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Nutrición Hospitalaria

ÓRGANO OFICIAL DE LA SOCIEDAD ESPAÑOLA DE NUTRICIÓN PARENTERAL Y ENTERAL
ÓRGANO OFICIAL DE LA SOCIEDAD ESPAÑOLA DE NUTRICIÓN
ÓRGANO OFICIAL DE LA FEDERACIÓN LATINO AMERICANA DE NUTRICIÓN PARENTERAL Y ENTERAL
ÓRGANO OFICIAL DE LA FEDERACIÓN ESPAÑOLA DE SOCIEDADES DE NUTRICIÓN, ALIMENTACIÓN Y DIETÉTICA

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Esta publicación recoge revisiones y trabajos originales, experimentales o clínicos, relacionados con el vasto campo de la nutrición. Su número extraordinario, dedicado a la reunión o Congreso Nacional de la Sociedad Española de Nutrición Parenteral y Enteral, presenta en sus páginas los avances más importantes en este campo.

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Nutrición Hospitalaria

Nutrición Hospitalaria, es la publicación científica oficial de la Sociedad Española de Nutrición Parenteral y Enteral (SENPE), de la Sociedad Española de Nutrición (SEN), de la Federación Latino Americana de Nutrición Parenteral y Enteral (FELANPE) y de la Federación Española de Sociedades de Nutrición, Alimentación y Dietética (FESNAD).

Publica trabajos en castellano e inglés sobre temas relacionados con el vasto campo de la nutrición. El envío de un manuscrito a la revista implica que es original y no ha sido publicado, ni está siendo evaluado para publicación, en otra revista y deben haberse elaborado siguiendo los Requisitos de Uniformidad del Comité Internacional de Directores de Revistas Médicas en su última versión (versión oficial disponible en inglés en http://www.icme.org; correspondiente traducción al castellano en: http://www.metodo.uab.es/enlaces/Requisitos_de_Uniformidad_2006.pdf).

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Cada parte del manuscrito empezará una página, respetando siempre el siguiente orden:

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En la parte inferior se especificará el número total de palabras del cuerpo del artículo (excluyendo la carta de presentación, el resumen, agradecimientos, referencias bibliográficas, tablas y figuras).

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Será estructurado en el caso de originales, originales breves y revisiones, cumplimentando los apartados de Introducción, Objetivos, Métodos, Resultados y Discusión (Conclusiones, en su caso). Deberá ser comprensible por sí mismo y no contendrá citas bibliográficas.

Encabezando nueva página se incluirá la traducción al inglés del resumen y las palabras clave, con idéntica estructuración. En caso de no incluirse, la traducción será realizada por la propia revista.

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Debe incluirse al final de resumen un máximo de 5 palabras clave que coincidirán con los Descriptores del Medical Subjects Headings (MeSH): http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=mesh

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Se deben citar aquellas referencias bibliográficas estrictamente necesarias teniendo en cuenta criterios de pertinencia y relevancia.

En la metodología, se especificará el diseño, la población a estudio, los métodos estadísticos empleados, los procedimientos y las normas éticas seguidas en caso de ser necesarias.

1.7 Anexos

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▶▶▶

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El contenido será autoexplicativo y los datos no deberán ser redundantes con lo escrito. Las leyendas deberán incluir suficiente información para poder interpretarse sin recurrir al texto y deberán estar escritas en el mismo formato que el resto del manuscrito.

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- Título
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- Texto máximo 400 palabras
- Una figura o una tabla
- Máximo cinco citas

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Tipo de artículo	Resumen	Texto	Tablas y figuras	Referencias
Original	Estructurado 250 palabras	Estructurado 4.000 palabras	5	35
Original breve	Estructurado 150 palabras	Estructurado 2.000 palabras	2	15
Revisión	Estructurado 250 palabras	Estructurado 6.000 palabras	6	150
Notas clínicas	150 palabras	1.500 palabras	2	10
Perspectiva	150 palabras	1.200 palabras	2	10
Editorial	–	2.000 palabras	2	10 a 15
Carta al Director	–	400 palabras	1	5

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Nutrición Hospitalaria

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Editorial

Bienvenida al nuevo gestor de contenidos de Nutrición Hospitalaria

Jesús M. Culebras[1] y Abelardo García de Lorenzo[2]

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Como ya anticipábamos en nuestro Editorial de octubre de 2013[1], NUTRICION HOSPITALARIA, en un continuo esfuerzo por adaptarse a los nuevos tiempos y modernizarse, ha estrenado el año con un nuevo Gestor de Contenidos Web.

La antigua plataforma, a la que agradecemos los servicios prestados, ha pasado a mejor vida.

Durante años ha sido de gran utilidad pero había llegado el momento de que gozase de un merecido descanso ya que es bien cierto que en los últimos tiempos, y debido a su clara obsolescencia, adolecía de importantes carencias entre las cuales y por no extendernos citaremos solamente las dos más importantes:

– No funcionaba de forma correcta con todos los navegadores Web. Solamente era operativa al 100% en *Internet Explorer*, navegador que en los últimos años había perdido el monopolio de que gozó tradicionalmente a favor de otros navegadores, hasta el punto de que incluso ya ni siquiera era el mayoritario puesto que en mayo de 2013 había perdido en favor de *Google Chrome*, como se puede apreciar en la figura 1.
– Los archivos enviados a la plataforma en versiones de *Office* posteriores a la versión 2003 quedaban gravemente dañados, obligando a intentar recuperarlos posteriormente o a pedir a los autores que los enviasen en otros formatos. Este problema, dado que cada vez es más frecuente la utilización por parte de los autores de versiones posteriores a Office 2003, era así mismo un importante hándicap, al igual que el punto indicado anteriormente.

Por estas razones llevábamos ya un tiempo estudiando la posibilidad de acometer la implantación de un Nuevo Gestor de Contenidos. Para ello se analizaron en principio dos vías:

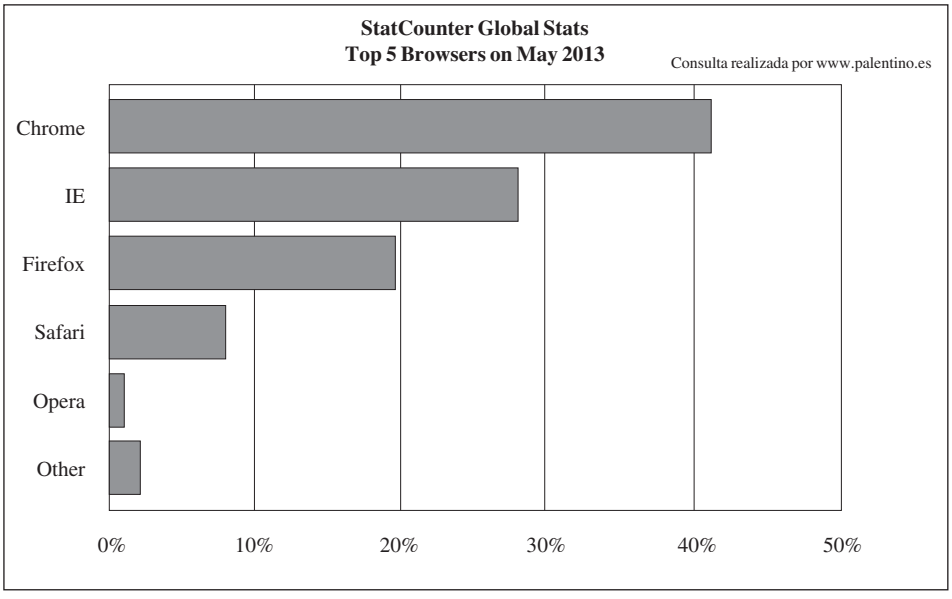


Fig. 1.—Porcentaje de utilización de Navegadores Web. Mayo 2013.

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Aceptado: 2-III-2014.

– Un desarrollo propio a medida
– La adquisición de alguno de los Gestores de Contenidos existentes en el mercado.

La primera de las dos opciones suponía un mayor tiempo de puesta en marcha y un coste inicial más elevado. Por el contrario la segunda implicaba unos costes de licencia anuales que, a la larga, suponían un sobrecoste adicional importante además de conllevar una dependencia del proveedor.

Durante el proceso de búsqueda encontramos Open Journal System, que aportaba las ventajas de las dos opciones mediante una inteligente solución: un esqueleto con las principales funciones necesarias en el Gestor de Contenidos, en código libre y gratuito, totalmente personalizable y sin costes posteriores de licencia. Como esta decisión parecía un poco arriesgada, contaremos con mayor detalle lo que hay detrás de esta opción.

Open Journal System (en adelante OJS) es un sistema de gestión y publicación de revistas que ha sido desarrollado por el organismo *Public Knowledge Project* (en adelante PKP) con fondos del Gobierno Federal de Canadá para ampliar y mejorar el acceso a la investigación. El proyecto PKP, comienza a gestarse en 1989 en la Universidad de la Columbia Británica (UCB) y la primera versión del software operativo es lanzada en 2001, estando desde entonces en continua evolución.

