol)[9], ajustarse a las pautas de alimentación saludable (distribución en 5 comidas, variada, equilibrada, cantidades adecuadas de los diferentes grupos de alimentos)[10] y cumplir el patrón de la dieta mediterránea (rica en alimentos vegetales, empleo de aceite de oliva, utilización de alimentos de temporada, uso de recetas sencillas)[11, 12].

Para comprobar que la calidad de los menús era adecuada se analizaron mediante 4 fórmulas indicadoras de calidad, en concreto para evaluar la proporcionalidad de las proteínas presentes además de la fuente de ácidos grasos. Con respecto a los ácidos grasos, el índice AGP/AGS y el índice AGM + AGP/AGS. En cuanto a las proteínas los índices realizados fueron: (proteína animal + proteína vegetal)/total proteína, y Ratio B6/proteínas totales[13].

Para conocer si cumplían las características propuestas, se calculó el contenido en energía, y macro nutrientes utilizando la base de datos del programa informático DIAL[13].

Como se propuso elaborar un menú económico, para conocer el precio de los alimentos de elección más favorable a esta característica, se realizó un estudio de mercado, durante el cual se visitaron cuatro grandes superficies dentro de la ciudad de Madrid en los meses de noviembre y diciembre de 2011, y marzo y julio de 2012. De cada alimento que iba a ser empleado en la realización de la dieta, se recogieron los siguientes datos: precio de venta al público (PVP), presentación de formato, marca, nombre del establecimiento y la presencia de alguna oferta en el producto.

Se estableció, que el precio medio de cada menú debía ser inferior al gasto medio de las personas mayores de 65 años en alimentos y bebidas no alcohólicas durante el año 2010, que fue de 2036,30 € al año, lo que supone 5,57 € al día[14].

El análisis estadístico de los datos, se realizó con el programa SPSS 18.0 (SPSS Inc.). Las variables continuas se presentan como media ± desviación estándar (DE) o mediana.

Resultados

Valoración nutricional

En las tablas I y II se describe de forma detallada el menú de otoño-invierno y de primavera-verano, respectivamente.

Para la elección de las recetas se ha optado por contemplar tanto preparaciones simples como platos más elaborados con el fin de promover la cocina activa y casera. Para ello se han utilizado recetas tradicionales (conejo guisando o lentejas estofadas), pero también preparaciones más modernas, como pollo al curry. Las preparaciones culinarias propuestas son sencillas, rápidas y saludables como la cocción con vapor, al horno o a la plancha. También se incluyen técnicas culinarias más actuales y menos usadas por el colectivo como el microondas.

Según los valores nutricionales utilizados como referencia para la realización de este estudio[1,2], se comprobó que las Ingestas Diarias Recomendadas (IDR) para la población diana se cumplían en su totalidad

tanto en el menú de otoño-invierno como en el menú de primavera-verano, como se ve en la tabla III.

Más allá da la variedad gastronómica, cabe mencionar que esta se refleja en un aporte nutricional adecuado. Según las 4 fórmulas indicadoras de calidad, con respecto a los ácidos grasos obtenemos una puntuación de 0,63 y 0,63 (recomendado > 0,5) para el índice AGP/AGS, y de 2,5 y 2,6 (recomendado > 2) para el índice AGM + AGP/AGS, para el menú de invierno y verano, respectivamente. En cuanto a las proteínas los índices realizados fueron: (proteína animal + proteína vegetal)/total proteína igual a 0,66 y 0,65 (recomendado > 0,7), y Ratio B6/proteínas totales, obteniendo 0,035 y 0,031 (recomendado > 0,02), para el menú de invierno y verano respectivamente.

Valoración económica

En el menú de otoño-inviernos los valores obtenidos son, en su mayoría, inferiores al presupuesto establecido por el INE, con la excepción de dos días, el miércoles y el domingo con un valor de 5,92 € y 5,76 €, respectivamente. Los valores correspondientes al lunes, martes, jueves, viernes y sábado son los siguientes: 4,92 €, 4,16 €, 4,86 €, 5,53 € y 4,70 €.

En cuanto al menú de primavera-verano los valores obtenidos por día también se encuentran por debajo de los 5,57 € establecidos por el INE, excepto en el viernes presentando un valor de 5,75 €. El resto de los días presentan los siguientes valores: lunes: 4,92 €; martes: 5,57 €; miércoles: 3,89 €; jueves: 5,12 €; sábado: 5,13 €; domingo: 5,07.

De esta manera, la valoración económica semanal de ambos menús presentan un valor inferior a los 5,57 € que hace referencia el INE como gasto invertido por las personas mayores en alimentación y bebidas sin alcohol. La media semanal para el menú de otoño-invierno y el menú de primavera-verano ha sido de 5,02 € (DT = 0,405) y de 5,06 € (DT = 0,596), respectivamente.

Con los resultados obtenidos podemos decir que realizar una alimentación saludable y equilibrada tanto en la temporada de otoño-invierno como en la temporada de primavera-verano, también puede ser económica,

Tabla I
Menú otoño/invierno

	Lunes	*Martes*	*Miércoles*	*Jueves*	*Viernes*	*Sábado*	*Domingo*
Desayuno	– Una pera – Un vaso de leche semidesnatada – Pan integral – Aceite de oliva + tomate triturado	– Zumo de naranja natural – Yogur desnatado – Pan integral – Queso fresco + mermelada	– Una naranja – Un vaso de leche semidesnatada – Pan integral – Aceite de oliva + tomate triturado	– Un kiwi – Yogur desnatado – Pan integral – Queso fresco + mermelada	– Zumo de naranja natural – Un vaso de leche semidesnatada – Pan integral – Aceite de oliva + tomate triturado	– Un kiwi – Yogur desnatado – Pan integral – Queso fresco + mermelada	– Dos mandarinas – Un vaso de leche semidesnatada – Pan integral – Aceite de oliva + tomate triturado
	0,61 €	**1,14 €**	**0,54 €**	**0,93 €**	**0,78 €**	**0,98 €**	**0,67 €**
Media mañana	– Una mandarina	– Cuajada con miel y nueces	– Un plátano	– Yogur desnatado	– Una manzana	– Dos mandarinas	– Yogur desnatado
	0,30 €	**0,36 €**	**0,43 €**	**0,27 €**	**0,30 €**	**0,30 €**	**0,36 €**
Comida	– Garbanzos con espinacas – Pechugas de pollo plancha – Ensalada tomate y lechuga – Una naranja – Pan integral	– Crema de coliflor con tacos de jamón – Dorada al horno con calabacín a la plancha – Yogur desnatado – Pan integral	– Judías verdes con patata y zanahoria – Pimiento relleno de carne – Fresas – Pan integral	– Pasta con verduras – Tortilla de espárragos – Ensalada multicolor – Dos mandarinas – Pan integral	– Patas a la riojana – Ensalada variada – Yogur desnatado – Pan integral	– Lentejas con verdura – Filete de ternera a la plancha – Ensalada – Yogur desnatado – Pan integral	– Cardo con piñones – Conejo guisado con verduras y patata – Una pera – Pan integral
	1,86 €	**1,72 €**	**2,78 €**	**1,68 €**	**1,90 €**	**1,62 €**	**2,40 €**
Merienda	– Pan integral con queso fresco y miel	– Una manzana	– Yogur desnatado – Cereales	– Un vaso de leche con galletas María	– Batido de fresas y plátano	– Yogur desnatado – Manzana	– Macedonia con galletas María
	1,86 €	**1,72 €**	**2,78 €**	**1,68 €**	**1,90 €**	**1,62 €**	**2,40 €**
Cena	– Patata y zanahoria al ajo arriero – Merluza horno con tomates – Yogur desnatado – Pan integral	– Huevo escalfado con arroz blanco – Ensalada verde – Una pera – Pan integral	– Berenjenas rellenas de verdura y atún – Ensalada de lechuga – Yogur desnatado – Pan integral	– Porrusalda "vegetariana" – Lenguado al horno con espinacas – Yogur desnatado – Pan integral	– Salmón con verduras en papillote y arroz – Yogur desnatado – Pan integral	– Ensalada de verduras con huevo – Cuajada con miel – Pan integral	– Sopa de fideos – Bacalao a la plancha con verduras al horno – Ensalada – Yogur desnatado – Pan integral
	1,74 €	**0,74 €**	**1,78 €**	**1,75 €**	**2,22 €**	**1,33 €**	**2,05 €**
Total	**4,92 €**	**4,16 €**	**5,92 €**	**4,86 €**	**5,53 €**	**4,70 €**	**5,76 €**

Tabla II
Menú primavera/verano

	Lunes	*Martes*	*Miércoles*	*Jueves*	*Viernes*	*Sábado*	*Domingo*
Desayuno	– Zumo de manzana – Un vaso de leche semidesnatada – Pan integral – Aceite de oliva + tomate triturado	– Raja de melón – Yogur desnatado – Pan integral – Queso fresco + mermelada	– Rodaja de piña – Vaso de leche semidesnatada – Pan integral – Aceite de oliva + tomate triturado	– Ciruelas – Yogur desnatado – Pan integral – Queso fresco + mermelada	– Zumo de naranja – Un vaso de leche semidesnatada – Pan integral – Aceite de oliva + tomate triturado	– Una pera – Yogur desnatado – Pan integral – Queso fresco + mermelada	– Rodaja de piña – Un vaso de leche semidesnatada – Pan integral – Aceite de oliva + tomate triturado
	0,98 €	**135 €**	**0,83 €**	**1,33 €**	**0,98 €**	**0,89 €**	**0,83 €**
Media mañana	– Yogur desnatado	– Brocheta de plátano y kiwi – Nueces	– Yogur desnatado	– Raja de melón – Pan con tomate y aceite de oliva	– Yogur desnatado – Galletas integrales	– Yogur desnatado – Una manzana	– Rodaja de sandía – Magdalena
	0,27 €	**0,53 €**	**0,27 €**	**0,28 €**	**0,34 €**	**0,27 €**	**0,15 €**
Comida	– Lacitos con verdura – Pollo al limón – Ensalada de tomate – Yogur desnatado – Pan integral	– Lentejas con almejas – Tortilla francesa – Ensalada – Cerezas – Pan integral	– Arroz morado con especias – Caballa a la plancha – Ensalada – Una naranja – Pan integral	– Patata rellena con cerdo magro – Raja de sandía – Pan integral	– Alubias encebolladas con huevo rallado – Un melocotón – Pan integral	– Fideuá con ternera y verduras – Yogur desnatado – Pan integral	– Arroz salvaje con guisantes y huevos escalfados – Yogur desnatado – Pan integral
	1,64 €	**1,80 €**	**1,28 €**	**1,01 €**	**1,45 €**	**1,80 €**	**1,08 €**
Merienda	– Una manzana – Rollito de pavo con queso fresco	– Leche semidesnatada – Galletas integrales	– Nueces –Una nectarina	– Leche desnatada – Cereales integrales	– Una pera – Pan integral con queso fresco	– Galleta integral – Cereales	– Leche semidesnatada – Cereales integrales
	0,58 €	**0,26 €**	**0,33 €**	**0,26 €**	**0,66 €**	**0,50 €**	**0,26 €**
Cena	– Ensalada campera con bonito – Una nectarina – Pan integral	– Conejo al ajillo con patatas al microondas – Un flan – Pan integral	– Espaguetis con pavo al curry y zanahoria – Yogur desnatado – Pan integral	– Merluza en salsa verde – Yogur desnatado – Pan integral	– Remolacha con vinagreta de albahaca – Pollo a la plancha – Yogur desnatado – Pan integral	– Gazpacho – Sardinas a las finas hierbas – Raja de melón – Pan integral	– Garbanzos a la vinagreta – Chirlas con champiñones – Una pera – Pan integral
	1,21 €	**1,63 €**	**0,94 €**	**2,00 €**	**1,87 €**	**1,43 €**	**2,52 €**
Total	**4,92 €**	**5,57 €**	**3,89 €**	**5,12 €**	**5,75 €**	**5,13 €**	**5,07 €**

Tabla III
IDR

Ingestas Diarias Recomendadas (IDR)		*Menú otoño-invierno*	*Menú primavera-verano*
Calorías	2.000 kcal	1.995 kcal	2.032 kcal
Proteínas	15-20%	17%	17%
Hidratos de carbono	50-60%	53,4%	51,1%
Lípidos	30-35%	29,7%	28%
Fibra	> 30 g/día	37,3 g/día	37,3 g/día
Ácidos grasos saturados (AGS)	< 10%	7,7%	7,13%
Ácidos grasos monoinsaturados (AGM)	13-20%	14,3%	13,8%
Ácidos grasos poliinsaturados (AGP)	< 7%	4,9%	4,5%
Colesterol	< 300 mg/día	217 mg/día	244 mg/día
Índice AGP/AGS	> 0,5	0,63	0,63
Índice (AGM + AGP)/AGS	> 2	2,5	2,6

sobre todo si se recurren a los alimentos de temporada, a una planificación en la compra y a la elaboración de recetas sencillas y saludables.

Discusión

El estudio plantea limitaciones de diseño y sesgos, especialmente en la valoración económica del estudio de mercado. Estas son debidas mayoritariamente a:

- Los precios son cambiantes por muchos factores (estacionalidad, clima, proveedores, fabricantes, etc). Un ejemplo lo comprobamos en los productos frescos, donde el precio de la fruta en el menú de verano resultó ser entre el doble y el triple del precio de la usada en el menú de invierno, seleccionando los datos recogidos durante los meses de noviembre-diciembre de 2011 o los de marzo de 2012, en lugar de los de julio 2012 para las frutas específicas del menú de verano como finalmente se hizo. Siendo esta diferencia en el precio semanal final del menú de verano de 5,42 € a 5,06 €.
- Estudio de mercado puntual, cuya recogida de datos se limitó a máximo tres días por cada grupo de alimentos, superficie visitada y mes de realización, por lo que los datos recopilados son solo representativos de las fechas y lugares próximos en los que se realizó.
- Diferencia inter-comercios: grandes superficies frente a mercados tradicionales y pequeño comercio. Incluso intra-comercios situados en diferentes zonas geográficas.
- Diferencias en formatos y ofertas. Elección final dependiente del consumidor, que evaluará el formato, oferta, descuento... en base a su situación personal.
- Diferencias entre productos de marca y marca blanca.
- Calibración de sólo dos menús de una semana.

Para solucionar la mayoría de ellos, y en los casos en los que contamos con diferentes referencias de precios, la elección del precio fue siempre el más elevado.

Además, aunque está calculado por ración, hay productos que no son monodosis, y para los que es necesario comprar y asumir el gasto del envase entero, donde el diseño de platos que tengan en cuenta toda la materia prima disponible comprada sin usar, influiría en el precio.

Algunos autores[15,16] han reportado que es necesario atender a ciertos micronutrientes frecuentemente deficitarios en esta población. En nuestros menús se ha conseguido un aporte adecuado de ellos: 132% y 128,3% magnesio, 80% y 86% zinc, 175% y 198% hierro, 144,25% y 126,5% calcio, 176,47% y 158,8% vitamina B_6, 180% y 200% tiamina, 191,67% y 183,3% riboflavina, 125,75% y 100,25% ácido fólico, 120% y 68,3% vitamina E correspondiendo a la CDR del menú de invierno y verano, respectivamente. En 2009, se publicaban nuevos datos sobre la prevalencia de desnutrición, el 4,3 por ciento de los españoles con 65 o más años y el 25,4% se hallaban en riesgo de padecerla[17]. Además los cambios fisiológicos ligados a la edad de este colectivo se asocia al desarrollo de diversas enfermedades como la obesidad, la sarcopenia y la osteoporosis, asociadas a una disminución de la calidad de vida, un mayor grado de dependencia y un riesgo aumentado de mortalidad[18].

Gran parte de nuestra población diana presenta simultáneamente dos de las patologías más frecuentes, exceso de grasa corporal y una significativa pérdida de masa muscular, lo que se ha denominado obesidad sarcopénica y cuya prevalencia se midió en el Estudio EXERNET en personas mayores no institucionalizadas alcanza valores medios del 15%[19]. Es por ello que resulta importante el fomentar estilos de vida saludable de forma combinada, para disminuir la obesidad general, la abdominal y mejorar el ratio músculo/grasa[20].

Creemos imprescindible trabajar para influir en disminuir las cifras actuales de desnutrición. Campañas como "5 raciones de frutas y verduras al día", "plan cuídate +", para restringir el consumo de sal, las campañas para aumentar la ingesta de agua o para mantenerse activos son de gran valor preventivo[21], así como los autocribados del estado nutricional, con un ítem "¿Me falta alguna vez dinero para comprar comida?"[22] que como ponemos de manifiesto en este trabajo, es fundamental tener en cuenta tanto a nivel de difusión como de intervención y criterio profesional.

Conclusiones

Hemos demostrado que es posible ajustar el gasto diario alimentario de personas mayores que estableció el INE en 2010 de forma equilibrada. Adaptándolo a las necesidades de la población de estudio, ofreciendo dos propuestas modelo variadas. La importancia que la nutrición adquiere en la población de edad avanzada por el riego de malnutrición está ampliamente recogida en la literatura científica. Sin embargo, con la complicada situación económica que vivimos en España, es necesario poder planificar adecuadamente la alimentación de este colectivo atendiendo la alimentación como algo más que el aspecto nutricional, y debido a la inexistencia de trabajos similares en la bibliografía actual al aquí propuesto, teniendo en cuenta la parte económica, creemos que puede ser útil para profesionales encargados del diseño alimenticio tanto en colectividades como a particulares en un programa nutricional o tratamiento. Aunque es necesario mejorar el diseño del estudio, sus limitaciones, desmitificamos el concepto que "saludable es igual a caro".

Agradecimientos

Queremos agradecer el trabajo de María González Neira, Ivana Verónica Carasa, Beatriz Utrilla , Dayana

Gomes Gomes, Laura Berninches Pintado y Sara Martínez Garrido Olaiz, voluntarios en el equipo de Madrid de la ONG Nutrición Sin Fronteras, en la elaboración del estudio de mercado.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2122-2129
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original

Food and nutritional safety of hospitalized patients under treatment with enteral nutrition therapy in the Jequitinhonha Valley, Brazil

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Abstract

The Enteral Nutrition Therapy (ENT) has been widely used in hospital and home care assistance. However, research works are needed to make this technique more efficient and cheaper.

Objective: **Evaluate the nutritional quality of handmade enteral diets used in a charity hospital in the Jequitinhonha Valley, Brazil, and propose qualitative and quantitative adjustments, when necessary, and compare the data available in tables of chemical composition of foods with the data achieved by laboratory analyses.**

Materials and methods: **The study was carried out in partnership with a charity organization of the region and the Universidade Federal dos Vales do Jequitinhonha e Mucuri, where the collection of the handmade enteral diets was performed. The analyses of the physical-chemical and centesimal composition of 36 samples of diets were carried out in the laboratories of the university.**

Results: **It was observed that the daily energy offer of the diets was below the recommended standards and presented a percentage distribution different from that estimated for patients receiving ENT. Besides, it can be seen that the nutrient values of the data achieved in laboratory do not agree with those available in tables of food chemical composition.**

Conclusions: **Significant losses of nutrients were verified during the processing and preparation of handmade enteral diets. It challenges nutritionists to standardize these diets and corroborates the relevance of new studies to determine the nutritional content of handmade enteral diets, since these diets have been widely used in poor regions of Brazil and in other countries.**

(*Nutr Hosp.* 2012;27:2122-2129)

DOI:10.3305/nh.2012.27.6.6118

Key words: *Enteral nutrition. Handmade. Diets. Standard formulas.*

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Recibido: 21-III-2012.
1.ª Revisión: 27-VI-2012.
Aceptado: 13-VII-2012.

SEGURIDAD ALIMENTARIA Y NUTRICIONAL DE LOS PACIENTES HOSPITALIZADOS DE UN TRATAMIENTO CON NUTRICIÓN ENTERAL EN EL VALLE DEL JEQUITINHONHA, BRASIL

Resumen

La terapia de nutrición enteral (TNE) se ha utilizado ampliamente en la asistencia hospitalaria y domiciliaria. Sin embargo, se necesitan trabajos de investigación para hacer que esta técnica sea más eficiente y barata.

Objetivo: **Evaluar la calidad nutricional de dietas enterales elaboradas de forma casera en un hospital de caridad del valle de Jequitinhonha, Brasil, y proponer ajustes cualitativos y cuantitativos, cuando sean necesarios, y comparar los datos disponibles en las tablas de la composición química de los alimentos con los datos obtenidos en los análisis de laboratorio.**

Materiales y métodos: **El estudio se realizó en colaboración con la organización de caridad de la región y la Universidad Federal dos Vales do Jequitinhonha e Mucuri, donde se realizó la recogida de las ditas enterales caseras. Los análisis de la composición fisicoquímica y centesimal de las 36 muestras de las dietas se realizaron en los laboratorios de la universidad.**

Resultados: **Se observó que la oferta energética diaria de las dietas estaba por debajo de las recomendaciones estándar y presentaba un porcentaje de distribución diferente de la estimada para pacientes que reciben TNE. Además, se pudo ver que los valores nutricionales de los datos obtenidos en el laboratorio no concordaban con los disponibles en las tablas de composición química de los alimentos.**

Conclusiones: **Se comprobó una pérdida significativa de nutrientes durante el procesamiento y preparación de las dietas enterales realizadas caseramente. Supone un reto para los nutricionistas para estandarizar estas dietas y corroborar la relevancia de nuevos estudios para determinar el contenido nutricional de las dietas enterales de realización casera, puesto que estas dietas se han empleado ampliamente en regiones pobres de Brasil y otros países.**

(*Nutr Hosp.* 2012;27:2122-2129)

DOI:10.3305/nh.2012.27.6.6118

Palabras clave: *Nutrición enteral. Elaboración casera. Dietas. Fórmulas estándar.*

Abbreviations

EN: Enteral Nutrition.
ENT: Enteral Nutrition Therapy.
UFVJM: Universidade Federal dos Vales do Jequitinhonha e Mucuri.
AOAC: Association of Official Analytical Chemists.
TSS: Total Soluble Soils.
ANVISA: Agência Nacional de Vigilância Sanitária.
Kcal: Kilocalories.

Introduction

Enteral Nutrition (EN) is the introduction of nutrients by means of a catheter or probe into the gastric or intestinal region of individuals unable to achieve their daily nutritional demands orally.[1] Thus, the Enteral Nutrition Therapy (ENT) is indicated for individuals whose oral ingestion does not supply at least two thirds of their daily energy needs,[2] and those under specific conditions, such as extensive burns, cancer, injuries to the central nervous system, food disturbances, impaired swallowing, among others.[3]

Enteral diets should be nutritionally balanced and present good hygienic conditions to assure or reestablish the supply of macronutrients, vitamins and minerals necessary to the metabolism of thepatient.[4] The chemical composition, osmolality and stability of industrialized formulas are well defined, while handmade diets are still unreliable in these aspects.[5] These diets are made from foods "in natura", which are subject to variations in their nutritional content due to environmental changes, modules of nutrients and food products. Besides, many hospitals do not have standardized manuals for the preparation of enteral diets.[6]

One of the main advantages of handmade formulas is the individual preparation, since the makers can mix several foods and prepare diets with different colors and tastes. Besides, they are cheaper than industrialized products.[7] In a study carried out by Henriques and Rosado[5] on the cost of handmade diets, considering the raw material suppliers, it was observed an average price variation of R$ 6.12 per day, in three months. Such cost presented a value four times smaller than that observed for the industrialized diets available in the market.

However, the real nutrient composition and hygiene[4,8] of handmade diets are questionable. Therefore, the adequate techniques involving all the preparation process, storage and administration of diets must be followed to avoid the contamination of the formulas and guarantee the quality of their enteral diets.[9]

Today, the Enteral Nutrition Therapy (ENT) has expanded to the home care assistance, which is a current trend, due to the benefits for the patients, such as the familiar environment, comfort and reduced risk of hospital-acquired infections.[10] Thus, the use of these diets still prevails in Brazil, mainly in poorer regions, such as the Jequitinhonha Valley,[11] with its several poor cities and high prevalence of malnutrition.[11,12]

The significance of nutritional therapy is already known, but there is little knowledge about the true losses in foods due to processing. Consequently, the real nutritional value of the diet offered to patients in handmade ENT is still questionable. Besides, the calculations of the nutritional values of diets are performed based on tables of food composition, which many times limits the achievement of data.[13,14]

Considering that the nutritive value of foods is essential for health and the improvement of patients' quality of life, the present study aimed at determining the nutritional quality, through chemical and centesimal determination, of the homemade enteral diets used in a charity hospital in the Jequitinhonha Valley, Brazil, and proposing qualitative and quantitative adjustments, when necessary. It also aims at comparing the data available in tables of food chemical composition with the data achieved through the laboratory analyses.

Materials and methods

This study was carried out from March to September 2009, in a charity hospital in the Jequitinhonha Valley-Brazil and in the Laboratories of Food and Nutritional Security and Technology and Cerrado Biomasses, at the Universidade Federal dos Vales do Jequitinhonha e Mucuri-UFVJM, Brazil.

Preparation and collection of samples of diets in the charity hospital

The homemade enteral diets used in the hospital are prepared as follows: first, the meat and vegetables are cooked separately. Next, they are blenderized together with the water used for cooking. The fruits are cleaned and blenderized with some water and the milk is heated to boiling. The foods were blenderized and passed through plastic sieves of various sizes. Finally, the modules of Nutren Active®, Albumax®, Nutri Soya® nutrients are added, when prescribed and/or available. If necessary, they are blenderized again. According to the characteristic of the foods used in the preparation of the diets, they can be separated into three different groups: vitamins, served in the breakfast and supper–containing milk and food supplement; juices and snack —containing water and fruits—; and soups, offered for lunch and dinner —containing meat and several vegetables. Table I describes the food and the quantities used to prepare these meals. After the preparation of each one of the six meals served during the day, the samples were collected in individual plastic pots with the capacity of 500 mL and stored in a freezer. The sample collection was performed for three consecutive days (n = 18).

Table I
Food used in handmade enteral diets at a charity hospital in the Jequitinhonha Valley, Brazil

Meal	*Food*	*1º day of collection*	*2º day of collection*	*3º day of collection*
Breakfast	Whole milk	300 mL	300 mL	–
	Skimmed Milk	–	–	300 mL
	Nutren Active®	54 g	54 g	–
	Albumax®	–	–	54 g
	Nutri Soya®	–	–	–
Collation	Apple	65 g	70 g	75 g
	Orange	65 g	70 g	75 g
	Guava	20 g	20 g	–
	Papaya	35 g	–	–
	Albumax®	27 g	27 g	–
	Nutren Active®	–	–	–
	Nutri Soya®	–	–	27 g
	Sugar	50 g	50 g	–
	Water	120 mL	140 mL	150 mL
Lunch/Dinner	Potato	45 g	37 g	35 g
	Carrot	15 g	15 g	20 g
	Chayote	17 g	15 g	20 g
	Corn oil	1 mL	1 mL	1 mL
	Seasoning®	–	–	–
	Garlic®	–	–	–
	Urucum®	–	–	–
	Water	230 mL	230 mL	230 mL
Collation	Apple	75 g	70 g	75 g
	Orange	75 g	70 g	75 g
	Guava	–	20 g	–
	Papaya	–	–	–
	Albumax®	–	–	–
	Nutren Active®	27 g	27 g	–
	Nutri Soya®	–	–	27 g
	Sugar	–	–	50 g
	Water	150 mL	140 mL	150 mL
Supper	Whole milk	300 mL	300 mL	300 mL
	Skimmed milk	–	–	–
	Nutren Active®	54 g	54 g	–
	Albumax®	–	–	–
	Nutri Soya®	–	–	54 g

*Products used to attibute flavor and color to meals.

Centesimal and physico-chemical analysis

The centesimal composition was determined according to the Association of Official Analytical Chemists (AOAC):[15] the humidity achieved by drying at 65º C in a greenhouse with forced air circulation up to constant weight. The content of ashes, or fixed mineral residue, was quantified after the incineration of the organic matter into muffle at 550º C and the content of crude protein, by the Semi-micro Kjeldahl method. The ether extract, or crude fat, was achieved through the continuous extraction in ethyl ether using the Soxhlet Extractor. The crude fiber was determined by acid hydrolysis and subsequent filtration in Gooch crucibles. The carbohydrates were achieved by difference. The pH was quantified by direct reading in a Peagatekph meter, according to the norms of the Instituto Adolfo Lutz.[16] And the total soluble solids (TSS) were determined in the diets by direct reading in a bench top refractometer and expressed in ºBrix.[16]

The energy value of the homemade diets was achieved according to Angelis,[17] using the Atwater conversion factors. All the analyses were carried out with three repetitions. The results were expressed by the averages and standard deviations. The Tukey testat 5% probability was applied for the statistical analysis.

Estimate of the chemical composition

The estimate of the chemical composition of the diets was calculated based on the tables of Pinheiro [18]

and Philippi,[19] besides the nutritional information present in the packagings of the nutrient modules used.

Elaboration of new standardized homenade diets

After finding that the diets offered to patients were inadequate, the researchers proposed new formulas to the hospital, so that the specific demands of the hospitalized patients could be better met, as well as the needs of those patients under home care assistance.

The diets were prepared in the Laboratory of Food and Nutritional Security of the UFVJM, in accordance with the hygienic and sanitary standards established by the resolution 337 of the Agência Nacional de Vigilância Sanitária-ANVISA[20] (National Agency of Sanitary Surveillance).

The formulas were divided into: Standard 1,500 kilocalories (kcal) (A), Standard 2,000 kcal (B), Constipating 2,000 kcal (C), Laxative 2,000 kcal (D), Hyperprotein 2,500 kcal (E) and Hypoprotein 2,500 kcal (F). Three samples of each type of diet (n = 18) were collected into individual plastic pots with the capacity of 500 mL and stored in a freezer in the UFVJM Laboratory of Technology and Biomasses of the Cerrado for centesimal and physical-chemical determination, according to the item 4.2.

Nutritional adjustment of the formulas

For the analysis of the adjustment of the diets used in the institution and those proposed to the hospital, the references of Teixeira Neto[21] and Baxter et al. [22] were used for the caloric distribution: 40 to 60% of carbohydrates, 30 to 35% of lipids and 14 to 20% of proteins. The energy density was calculated according to the calorie supply per mL, considering the value from 0.9 to 1.2 kcal/mL for normocaloric diets.[21,22]

Results

The results are shown in tables II, III, IV and V.

Discussion

Since these diets need to pass through fine probes, they were supposed to present high humidity levels. However, the average humidity found in diets composition (table II) was higher than normocaloric diets recommended by Mitne.[6] The same author considers that the volume of water in the prepared diets may decrease their nutritional quality, and there may be a hyperdilution to facilitate the passage through fine probes, directly affecting the caloric density, which becomes lower than expected.

The fiber content of the preparations (table II) had mean values consistent with the recommendations for home enteral feeding from 4 to 20 g/L.[22]

The average content of mineral (table II) was lower than the total observed by Araújo and Menezes,[13] Atzingen et al.[23] and Menegassi et al.,[24] 1.62, 0.84 and 0.98 g/100 g, respectively.