El software es de acceso libre, es decir, no hay un coste de licencia y cualquier editorial o revista puede descargar y utilizar el software teniendo acceso a las futuras actualizaciones del mismo. El coste anual estimado para el continuo desarrollo de la herramienta, según PKP es de un millón de dólares. En la actualidad el soporte económico y técnico a este proyecto es el siguiente.

Socios principales

– California Digital Library
– Ontario Council of University Libraries
– Simon Fraser University Library
– Stanford University School of Education
– University of British Columbia
– University of Pittsburgh Library

Además de estos socios principales hay una estructura de apoyo formada por los siguientes tipos de patrocinadores (*sponsors*):

– Platinum Sponsors ($15,000)
– Gold Sponsors ($10,000)
– Silver Sponsors ($5,000)
– Bronze Sponsors ($2,500)
– Friends of PKP (hasta $2,500)

Dentro de cada una de estas categorías se encuentran importantes universidades. Para más información a este respecto, se puede visitar:

http://pkp.sfu.ca/sponsorships

En la figura 2 se muestra la evolución del número de usuarios de OJS. En la figura 3 aparece la distribución de usuarios por continente. Los datos con que se elaboran estos gráficos se obtienen de forma automática a través de las instalaciones que los usuarios realizan de OJS.

En España –por ejemplo– lo utilizan para sus publicaciones varias universidades, como las de Salamanca, Granada o Murcia y organismos como el Centro Superior de Investigaciones Científicas (CSIC). El CSIC lo podemos ver como ejemplo de instalación en http://revistas.csic.es/ porque edita más de 30 revistas con OJS:

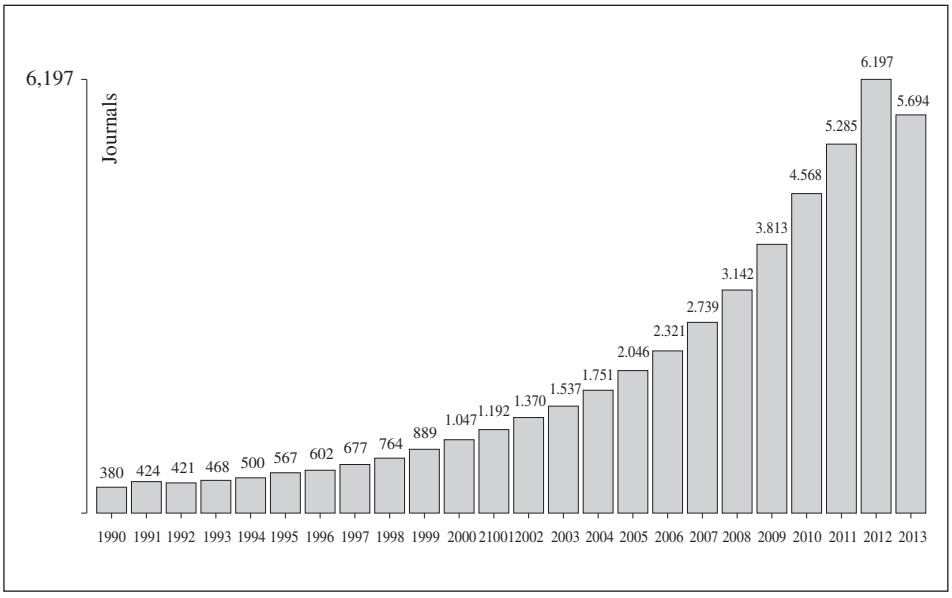


Fig. 2.—Revistas que usan OJS-Número total de revistas. Este cuadro muestra las revistas que usan (OJS) para publicación online hasta finales de 103. Cada año solamente muestra las revistas con contenido publicado ese año. Las cantigades no muestran las instalaciones totales de OJS (muchas revistas solo muestran contenido anterior sin actualizar contenidos, saltan algún año, o dejan de publicar on line).

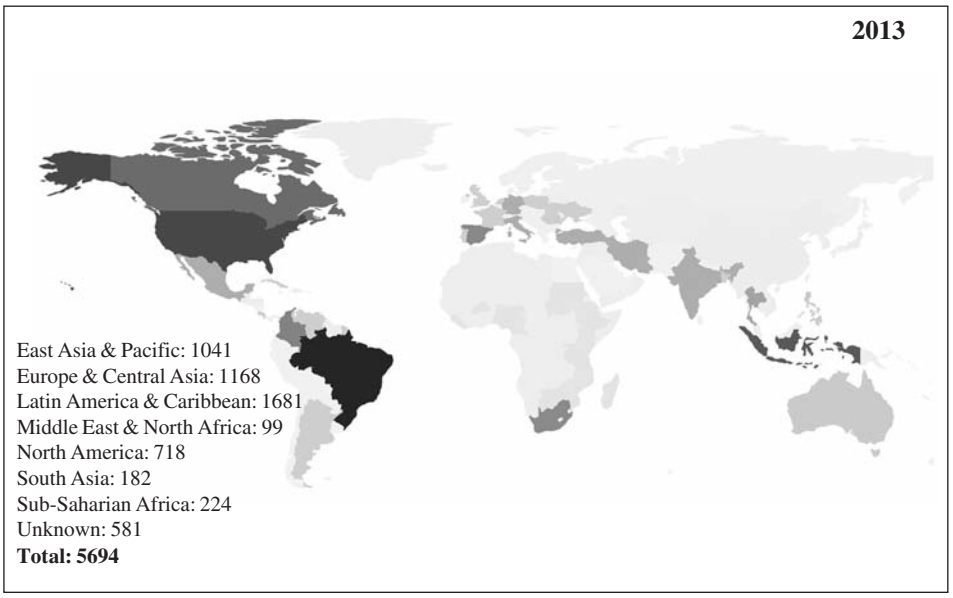


Fig. 3.—Revistas que usan OJS-Distribución por continentes. Este cuadro muestra las revistas que usan (OJS) para publicación online hasta finales de 2013. Cada año solamente muestra las revistas con contenido publicado ese año. Las cantidades no muestran las instalaciones totales de OJS (muchas revistas solo muestran contenido anterior sin actualizar contenidos, saltan algún año, o dejan de publicar on line).

OJS es un software desarrollado especialmente para la gestión y publicación del contenido de revistas científicas. Está desarrollado según la filosofía *Open Source*, es decir, que los usuarios tienen acceso libre, completo y gratuito al software y sus futuras actualizaciones. Permite su utilización para una o varias revistas. Al tener libre acceso al código, permite su configuración y adaptación a las necesidades de cada revista. Utiliza distintos perfiles de usuario con acceso a las distintas funciones: Autor, Revisor, Editor, Administrador, etc., asignando a los usuarios el perfil que le corresponda y, en función de esta asignación, definiendo que es lo que puede hacer cada usuario. Soporta todos los puntos del proceso editorial, desde el envío inicial del artículo por parte del autor a la edición final del artículo una vez aprobado para su publicación. La basta red de usuarios que lo utilizan es una garantía del buen funcionamiento del software y de su validez para gestionar todo el proceso editorial de una revista. Así mismo este gran número de usuarios, distribuidos por todo el mundo, y la estructura financiera que soporta el proyecto, dan una seguridad respecto a su continuidad en el futuro. En cualquier caso y aun cuando esto no fuese, disponer de todo el código permite la continuidad de su utilización y su modificación.

Tras analizar todas estas características, la decisión final fue adoptar OJS como solución de futuro. Tras 6 meses de adaptación y personalización y el oportuno traspaso de datos entre los dos sistemas, al final estrenamos el año con nuestro nuevo gestor de contenidos. El cambio ha sido algo traumático, como lo son todos los cambios, pero no tenemos la menor duda de que hemos hecho una apuesta de futuro y que, pasado este periodo inicial de adaptación, notaremos la mejora. Pedimos a los lectores y contribuyentes de NUTRICIÓN HOSPITALARIA paciencia y comprensión durante esta fase de adaptación, al tiempo que nos ponemos a disposición de quien necesite nuestra ayuda.

Referencias

1. Jesús M. Culebras, Ángeles Franco-López, Abelardo García de Lorenzo. Un año más la revista Nutrición Hospitalaria aumenta sus contenidos, su visibilidad y su mpacto. *Nutr Hosp* 2013; 28 (5): 1361-4.

Nutrición Hospitalaria

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Revisión

Cortisol salival como indicador de estrés fisiológico en niños y adultos; revisión sistemática

M. J. Aguilar Cordero[1], A. M. Sánchez López[2], N. Mur Villar[3], I. García García[4], M. A. Rodríguez López[5], A. Ortegón Piñero[6] y E. Cortes Castell[7]

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Resumen

El cortisol salival es una hormona esteoridea producida en el eje hipotálamo-pitutitario-adrenal que se segrega en la saliva, sobre todo cuando las personas se estresan. Un nivel elevado de cortisol en saliva puede ser producido por muchos factores diferentes, entre los que se encuentran algunas alteraciones, como la obesidad y otras afecciones psicológicas. Los artículos seleccionados para ser incluidos en esta revisión se tomaron de Google Scholar y Medline, y con un total de 57 artículos. La validez de los mismos viene dada por el grado de evidencias demostrado, por las recomendaciones allí recogidas y por la aplicabilidad a nuestro contexto. En esta revisión se han considerado los estudios que investigan el cortisol salival y el estrés en niños y adultos. También se han tenido en cuenta los que relacionan unos niveles altos de cortisol salival con otras alteraciones, como ansiedad, TDAH, fobia social o la carencia afectiva. Los estudios demuestran que el cortisol salival es un claro indicador de estrés, tanto en niños como en adultos. Las principales consecuencias de un alto nivel de esta hormona en la saliva son las siguientes: reducción de la función inmunológica, que afecta a la cicatrización y, como consecuencia, a un mayor tiempo de recuperación. También se relaciona con un déficit en el crecimiento físico de los niños, así como con un aumento de la presión arterial y de la frecuencia cardíaca, tanto en niños como en adultos.

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Palabras clave: *Cortisol. Saliva. Estrés. Estrés fisiológico.*

SALIVARY CORTISOL AS AN INDICATOR OF PHYSIOLOGICAL STRESS IN CHILDREN AND ADULTS; A SYSTEMATIC REVIEW

Abstract

Salivary cortisol is a steroid hormone that is produced in the hypothalamic-pituitary-adrenal axis and secreted into saliva when persons are under stress. High levels of cortisol in saliva can be produced by many different factors, including obesity and certain psychological disorders. The articles selected for inclusion in this review were identified using Google Scholar and Medline, and this search obtained a total of 57 items. The validity of these studies was established according to the degree of evidence presented, by citations and by their applicability to the healthcare context in Spain. Specifically, this review takes into consideration studies of salivary cortisol and stress in children and adults, and those examining the relation between high levels of salivary cortisol and other disorders such as anxiety, attention-deficit/hyperactivity disorder, social phobia or emotional deprivation. These studies show that salivary cortisol is a clear indicator of stress in both children and adults. High levels of this hormone in saliva are associated with the following main consequences: reduced immune function, affecting healing and thus prolonging recovery time; delayed growth in children; increased blood pressure and heart rate in both children and adults.

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Key words: *Cortisol. Saliva. Stress. Physiological stress.*

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Introducción

El estrés se define como la percepción de una dificultad o incapacidad para dominar ciertas demandas que conlleva una activación fisiológica y conductual características, equiparándose a cualquier situación que desborde los recursos de un individuo, como ocurre con la ansiedad, las preocupaciones, la irritabilidad, etc[1,2]. El estrés es un término genérico que designa a los síntomas divergentes, como latidos rápidos del corazón, mareos, dolores, nerviosismo, agitación, irritabilidad, preocupación, problemas de concentración y mal humor. Todos estos síntomas se conocen como estrés y sugiere que reflejan un mecanismo subyacente único.

Los índices fisiológicos de estrés son más difíciles de evaluar que los de carácter psicológico. El estrés percibido a menudo es la medida inicial de la valoración de los estados de estrés, tanto en la investigación como en la práctica clínica[3]. La medición de la actividad del eje hipotalámico-pituitario-adrenal (HPA), que mide el estrés, se puede realizar de forma no invasiva a través de la recolección de cortisol en la saliva mediante el método ELISA[4-7]. En la actualidad, la valoración del estrés se efectúa mediante la medición del cortisol en una muestra de saliva. La evaluación del estrés percibido también se puede llevar a cabo por medio de una evaluación psicológica, con test validados para ese fin.

El eje hipotalámico-pituitario-adrenal (Eje HPA) es un conjunto complejo de influencias directas e interacciones retroalimentadas entre el hipotálamo, una parte del cerebro hueca con forma de fuelle, la glándula pituitaria, una estructura en forma de haba localizada bajo el hipotálamo y la glándula adrenal o suprarrenal, una glándula pequeña, pareada y de forma piramidal localizada en la parte superior de los riñones. Las interacciones homeostáticas finas entre estos tres órganos constituyen el eje HPA, una parte esencial del sistema neuroendocrino que controla las reacciones al estrés[8].

Con la respuesta fisiológica al estrés se liberan glucocorticoides en el torrente sanguíneo a través del citado eje HPA, especialmente cortisol, el glucocorticoide más activo[9,10]. La liberación de cortisol es pulsátil, su regulación es genética y ambiental, e influyen en ella el ciclo sueño vigilia y la percepción del propio estrés[1,11]. La hormona cortisol, en condiciones normales, muestra un marcado ritmo circadiano, con un incremento que oscila entre el 50 y el 75% durante los 30 minutos siguientes al despertar, seguido de un descenso abrupto inmediato, que se hace luego gradual a lo largo del resto del día, hasta alcanzar un mínimo por la noche[12]. El aumento al despertar tiene carácter genético, mientras que la variabilidad en el descenso a lo largo del día se relaciona con las influencias ambientales. En condiciones fisiológicas estables, este ritmo se presenta con una significativa regularidad, pues no se ve afectado por la edad, el género, la etapa de desarrollo o la composición corporal[13,14]. Se ha sugerido que la respuesta matutina de la secreción de cortisol salival sea un indicador de estrés crónico o bien depresión[15-22]. Asimismo, variaciones de cortisol a lo largo del día pueden ser un indicador de un estado de ánimo negativo o de un elevado estrés percibido[1,23,24]. Una mayor duración del sueño se puede relacionar con una secreción de cortisol más dinámica[25].

Las consecuencias negativas de un funcionamiento anormal del eje HPA suelen ser mayores durante la infancia[26,27]. Una considerable evidencia ha sugerido que el estrés psicosocial puede afectar a una variedad de funciones inmunes, a través de procesos neuroendocrinos, tales como la activación del eje HPA o el sistema adrenérgico[28-30]. Funciones inmunitarias reguladas por el sistema neuroendocrino también incluyen procesos inmunes pertinentes, tales como la secreción de anticuerpos, función de las células T helper, o reactividad de los macrófagos o eosinófilos[31-34]. La hipersecreción de cortisol ha sido observada como una vía fisiológica relacionada con los efectos del estrés crónico, es decir, con resultados nocivos para la salud por la reducción de la eficacia inmunológica[35,36]. Con el tiempo, la hipersecreción de cortisol puede dar lugar a que, en función de la sensibilidad a la retroalimentación[37], la salida HPA rebote a niveles inferiores a los normales[38]. La hiposecreción de cortisol y la desinhibición concomitante de la respuesta inmune ha sido apreciada como una vía fisiológica que vincula el estrés de larga duración con una serie de trastornos relacionados con la fatiga corporal y el agotamiento[39,40].

Metodología

Diseño

Revisión sistemática

- Selección de los estudios y estrategia de búsqueda

Los artículos de la presente revisión se identificaron a través de la búsqueda automatizada en las bases de datos de los motores de búsqueda Google Scholar y Medline, a los que se añadieron artículos y libros propios. La revisión se efectuó durante los meses de junio a noviembre de 2013.

Se combinaron las palabras claves: cortisol salival, estrés fisiológico, niños, adultos, Salivary cortisol, physiological stress, kids, adults según la pagina: decs.bvs.br./ E / homepage.htm

Para la búsqueda de bibliografía se utilizaron los siguientes métodos:

– Análisis de documentos, que permitió extraer la información más relevante y separarla en elementos constituyentes.
– Síntesis de la información, lo que hizo posible la ordenación y combinación de la información extraída y la evaluación comparativa.

Concluida la búsqueda, se estableció una selección de los artículos que debían incluirse en la revisión. Para

ello, se consideró de utilidad y con relevancia para nuestro tema, la credibilidad y experiencia de los autores en la temática; también se analizó en el resumen la aplicabilidad de los resultados al tema de estudio.

El número total de referencias identificadas por los diferentes medios fue de 1800. Como resultado del proceso de búsqueda, se eligieron 57 estudios que cumplieron con los criterios de selección. A continuación, se procedió a la lectura crítica de todo el documento.

La validez de los artículos seleccionados estuvo dada por el grado de evidencias demostrado, por las recomendaciones que dejan los mismos y la aplicabilidad a nuestro contexto. La búsqueda se llevó a cabo por los autores de la investigación.

Resultados

Se evaluaron 57 artículos que cumplieron los criterios de selección. Del total, 41 estaban en idioma inglés y 16, en español. El análisis de la distribución geográfica pone de manifiesto la preocupación de la comunidad científica con el cortisol salival.

Los principales artículos seleccionados para esta revisión establecen que el cortisol salival es un indicador fiable del estrés fisiológico. También se asocia con problemas de ansiedad, con trastornos psicológicos y con algunas enfermedades, como la obesidad. En la tabla I se describen los artículos más relevantes incluidos en esta revisión.

A continuación, llevamos a cabo una breve descripción de los resultados y conclusiones de los principales estudios seleccionados.