The pH of the diets varied from slightly acid to neutral (table II), which is close to the values found by Araújo and Menezes (6.00)[13] and Montejo et al. (6.71)[25]. It may favor the growth and dissemination of microorganisms in the preparations. Thus, enteral diets must be prepared in locations with ideal conditions, in accordance with the standards for the production and adequate cleaning of utensils, surfaces and handlers. A study carried out by Maurício et al.[8] evaluated enteral diets in three private hospitals in Paraná, Brazil. This study led to the conclusion that the samples of the three hospitals were contaminated and that the diets had not been prepared according to the norms. Besides, the physical structure it self represented a risk factor for the contamination of the diets produced.

In their research work, Medina, Nascimento and Oliveira[26] demonstrated that 91% of the enteral diets used in a public service for home care assistance were contaminated by mesophilic aerobic microorganisms, total and faecal coliforms, *Salmonella sp*, *Staphylococcus aureus* and *Listeria monocytogenes,* compromising the nutritional quality of these formulas. Besides, Oliveira and Waitzberg[27] highlighted another potential factor of microbiological contamination, the non-sterile nutrient modules added to the enteral preparations, in which pathogenic microorganisms, such as *Bacillus ssp, Pseudomonas ssp, Bacillus Cereus* and *Enterobacter ssp* have been isolated.

As for the content of Total Soluble Solids (TSS), the recommended value found in Literature is about 20%.[28] In this case, the diets presented more fluidity of the preparations (table II).

No statistical difference was observed in the nutritional content of the diets on the days of the collection, according to the Tukey test.

In the comparison between the data of the centesimal/physical-chemical analysis and the estimate of the chemical composition, it is possible to observe that the total caloric value (TCV) was overestimated by both food composition tables, adjusting in 40.76%, according to Pinheiro[18] and in 45.87%,according to Philippi[19] (table III).

However, as for the protein content (table III), the average values found presented adjustment of 107.52%, according to the table of Pinheiro[18] and 91.98%, according to Philippi.[19] It may be associated to the presence of food supplements with a determined amount of proteins. Consequently, their composition in the formulas is more accurate.

The carbohydrate values achieved by the centesimal composition (table III), achieved adjustment of 108.42% and 102.5%, according to Pinheiro[18] and Philippi[19],

Table II

Centesimal and physical-chemical characteristics (mean = standard deviation) of handmade enteral diets (current and proposed diets), according to the day of collection, in a hospital in Jequitinhonha Valley-Brazil

Current diets	*1st day of collection*	*2nd day of collection*	*3rd day of collection*
Protein	6.54 ± 1.86	6.63 ± 4.65	4.20 ± 5.58
Carbohydrate	19.35 ± 12.48	14.01 ± 14.22	16.89 ± 10.47
Lipid	2.01 ± 1.86	2.40 ± 3.54	2.73 ± 4.56
Fiber	1.86 ± 2.52	3.24 ± 5.10	2.70 ± 3.99
Ash	1.71 ± 1.38	2.70 ± 1.77	2.19 ± 1.02
Humidity	268.50 ± 18.45	270.96 ± 31.17	271.29 ± 23.55
pH	6.63 ± 0.71	5.88 ± 1.16	5.61 ± 0.64
TSS	18.36 ± 15.57	21.36 ± 25.11	18.54 ± 12.57
Energy	121.83 ± 68.88	104.34 ± 122.07	109.02 ± 98.46

Proposed diets	*A*	*B*	*C*	*D*	*E*	*F*
Protein	9.36 ± 3.6	7.62 ± 2.31	10.47 ± 0.66	9.42 ± 1.98	17.28 ± 2.1	6.87 ± 0.45
Carbohydrate	38.44 ± 10.11	44.28 ± 14.17	49.60 ± 17.65	41.74 ± 18.90	63.94 ± 2.11	43.81 ± 9.89
Lipid	3.92 ± 1.49	3.99 ± 1.54	2.17 ± 1.52	5.58 ± 1.67	1.15 ± 1.11	5.73 ± 1.92
Fiber	4.11 ± 1.08	2.91 ± 1.74	1.53 ± 0.37	3.94 ± 1.68	1.37 ± 0.22	3.74 ± 1.45
Ash	2.29 ± 0.73	1.90 ± 0.48	2.40 ± 0.37	1.89 ± 0.70	3.23 ± 1.76	1.58 ± 0.15
Humidity	241.88 ± 15.28	239.28 ± 15.32	233.97 ± 18.98	237.42 ± 18.98	213.05 ± 4.54	238.27 ± 8.71
pH	5.95 ± 0.17	6.36 ± 0.27	6.68 ± 0.73	5.94 ± 0.53	6.35 ± 0.41	5.19 ± 0.42
TSS	55.50 ± 6.85	47.40 ± 5.1	47.70 ± 6.81	51.30 ± 7.84	70.95 ± 6.12	56.40 ± 6.24
Energy	226.50 ± 21.23	243.53 ± 64.60	259.20 ± 78.10	254.87 ± 71.63	335.34 ± 14.08	254.26 ± 36.61

Macro and micronutrients expressed in grams: humidity in milliliters; TSS: (Total soluble solids) in ºBrix; energy in kcal; A: Standard 1,500 kilocalories (kcal); B: Standard 2,000 kcal; C: Constipating 2,000 kcal; D: Laxative 2,000 kcal; E: Hyperprotein 2,500 kcal; F and hypoprotein: 2,500 kcal. Values are expressed as a portion of 300 ml of diet.

Table III

Comparison of the daily (kcal) total caloric value (TCV), macronutrients (%) and energy density (kcal/mL), according to centesimal composition and the estimated chemical composition of the diets offered in a hospital in the Jequitinhonha Valley-Brazil

	Centesimal composition	*Chemical composition*	
		Pinheiro (2005)	*Philippi (2002)*
Daily TCV	670.5	1,461.93	1,645.01
Proteins	23.29	25.53	21.66
Carbohydrates	66.99	65.35	61.79
Lipids	9.72	9.12	14.46
Density	0.37	0.81	0.91

respectively. Thus, both of them underestimated the values of carbohydrate present in the foods. On the other hand, the average found for lipids (table III) was adequate in 67.21% by the table of Pinheiro[18] and in 107.23%, by the table of Philippi.[19] Comparing the values achieved by the centesimal composition and by the table of Pinheiro,[18] it was suggested a nutritional loss of 32.79% of lipids during food processing.

Composition tables are an important source of data. However, studies reveal that the data available in these tables in Brazil are not reliable, since they have not been updated and are not very clear, which make them unsafe for clinical use.[13,29]

The energy density (table III) was adjusted in 40.66%, according to Pinheiro[18] and in 45.68%, according to Philippi.[18] This low energy density requires higher volume of the meals offered to the patients to compensate the low caloric supply. According to Mitne[6], the offer of diets with low energy density presents a negative impact on osmolality, load of solutes and viscosity of the diets.

Another important aspect to be considered is the energy content of the diets offered to hospitalized patients (table III), which is below the recommended amount for adults, considering the reference of 2,000 kcal[30] for the Brazilian population. It is a paradox, since

Table IV
Food used in the preparation of new enteral feedings proposed to a charity hospital in Jequitinhonha Valley-Brazil

Diet	*Breakfast/ supper*	*Portion - 300 mL*	*Collation*	*Portion - 300 mL*	*Lunch/ dinner*	*Portion - 300 mL*
A	Whole milk	200 mL	Whole milk	165 mL	Wheatflour	20 g
	Comflour	20 g	Oat	18 g	Beef	25 g
	Banana	56 g	Sustagen®	18 g	Comflour	20 g
	Water	45 mL	Banana	30 g	Carrot	25 g
	–	–	Water	50 mL	Pumpkin	72 g
	–	–	–	–	Water	210 mL
B	Whole milk	200 mL	Whole milk	165 mL	Comflour	40 g
	Banana	30 g	Apple	90 g	Bolied egg	45 g
	Comflour	40 g	Sustagen®	18 G	Potato	60 g
	Oat	18 g	Comflour	40 g	Carrot	25 g
	Water	50 mL	–	–	Sustagen®	18 g
C	Whole milk	200 mL	Nutren Active®	31.5 g	Rice	50 g
	Oatmeal cookie	20 g	Comflour	20 g	Potato	60 g
	Mucilon Arroz®	18 g	Biscuit	20 g	Carrot	25 g
	Sustagen®	18 g	Oat	18 g	Chicken breast	30 g
	Water	50 mL	Fiber Mais®	5 g	Comflour	40 g
	Fiber Mais®	15 g	Water	200 mL	Water	150 mL
	–	–	–	–	Fiber Mais®	10 g
D	Whole milk	200 mL	Whole milk	200 mL	Pumpkin	40 g
	Papaya	50 g	Apple	45 g	Tomato	30 g
	Oat	30 g	Oat	36 g	Comflour	30 g
	Fiber Mais®	15 g	Nutren Active®	15.7 g	Beef	25 g
	Banana	30 g	Papaya	50 g	Cornmeal	30 g
	Nutren Active®	15.17 g	–	–	Corn oil	8 g
E	Whole milk	200 mL	Whole milk	200 mL	Wheatflour	40 g
	Sustagen®	36 g	Apple	65 g	Chicken breast	30 g
	Nutren Active®	31.5 g	Oat	36 g	Rice	50 g
	Oatmeal cookie	10 g	Nutren Active®	63 g	Beetroot	40 g
	Banana	30 g	–	–	Comflour	40 g
	Water	50 mL	–	–	–	–
F	Whole milk	200 mL	Orange	100 g	Rice	68 g
	Mucilon Arroz®	18 g	Apple	45 g	Pumpkin	36 g
	Apple	65 g	Nutren Active®	15 g	Beetroot	20 g
	Cream	30 g	Oat	15 g	Boiled egg	45 g
	Comflour	40 g	Comflour	30 g	Milk cream	15 g
	–	–	Biscuit	30 g	Comflour	30 g
	–	–	–	–	Apple	45 g

A: Standard 1,500 (kcal); B: Standard 2,000 (kcal); C: Constipating 2,000 (kcal); D: Laxative 2,000 (kcal); E: Hyperprotein 2,500 (kcal); F: Hypoprotein 2,500 (kcal).

the nutritional therapy recommends the maintenance or recovery of the nutritional status, which is inconsistent with the nutritional characteristics of the diets provided to patients. Besides, in a broader sense, it may represent a risk factor for the occurrence of new pathologies, such as malnutrition and other specific problems, thus increasing mortality rate.

Several studies demonstrate that the enteral diets offered in hospitals present caloric value lower than the prescribed amount, besides an infused volume deficit. These factors decrease the amount of energy available to the patients and may aggravate their health condition.[31,32,33]

After the inadequacy of the diets available at the hospital was observed, new homemade enteral formulas

Table V
Proposed and achieved daily total caloric value (TCV) (kcal), distribution of macronutrients (%), and energy density (kcal/mL) of the diets proposed to a hospital in the Jequitinhonha Valley-Brazil

	Standard 1,500 kcal	*Standard 2,000 kcal*	*Constipant*	*Laxative*	*Hyperprotein*	*Hypoprotein*
Proposed TCV	1,500	2,000	2,000	2,000	2,500	2,500
Real TCV	1,358.97	1,461.17	1,555.18	1,529.2	2,012.02	1,525.56
Proteins	18.11	13.64	16.62	16.6	21	12.16
Carbohydrates	73.31	79.22	79.88	73.57	77.61	77.68
Lipids	7.57	7.14	3.5	3.5	1.4	10.16
Density	0.75	0.81	0.86	0.85	1.12	0.84

were proposed. In the elaboration of new diets, priority was given to regional foods, foods of the season and those usually available in the hospital, besides some calorie supplements (Nutren Active®, Sustagem®) and fiber modules (Fiber Mais®). The food used to prepare these meals and quantities are described in table IV.

It was observed that the new diets presented average humidity 78% (table II) which is below the value found by Araújo and Menezes,[13] 79%, and by Menegassi et al.,[24] 83%. The literature mentions the value of about 80 to 85% of humidity for normocaloric diets.[6] Comparing the diet offered in the hospital with the new standard proposal of 2,000 kcal (B), it can be seen that it is closer to the values found by other authors.

The pH average is similar to the pH values of the diets used in the hospital (table II). This is something expected, considering that most foods used to make the preparations presented pH close to neutral. Therefore, all the processing and preparation of foods need careful handling, observing the critical points of control to guarantee the microbiological quality of the diets[34], since they are subject to more manipulation than the industrialized formulas[24] and, consequently, are more susceptible to contamination. Besides, these diets are intended to weak patients, who present lower immunity.[27]

The TSS present values more satisfactory than those of the diets offered in the hospital (table II). In the study carried out by Araújo and Menezes,[14] the values of soluble solids ranged between 18 and 22%, for homemade enteral diets.

The new formulas proposed to the hospital showed an average fiber content similar to the diets offered in the hospital (table II). In this context, some authors claim that fibers are essential to stimulate the local immune system, balance the pH, maintain the colonic microflora and avoid the bacterial translocation, helping in the treatment of patients.[22,35]

The average value of total minerals is similar to the value presented by the diets offered in the hospital (table II). Mitne[6] suggests that mineral and/or vitamin supplements may be necessary for patients with deficiencies or those under a long-term nutritional therapy, since the deficit of these nutrients usually occurs in handmade diets.

It was observed that the profile of macronutrient distribution was different from the recommendation proposed for non-industrialized enteral diets[21,22], and the diets were classified as hyperglicidic and hypolipidic (table V), presenting variable protein content. Araújo and Menezes[13] mentioned that the adequate distribution of macronutrients in the diets plays a fundamental role in their nutritional quality and confers more credibility to the ENT.

However, when the diet offered to hospitalized patients is compared to the proposed standard diet 2,000 kcal, a significant improvement is verified in the energy offer (table V). In the first case, TCV achieved about 34% of the daily energy needs (table III). But in the second, it achieved about 73%, although it did not adjust to the macronutrient expected distribution, either[21,22] (table V).

The energy density of the new diets allowed them to be classified into slightly hypocaloric (table V), which is similar to the results found by other authors.[23,24] The hyperprotein formula was an exception. It was classified as normocaloric. By comparing the density value of the standard diet 2,000 kcal proposed (table V) and the diets currently available in the hospital (table III), it is possible to verify a significant improvement in the kcal/mL diet relation.

Considering that these diets were prepared and adjusted nutritionally through previous calculations using chemical composition tables, it was observed in the present work that not only the percentage distribution, but also the caloric value achieved were not compatible with those found in the laboratory analyses (table V), corroborating the results of Menegassi et al.[24]. Therefore, there are some factors that may have contributed to the variability of the data, such as the time for cooking food, fruit maturation and the losses occurred during the processes of diet production.

Conclusions

The diets offered in the hospital presented insufficient caloric values for the supply of the energy needs of the hospitalized patients, which makes them vulner-

able to food insecurity and to the aggravation of their nutritional status. Besides, the data of the chemical composition suggest that there are significant losses of nutrients during the processing and preparation of homemade enteral formulas, which is a challenge for nutritionists regarding the standardization and adjustment of these formulas.

To implement the use of the new formulas proposed to the hospital, quantitative adjustments must be carried out aiming at improving their nutritional value and ensure the quantitative and qualitative offer provided to patients under nutritional therapy. It is also highlighted the importance of the development of other studies to determine the nutritional content of homemade enteral diets, since they are widely used in clinical practice in poor regions of Brazil and other countries.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2130-2132
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Caso clínico

Síndrome de la orina morada en bolsa en paciente anciana con suplementos nutricionales

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Resumen

El síndrome de la orina morada en bolsa es una entidad poco frecuente que afecta característicamente a mujeres de edad avanzada con sondaje vesical prolongado y debilitadas por enfermedades crónicas. La presencia de patología urológica previa, el encamamiento prolongado y el estreñimiento crónico son factores predisponentes. El color morado de la orina se debe a la presencia de elevadas concentraciones de bacterias con actividad indoxilsulfatasa/fosfatasa que se desarrollan en un ambiente alcalino en presencia de otros factores. En el caso que presentamos la administración de suplementos nutricionales ricos en triptófano tuvieron un papel relevante en la generación de este síndrome.

(*Nutr Hosp.* 2012;27:2130-2132)

DOI:10.3305/nh.2012.27.6.6054

Palabras clave: *Síndrome de la orina morada. Sondaje vesical. Malnutrición. Triptófano.*

PURPLE URINE BAG SYNDROME IN ELDERLY WOMAN WITH NUTRITIONAL SUPPLEMENTS

Abstract

The purple urine bag syndrome is a rare entity which typically affects elderly women with prolonged urinary catheterization and weakening chronic diseases. Other predisposing factors are previous urologic pathology, immobility syndrome and chronic constipation. The purple color is due to the presence of high loads of bacteria with sulphatase - phosphatase activity which develop in an alkaline environment as well as the presence of other factors. In the case we present the administration of nutritional supplements containing tryptophan conditioned the generation of this syndrome.

(*Nutr Hosp.* 2012;27:2130-2132)

DOI:10.3305/nh.2012.27.6.6054

Key words: *Purple urine bag syndrome. Urinary catheter. Malnutrition. Triptophan.*

Introducción

La prevalencia de riesgo de malnutrición es elevada en pacientes ancianos hospitalizados[1]. Se trata de un grupo de riesgo debido a una serie de cambios fisiológicos, sociales, económicos y psicológicos relacionados con el proceso de envejecimiento. Dicha malnutrición favorece la aparición de enfermedades que a su vez repercutirán negativamente en el estado nutricional del anciano, instaurándose de esta manera un círculo vicioso malnutrición-enfermedad. Los suplementos nutricionales se convierten en este sentido en el aporte extra de macro y micronutrientes que en ocasiones precisa este segmento de la población para alcanzar los requerimientos mínimos diarios. Las fórmulas hipercalóricas e hiperproteicas en concreto, permiten cubrir las necesidades de energía y proteínas para pacientes con posible riesgo de desnutrición o ya desnutridos. Estas fórmulas son ricas en aminoácidos esenciales como el triptófano.

El síndrome de la orina morada en bolsa es una entidad rara, que fue descrita por primera vez en 1978[2]. Afecta principalmente a mujeres debilitadas por enfermedades crónicas, con sondajes vesicales prolongados, insuficiencia renal crónica y estreñimiento crónico[3]. Consiste en la aparición de orina morada en la bolsa del sondaje vesical, en presencia de elevadas concentraciones de bacterias con actividad indoxilsulfatasa/fosfatasa (de los géneros Proteus, Providencia, Pseudomonas, Morganella, Citrobacter, Enterococcus, así como en E. coli, K. pneumoniae y Streptococos del grupo B) que se desarrollan en un ambiente alcalino[4]. En general no se asocia a una mayor morbilidad, y en la mayoría de los casos se resuelve con recambio del sondaje vesical[5], cuidados higiénicos de la sonda y tratamiento antibiótico. No suele asociarse a infecciones sintomáticas,

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Recibido: 12-VII-2012.
Aceptado: 11-IX-2012.

estando la mayoría de los pacientes afebriles, sin leucocitosis ni otros datos relevantes. A pesar de ello, se han descrito dos casos de orina morada asociada a gangrena de Fournier[6], por lo que podría ser necesario administrar tratamiento antibiótico a estos pacientes a pesar de que no presenten infecciones sintomáticas[7].

El color morado de la orina se debe a la conversión del indoxil sulfato, metabolito de excreción natural del triptófano, en indoxil por la acción de enzimas sulfatasas/fosfatasas bacterianas. Una vez en la bolsa, al entrar en contacto con el oxígeno, el indoxil se transforma en índigo (color azul) e indirrubina (rojo), cuya mezcla origina un tono morado. El proceso de oxidación tarda unas horas, por lo que la orina tiene un aspecto normal inicialmente y el color morado sólo se aprecia tiempo después en la bolsa recolectora[8].

Dado lo excepcional del caso, al presentarse el citado síndrome tras la suplementación nutricional y no haberse señalado en la literatura previamente, consideramos de interes su publicación.

Caso clínico

Mujer de 78 años, 40 kilogramos de peso y 1,65 m de altura, con antecedentes de gastrectomía por úlcera gástrica con reconstrucción tipo Billroth II hace más de 30 años, que se convierte a Y de Roux posteriormente por reflujo alcalino. Un año después comienza con cuadros suboclusivos, llegando a precisar cirugía por obstrucción intestinal. Secundariamente presenta malnutrición con hipoalbuminemia grave, anemia de trastornos crónicos severa, úlceras por presión en región sacra y talones, incontinencia urinaria y síndrome de inmovilidad. Destaca además TBC renal hace mas de 20 años, con pielonefritis de repetición, que precisó cirugía por estenosis ureteral.

Ingresa por anemización con una hemoglobina de 4,8 g/dl (VN: 12-18 gr/dl) secundaria a sangrado digestivo. Presenta desnutrición proteico-calórica grave (IMC: 14,7 kg/m^2), con albúmina de 2,48 g/dl (VN: 3,30-5,20 g/dl). Al ingreso porta sondaje vesical con orina en bolsa recolectora de color morada. Tres meses antes, había ingresado por cuadro de anasarca en relación con desnutrición por síndrome malabsortivo, y en ese momento se inició la administración de suplementos nutricionales hipercalóricos/hiperproteicos (Fortimel® 1 cada 8 horas). La tabla I refleja la mejoría de los marcadores nutricionales bioquímicos desde este primer ingreso y el inicio de los suplementos nutricionales hasta el alta del hospital.



Fig. 1.—Orina de color morada en bolsa recolectora del sondaje vesical.

Durante el primer ingreso precisó un sondaje vesical para control de diuresis, que se mantuvo posteriormente para favorecer la curación de las úlceras en región sacra. Poco antes del alta se objetivó el color morado de la orina en la bolsa del sondaje vesical, por lo que empíricamente se administró fosfomicina en pauta larga por sospecha de infección del tracto urinario. En el presente ingreso se evidencia la persistencia del color morado de la orina en la bolsa de la sonda vesical a pesar del tratamiento antibiótico (fig. 1). La paciente describe haber notado este cambio en la coloración desde el alta previa y que éste persiste al cambiar la misma, reapareciendo a los tres o cuatro días de cada cambio. No presentó fiebre ni leucocitosis en ningún

Tabla I
Indicadores de estado nutricional

	Albúmina (g/dl)	*Prealbúmina (mg/dl)*	*Transferrina (mg/dl)*	*Proteína ligada retinol (mg/dl)*	*Colesterol (mg/dl)*	*Triglicéridos (mg/dl)*	*Linfocitos (cels/mm^3)*
1er ingreso	1,37	4,83	20	< 1,10	31	60	300
2.º ingreso	2,48	13,20	131	3,99	80	49	1.000
Alta 2.º ingreso	3,43	28,60	164	5,62	109	54	1.690

momento. El análisis bioquímico de la orina muestra un pH alcalino (8,5), que se puede observar también en los análisis de meses previos. Además en el sedimento se encuentran cristales de fosfato amónico magnésico, 10-25 hematíes por campo, 10-25 leucocitos por campo y bacteriuria abundante. La reacción de nitritos es negativa. En el urocultivo se aísla Proteus vulgaris, resistente a fosfomicina. Se inicia tratamiento con ciprofloxacino (sensible según antibiograma) y cambio de la sonda vesical. A las 48 horas la orina adquiere un color normal.

Discusión

El síndrome de la orina morada en bolsa es una entidad poco frecuente cuyo hallazgo se caracteriza por ser sumamente llamativo. El caso que presentamos cumple los criterios señalados en la literatura al tratarse de una mujer, de edad avanzada, con patología crónica debilitante (desnutrición grave), inmovilidad (con úlceras por presión por este motivo), sondaje vesical de larga evolución (más de tres meses), y episodios de suboclusión y oclusión intestinal, características predisponentes a la aparición de este síndrome[2,3,4,5,7]. Así, en nuestro caso encontramos una bacteria del género Proteus, capaz de producir las enzimas necesarias para trasformar el indoxil sulfato en los metabolitos coloreados que se pudieron observar en la bolsa de orina con un pH alcalino[4]. Es importante destacar los antecedentes urológicos de la paciente, habiendo padecido una tuberculosis renal y pielonefritis de repetición, lo que produjo alteraciones estructurales que la predisponían a padecer infecciones urinarias como sucedió en este caso. Otros autores describen también cómo alteraciones en la función renal pueden favorecer la aparición del síndrome[9].

En nuestro caso los cambios del sondaje vesical y cuidados higiénicos de la sonda no fueron suficientes para la resolución del cuadro, tal y como describen otros autores, y fue necesario el uso de tratamiento antibiótico dirigido, medida que consideramos de vital importancia en la resolución del cuadro.

Es de destacar el papel de los suplementos hiperproteicos ricos en triptófano, no señalados previamente en la literatura, como mecanismo predisponente al desarrollo de esta entidad. Las necesidades diarias establecidas por la Organización Mundial de la Salud para este aminoácido son de 4 mg/kg de peso[10]. En la literatura se señala una relación entre la ingesta de triptófano en la dieta y la aparición de la orina morada[7]. En nuestro caso pudimos asegurar una ingesta mínima diaria de 840 mg de triptófano a través de los suplementos. Por todo ello, concluimos que la suplementación enteral de triptófano en la dieta, junto con el resto de factores predisponentes, puede contribuir a la aparición del síndrome de la orina morada en la bolsa.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2133-2138
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Caso clínico

Homocistinuria; curso clínico y tratamiento dietético; a propósito de dos casos

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Resumen

La homocistinuria es un error congénito del metabolismo de la metionina que conduce al acúmulo de metionina y de su principal metabolito, homocisteína, en plasma, orina y tejidos. El acúmulo de homocisteína posee toxicidad sobre los sistemas óseo (osteoporosis), ocular (luxación del cristalino), nervioso (convulsiones, alteraciones psiquiátricas) y vascular (accidentes cerebrovasculares, enfermedad cardiovascular).

Presentamos 2 casos de homocistinuria en 2 pacientes hermanos y, a continuación, revisamos las estrategias terapéuticas disponibles.

(*Nutr Hosp.* 2012;27:2133-2138)

DOI:10.3305/nh.2012.27.6.6098

Palabras clave: *Homocistinuria. Homocisteína.*

CLINICAL MANAGEMENT OF HOMOCYSTINURIA; CASE REPORT AND REVIEW OF THE LITERATURE

Abstract

Homocystinuria is a congenital disorder of methyonine metabolism that leads to increased plasmatic, urinary and tissue deposits of methyonine and its main metabolite: homocysteine. Homocysteine deposits are toxic for the skeletal system (osteoporosis), the eyes (lens dislocation), central nervous system (seizures, psychiatric disorders) and also induce vascular damage (stroke and other cardiovascular events).

This article reports two patients with homocystinuria in two siblings, followed by a concise review on the therapeutic strategies available for this disorder.

(*Nutr Hosp.* 2012;27:2133-2138)

DOI:10.3305/nh.2012.27.6.6098

Key words: *Homocystinuria. Homocysteine.*

Introducción

La homocistinuria es un error congénito del metabolismo de la metionina que conduce al acúmulo de metionina y de su principal metabolito, homocisteína, en plasma, orina y tejidos[1]. La hiperhomocisteinemia se caracteriza por un aumento de los niveles de homocisteína en sangre. Puede producirse por errores genéticos o por trastornos adquiridos. Los trastornos genéticos del metabolismo de la metionina (homocistinuria) cursan con elevaciones de homocisteína de diferente grado en función de la gravedad del defecto metabólico, y se originan por mutaciones de herencia autosómica recesiva en las enzimas más relevantes del metabolismo de la metionina (fig. 1). La homocistinuria se clasifica en tipo I, II y III en función de la enzima afectada por la mutación. Asimismo, también existen causas adquiridas de hiperhomocisteinemia, como el déficit de vitamina B6, de ácido fólico y/o vitamina B12[2] (cofactores en el metabolismo de la metionina y la homocisteína), hipotiroidismo[3], enfermedad renal crónica, edad avanzada o toxicidad por fármacos (principalmente fibratos e inhibidores de la bomba de protones)[4].

Las características clínicas más llamativas de la homocistinuria son la ectopia del cristalino, la osteoporosis, la presencia de fenómenos tromboembólicos y el retraso psicomotor[1].

El tratamiento de estos trastornos se fundamenta en el empleo de betaína, en la suplementación de las vitaminas que actúan como cofactores en el metabolismo de la metionina y en la restricción dietética de metionina. Mientras que el tratamiento dietético trata de restringir la entrada de alimentos que contengan cantidades excesivas de metionina (tabla I), los cofactores y vitaminas empleados aceleran su metabolismo, lo cual resulta en un mejor control de la hiperhomocisteinemia[5].

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Recibido: 13-V-2012.
1.ª Revisión: 5-VIII-2012.
Aceptado: 7-VIII-2012.

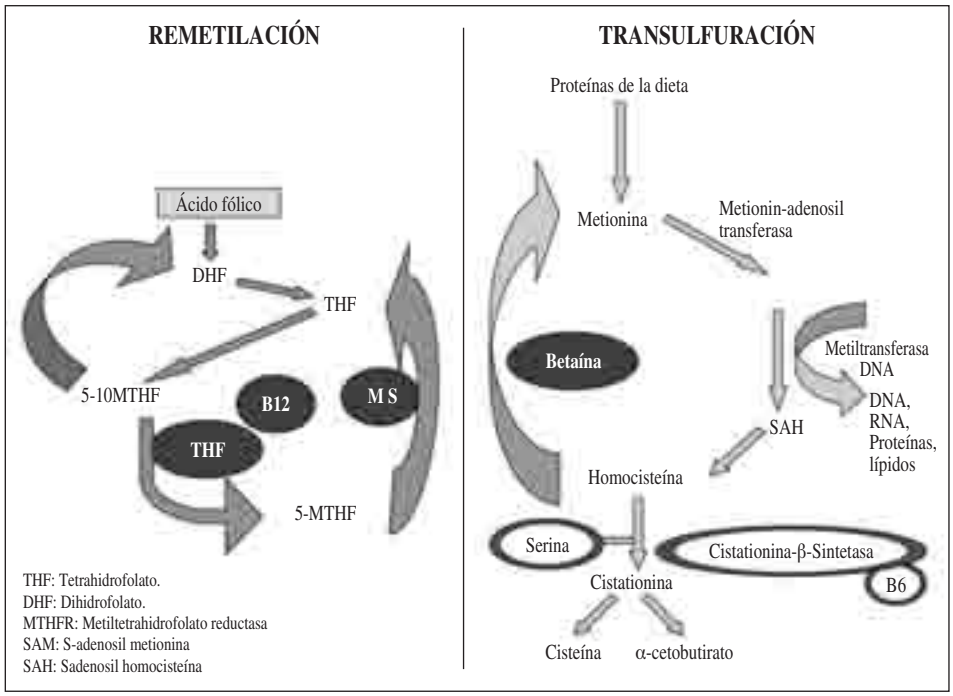


Fig. 1.—Metabolismo de la metionina.

A continuación describimos dos casos clínicos de homocistinuria en 2 pacientes hermanos. La clínica es más florida en el caso 1 puesto que el diagnóstico se estableció por clínica sospechosa a una edad más tardía. En el caso 2 el diagnóstico se efectuó tempranamente en el contexto del estudio familiar.