Brydon realizó un estudio con 67 mujeres con edades comprendidas entre 18 y 25 años donde se examinó la relación entre la adiposidad, la leptina y las respuestas fisiológicas al estrés agudo en laboratorio. Se concluyó que existía una relación positiva entre la obesidad central y las diferencias individuales en las respuestas fisiológicas al estrés, de modo que las mujeres con una circunferencia de cintura mayor tenían mayores niveles plasmáticos de IL-1Ra y de leptina inducidas por el estrés[41].

El estudio realizado por Tarazona y cols. con 39 estudiantes (20 varones y 19 mujeres) con edades comprendidas entre 17 y 24 años determinó los efectos del estrés social agudo en el rendimiento de una tarea de atención sostenida y dividida. Los resultados mostraron que los niveles de cortisol sistémico aumentaban en los varones cuando realizaban el protocolo de inducción al estrés TSST (Trier Social Stress Test) mientras que en las mujeres no se encontraron diferencias significativas en los niveles de cortisol al efectuar esa prueba[42].

Vreeburg y cols. examinaron la asociación entre los diversos subtipos de trastornos de ansiedad y varios indicadores de cortisol en un gran estudio de cohortes con 342 participantes dell grupo control sin trastornos psiquiátricos, 311 personas en el grupo de estudio 1 con un trastorno de ansiedad remitido (fobia social, trastorno de ansiedad generalizada, trastorno de pánico), y 774 personas en el grupo de estudio 2 con un trastorno de ansiedad actual. Encontraron que los niveles de cortisol al despertar eran más altos en las personas con un trastorno de ansiedad actual y una significación marginal para las personas con ansiedad remitido, en comparación con los participantes del grupo control[15].

Pérez Lancho y cols. estudiaron un grupo de 42 estudiantes (22 chicos y 20 chicas) para analizar el nivel de estrés, en distintos momentos académicos, mediante la determinación del cortisol salivar. Este estudio estableció que los valores medios de cortisol en saliva dependían de la situación académica, con niveles mayores en la etapa final (próxima a los exámenes finales). En cuanto a la diferencia por sexos, las mujeres tuvieron valores más altos que los varones en las mismas etapas académicas[11].

Allwood y cols. seleccionaron un grupo de 56 niños sanos (7-16 años de edad) para realizar una investigación en donde examinar las diferencias individuales en la alfa-amilasa salival y la reactividad del estrés a través del cortisol salival, en relación con el ajuste conductual y emocional de los jóvenes. Los niveles de alfa-amilasa salival y cortisol aumentaron significativamente en las situaciones de estrés. Aunque la alfa-amilasa se mostró más sensible a los factores estresantes que el cortisol salival[6].

Lemmens y cols. investigaron los efectos del consumo de una comida rica en proteínas y alta en hidratos de carbono en la respuesta del cortisol salival. Los sujetos fueron 38 (19/19) con una edad media de 25 años. En este estudio se concluyó que el consumo de una dieta de harinas con diferentes contenidos de macronutrientes, es decir, de alto valor proteico y alta en hidratos de carbono, no influye en la respuesta fisiológica y psicológica del estrés. Aún así, los hombres mostraron una mayor respuesta del cortisol salival frente a las mujeres[43].

McBurnett y cols. evaluaron la relación entre los niveles de cortisol salival y la agresividad en 38 niños en edad escolar. La baja actividad del eje hipotalámico-pituitario-adrenal (cortisol salival) fue indicador de un nivel de agresividad grave y persistente en niños y adolescentes varones. Aunque la baja variabilidad de cortisol puede ser más indicativa de la agresividad persistente que una baja concentración de cortisol en un solo punto en el tiempo[44].

Camacho y cols. investigaron 160 estudiantes universitarios sanos de Zaragoza (España) y Guadalajara (Mexico) para ver si existen diferencias en los niveles de cortisol salival y si estas diferencias se pueden atribuir al estilo de vida diferente. Los resultados mostraron niveles superiores significativamente en cortisol salival de los estudiantes mexicanos con respecto a los estudiantes españoles. También se encontraron diferencias significativas en horas de sueño, hora del despertar y consumo de alcohol, pero no se pueden atribuir estas causas como las causantes de las diferencias en

Tabla I
Principales estudios que relacionan el cortisol salival con el estrés fisiológico

Artículo	*Lugar*	*Muestra*	*Método*	*Conclusiones*
Allwood MA et al. (2011)[6]	Nueva York, Estados Unidos	56 niños sanos (7-16 años)	Examen de las diferencias individuales en alfa-amilasa salival y la reactividad del estrés cortisol, en relación con el ajuste conductual y emocional de los jóvenes.	Alfa-amilasa salival es más sensible que el cortisol a los factores estresantes de laboratorio.
Bakker L et al. (2012)[26]	Buenos Aires, Argentina	10 niños con diagnóstico de TDAH y la muestra control integrada por 10 niños sin diagnóstico de TDAH	Consistió en evaluar posibles asociaciones entre el grado de percepción de estrés escolar y alteraciones en el ritmo circadiano de cortisol en niños con dignóstico de TDAH.	Los resultados obtenidos muestran que los niveles generales de percepción de estrés escolar en los niños con TDAH son significativamente más altos que en la muestra control.
Brydon L. (2010)[41]	Londres, Reino Unido	67 mujeres (18-25 años)	Se examinó la relación entre la adiposidad, la leptina y las respuestas fisiológicas al estrés agudo en el laboratorio.	Mujeres con una circunferencia de cintura mayor tenían más estrés y mayores niveles plasmáticos de IL-1Ra y de leptina.
Buske-Kirschbaum A et al. (1997)[34]	Trier, Alemania	16 niños sanos (9 niños y 7 niñas), con edades entre 9 y 14 años (edad media 12,4 años)	Relación entre la respuesta adrenocortica, l el estrés, la frecuencia cardíaca y los parámetros psicológicos de los niños con dermatitis atópica.	Los niños que sufren de AD muestran una reducción de los niveles de cortisol en respuesta a un estres psicosocial estandarizado.
Camacho, E. (2011)[45]	Guadalajara, México	160 estudiantes universitarios	Diferencias en los niveles de cortisol salival y si estas diferencias se pueden atribuir al estilo de vida.	Se encontraron diferencias significativas en horas de sueño, hora del despertar y consumo de alcohol.
Himani Kariyawasam S et al. (2002)[46]	Birmingham, Reino Unido	32 niños con comorbilidad TDAH y trastorno de oposición desafiante (ODD), en comparación con veinticinco controles sanos de la misma edad y origen étnico.	Se Propusimos determinar si el cortisol salival se reduciría en un grupo de niños con TDAH /ODD (trastorno de oposición desafiante) y para examinar el efecto de la medicación estimulante sobre dicha relación.	Los resultados apoyan la posibilidad de una disfunción del control del eje HPA en estos niños con trastornos conductuales.
Krämer M et al. (2011)[47]	Friburgo, Alemania	41 niños con fobia social y 40 niños sanos (8-12 años).	Diferencias entre los niños sanos de los niños con fobia social, no sólo en términos de la ansiedad subjetiva, sino también sobre las medidas de estrés autonómicas y endocrinas.	Los niños con fobia social mostraron reactividad elevada sobre la ansiedad subjetiva en comparación con los niños sanos, pero no una reactividad elevada de la frecuencia cardiaca, alfa-amalisa salival o cortisol.
Lemmens SG et al. (2011)[43]	Wageningen, Países Bajos	38 sujetos (19m/19f, edad=25 ± 9 años, IMC=25,0 ±3,3 kg/m^2).	Efectos del consumo de una dieta rica en proteínas frente a otra rica en hidratos de carbono y la respuesta del cortisol.	El consumo de harinas con diferentes contenidos de macronutrientes, es decir, de alto valor proteico frente a la alta en hidratos de carbono, no influye en la respuesta fisiológica y psicológica diferente.