Casos clínicos

Caso 1: Varón de 26 años en seguimiento por la Unidad de Nutrición desde los 19 años de edad por homocistinuria. A los 6 años de edad presentó un glaucoma agudo bilateral secundario a luxación del cristalino. Dicho cuadro clínico, junto con la presencia de hábito marfanoide, llevó a la sospecha de homocistinuria, confirmada tras el estudio metabólico pertinente, que clasificó el cuadro como homocistinuria tipo I (déficit de cistationina β sintetasa), la forma más frecuente de homocistinuria. El estudio de la afectación familiar detectó el estado de portador en ambos progenitores y un hermano afecto (ver caso 2). Otros problemas presentados en el contexto de la enfermedad incluyen trombosis del seno venoso longitudinal a los 7 años, neumotórax espontáneo a los 15 años y hábito marfanoide. Desde el momento del diagnóstico seguía tratamiento con vitamina B6, ácido fólico, L-cistina y dieta con restricción de proteínas (20-40 gramos diarios). La ausencia de respuesta a vitamina B6 motivó la adición de betaína. En el momento actual ha finalizado sus estudios universitarios con éxito, no realiza actividad física programada, no presenta sintomatología en la anamnesis por aparatos y su estado de ánimo es normal. Reconoce no seguir ningúna restricción dietética a pesar de que se le ha explicado la importancia de la misma para reducir el riesgo de complicaciones. En la exploración física destaca hábito marfanoide, peso 73,1, talla 1,77, IMC 23,3, TA 105/69. Realiza tratamiento con 900 mg diarios de vitamina B6, 5 gramos diarios de cistina, 5 mg diarios de ácido fólico y betaína (6 gramos diarios). Durante su seguimiento en las Consultas de Nutrición ha presentado parámetros antropométricos (peso, IMC, pliegue tricipital, circunferencia muscular del brazo) y analíticos nutricionales (linfocitos, proteínas, albúmina, prealbúmina, colesterol) dentro de la normalidad. Sin embargo los niveles de homocisteína total en plasma han oscilado entre 353,9 y 135 µmol/l (rango 5-15 µmol/l) según el contenido proteico de la dieta. La metionina se ha mantenido en valores inferiores a 600 µmol/l (10-40 µmol/l). Además, realiza seguimiento activo por el Servicio de Oftalmología.

Caso 2: Varón de 20 años de edad diagnosticado de homocistinuria tipo I en la infancia en seguimiento en la Unidad de Nutrición desde los 13 años. Se estableció el diagnóstico con un mes de vida tras la confirmación de la enfermedad en su hermano. Entre los problemas asociados a este error congénito del metabolismo de la metionina sólo presenta miopía magna y una escoliosis severa que ha precisado medidas ortopédicas. No tiene otros antecedentes personales reseñables. Hasta los 12 años realizó seguimiento en otro centro hospitalario y según consta en los informes el desarrollo ponderoestatural y psicomotor fueron normales. Recibió tratamiento con restricción dietética 20-40 gramos diarios con escaso cumplimiento asociado a vitamina B6, ácido fólico y cistina. El tratamiento con betaína se comenzó cuando el paciente tenía 11 años de edad observándose importante mejoría de los niveles de

Tabla I
Alimentos desaconsejados, limitados y permitidos en la homocistinuria

Lista Roja - ¡Stop! *(Alimentos no permitidos. Alto contenido en metionina)*	*Lista Ámbar - ¡Vaya con cuidado!* *(Alimentos que contienen metionina en cantidad moderada)*	*Lista Verde* *(Libres pero nunca en exceso. Alimentos con contenido pequeño de metionina*
Carne: todo tipo (ternera, cordero, cerdo, jamón, bacon, pollo, pato, faisán, ganso, conejo, vísceras, salchichas, carne enlatada, carne picada (cualquier producto que contenga carne). *Pescados:* todo tipo (frescos, congelados), incluyendo mariscos. *Huevos:* Todo tipo. *Quesos:* Todos, incluyendo los de untar. *Frutos secos.* *Pan, harinas, bizcoches y galletas normales.* *Legumbres:* lentejas, judías blancas, soja y derivados. *Otros:* gelatina, caramelos, chocolates, cacao, regaliz	*Lácteos:* leche, crema de leche, nata, yogurt. *Verduras, tubérculos y legumbres:* patatas, batata, brócoli, coliflor, remolacha, coles de Bruselas, espinacas, champiñones, guisantes, judías rojas, maíz (mazorca o dulce en lata). *Cereales y arroz.* *Frutas:* aguacate, plátano, melocotones, nectarinas, pasas, sulfatanas, higo seco, dátiles secos, albaricoque seco (orejones).	*Frutas:* la mayoría (fresca, en lata, cruda o en almíbar): manzanas, peras, naranjas, mandarinas, kiwis, piña, uva, albaricocques (no secos), fresas, frambuesas, cerezas, arándanos, higos (frescos, no secos), ciruelas, guayaba, melón, sandía, papaya, mango, lichis, pasas, limones, lima, maracuyá (fruta de la pasión). *Verduras:* acelgas, chicoria, alcachofas, apio, ajo, (calabacín), berenjena, berros, cebolla, col, endibias, espárragos, judías verdes, lechuga, pepino, puerros, pimiento, rábano, tomate, perejil, hierbas aromáticas. *Cereales:* maizena, tapioca. *Grasas:* mantequilla, margarina (no las que contenga leche), cebo, manteca, grasas vegetales y aceites. *Bebidas:* agua, agua mineral, soda, refresco de limón, de frutas, de té, coca-cola, café negro, y zumos de frutas. *Miscelánea:* azúcar (blanca, morena, glasé), glucosas, mermelada, miel, sirope, esencias y colorante (vainilla, menta, almendra, cochinilla). Sal, pimienta, vinagre, mostaza, sal de menta, crema de tártara, curry, hierbas y especias, caramelos de crista, algodón de azúcar.

homocisteína en plasma y en orina (374 µmol/l y 1131 µmol/l g de creatinina versus 104 y 515). En nuestra Unidad el paciente ha seguido tratamiento con vitamina B6 (900 mg/d), ácido fólico (5 mg/d), L-cistina (5 gramos/día) y betaína. Al igual que su hermano, el caso 2 presenta baja adherencia a la restricción proteica de la dieta, lo cual justifica sus niveles elevados de homocisteína plasmática (374 y 98 µmol/l). Desde hace 2 años su análisis nutricional revela un déficit de vitaminas A y E que ha respondido adecuadamente a la suplementación.

En los dos pacientes se realizan visitas anuales en las que se los interroga clínicamente sobre síntomas neurológicos, osteomusculares y de otras posibles complicaciones, y se les pregunta sobre posibles incidencias médicas y personales de relevancia. Se efectúan medidas antropométricas y exploración física básica. Con frecuencia anual se solicita analítica con bioquímica, iones, coagulación, vitaminas B12, fólico, D, A, E, prealbúmina, zinc, magnesio, homocisteína en plasma, en orina y metionina plasmática y pruebas de función tiroidea.

En los dos pacientes se ha realizado densitometría con frecuencia bianual, que ha indicado la presencia de una osteopenia estable, y ecocardiogramas periódicos, con un resultado normal.

En ambos casos destaca una baja adherencia a la dieta pautada con restricción proteica. Dicha baja adherencia ha persistido aunque se les han explicado las consecuencias negativas de la misma sobre el pronóstico de la enfermedad, se ha realizado una adecuada educación dietética por el personal de la Unidad de Nutrición y se le han facilitado diferentes recetas culinarias para facilitar un mayor cumplimiento dietético.

Discusión

La homocisteína es un aminoácido azufrado que no forma parte de las proteínas dietéticas y que se sintetiza a partir de la metionina presente en las proteínas de los alimentos[5]. A continuación expondremos las rutas metabólicas de ambos aminoácidos para poder comprender adecuadamente la fisiopatología y el tratamiento de la homocistinuria.

La metionina, procedente de la dieta o del catabolismo de las proteínas endógenas, es transformada a homocisteína. La homocisteína puede metabolizarse por dos vías diferentes: la transulfuración y la remetilación[5] (fig. 1).

En la transulfuración, la homocisteína se transforma a cisteína por medio de dos reacciones dependientes de vitamina B6. La primera de estas reacciones es catalizada por la cistationina-β-sintetasa y en ella, la homo-

cisteína se condensa con una molécula de serina para formar cistationina. En la segunda reacción, la cistationina es transformada a cisteína por acción de la cistationina-β-liasa[5]. La cisteína es precursora del glutation y la taurina, compuestos de gran importancia metabólica como antioxidantes (glutation) y neurotransmisor (taurina). La cisteína es finalmente catabolizada, y se elimina por la orina en forma de sulfato.

En la ruta de la remetilación, la homocisteína se metila para formar metionina mediante dos rutas metabólicas independientes, en las que participan respectivamente las encimas 5-metiltetrahidrofolato-reductasa y la betaína-homocisteína-metiltransferasa[5]. La primera de estas enzimas requiere 5-metiltetrahidrofolato y metilcobalamina como fuentes de grupos metilo. La segunda se encuentra en el hígado y, en menor proporción, en riñones y glándulas suprarrenales, y emplea betaína como fuente de grupo metilo. Por tanto, las vitaminas del grupo B (piridoxina, ácido fólico y metilcobalamina) son necesarias en el metabolismo de la metionina y la homocisteína, que como veremos a continuación tienen un importante papel terapéutico en los pacientes afectos de homocistinuria.

En humanos, aproximadamente el 50% de la homocisteína es convertida en metionina mediante remetilación. La concentración plasmática de metionina determina la ruta metabólica (transulfuración o remetilación) que debe seguir la homocisteína. La regulación de estas vías metabólicas ayuda a mantener concentraciones de metionina y homocisteína en intervalos fisiológicos, es decir, no tóxicos para la fisiología celular.

De acuerdo con el metabolismo de la homocisteína podemos encontrar tres mecanismos diferentes de producción de homocistinuria:

1) Homocistinuria tipo I: Déficit de la enzima cistationina-β-sintetasa, que ocasiona la forma clásica de homocistinuria. El gen que codifica dicha encima se localiza en el brazo largo del cromosoma 21.
2) Homocistinuria tipo II: Déficit de la enzima tetrahidrofolato-reductasa.
3) Homocistinuria tipo III: Errores innatos en el metabolismo de la vitamina B12.

La homocistinuria tipo I es la más frecuente, por lo que también se denomina homocistinuria clásica[5], y presenta un patrón de herencia autosómico recesivo. Se han descrito 140 mutaciones de la cistationina-β-sintetasa, aunque el listado de mutaciones y su expresividad clínica se actualizan regularmente, y pueden consultarse en la página siguiente: www.uchsc.edu/sm/ cbs/cbs. Las dos mutaciones más frecuentes son I278T, que se asocia a respuesta al tratamiento con B6, y la G307S, que no responde a B6[1,6]. Aún comprendiendo todas sus variantes, la homocistinuria es una enfermedad rara, con una frecuencia de 1 caso por 334.000 habitantes[1]. En Irlanda, que dispone de estudios de cribaje neonatal desde 1971[7], la frecuencia es mayor, con 1 caso por 65.000 habitantes.

Los pacientes homocigotos se caracterizan por hiperhomocisteninemia grave de hasta 500 µmol/l, con homocistinuria y varias manifestaciones clínicas, entre las que destaca la afectación cardiovascular. Los pacientes heterocigotos, portadores, desarrollan una hiperhomocisteinemia moderada con una expresividad clínica intermedia[1].

Los recién nacidos típicamente no presentan manifestaciones cínicas, ya que durante el embarazo es la madre la que metaboliza las proteínas, y aunque sea portadora lo realiza correctamente. Cuando el bebé comienza a alimentarse, comienza a utilizar su propio sistema enzimático para el metabolismo de la metionina; las proteínas de la dieta contienen metionina, que se metaboliza a homocisteína. Dicho aminoácido no se degrada bien por el déficit enzimático, con el consiguiente acúmulo de homocisteína y su precursor metionina.

El acúmulo de homocisteína es tóxico a nivel del sistema óseo (osteoporosis), sistema ocular (luxación del cristalino, miopía, glaucoma), sistema nervioso (convulsiones, alteraciones psiquiátricas), y sistema vascular (accidentes cerebrovasculares, enfermedad cardiovascular). Los mecanismos por los que la homocisteína es responsable de dichas manifestaciones clínicas son variados. A nivel vascular, produce mayor adhesión plaquetaria, activa la cascada de la coagulación, daña el endotelio, incrementa la oxidación de partículas LDL y precipita su depósito de las mismas en la pared arterial[8]. La hiperhomocisteinemia también afecta al colágeno del tejido conjuntivo, y por ello, estos pacientes muestran alteraciones óseas y ectopia del cristalino.

Desde el punto de vista neurológico destacan retraso psicomotor leve o moderado en la mayoría de los casos y que suele manifestarse a los 2-3 años de vida y los problemas vasculares cerebrales de origen tromboembólico. También se han descrito síntomas extrapiramidales como debilidad muscular. El coeficiente intelectual está discretamente descendido en más de la mitad de los pacientes, aunque los dos casos comentados tienen una inteligencia normal.

El síntoma oftalmológico más llamativo es la subluxación o ectopia del cristalino[5], que se define por el desplazamiento del mismo dentro de la pupila ocasionando disminución de la agudeza visual o incluso dolor por glaucoma agudo secundario, como el Caso 1 que presentamos. La ectopia del cristalino está presente en el 100% de los pacientes con homocistinuria y en el 80% de los pacientes con síndrome de Marfan, principal diagnóstico diferencial de la homocistinuria. Ambas entidades también comparten rasgos osteomusculares comunes, como la aracnodactilia, pero dichas manifestaciones esqueléticas suelen ser más llamativas en los casos de síndrome de Marfan.

Las manifestaciones osteomusculares de la homocistinuria incluyen extremidades largas con hábito marfanoide, *pectus excavatum* o *carinatum*, *genu valgo* y osteoporosis.

Otros hallazgos descritos en la homocistinuria son la pancreatitis, el neumotórax espontáneo y la hipopig-

mentación de piel y cabello. La hipomelanosis es ocasionada por la inhibición que la homocisteína ejerce sobre la enzima tirosinasa[9]; dicha inhibición es reversible con la disminución de niveles de homocisteína.

En 1985 Mudd y cols., publicaron un estudio sobre la historia natural de la homocistinuria tras estudiar 629 pacientes con dicho trastorno[10]. El 82% de los afectados presentaban ectopia del cristalino a los 10 años de edad. La prevalencia de osteoporosis fue del 50% a los 15 años. En cuanto a los fenómenos tromboembólicos el 30% de los pacientes a los 20 años había padecido un evento de dicha naturaleza y la mitad a los 30 años. A los 30 años de edad, un 18% de la serie había fallecido.

El principal motivo de morbimortalidad en la homocistinuria está representado por los fenómenos tromboembólicos. En un estudio de 253 fenómenos tromboembólicos ocurridos a 158 pacientes con homocistinuria se observó que el episodio más frecuente eran los accidentes cerebrovasculares (32%) junto con la trombosis venosa profunda (51%) y con menor frecuencia tromboembolismo pulmonar (25%), infarto agudo de miocardio (4%) y enfermedad vascular periférica (11%)[11].

El diagnóstico se basa en la sospecha clínica y las determinaciones de laboratorio que característicamente presentan elevación de metionina en plasma y de homocisteína en plasma y en orina. El diagnóstico se confirma determinando la actividad de la enzima cistationina-β-sintetasa en fibroblastos de piel.

Dado el beneficio obtenido del diágnóstico y tratamiento precoces[12] se propone el diagnóstico neonatal mediante la medicción de metionina en dicho periodo. De hecho, la progresiva instauración de los programas de cribado neonatal, y la búsqueda sistemática de esta patología en los pacientes con manifestaciones clínicas compatibles (y no sólo en los que presentan un fenotipo "clásico"), muestra que su incidencia real es mucho más elevada de lo que se pensaba, alrededor de 1/20.000 recién nacidos y, después de la hiperfenilalaninemia, es probablemente la aminoacidopatía más frecuente[13].

Desde el punto de vista clínico, el diagnostico diferencial de la homocistinuria debe hacerse con las entidades que presentan las alteraciones esqueléticas citadas, es decir, con el síndrome de Marfan. Ambas entidades comparten carácterísticas clínicas: aracnodactilia, problemas cardiovasculares, pero en la enfermedad de Marfan las alteraciones óseas son más llamativas y en la esfera cardiovascular destaca aneurisma de aorta e insuficiencia mitral. En este caso la determinación analítica es definitoria puesto que en el síndrome de Marfan los niveles de homocisteína son normales.

Desde el punto de vista bioquímico el diagnóstico diferencial se realiza con otras enfermedades que cursan con homocisteína elevada en plasma. Destacan la homocistinuria II y III pero la hiperhomocisteinemia es menos llamativa en el tipo I o clásica con cifras que oscilan entre 50-200 μmol/litro. En los tipos II y III el paciente no presenta el fenotipo clásico de homocistinuria. Además, el aumento de homocisteína puede deberse a otras situaciones médicas: hipotiroidismo, insuficiencia renal crónica, déficit de ácido fólico o cobalamina y fármacos.

El objetivo del tratamiento es mantener los niveles de homocisteína dentro del rango de la normalidad o lo más cercano a éste posible, considerándose control metabólico aceptable si los niveles de homocisteína total son inferiores a 50 μmol/l.

El tratamiento dietético es fundamental para lograr dicho objetivo, porque como vemos en los casos que presentamos la falta de adherencia a la dieta implica niveles muy elevados de homocisteína a pesar de emplear adecuadamente el resto de herramientas terapeúticas de las que disponemos.

Se recomienda restringir las proteínas de alto valor biológico puesto que son las más ricas en metionina. La cantidad de metionina tolerada para mantener un buen control metabólico varía de unos pacientes a otros (150-900 mg/día). En general, en la edad adulta se recomienda 8-10 mg/kg/día de metionina. Los alimentos con un alto contenido en metionina son huevos, pescados, carnes, quesos, frutos secos y legumbres, cuyo consumo debe limitarse en estos pacientes. En la tabla 1 se exponen los alimentos clasificados según su contenido en metionina. En España están comercializados pasta, harina, galletas y cereales con muy bajo contenido proteico y que consumidos con los alimentos naturales facilitan el cumplimiento de la restricción proteica.

No obstante, los aminoácidos son indispensables en la formación de proteínas, por lo que se aportan mediante una fórmula especial que contiene todos los demás aminoácidos a excepción de la metionina (XMET homidon®, XMET maxamun®, ambos del laboratorio SHS).

La homocisteína es precursor de la cistina y ésta a su vez de la taurina (indispensable en el metabolismo cerebral) y de glutatión (con importante función antioxidante) por lo que la cistina se convierte en aminoácido esencial y se aporta a dosis de 5 gramos diarios (Cistina®, laboratorio SHS.

Respecto al tratamiento de la homocistinuria los pacientes se clasifican generalemente en piridoxina sensibles y piridoxina resistentes[1,12]. En el primer grupo en el que se incluyen hasta el 50% de los pacientes, el tratamiento con piridoxina reduce los niveles de homocisteína. La dosis de piridoxina a emplear es la menor para normalizar los niveles de homocisteína. Los adultos suelen precisar 500 a 1.200 mg/día, puesto que aportes mayores se han asociado a neuropatía sensorial[14]. Se ha demostrado que la piridoxina previene los fenómenos tromboembólicos por lo que se recomienda en todos los pacientes, respondedores o no.

La respuesta a la piridoxina está influenciada por los valores de folato, por lo que en ambos grupos se debe aportar ácido fólico a razón de 5 mg diarios y se

han de monitorizar estrechamente los niveles de vitamina B12, suplementándose en caso de que exista déficit.

En el segundo grupo se emplea la suplementación con betaína[15], que actúa como donador de grupos metilo y favorece la remetilación de homocisteína descendiendo así los niveles de ésta. El empleo de betaína reduce el riesgo de fenómenos tromboembólicos que constituyen la primera causa de mortalidad. La betaína disminuye los niveles de homocisteína pero incrementa las concentraciones de metionina, que si bien no es tóxica debe monitorizarse puesto que en la literatura científica se han descrito 3 casos de edema cerebral asociado a hipermetioninemia, especialmente si los valores en plasma exceden 1.000 µmol/l. Se deben vigilar datos clínicos de hipertensión intracraneal y las cifras de metionina plasmáticos[15]. La dosis que se emplea en adultos es 6-9 g/día de betaína anhidra oral (Cystadane®, Orphan). Es un fármaco de utilidad en los pacientes no sensibles a vitamina B6.

Además se recomienda actuar sobre otros factores de riesgo cardiovascular asociados y es fundamental la prevención de fenómenos tromboembólicos en los periodos perioperatorios, incluso con cirugía menor.

En conclusión, la homocistinuria es un conjunto de trastornos congénitos en el metabolismo de la homocisteína con una importante morbimortalidad asociada. La prevención de sus complicaciones depende en último término de mantener niveles fisiológicos de homocisteína mediante el tratamiento dietético y las medidas farmacológicas, que serán más eficaces cuanto más precoz sea el diagnóstico. Por tanto, resulta de particular importancia sospechar la presencia de homocistinuria en niños y adolescentes con fenómenos tromboembólicos y/o ectopia del cristalino. Por último, el seguimiento de los pacientes con homocistinuria participa de un enfoque multidisciplinar en el que el tratamiento dietético desempeña un papel cardinal para el control metabólico y para modificar el curso natural de la enfermedad.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2139-2141
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Comunicación breve

Prevalence of *Listeria monocytogenes* in Idiazabal cheese

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Abstract

Introduction: **Raw-milk cheese has been identified in risk assessment as a food of greater concern to public health due to listeriosis.**

Objective: **To determine the prevalence and levels of *Listeria monocytogenes* in semi-hard Idiazabal cheese manufactured by different producers in the Basque Country at consumer level.**

Methodology: **A total of 51 Idiazabal cheese samples were obtained from 10 separate retail establishments, chosen by stratified random sampling. Samples were tested using the official standard ISO procedure 11290-1 for detection and enumeration methods.**

Results and conclusion: **All cheese samples tested negative for *L. monocytogenes*. However, 9.8% tested positive for *Listeria spp.*, different from *L. monocytogenes*. Positive samples came from two brands, two were natural and three were smoked. The presence of *Listeria spss*. suggests that the cheese making process and the hygiene whether at milking or during cheese making could be insufficient.**

(*Nutr Hosp.* 2012;27:2139-2141)

DOI:10.3305/nh.2012.27.6.6052

Key words: *Food microbiology. Listeria monocytogenes. Cheese. Consumer.*

PREVALENCIA DE *LISTERIA MONOCYTOGENES* EN QUESO IDIAZABAL

Resumen

***Introducción: Listeria monocytogenes* se ha asociado a quesos elaborados a partir de leche cruda, lo que supone un importante riesgo de salud pública debido a la listeriosis.**

Objetivo: **Estudiar la prevalencia y los niveles de *L. monocytogenes* en quesos Idiazabal semi-curados de distintos productores del País Vasco, a nivel de consumidor.**

Metodología: **Se analizaron 51 muestras de queso Idiazabal procedentes de 10 establecimientos de venta al público; el muestreo fue aleatorio y estratificado. Los análisis se hicieron según el método de detección y de enumeración del procedimiento estandarizado ISO 11290-1.**

Resultados y conclusión: **Todas las muestras dieron negativo para *L. monocytogenes*. Sin embargo, el 9,8% dio positivo para *Listeria spp.*, distinta de *L. monocytogenes*. Las muestras positivas procedían de dos marcas, dos eran quesos naturales y tres ahumados. La presencia de *Listeria spss.* sugiere que el procesado del queso y la higiene durante el ordeño o durante la fabricación podría ser insuficiente.**

(*Nutr Hosp.* 2012;27:2139-2141)

DOI:10.3305/nh.2012.27.6.6052

Palabras clave: *Microbiología de los alimentos. Listeria monocytogenes. Queso. Consumidor.*

Abbreviations

DO: Denomination of Origin.
RE: Retail establishments.

Introduction

Raw-milk cheese has been identified in risk assessment as a food of greater concern to public health due to listeriosis.[1,2] *Listeria monocytogenes* has been isolated from sheep and goat cheese from raw milk.[3,4] However, other authors have not found *Listeria monocytogenes* in cheese made from unpasteurized milk.[5]

Idiazabal cheese is a traditional semi-hard cheese from the Basque Country region of Northern Spain made with raw ovine milk which can be manufactured either with any commercial animal rennet or with artisan-produced lamb rennet paste, as approved by its Denomination of Origin.[6] The Idiazabal Denomination of Origin (DO), which was created in 1987, defines the basic regulations for the product's manufacturing and permits external smoking of the cheese.

The pH levels (pH 4.9 to 5.5), the aw (0.96)[7] and low salt content (1.8%),[8] and considerable hand manipulation during manufacturing by small processors are factors that may all contribute to providing a favourable environment for contamination and survival/growth of *L. monocytogenes* in Idiazabal cheese. However, to the

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Recibido: 10-VII-2012.
Aceptado: 7-VIII-2012.

Table I
Idiazabal cheese samples analyzed

Region	*Total no. of REs per region*	*No. of natural cheese samples taken*	*No. of smoked cheese samples taken*	*No. of brands*
Álava	17	7	10	15
Vizcaya	17	10	7	9
Guipúzcoa	17	9	8	16

RE: Retail establishment.

best of our knowledge, there are even fewer studies about the hygienic quality of Idiazabal cheese[9] and there are no studies at consumer level.

Based on the association of *Listeria monocytogenes* with raw-milk cheese and, in turn, on the potential threat of listeriosis, the objective of this study was to determine the prevalence and levels of *Listeria monocytogenes* in semi-hard Idiazabal cheese manufactured by different producers in the Basque Country at consumer level.

Methodology

Retail sampling

A total of 51 Idiazabal cheese samples representing 16 different brands (two to three samples per brand) were obtained from 10 separate retail establishments (REs) (table I), chosen by stratified random sampling, located in the three autonomous region of the Basque Country (Álava, Vizcaya and Guipúzcoa). Commercial vacuum-packed cheeses were transported to the Microbiology Laboratory (University of the Basque Country, UPV/EHU) for microbiological analyses where they were stored at 3-4º C.

Isolation, identification and enumeration of L. monocytogenes

Cheese samples were collected as finished packaged products at the above-mentioned REs. Samples were tested using the official standard ISO procedure 11290-1 for detection and enumeration methods (ISO 1998 ISO 11290-1) and triplicate analyses were performed. Agar Listeria according to Ottaviani & Agosti (ALOA) chromogenic agar (AES Chemunex España, S.A., Barcelona, Terrassa) and polymyxin acriflavine lithiumchloride ceftazidime aesculin manitol PALCAM Listeria selective agar (OXOID S.A, Madrid, Spain) were used as culture plates. *L. monocytogenes* identification was based on colony morphology and results of gram-staining, catalase test, beta -haemolysis, carbohydrate utilisation and CAMP reaction.[10]

Results and discussion

Our survey of 10 REs in the Basque Country revealed that all 51 cheese samples from 16 brands tested negative for *L. monocytogenes*, by both direct plating and enriched cultures. However, 9.8% (5 out of 51 samples) tested positive for *Listeria* species. Positive samples came from two brands, two were natural and three were smoked. These samples positive for *Listeria* were analyzed, although it was not possible to identify the species, it was confirmed that they were not *L. ivanovii, L. innocua, L. welshimeri, L. seeligeri* or *L. grayi.*

The most recent official data of *L. monocytogenes* refer to the year 2010 wherein 21 cases were declared.[11] Although *L. monocytogenes* is widespread in nature as well as in the dairy environment, our results and those of other investigators confirm that all raw-milk cheese is not a common source of this pathogen,[5,9] probably because the procedure eliminates it. The literature data indicate that *L. monocytogenes* contamination may occur both during and after cheese processing[12,13] and that the introduction of *L. monocytogenes* can be produced via contaminated raw milk.[14,15]

Our data also confirmed that these cheeses can be a source of *Listeria* spp., different from *Listeria monocytogenes*, to consumers even they are smoked. The presence of *Listeria* spss. suggests that the cheese making process and the hygiene whether at milking or during cheese making could be insufficient.

In conclusion, this work has increased our knowledge of the prevalence of *L. monocytogenes* in Idiazabal cheese at consumer level and gives an account of the hygiene status during production. However, continued efforts are needed to decrease *Listeria* in RTE foods, also populations vulnerable to listeriosis need to be appropriately educated.

Acknowledgements

We gratefully acknowledge the contributions of Celia Sánchez, Nuria López-Molina and Ana Rocandio who contributed significantly to the initiation and conduct of the study per se. This work was financially supported by ERA-NET SAFEFOODERA (7PM, EU Framework Programme) (LisRisk 08196). The men-

tion of trade names or commercial products in this publication is solely for the purpose of providing specific information and does not imply recommendation.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2142-2145
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Comunicación breve

Intronic SNP rs3811647 of the human transferrin gene modulates its expression in hepatoma cells

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Abstract

Introduction: **Transferrin (Tf) exerts a crucial function in the maintenance of systemic iron homeostasis. The expression of the Tf gene is controlled by transcriptional mechanism, although little is known about genetic factors influence.**

Objective: **To study the role of rs3811647 in Tf expression using an *in-vitro* assay on hepatoma cells.**

Design and Methods: Hep3B cells were co-transfected with constructs containing A *(VarA-Tf-luc)* and G *(VarG-Tf-luc)* variants of rs3811647, using luciferase as a surrogate reporter of Tf expression.

Results: **Luciferase assays showed a higher intrinsic enhancer activity ($p < 0.05$) in the A compared with the G variant. In silico analysis of SNP rs3811647 showed that the A allele might constitute a binding site for the transcription factor glucocorticoid receptor (GR).**

Conclusion: **The A allele of SNP rs3811647 increases Tf expression in a manner that might underlie inter-individual variation in serum transferrin levels observed in different population groups.**

(*Nutr Hosp.* 2012;27:2142-2145)

DOI:10.3305/nh.2012.27.6.6154

Key words: *Transferrin gene. SNP rs3811647. Serum transferrin. Iron metabolism. Gene expression.*

EL SNP INTRÓNICO rs3811647 DEL GEN DE LA TRANSFERRINA HUMANO, MODULA SU EXPRESIÓN EN CÉLULAS HEPÁTICAS

Resumen

Introducción: **La transferrina (Tf) ejerce una función crucial en el mantenimiento de la homeostasis sistémica del hierro. La expresión del gen de la transferrina es controlada a nivel transcripcional, aunque la posible influencia de factores genéticos todavía se desconoce.**

Objetivo: **Estudiar el papel del rs3811647 en la expresión de la transferrina mediante un ensayo *in-vitro* en células de hepatoma.**

Diseño y métodos: **Células Hep3B fueron co-transfectadas con vectores que contenían las variantes A *(VarA-Tf-luc)* y G *(VarG-Tf-luc)* del rs3811647, utilizandose la luciferasa como marcador de la expresión del gen Tf.**

Resultados: **Los ensayos con la luciferasa mostraron un mayor aumento de la expresión del gen Tf en presencia de la variante A comparada con la G ($p < 0,05$). El análisis in silico del SNP rs3811647 mostró que la presencia del alelo A puede constituir un sitio de unión del receptor de glucocorticoides (GR).**

Conclusión: **El alelo A del SNP rs3811647 incrementa la expresión del gen Tf de modo que podría modular la variación interindividual en los niveles de transferrina sérica observados en diferentes poblaciones.**

(*Nutr Hosp.* 2012;27:2142-2145)

DOI:10.3305/nh.2012.27.6.6154

Palabras clave: *Gen de la transferrina. SNP rs3811647. Transferina sérica. Metabolismo del hierro. Expresión génica.*

Abbreviations

Tf: Transferrin.
GR: Glucocorticoid receptor.