Tabla I (cont.)
Principales estudios que relacionan el cortisol salival con el estrés fisiológico

Artículo	*Lugar*	*Muestra*	*Método*	*Conclusiones*
Lovell B et al. (2011)[40]	Newcastle, Reino Unido	35 participantes del sexo femenino (Edad media = 9.22 años)	Este estudio investigó si los patrones diferenciales de la secreción de cortisol en parte podría mediar en las diferencias relacionadas con el estrés percibido en los problemas de salud comunes en individuos jóvenes y sanos.	Los participantes que reportaron mayores niveles de percepción de estrés muestran una elevación de la producción media diurna de cortisol, impulsada por la hiperactividad del eje HPA durante la noche.
Mangold D et al. (2011)[48]	San Antonio, Estados Unidos	55 sujetos mexicanos de entre 18 y 38 años, sin diagnóstico de depresión clínica.	Se evaluó la medida en que el despertar de respuesta del cortisol (CAR) predice la sintomatología depresiva subclínica más allá de la influencia de los traumas de la infancia.	Los análisis muestran la atenuación de la subida inicial del cortisol en el despertar. Era el mejor predictor de mayor sintomatología depresiva subclínica, más allá de la influencia de un trauma de origen mexicano.
McBurnett K et al. (2000)[44]	Chicago, Estados Unidos	38 niños en edad escolar	Relación entre los niveles de cortisol salival y la agresividad, mediante la recopilación de los síntomas del trastorno de comportamiento perturbador en 4 evaluaciones clínicas anuales.	La baja actividad del eje hipotalámico-pituitario-adrenal es un indicador de agresividad grave y persistente en niños y adolescentes varones.
Oldehinkel AJ et al. (2011)[3]	Groningen, Holanda	715 adolescentes (niñas, el 50,9%, con una edad media de 16,11 años)	Evaluar cómo los diversos índices de estrés psicológico y fisiológico están relacionados entre sí.	Los resultados sugieren una covariación de estrés percibido y concurrentes respuestas fisiológicas, tanto en la navegación aérea como en el eje HPA, así como asociaciones inversas entre la capacidad de respuesta de frecuencia cardíaca y la evaluación posterior de estrés.
Perogamvros I et al. (2010)[30]	Manchester, Reino Unido	537 sujetos	El presente estudio fue diseñado para evaluar el impacto de la actividad parótida en la medición de cortisol salival.	El cortisol salival es un compuesto útil para valorar el cortisol libre en sangre.
Pérez Lancho MC et al. (2013)[1]	Sevilla, España	42 alumnos, de los cuales 22 fueron chicas y 20 chicos	Analizar el nivel de estrés, en distintos momentos académicos, mediante la determinación del cortisol salivar y evaluar la influencia en la eficacia de un programa de educación nutricional en adolescentes.	Se puede observar que los valores medios de cortisol en saliva dependen de la situación académica, con niveles mayores en la etapa final (próxima a los exámenes finales).
Plusquellec P et al. (2011)[11]	Quebec, Canadá	376 niños (edad: 19 meses)	Los niveles de cortisol en los niños se relaciona con la dominancia social en una situación de recursos competitivos.	Asociación significativa entre los niveles de cortisol y la capacidad de controlar los recursos.
Rask E et al. (2001)[49]	Umea, Suecia	34 hombres	Este estudio abordó si la 11β-hidroxiesteroide-deshidrogenasa de tipo 1 (11β- HSD1), regeneradora del cortisol, se reduce en el hígado pero se refuerza en el tejido adiposo en la obesidad humana.	Llegamos a la conclusión de que en la obesidad la reactivación de la cortisona en cortisol or 11β-HSD1 en el hígado se deteriora, por lo que los niveles de cortisol en plasma tienden a caer, y puede haber un aumento compensatorio en la secreción de cortisol mediada por un funcionamiento normal del eje HPA.

Tabla I (cont.)
Principales estudios que relacionan el cortisol salival con el estrés fisiológico

Artículo	*Lugar*	*Muestra*	*Método*	*Conclusiones*
Tarazona OM. (2012)[42]	Bogotá, Colombia	39 estudiantes (20 hombres y 19 mujeres) con edades entre 17 y 24 años (19.8 ± 1.8).	Determinar los efectos del estrés social agudo en el rendimiento de una tarea de atención sostenida y dividida.	Incrementos en la los niveles sistémicos de cortisol, al menos en los del sexo masculino, mientras que los efectos en las mujeres no fueron significativos.
Vreeburg SA et al. (2010)[14]	Amsterdam, Países Bajos	342 participantes de control sin trastornos psiquiátricos, 311 personas con un trastorno de ansiedad remitido y 774 con un trastorno de ansiedad actual.	Examinar la asociación entre los diversos subtipos de trastornos de ansiedad y varios indicadores de cortisol en un gran estudio de cohortes.	Más altos niveles de cortisol al despertar en las personas con un trastorno de ansiedad actual y significación marginal para las personas con ansiedad remitido, en comparación con los participantes del grupo control.

los niveles de cortisol salival de forma significativa, aunque deben influir[45].

Lovell y cols. estudiaron si los patrones diferenciales de la secreción de cortisol, en parte, podría mediar en las diferencias relacionadas con el estrés percibido en los problemas de salud comunes en 35 individuos jóvenes (19,22 años de media) y sanos del sexo femenino. Las participantes que reportaron mayores niveles de percepción de estrés mostraron una elevación de los niveles medios de cortisol diurnos, impulsados por la hiperactividad del eje Hipotálamo Pituitario Adrenal durante la noche.[41].

Bakker y cols. realizaron un estudio que consistió en evaluar posibles asociaciones entre el grado de percepción del estrés escolar y las alteraciones en el ritmo circadiano de cortisol en niños con diagnóstico de trastorno de déficit de atención e hiperactividad (TDAH). Se efectuó un estudio retrospectivo con 10 niños diagnosticados con TDAH y con 10 niños sin tal diagnóstico, y con edades comprendidas entre 8 y 14 años. Los niños con TDAH mostraron un mayor estrés escolar evaluado de forma subjetiva y un mayor estrés fisiológico evaluado por un aumento de los niveles diurnos de cortisol salival, con respecto a los niños sin ese trastorno. Por ello, se aprecia una relación entre las técnicas subjetivas y las pruebas fisiológicas de percepción del estrés[27].

Kariyawasam y cols. propusieron determinar si el cortisol salival se reduciría en un grupo de 32 niños con TDAH/TOD (trastorno de oposición desafiante) mediante el efecto de la medicación, en comparación con 25 niños sanos de la misma edad y origen étnico. Los resultados apoyan la posibilidad de una mayor actividad del eje Hipotálamo Pituitario Adrenal en estos niños con trastornos conductuales, respecto al grupo control. El uso de medicación estimulante mejora los niveles de cortisol, por lo que debe ser tomado en cuenta en estudios con cortisol salival en los niños con trastornos conductuales[46].

En el estudio realizado por Plusquellec y cols. con 376 niños de 19 meses de edad, en el que cada uno fue expuesto a 2 situaciones desconocidas, pero que se sabe que son moderadamente estresantes a esa edad, reflejó que existe una relación entre los niveles de cortisol y el estrés producido por querer dominar una situación desconocida, para estos niños de edades tan tempranas. También se observó que la relación solo se producía en los varones, y no en las niñas[12].

Oldehinkel y cols. evaluaron cómo los diversos índices de estrés psicológico y fisiológico están relacionados entre sí. Este estudio explora estas relaciones en una muestra de 715 adolescentes con 16,11 años de media. Aunque los tamaños del efecto fueron pequeños, los resultados reflejaron una relación entre el estrés percibido y las respuestas fisiológicas, así como asociaciones inversas entre la capacidad de respuesta de la frecuencia cardíaca y la evaluación posterior del estrés[3].

Krämer y cols. midieron la ansiedad subjetiva, la frecuencia cardiaca, la alfa-amilasa salival y el cortisol salival, en 41 niños de 8-12 años de edad con fobia social en comparación con 40 niños sanos de la misma edad. Los niños con fobia social mostraron una reacción elevada con ansiedad subjetiva, en comparación con el grupo control, pero no una reacción elevada de la frecuencia cardiaca, alfa-amilasa salival o cortisol salival[47].

Mangold y cols. evaluaron la medida en que la respuesta del cortisol al despertar predice la sintomatología depresiva subclínica, más allá de la influencia de los traumas de la infancia en una muestra de 55 sujetos de 18-38 años, sin diagnóstico de depresión clínica. Los análisis muestran que la subida inicial de cortisol en el despertar era el mejor predictor de la sintomatología depresiva subclínica, más allá de la influencia de un trauma, e independiente de un diagnóstico actual de depresión mayor[48].

Rask y cols. estudiaron si, como ocurre en las ratas, en la obesidad humana se reducía en el higado la actividad de la enzima 11β-hidroxiesteroide deshidrogenasa de tipo 1 (11β-HSD1), a través de la cual se regenera el cortisol en el hígado y el tejido adiposo. El estudio, conformado por 34 hombres, estableció que en la obesidad, la reactivación del cortisol a través de esta enzima en el hígado se deteriora. Por lo que, al caer la concentración de cortisol en el plasma, se produce un aumento en la secreción del mismo a través del eje hipotálamo-pitutitario-adrenal para compensar. La reactivación del cortisol en el tejido adiposo puede exacerbar la obesidad. Por ello, puede ser beneficiosa la segregación de cortisol a través del eje hipotálamo-pitutitario-adrenal para inhibir esta enzima en los pacientes obesos[49].

Conclusiones

Al revisar y analizar la bibliografía seleccionada para este artículo, la principal conclusión que se obtiene es que el cortisol salival es un indicador de estrés y tiene una relación directa con el diagnóstico de problemas psicológicos, tales como depresión o ansiedad, entre otras enfermedades. Así pues, una situación estresante o enfermedad puede detectarse observando los niveles de cortisol en la saliva.

Numerosos estudios han comprobado que la evaluación psicológica a través de pruebas subjetivas (test psicológicos), tienen una relación directa con las pruebas fisiológicas mediante los niveles de cortisol salival. Se puede decir que la fórmula ideal para evaluar el estrés es unificar las dos pruebas, las psicológicas y las fisiológicas[50].