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Recibido: 5-IX-2012.
Aceptado: 11-IX-2012.

Introduction

Transferrin (Tf) is an iron-binding plasma protein that delivers iron to cells via the transferrin receptor pathway.[1] A molecule of Tf can bind two atoms of ferric iron with high affinity. Iron chelation by transferrin serves three main purposes: to maintain ferric iron in a soluble form under physiologic conditions; to facilitate regulated iron transport and cellular uptake, and to maintain ferric iron in a redox-inert state, avoiding the generation of free radicals.[2] Moreover, diferric Tf stimulates hepcidin expression, the central regulatory molecule of systemic iron homeostasis, through a TfR2/HFE mediated pathway.[3]

The expression of the Tf gene is controlled by transcriptional mechanisms and is tissue-specific.[4] Many environmental factors are known to affect plasma Tf levels: in iron deficiency, the rate of Tf synthesis in the liver increases significantly,[5] whereas inflammatory or immunologic stimuli may decrease the levels of circulating Tf.[6] Recent studies observed increased Tf levels under hypoxia, a response that may facilitate iron supply for erythropoiesis.[7] Nevertheless, little is known about the genetic factors that influence Tf levels in humans, although its expression pattern appears to show sexual dimorphism.[8] Our research group recently published that only a few SNPs could explain a large percentage of the heritable variation of serum transferrin levels; one of these loci is SNP rs3811647, located in intron 11 of the human transferrin gene (*Tf*),[9] which as in agreement with other data from the bibliography.[10] Based on these studies, we hypothesised that SNP rs3811647 increases transferrin expression. Here we show that this SNP constitutes an intronic enhancer that modulates *Tf* expression in hepatoma cells.

Design and methods

Plasmid constructs

A fragment of approximately 500 bp of intron 11 of the human transferrin gene (*Tf*), encompassing the SNP rs3811647, was amplified from placental genomic DNA with the following primers: sense, CATGCTAGCGGCTTGCACACAGGATTTTT; antisense, CATCTCGAGAATCAGTGGAAGTGGCAAGG; *NheI* and *XhoI* restriction sites are underlined. The cycling parameters were: 95° C for 5 minutes, then 95° C for 5 minutes (denaturation), 62° C for 1 minute (annealing), and 72° C for 1 minute (extension); 35 cycles of PCR were performed with a final extension for 10 minutes at 72° C. The PCR product was subcloned into pGEM-T Easy vector (Promega, Southampton, United Kingdom) and sequenced for verification of the nucleotide sequence (MWG Biotech, Ebersberg, Germany) and to confirm the presence of the A allele. The construct was digested with *NheI* and *XhoI* (New England Biolabs, Hitchin, United Kingdom), and the insert was purified with Geneclean (BIO101; Anachem, Luton, United Kingdom) and ligated into the *NheI* and *XhoI* sites of pGL3Promoter (Promega) to generate *VarA-Tf-luc*.

Site-directed mutagenesis

VarA-Tf-luc was subjected to site-directed mutagenesis using the QuikChange Multi Site-Directed Mutagenesis system (Stratagene, Amsterdam, The Netherlands) as instructed by the manufacturer. To change the A to G alleles we synthesized a mutagenic primer (mutations in lowercase) as follows: GGGAGTTTACAGACAGATCgTCTAGGATTATACATCTAGGAAGGG. After initial denaturation for 5 minutes at 95° C, PCR cycling parameters were 95° C (5 minutes), 55° C (1 minute), and 65° C (11 minutes and 12 seconds), for a total of 30 cycles. Plasmids were sequenced to verify that the intended mutation had occurred. The resulting construct was designated *VarG-Tf-luc*.

Cell culture, transfection and luciferase assay

The human hepatoma cell line Hep3B was obtained from Antonello Pietrangelo and cultured in Dulbecco's Modified Eagle Medium (DMEM), supplemented with 10% foetal calf serum (FCS) and antibiotics/antimycotics (Invitrogen). Cells were grown under standard cell culture conditions of 37° C and 5% CO2; for transfection, cells were seeded in 24-well plates at densities of approximately 10^4 cells/well. Cells were transfected with 100 ng/well of *VarA-Tf-luc or VarG-Tf-luc* with Lipofectamine 2000 (Invitrogen), as instructed by the manufacturer. As internal control, 50 ng of pSV gal vector (Promega) was included in all transfections to normalize transfection efficiencies. Cells were harvested after 48 hours for reporter assays; luciferase activities were determined with the luciferase assay reagent and β-galactosidase (βgal) activity was measured using the Beta-Glo reagent (both from Promega). Luminescence was measured in a Tropix TR717 microplate luminometer (Applied Biosystems); luciferase levels were normalized with respect to gal activity in the samples.

In silico analysis

For the prediction of putative transcription factor binding sites, a sequence of 25 bases to either side of the SNP rs3811647 was submitted to a net-based search tool Patch 1.0 (http://www.gene-regulation.com/cgi-bin/pub/programs/patch/bin/patch.cgi).

Settings for core and pair similarities, matrix conservation, and factor class levels were adjusted according to factors predicted.

Statistical analysis

Pairwise comparisons of control and SNP constructs were made using ANOVA test. A *P* value of 0.05 was considered significant. Graphs were plotted with the GraphPad Prism software and data were analysed using the SPSS statistical package for Windows (version 19.0; SPSS Inc., Chicago, IL, USA).

Results

Using reporter assays in which fragments of the intron encompassing SNP rs3811647 were ligated to

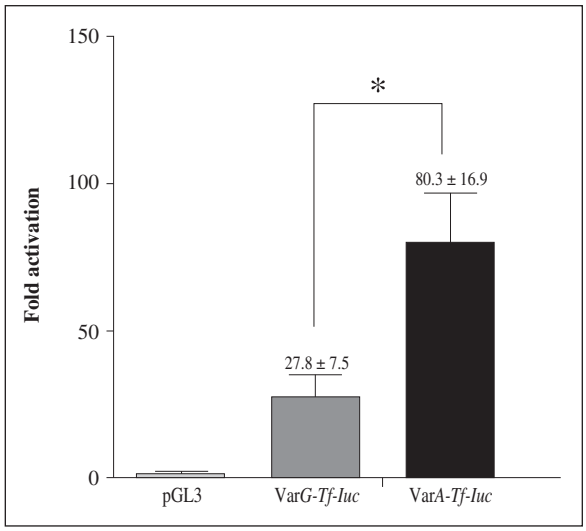


*Fig. 1.—SNP rs3811647 luciferase assay. Hep3B cells were transfected with VarA-Tf-luc or VarG-Tf-luc constructs; pGL3 (promoter) vector backbone was used as negative control. Data were normalized to the expression levels of β-galactosidase internal control, and represent the means of two independent experiments (± SEM), *p < 0.05.*

firefly luciferase as *Tf* surrogate, we found that the A allele enhanced gene expression compared with the G allele. The fold activation of the *VarA-Tf-luc* construct was significantly higher ($p < 0.05$) than that of the *VarG-Tf-luc* construct (fig. 1). In other words, the A allele of the SNP rs3811647 supports higher *Tf* expression than the G allele in hepatoma cells.

In silico analysis of this SNP showed that the A allele in rs3811647 could theoretically constitute a binding site for the glucocorticoid receptor (GR), also known as nuclear receptor subfamily 3 group C member 1 (NR3C1), whereas this binding site is lost with the G allele (fig. 2).

Discussion

The obtained results can be validated by the findings that our research group obtained in a group of menstruating women. We found that serum transferrin was significantly higher in AA homozygous women than in AG heterozygous and GG homozygous ($p < 0.01$), and serum transferrin saturation was significantly higher in GG than in AG and AA women ($p = 0.01$).[9] Also, the *in-vitro* results confirm previous observations in different population groups[10-13] and add new information concerning the functionality of rs3811647. We therefore suggest that basal differences in circulating Tf levels between individuals may be ascribed to SNP rs3811647, which is located in intron 11 of Tf gene (Chr3q22.1).

The tissue-specificity of *Tf* expression is accomplished by the recruitment of different combinations of transcription factors. In hepatocytes, binding sites of transcription factors that are well-known to regulate *Tf* expression have been described. Proximal region I (PRI) and proximal region II (PRII) within the *Tf* promoter positively regulate its expression in the liver whereas distal regions repress *Tf* expression.[14] However, our study shows that in addition to the positive regulation of *Tf* by proximal promoter elements, there are intronic elements such as rs3811647 that could act as enhancers of *Tf* transcription. This is intriguing because no known function especially in relation to relative risk would have been predicted for intronic sequences,[15] considering that disease associations have hitherto been limited to coding-region mutations only. We found that presence of the A allele of rs3811647 might constitute a binding site for the GR. Glucocorticoids influence the expression of a number of genes involved in iron metabolism including ferritin, ferroportin, DMT-1 and iron regulatory protein-1.[16,17] GR might therefore regulate glucocorticoid-dependent differences in *Tf* allele expression; further studies will ascertain this. Although it is more frequent to find regulatory regions upstream of the start site of transcription, in some cases transcription factors are able to drive gene expression from within coding regions.[18] It is therefore not entirely surprising that we found regulatory regions within the *Tf* intron.

In our previous study, the women that presented the A allele also had lower transferrin saturation, which may indicate a reduction in iron transport to tissues.[9] Since low ferritin levels have been associated with this

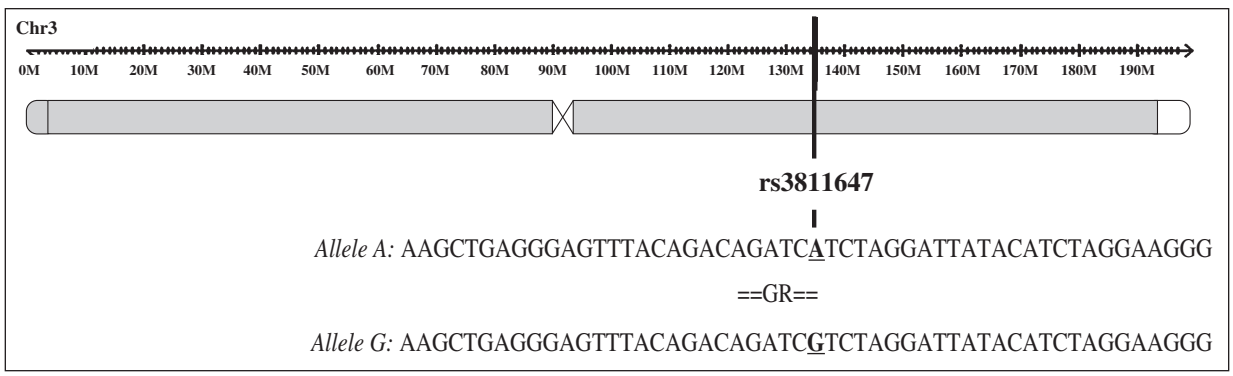


Fig. 2.—Genomic arrangement (upper panel) and sequences proximal to SNP rs3811647 (bold letter, lower panel). Sequence analysis with prediction algorithms showed that the A allele in rs3811647 might create a binding site for the glucocorticoid receptor (GR).

SNP, it could be related to low iron status.[10] Another important observation was made in a placebo-controlled nutritional intervention study an with iron-fortified food in iron-deficient women.[19] Dietary iron-fortification markedly increased the iron status in all women. However, carriers of the minor A allele showed Tf levels higher than the rest during the 16-week intervention period.[20] All of these observations suggest that this SNP may affect iron metabolism.

In conclusion, we found that the A allele of the SNP rs3811647 enhances *Tf* expression compared with the G allele, and that this might explain the association between this SNP and the high serum Tf levels observed in different population groups.

Acknowledgements

This study was supported by Project AGL2009-11437. R. Blanco-Rojo was supported by a JAE-predoc grant from CSIC and European Social Found.

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2146-2147
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

DOI:10.3305/nh.2012.27.6.6027

Cartas científicas

Nutrition and tracheal morphology; does malnutrition lead to characteristics of premature aging?

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Interest in tracheal surgery and invasive airway endoscopic procedures has increased in the last two decades. This is a direct consequence of the aging of population and improvement in intensive care units. The most prevalent airway disease requiring surgery or invasive endoscopic procedure is tracheal stenosis. The occurrence of this disease is related to abnormal healing after injury to mucosa, usually by orotracheal or tracheostomy tube. Importantly, this healing process is initiated in, and coordinated by, the extracellular matrix.[1,2]

Our initial studies revealed that the arrangement of extracellular matrix components in the Wistar rat trachea, such as elastic fibers, collagen and smooth muscle are essentially the same that are in human trachea.[2] Attempts to substitute a tracheal segment with aortic allograft have been performed in pigs, where the normal aortic tissue was replaced by a structure resembling a "new trachea" with histological characteristics of a normal trachea. Interestingly, this new trachea has developed amid islets of elastic fibers in the extracellular matrix of the aortic allograft.[3] In his work on tissue-engineered major airway replacement, Macchiarini and coworkers discuss the role of extracellular matrix as an active part in regulating diverse aspects of cell biology that are essential to the normal function of tissue.[4]

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Recibido: 14-VI-2012.
1.ª Revisión: 27-VI-2012.
Aceptado: 13-VII-2012.

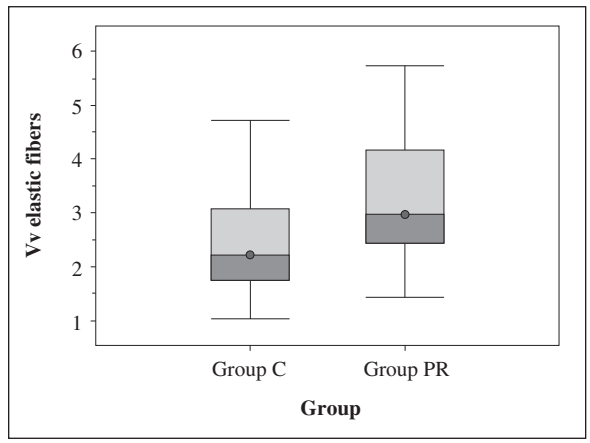


Fig. 1.—Volumetric density, expressed as percentage, of the elastic system fibers of the trachea of Wistar rats at the age of 21 days. Values expressed as the mean of volumetric density ± SD of 6 pups per group (P < 0.01). Vv %: Volumetric density, expressed as percentage; SD: standard deviation; Group C: Control group; Group PR: Protein restricted group.

Our initial research concerns maternal protein restriction in Wistar rats' offspring during lactation and tracheal extracellular matrix. We found an augmentation in tracheal elastic fibers concentration, measured by stereological method, of the malnourished rats, comparing to controls (fig. 1). Interestingly, augmentation in concentration of these fibers also occurs in the elderly; a population that is known to have a trachea with lesser elastic properties and more suitable to anastomotic problems when submitted to surgical procedures.[1] While this find could be interpreted as nonsense, it may be well explained by molecular characteristic of elastin: in the elderly, there are more elastic fibers, but the elastin is binding to calcium through cross-linked reactions. Therefore, the trachea in the elderly is less extensible and more difficult to manipulate during

surgical procedures.[1,4] If this augmentation in the elastic fibers leads to a tracheal tissue more prone to stenosis, malacia and other problems related to cicatricial process is not clear. Also, studies involving surgical procedures are necessary to evaluate the morphological tissue response to healing. Moreover, these findings about malnutrition and tracheal tissue alterations demonstrate the critical role of nutrition in tracheal tissue development, which has unique importance, given the prevalence of malnutrition among hospitalized patients and during childhood, especially in developing countries.[5]

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Nutrición Hospitalaria

Nutr Hosp. 2012;27(6):2148-2150
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

DOI:10.3305/nh.2012.27.6.6061

Cartas científicas

Influencia de las emociones en la ingesta y control de peso

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El propósito de esta carta ha sido presentar los resultados de un estudio longitudinal para mostrar como influyen las emociones en la ingesta y en el control del peso. Ha sido coordinado por el Colegio Oficial de Farmacéuticos de Madrid (Vocalía de Alimentación y Nutrición).