Se puede observar que enfermedades, como la obesidad o la dermatitis atópica, producen elevados niveles de esta hormona[51]. En concreto, la obesidad reduce la regeneración de cortisol en el hígado y en el tejido adiposo, lo que repercute en una reducción de su concentración en el plasma. Estos niveles bajos son compensados con un aumento de la secreción del cortisol a través del eje hipotálamo-pituitario-adrenal, que acarrea un aumento del cortisol en la saliva. La regeneración del cortisol en el tejido adiposo puede exacerbar la obesidad, por lo que una mayor producción del cortisol salival a través del HPA puede favorecer una mejora de la obesidad.

Varios estudios han demostrado que los niños que tienen diagnosticado TDAH/TOD, así como fobia social, generan mayores niveles de cortisol en la saliva, por lo que son niños con estrés y ansiedad producidos por esas alteraciones. Los estudios demostrarían que unos niveles de estrés elevados en esos niños repercutirán en su crecimiento físico.

Altos niveles de cortisol salival también tienen relación con los problemas del crecimiento físico de los niños. La hormona del crecimiento, al igual que el cortisol, se genera en el hipotálamo, que se ve alterado por la alta actividad producida por el eje HPA y que puede afectar a la correcta secreción de la hormona del crecimiento. Lo que daría lugar a un déficit en el crecimiento de los niños que padecen problemas psicológicos, obesidad o TDAH, entre otros[52,53].

Estos elevados niveles de la hormona esteroidea pueden producir otras enfermedades, ya que una de las funciones del cortisol es suprimir el sistema inmunológico, por lo que en situaciones estresantes se tienen más probabilidad de padecer otro tipo de afecciones, infecciosas y no infecciosas. Cuando la persona presenta un alto grado de ansiedad o estrés, puede ver afectada su presión arterial o la frecuencia cardiaca y la cicatrización de las heridas se demora más tiempo. También su sistema inmunológico estrá más debilitado y el post-operatorio será más largo[54]. El efecto de los fármacos anestésicos se reduce, ante el incremento en la percepción del dolor[55].

En cuanto al género, la mayoría de los estudios establecen que el cortisol es algo genético y no depende del sexo. Aunque se aprecian resultados controvertidos, ya que hay estudios en los que el hombre es más sensible a las reacciones del cortisol que la mujer, pero también se encuentran resultados que dicen lo contrario, aunque la mayoría afirman se decantan por lo primero.

Por último, hay que resaltar la importancia de la carencia afectiva en la actuación del eje HPA, tanto en niños como en adultos. La falta de afecto se relaciona con mayores niveles de cortisol salival, con sus citadas consecuencias. Esta carencia afectiva también afecta a la frecuencia cardíaca, a la presión arterial y a los niveles de epinefrina y norepinefrina en la sangre. El afecto, por el contrario, favorece prácticas saludables, como la mejora en la calidad del sueño, una actitud positiva hacia el ejercicio físico y llevar una dieta más equilibrada. Todas estas ventajas, finalmente, están relacionadas con una menor morbimortalidad y con menores niveles de cortisol[56,57].

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Revisión

Potenciales intervenciones alimentarias en el manejo y prevención de la alergia en lactantes

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Resumen

Durante las últimas décadas la incidencia de enfermedades atópicas como el asma, dermatitis atópica y alergias a alimentos ha aumentado de manera exponencial. Aunque las enfermedades atópicas tienen una clara base genética, los factores ambientales, principalmente la dieta, pueden tener una influencia importante en su desarrollo. Este artículo resume los principales estudios que investigan hasta qué punto las prácticas alimentarias de la madre y los lactantes intervienen en la aparición de enfermedades alérgicas, discutiendo su posible rol en la prevención y/o manejo de alergias en lactantes con y sin historia familiar de alergia. La evidencia existente se evaluó en relación a: 1) si el consumo de ácidos grasos esenciales y de pre y probióticos por parte de la madre durante el período de gestación o la lactancia, modularían la aparición de desórdenes alérgicos, 2) si la alimentación del lactante, alimentado con lactancia materna/fórmulas artificiales podría prevenir/gatillar la aparición de síntomas, y 3) si la edad de introducción de la alimentación complementaria y hacerlo con determinados alérgenos alimentarios podría influir en alcanzar la tolerancia oral del lactante. La evidencia acumulada en las últimas décadas sugiere que, contra la postura histórica en el tema, la exposición a alérgenos en etapas tempranas de la vida podría promover la tolerancia del sistema inmune del lactante y prevenir la sensibilización a alimentos.

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Palabras clave: *Alergia. Lactancia materna. Fórmulas artificiales. Alimentación complementaria. Historia familiar.*

POTENTIAL DIETARY INTERVENTIONS FOR PREVENTION AND TREATMENT OF INFANT ALLERGY

Abstract

The incidence of atopic diseases such as asthma, atopic dermatitis and food allergies has increased exponentially in recent decades. Although atopic diseases have a clear genetic basis, environmental factors such as the diet, seems to play an important role in its development. This article summarizes main studies exploring whether feeding practices of mothers and infants intervenes in the development of allergic diseases. The potential role of dietary practices of the mother and infants for the prevention and/or management of allergies in infants is discussed. The available evidence was analyzed for: 1) does mothers consumption of essential fatty acids, prebiotics and probiotics modulates the onset of allergic disorders?, 2) Does breastfeeding and artificial formula prevent/trigger the onset of allergy symptoms? 3) Does timing of introduction of solid feeding and the selection of certain common food allergens participate in achieving oral tolerance in infants? Accumulated evidence in recent years suggest that exposure to allergens early in life may promote immune tolerance and contribute to prevent infant food sensitization.

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Key words: *Allergy. Breast feeding. Artificial formulas. Food supplements. Family history.*

Abreviaturas

AA: Alergia Alimentaria.
Ig: Inmunoglobulina HLA: Human Leucocyte Antigen.
AGPI: Ácidos Grasos Poliinsaturados.
ω-3: Omega-3.
ω-6: omega-6.
AGPICL: Ácidos Grasos Poli-insaturados de Cadena Larga.
ALA: ácido α-linolénico.
EPA: Ácido Eicosapentaenoico.
DHA: Ácido Docosahexaenoico.
AL: Ácido Linoleico.
ARA: Ácido AraquidónicoTGF-β: Transforming growth factor beta.
IL: Interleuquina.
IFN-γ: Interferón gamma.
LGG: Lactobacillus Rhamnosus GG.

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TNF-α: Tumor necrosis factor alpha.
LM: Lactancia materna.
ESPACI: European Society of Pediatric Allergology and Clinical Inmmunology.
ESPGHAN**:** European Society for Pediatric Gastroenterology, Hepatology and Nutrition.
AAP: American Academy of Pediatrics.
APLV: Alergia a la proteína de la leche de vaca.
FL: Fórmula láctea.

Introducción

Las enfermedades alérgicas y autoinmunes han aumentado durante las últimas décadas, especialmente en sociedades occidentalizadas. En particular, la incidencia y prevalencia de desórdenes alérgicos tales como asma, atopía, rinoconjuntivitis alérgica y alergia alimentaria (AA), han aumentado en la población pediátrica[1]. En los EEUU la prevalencia publicada de AA varía entre un 6% de los niños y 4% de los adultos[2]. Desde el punto de vista clínico, la AA se entiende como una falla del fenómeno de tolerancia oral en individuos predispuestos genéticamente, reacción que puede ser mediada por anticuerpos del tipo Inmunoglubulinas (Ig) E, G, A o M o por células, dando una amplia variedad de manifestaciones clínicas[3-5]. Esta patología es más prevalente en etapas tempranas de la vida (6-8%) declinando con el paso de los años (2,5% en adultos)[6,7]. Aunque las presentaciones clínicas de la AA pueden ser con síntomas repentinos, agudos y potencialmente mortal, su prevalencia es baja, especialmente si se considera la complejidad del sistema inmune asociado a la mucosa intestinal[8]. Se ha propuesto que el aumento de las enfermedades alérgicas, podría tener su origen en la exposición durante etapas tempranas de la vida a diversos factores ambientales. Junto a ello, la predisposición genética y la historia familiar de alergia, promueven un mayor riesgo y determinan individuos susceptibles a desarrollar desórdenes alérgicos[9].

La dieta jugaría un rol importante en la relación entre ambiente y herencia. Factores como la alimentación materna durante la gestación, la lactancia materna, la edad de inicio y el tipo de alimentos sólidos incorporados a la dieta del lactante podrían impactar en el desarrollo de la respuesta inmune. Es por esto que se postula que el embarazo y la infancia temprana podrían ser períodos críticos para prevenir la aparición de enfermedad alérgica[10]. El presente artículo revisa la evidencia y los conceptos más relevantes en relación a si las prácticas alimentarias maternas e infantiles modularían la aparición de alergia en la infancia. Además se analizan posibles nuevas estrategias que podrían contribuir en la prevención y manejo dietario de los desórdenes alérgicos.

Historia familiar de alergia alimentaria

El carácter hereditario del asma, la fiebre del heno y la dermatitis atópica ha sido documentado en estudios de población[11]. De acuerdo con estudios realizados en gemelos, 70% de manifestaciones atópicas son atribuibles a factores hereditarios. Debido a que existe una asociación estrecha entre las enfermedades atópicas y las AA, se cree que todas estas condiciones comparten factores de riesgo comunes, incluidos los hereditarios[12].

A pesar de que la AA es a menudo la primera manifestación de alergia en la infancia, son pocos los estudios poblacionales que se han centrado en su herencia[13]. Un estudio en preescolares chinos con historia familiar de reacciones adversas a los alimentos, mostró una mayor prevalencia de denuncias de reacciones adversas a los alimentos en niños con historia familiar de alergia que en aquellos niños que no la poseían[14]. Algunos estudios proporcionan evidencia específicamente en relación a la heredabilidad de la alergia al cacahuete (maní), concluyendo que la alergia al cacahuete es más común en hermanos de sujetos con alergia que en los padres o en la población general[15]. Su creciente prevalencia, aparentemente puede reflejar un aumento general de atopia que se heredaría con mayor frecuencia desde la madre. La alergia al cacahuete se presenta temprano en la vida y posiblemente estaría reflejando el aumento del consumo de cacahuete por las madres, ya sea durante el embarazo o la lactancia[15,16]. Interesantemente, en pacientes con alergia a las nueces se ha reportado mayor frecuencia de ciertos tipos de HLA (Human Leucocyte Antigen) y polimorfismos genéticos en comparación a la población general[17-19].

Un estudio de 3.899 niños, realizado en Finlandia entre los años 2001 y 2006, recopiló información acerca de la presencia de manifestaciones alérgicas de ambos padres[20]. Paralelamente a la encuesta, se evaluó IgE, pruebas de punción cutánea y pruebas de tolerancia oral. Los resultados mostraron que hasta los 4 años, la incidencia de cualquier prueba positiva para AA fue tres veces mayor en aquellos niños que poseían ambos padres con una manifestación alérgica y dos veces mayor si la madre o el padre tenía una manifestación alérgica, comparado con niños cuyos padres no informaron ninguna de estas condiciones; el riesgo estimado de cualquier prueba de AA positiva aumentó por un factor de 1,3 (IC 95%: 1,2-1,4) para cada manifestación adicional alérgica en los padres[20]. Otro estudio, en una muestra de 581 familias examinó los patrones de agregación familiar, el grado de asociación con factores genéticos que contribuyen a la AA y a la sensibilización a alérgenos alimentarios[21]. Los resultados revelaron que la presencia de AA en un niño es un predictor significativo e independiente de AA en un hermano (OR = 2,6, IC95%:1,2–5,6, p = 0,01); junto a esto, se encontró una asociación positiva entre el perfil de IgE total e IgE específica y los principales alérgenos alimentarios evaluados en esta muestra (sésamo, cacahuete, trigo, leche, clara de huevo, soja, nuez, camarón y bacalao), entre miembros de la familia (padre/hijo, madre/hijo, caso índice/hermanos)[21].

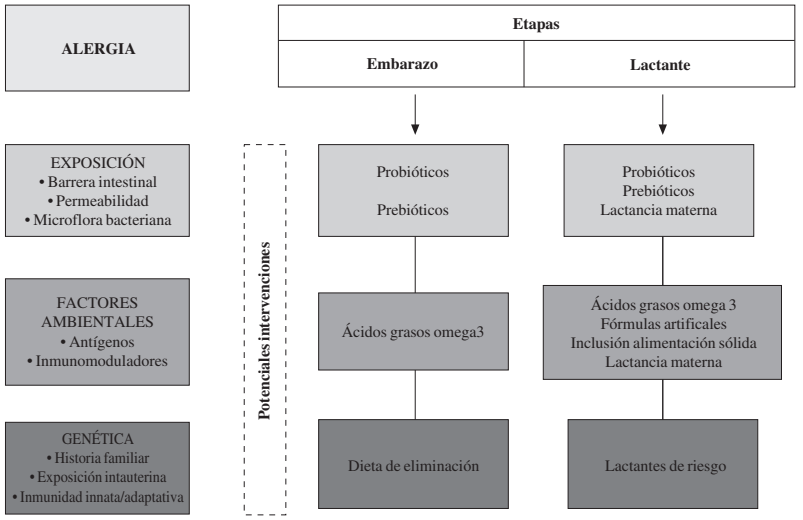
La determinación de un lactante de riesgo para desarrollar alergia según la Academia Americana de Pedia-

tría (AAP)[22], y las directrices conjuntas de la Sociedad Europea de Pediatría, Alergología e Inmunología Clínica (ESPACI)[23] y la Sociedad Europea de Gastroenterología Pediatría, Hepatología y Nutrición (ESPGHAN)[24,25], han definido a un lactante de riesgo si existe a lo menos un familiar de primer grado (padre o hermano) con una condición alérgica documentada. Esta clasificación permite direccionar el tratamiento de un lactante, el cual involucra estrategias de prevención o manejo de la alergia.

Prácticas alimentarias de la madre y desórdenes alérgicos

Las dietas modernas difieren en muchos aspectos de las dietas tradicionales y varios de los cambios en los componentes dietarios específicos se han relacionado con el aumento de las enfermedades alérgicas. Existe alguna evidencia de que componentes específicos de la dieta durante el embarazo, tales como los que se incluyen en la dieta mediterránea, protegerían contra el desarrollo de la alergia y cumplirían un papel en la prevención de la sensibilización alérgica y el asma[26,27]. En particular, es interesante que cambios en la dieta pueden transformarse en una de las causas ambientales capaces de inducir modificaciones epigenéticas, las que podrían sustentar el aumento de muchas enfermedades actuales, incluidas las alérgicas[28,29]. Modelos animales demuestran que la dieta materna tiene efectos epigenéticos en la función inmune y que predisponen a un fenotipo alérgico[30]. Lo anterior pone de manifiesto que el embarazo ofrece una importante oportunidad para la prevención de la enfermedad alérgica y que la dieta puede ser una estrategia no invasiva útil en este sentido[31] (fig. 1).

Se ha sugerido que la sensibilización atópica podría ocurrir en útero[32]. Esta idea es sostenida en algunos reportes que demuestran la capacidad del feto de producir IgE a partir del segundo trimestre de gestación[33]. Se ha descrito una asociación positiva entre IgE total en sangre de cordón umbilical y el desarrollo de atopia en niños[34-36]. Asimismo, se ha descrito que la IgE y los linfocitos T de memoria específicas para alérgenos en sangre de cordón umbilical, constituyen un factor predictor de enfermedad atópica[37,38].



El fenómeno alérgico tiene una etiopatogenia multifactorial, entre estos, factores genéticos, factores ambientales y factores asociados a la exposición a antígenos han sido descritos (columna a la izquierda). Los períodos (Etapas) del embarazo y la infancia temprana podrían ser períodos críticos para prevenir la aparición de la enfermedad alérgica o contribuir en su tratamiento. Se ilustran las potenciales intervenciones alimentarias durante la etapa del embarazo (columna central) y del lactante (columna a la derecha) que guardan relación con: a) la exposición a antígenos durante el período de gestación, tales como el uso de probióticos y prebióticos, y la LM exclusiva una vez nacido el lactante, contribuirían a alcanzar la tolerancia oral a proteínas foráneas; b) de los factores ambientales que modularían el sistema inmune, destacan el uso de AGPI ω-3 durante el embarazo y la lactancia materna, la inclusión de fórmulas lácteas y la alimentación sólida durante la infancia temprana . Una vez clasificado un lactante como de alto riesgo, c) los factores genéticos tomarían relevancia en las estrategias a seguir. Una dieta de eliminación durante el embarazo podría ser indicada, sin embargo no es recomendada, ya que podría ser deficiente en algunos nutrientes necesarios para el desarrollo normal del feto. En el caso de un lactante de riesgo, este debería ser intervenido nutricionalmente para recibir lactancia materna exclusiva y en caso que no pueda recibirla, incorporar el uso de fórmulas lácteas artificiales parcialmente hidrolizadas.

Fig. 1.—Potenciales intervenciones alimentarias en la prevención y manejo de la alergia.

La exposición intrauterina a alérgenos ha sido estudiada en sangre de cordón y líquido amniótico, aportando datos que sugieren que la sensibilización en útero es una posibilidad, al menos teóricamente[39] y merece ser estudiada.