Es bien sabido que nuestras emociones tienen un efecto poderoso sobre nuestra elección de alimentos y sobre los hábitos alimentarios. Se ha encontrado evidencia empírica de que la influencia de las emociones sobre la conducta alimentaria es más fuerte en las personas obesas que en las no obesas y en personas que hacen dieta en relación a las personas que no hacen dieta[1].

También se ha sugerido que la emoción en sí misma no puede ser responsable de excesiva ingesta sino más bien, la verdadera causante del sobrepeso, es la forma en que la emoción es afrontada por la persona[2].

Solamente conociendo los factores emocionales podremos reforzar los hábitos saludables que nos permitan controlar el peso. Por todo ello en los comedores emocionales para controlar el sobrepeso y la obesidad se recomienda seguir una terapia cognitiva para controlar mejor las emociones, una dieta sana y practicar de ejercicio regularmente.

El objetivo de este trabajo ha sido estudiar y comparar la influencia de las emociones en la ingesta de personas sedentarias y de personas físicamente activas.

Estudiar las estrategias de control de peso que suelen utilizar dichas personas.

Estudio longitudinal, con adultos sedentarios que piden ayuda en oficina de farmacia (OF) para perder peso. Intervención nutricional durante 6 meses. Para comparar se ha incluido grupo de cicloturistas de Campus de ciclismo Calpe2012. (www.echozas.com).

Encuesta "Comedor Emocional" (Garaulet M., 2010)[3] consistente en la respuesta a 10 preguntas (cada pregunta se ha evaluado entre 0 y 3) La puntuación acumulada permite clasificar en: Comedor Poco emocional (0-9 puntos); Moderadamente emocional(10-19 puntos); Muy emocional. (20-30 puntos).

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Recibido: 15-VII-2012.
Aceptado: 7-VIII-2012.

Han aceptado participar 41 personas sedentarias y 25 Cicloturistas activos físicamente.

Datos antropométricos

Personas sedentarias de edad = 53,9 ± 12,4 años, IMC = 33,6 ± 4,9 kg/m^2. Con 10 hombres y 31 mujeres. Cicloturistas de edad = 46,4 ± 9,1, IMC = 24,2 ± 2,5 kg/m^2. 25 todos hombres.

Tabla I
Datos antropométricos

	N	*Peso kg media ± DE*	*IMC kg/m^2 media ± DE*	*Perímetro de cintura (cm) media ± DE*
Personas sedentarias				
Total	41	87,5 ± 14,5	33,6 ± 4,9	104,5 ± 11,9
Hombres	10	101,6 ± 12,5	35.0 ± 4,1	114 ± 12,9
Mujeres	31	82,9 ± 13,5	33,2 ± 4,8	101 ± 9,9
Cicloturistas				
Total (todos hombres)	25	73,2 ± 10,5	24,2 ± 2,5	87,2 ± 3,5

DE = Desviación Estándar.

Como se muestra en los datos antropométricos los cicloturistas están en el normopeso, mientras que las personas sedentarias están en sobrepeso y obesidad.

El 10% de los hombres tienen IMC < 25, el 90% tienen IMC ≥ 25. El 3% de las mujeres tienen IMC < 25, el 97% tienen IMC ≥ 25. También se deduce por el perímetro de cintura que las personas sedentarias que tienen excesiva grasa abdominal (mucho mayor que la referencia de 88 cm para mujeres y 102 cm para hombres).

Se ha encontrado que el 64% de los cicloturistas tienen IMC < 25, mientras que solamente el 36% tienen IMC ≥ 25. Es decir hay mayor porcentaje con IMC < 25 en los cicloturistas, que en los hombres y mujeres sedentarios.

Perdida de peso ha dependido de su IMC y de su puntuación de comedor emocional

Si clasificamos al colectivo en tres Grupos según su IMC y observamos la perdida de peso en la intervención nutricional de 6 meses; se muestra que *cuanto más*

bajo era el IMC menor ha sido la perdida de peso (desde Sobrepeso con perdida de 5,7 kg, hasta Obesidad tipo 2,3 con perdida de 8,1 kg). La diferencia de perdida de peso entre el Sobrepeso y el Obesidad tipo 2,3 ha sido estadísticamente significativa ($p < 0,001$).

Tabla II
Pérdida de peso en la intervención nutricional según IMC

Grupos de personas sedentarias	*Porcentaje del colectivo sedentario*	*IMC kg/m² media ± DE*	*Pérdida peso en kg media ± DE*
Sobrepeso	22%	28 ± 1.6	5,7 ± 1,2
Obesidad tipo 1	45%	31 ± 1.4	7,2 ± 4,2
Obesidad tipo 2, 3	28%	40 ± 2.9	8,1 ± 2,2

DE = Desviación Estándar.

Si clasificamos al colectivo en tres Grupos según su puntuación de comedor emocional y observamos la perdida de peso en la intervención nutricional, se muestra que *cuanto mayor ha sido la puntuación emocional, menor ha sido la perdida de peso* (desde Poco emocional con perdida de 8,9 kg, hasta Muy emocional con perdida de 5,8 kg. La diferencia de perdida de peso entre el Poco emocional y el Muy emocional ha sido estadísticamente significativa ($p < 0,01$).

Tabla III
Pérdida de peso en la intervención nutricional según puntuación emocional

Grupos de personas sedentarias	*% del colectivo*	*Puntuación emocional media ± DE*	*Pérdida peso (kg) media ± DE*	*% del colectivo que desayuna*
Poco emocional	20%	8 ± 2,8	8,9 ± 1,2	100
Moderadamente	39%	12 ± 3,8	7,3 ± 2,3	89
Muy emocional	40%	17 ± 4,8	5,8 ± 3,2	73

DE = Desviación Estándar.

Diferencias de ingesta emocional entre los diferentes colectivos

En sedentarios la puntuación emocional ha sido 13,4 ± 5,3 puntos. En cicloturistas de 7,1 ± 3,7, lo que muestra que son menos emocionales en su ingesta ($p < 0,001$).

Existen factores emocionales que nos desinhiben y hacen que comamos mucho mas de lo debido, como por ejemplo cuando estamos cansados del trabajo, en situaciones de ansiedad o problemas. Contrariamente tenemos sentimientos de culpa por ejemplo al pesarnos y ver que hemos ganado peso, estas emociones actúan como freno a la ingesta excesiva y nos protegen del sobrepeso. Pero existen alimentos como el chocolate a los que no nos podemos resistir. El control de nuestro peso es el resultado de todo ello y cada persona utiliza estrategias para controlar su peso como dietas hipocalóricas, ejercicio físico o ambas cosas.

El factor emocional más influyente en hombres y mujeres sedentarios ha sido: Desinhibición en la comida y Antojos por ciertos alimentos como chocolate y pastelería. Sin embargo en cicloturistas las emociones de culpabilidad como el miedo a la báscula y comer dulces, han tenido mas influencia que las emociones de Desinhibición en la comida.

Diferencias en hábitos dietéticos y práctica regular de ejercicio físico

Las personas desarrollan conductas diferentes en respuesta a sus emociones dependiendo del medio ambiente socioeconómico donde viven y de su formación y como resultado pueden controlar mejor o peor su peso.

Los deportistas en general y los ciclistas en particular suelen hacer deporte en primer lugar porque les gusta y en segundo lugar para controlar el peso y por motivos de salud[4].

Los deportistas activos pueden variar el volumen y la intensidad de su entrenamiento para regular su peso y perder los kg que hayan ganado en determinadas circunstancias. Las personas sedentarias tienen que adoptar otras estrategias, como recurrir periódicamente a dietas hipocalóricas o de lo contrario acaban con sobrepeso y obesidad.

Se ha observado que cuanto más emocional es la persona en su ingesta, mas se salta el desayuno. Los cicloturistas desayunan habitualmente.

La media de tiempo dedicado al ejercicio físico de ocio en las personas sedentarias es de una hora y media a la semana.

Los cicloturistas por el contrario es de quince horas a la semana (10 veces mas que el de los sedentarios) y ha sido mayor el tiempo dedicado, cuanto menor es el IMC del cicloturista.

Se ha observado que cuando los cicloturistas han constatado que estaban aumentando su peso, han realizado mas volumen de ejercicio físico y con mas intensidad, como estrategia para controlar su peso.

Conclusiones

Las conclusiones más significativas han sido:

- A menor IMC mejor control emocional de la ingesta.
- A mayor puntuación emocional, menor cantidad de peso perdido.
- Las mujeres han sido mas influenciadas por sus emociones que los hombres.
- La estrategia de control de peso de personas sedentarias fue recurrir a dietas hipocalóricas. Los cicloturistas por el contrario lo hacen controlando la cantidad de ejercicio que realizan.

Las diez preguntas de la Encuesta "Comedor Emocional" de Garaulet M. y en Negrita el colectivo que más puntuación ha obtenido

1. ¿La báscula tiene un gran poder sobre ti? ¿es capaz de cambiar tu estado de humor? **Mujeres y cicloturistas**
2. ¿Tienes antojos por ciertos alimentos específicos? **Mujeres y hombres sedentarios**
3. ¿Te cuesta parar de comer alimentos dulces, especialmente chocolate? **Mujeres y cicloturistas**
4. ¿Tienes problemas para controlar las cantidades de ciertos alimentos? **Mujeres y hombres sedentarios**
5. ¿Comes cuando estás estresado, enfadado o aburrido? **Mujeres y hombres sedentarios**
6. ¿Comes más de tus alimentos favoritos, y con más descontrol, cuando estás solo? **Mujeres y hombres sedentarios**
7. ¿Te sientes culpable cuando tomas alimentos "prohibidos", es decir, aquellos que crees que no deberías, como los dulces? **Mujeres**
8. Por la noche, cuando llegas cansado de trabajar ¿es cuando más descontrol sientes en tu alimentación? **Hombres sedentarios**
9. Estás a dieta, y por alguna razón comes más de la cuenta, entonces piensas que no vale la pena y ¿comes de forma descontrolada aquellos alimentos que piensas que más te van a engordar? **Mujeres y hombres sedentarios**
10. ¿Cuántas veces sientes que la comida te controla a ti en vez de tú a ella? **Hombres y mujeres sedentarios**

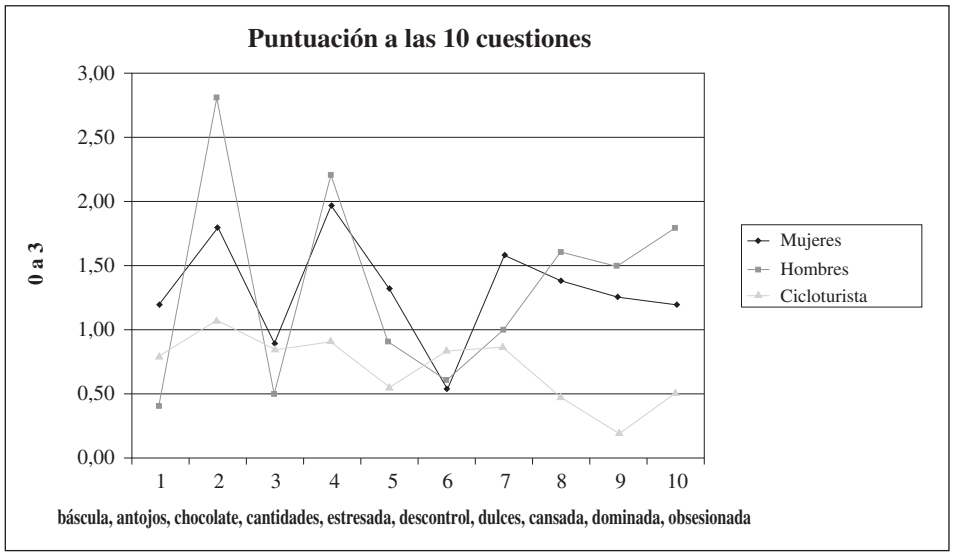


Fig. 1.—Puntuación a las 10 cuestiones de Comedor emocional.

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Nutr Hosp. 2012;27(6):2151-2152
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

DOI:10.3305/nh.2012.27.6.6141

Cartas científicas

The effect of vitamin A supplementation on retinol concentrations of children with anaemia

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Iron deficiency seems to impair vitamin A metabolism leading to an increase in retinol sequestration to the liver and/or impairment in the activity of hepatic retinyl ester hydrolases, decreasing vitamin A mobilization and blood concentration.[1] Such observations led to speculations regarding the efficacy of vitamin A supplementation in regions where iron deficiency coexist. In Brazil, a risk country for subclinical vitamin A deficiency —VAD, the Health Ministry implemented a supplementation programme— administration of mega doses of vitamin A (200,000 IU) to children ages 6 months-5 years in underprivileged regions.[2] This study aimed to evaluate the impact of vitamin A supplementation on anaemia of VAD children, 36-83 months, from Teresina city, Brazil. Excluded from the study were children who had received transfusions of blood/blood derivatives and iron and/or vitamin A supplements in the last 6 months, children under immunosuppressive or corticosteroid therapy, and with HIV infection, chronic diseases or severe infection. An adequate zinc status was inclusion criteria, according to serum zinc (atomic absorption spectrophotometry) and alkaline phosphatase (fluorescence) concentrations. Serum retinol, ferritin and haemoglobin-Hb were determined by HPLC, chemiluminescence and a haematological analyzer, respectively. The children received 200 000IU of vitamin A, and after two months, vitamin A concentration was determined again. The cut off points used to identify deficiencies were: retinol < 0.70 µmol/L; Hb < 110 g/L; ferritin < 12 g/dL. Difference between means was tested by the Mann-Whitney test, and correlations were determined by the Spearman's correlation coefficient. Forty eight children with VAD were included in the study; 60.42% of them were boys. Mean (SD) concentrations of retinol and Hb before supplementation were 0.52 (0.13) µmol/L and 113.42 (15.04) g/L, respectively, without difference between gender. Concomitant vitamin A deficiency and anaemia were observed in 25% of the children, reinforcing the knowledge that iron and vitamin A deficiencies are important nutritional problems in Brazil.[3] After supplementation all children reached acceptable/normal retinol concentrations [1.82 (0.82) µmol/L]. Retinol concentrations before, after and after/before difference was similar in children with and without anaemia (table I). The increase of retinol concentrations after supplementation suggests the efficacy of the intervention in the recovery of this vitamin deficiency, as reported in another study,[4] independent of anaemia. A study involving rats supplemented with iron and vitamin A showed a significant increase in retinol concentrations of those rats compared to controls.[5] Despite the limitations of our study, it confirms the efficacy of vitamin A supplementation in populations with adequate zinc status and high prevalence of anaemia.

Table I
Mean (standard deviation) concentrations of serum retinol, according to haemoglobin (Hb) concentrations in preschool children (n = 48)

Variables	*Hb < 110 g/L mean (SD) n = 12*	*Hb ≥ 110 g/L mean (SD) n = 36*	*P value[(1)]*
Serum retinol (µmol/L)			
Before supplementation	0.50 (0.12)	0.54 (0.14)	0.167
After supplementation	2.08 (1.00)	1.74 (0.73)	0.317
After/before difference	1.59 (1.04)	1.19 (0.75)	0.238

[(1)]Mann-Whitney test.

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Recibido: 11-VI-2012.
1.ª Revisión: 30-VIII-2012.
Aceptado: 2-IX-2012.

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DOI:10.3305/nh.2011.27.6.????

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