Alimentación de la madre durante el embarazo y lactancia

La dieta materna representa el factor dietario que actúa más tempranamente en el individuo en gestación. Sin embargo, a la fecha no es claro que la exclusión de alérgenos alimentarios de la dieta de la madre embarazada tenga un efecto protector en el desarrollo de enfermedad atópica en lactantes[40]. Estudios realizados con alimentos específicos, como cacahuete, no mostraron asociación entre su consumo durante el embarazo y la alergia al cacahuete en la descendencia[22]. Dos estudios que evaluaron a 334 mujeres embarazadas que evitaron el consumo de antígenos dietarios durante el embarazo, no demostraron efecto protector en eczema atópico o asma durante los primeros 18 meses de sus hijos[41,42]. Sin embargo, un estudio reciente mostró que el aumento en el consumo de frutas cítricas y frutas totales durante el embarazo estuvo positivamente asociado con la sensibilización a alérgenos aéreos. Por otro lado, la ingesta materna de Vitamina D se asoció inversamente con la sensibilización a alérgenos alimentarios[43]. Existe escasa evidencia que respalde el uso de dietas de eliminación en embarazadas con riesgo de tener un hijo alérgico. Contrariamente a los efectos esperados, las dietas de eliminación han mostrado un menor incremento de peso materno, y un aumento no significativo de nacimientos de pre-término y un menor peso de nacimiento[40].

Existe un amplio rango de nutrientes en los que se han documentado efectos en la función inmune[44]. Entre ellos, el ácido retinoico (Vitamina A)[45,46], la Vitamina E[47,48] y los polifenoles[49] han mostrado efectos prometedores en la modulación del sistema inmune y desórdenes alérgicos en modelos animales y en humanos. Además, los ácidos grasos poli-insaturados (AGPI) han sido extensamente investigados debido al bajo consumo de ácidos grasos ω-3, característico de las dietas modernas occidentales típicamente ricas en AGPI omega-6 (ω-6)[50]. Algunos estudios han sugerido que estos nutrientes influirían en el desarrollo de alergia y asma, sugiriendo que un bajo consumo de alimentos ricos en ω-3 representaría un factor de riesgo para la aparición de asma más que cualquier otro nutriente.[51] Estos datos han llevado a proponer el uso de aceite de pescado como una estrategia preventiva para restaurar el equilibrio de AGPI ω-6/ω-3. Este enfoque es apoyado por los reconocidos efectos anti-inflamatorios de los AGPI ω-3 y de las características pro-inflamatorias de productos metabólicos derivados de los AGPI ω-6[52,53] (fig. 1).

Ácidos Grasos Poli-insaturados de Cadena Larga (AGPICL)

De los principales AGPICL (ácidos grasos ω-3 y ω-6), el ácido α-linolénico (ALA) es el más representativo de los ω-3 y es precursor metabólico del ácido eicosapentaenoico (EPA) y del ácido docosahexaenoico (DHA). En el caso de los ω-6, el ácido linoleico (AL) es precursor metabólico del ácido araquidónico (ARA) y docosapentaenoico[54]. Tanto el ALA como el AL son considerados ácidos grasos esenciales, debido a que los mamíferos carecen de las enzimas necesarias para sintetizarlos y deben ser aportados por la dieta. La ingesta de AGPI ω-3 ha disminuido en la población general y en mujeres gestantes, asociándolos al incremento que se observa actualmente de alergia en los niños[55]. Un estudio clínico aleatorizado, placebo-control realizado en Suecia, evaluó a 145 mujeres embarazas con diagnóstico de alergia o con un hijo o esposo con alergia. Las mujeres recibieron una suplementación diaria, con EPA (1,6 g/día) y DHA (1,1 g/día) o placebo, a partir de la semana 25 de gestación y durante 3-4 meses del período de lactancia.[55] Los resultados mostraron que la prevalencia de AA durante el periodo de suplementación fue inferior en el grupo que recibió ω-3 (1/52, 2%) en comparación con el grupo placebo (10/65, 15%), así como también la incidencia de IgE asociada a eczema (grupo ω-3: 4/52, 8%; grupo placebo: 15/63, 24%). Los autores concluyeron que la suplementación materna con AGPICL ω-3 puede disminuir el riesgo de alergia a los alimentos y eczema asociada a IgE durante el primer año de vida, en niños con antecedentes familiares de la enfermedad alérgica[55].

En otro estudio se evaluó el efecto de la suplementación con AGPICL durante el embarazo en la composición de ácidos grasos y su relación con la función inmune materna; se incluyeron a 70 mujeres embarazadas con antecedente de un familiar de primer grado con enfermedad alérgica y fueron suplementadas diariamente con 2,7 g de AGPICL ω-3 o 2,8 g de aceite de soja como placebo (n = 75) a partir de la semana 25 de gestación[56]. Los resultados mostraron un incremento en la proporción de EPA y DHA y una disminución de ARA en membranas de fosfolípidos de eritrocitos en el grupo suplementado con AGPICL ω-3. La secreción de prostaglandina E2 en la sangre materna (inducida por lipopolisacárido) disminuyó en la mayoría de las madres suplementadas con AGPICL ω-3. Estos resultados indican que la suplementación con AGPICL ω-3 durante el último trimestre de la gestación podría disminuir algunas respuestas inmunes implicadas en la inflamación alérgica[56]. Sin embargo, un ensayo placebo controlado, en el que se suplementó embarazadas con 900 mg de AGPICL ω-3 o con aceites vegetales sin AGPICL ω-3 (placebo), no logró demostrar una reducción en alergias IgE mediadas al primer año de vida, aunque la sensibilización al huevo y el eczema atópico tuvieron menor frecuencia en el grupo suplementado[57]. Siendo una estrategia de fácil implementación, clara-

mente son necesarios estudios de seguimiento a largo plazo para determinar si la suplementación con ácidos grasos ω-3 tiene efecto en enfermedades alérgicas del tracto respiratorio y en la sensibilización a aeroalérgenos en niños[57].

Microbiota y tolerancia oral

La microbiota intestinal juega un rol crucial en el establecimiento de la tolerancia a antígenos de alimentos. Existe amplia evidencia en animales (tanto de tipo silvestre como libres de gérmenes) que demuestra que la ausencia de la microbiota habitual produce una falla en la adquisición de la tolerancia a algunas proteínas alimentarias[58]. Tanto la occidentalización de las dietas como la enfermedad alérgica se asocian a una alteración del "equilibrio" de la microbiota, incluyendo patrones de colonización temprana distintos a los habituales y una reducción en la diversidad de las bacterias adquiridas. Por este motivo, intentar restaurar el patrón de microflora que adquiere el recién nacido de término alimentado con leche materna se ha planteado como estrategia para prevenir y/o manejar la AA[59]. He y cols.,[60] compararon la flora fecal de niños alérgicos y saludables, describiendo diferencias en los perfiles de las especies de bifidobacterias y su capacidad adherente a la mucosa intestinal humana (más adherente en niños sanos). Los autores concluyeron que la suplementación dietaria de bifidobacterias típicas de lactantes saludables, podría ser beneficioso en el tratamiento de desórdenes alérgicos.

A partir del monitoreo de la flora intestinal de niños alérgicos y sanos en Estonia y Suecia, Bjorksten y cols.[61] reportaron una menor colonización por bacterias anaerobias (bifidobacterias) y mayores recuentos de algunas especies aeróbicas (coliformes) en los niños que desarrollaron alergia en los primeros dos años de vida.

El epitelio intestinal está constantemente expuesto a una gran carga de agentes externos que pueden ser dañinos o beneficiosos para el organismo. Por consiguiente, el sistema inmunitario intestinal debe encontrar un equilibrio entre las respuestas protectoras inmunes, inducidas después del encuentro con el patógeno o toxinas intestinales, y la tolerancia propia de las bacterias comensales y antígenos alimentarios. Estos dos factores aportan la mayor carga antigénica en el intestino, promoviendo en la mayoría de los casos el fenómeno denominado *tolerancia oral*, que se traduce en una falta de respuesta del sistema inmunológico (anergia) y constituye una característica clave de la inmunidad intestinal[62].

La interacción del contenido intestinal y las células epiteliales e inmunes presentes en la mucosa proveen un ambiente que promueve la tolerancia inmunológica, por ejemplo a través de la inducción de IgA, la presencia de linfocitos Th3 secretores de TGF-β (Transforming growth factor beta), linfocitos T reguladores y la secreción de interleuquina (IL) 10 e INF-γ (Interferón gamma). Ellos aseguran la posibilidad de un equilibrio homeostático entre el sistema inmune intestinal y su carga antigénica, manteniendo la capacidad de reconocer antígenos dañinos y preservando la integridad de la mucosa intestinal. La respuesta inmune inapropiada a componentes alimentarios y bacterias comensales es responsable de algunas patologías, tales como la enfermedad celíaca, enfermedad de Crohn y la AA, en las que se altera el fenómeno de tolerancia[63,64].

Hasta el momento, una de las estrategias de prevención de AA ha sido la administración de suplementos probióticos microbianos (en el embarazo y/o lactancia) u oligosacáridos prebióticos (en la infancia), que buscan favorecer una microflora favorable que promueva la tolerancia[65-67]. Un estudio de la descendencia de ratones hembras evaluó el efecto de la suplementación de Lactobacillus rhamnosus GG (LGG) en el desarrollo de desórdenes alérgicos[68]. Se suministró LGG intragástricamente en forma diaria antes de la concepción, durante el embarazo y lactancia (grupo de suplementación perinatal), o bien después de la concepción y sólo durante el embarazo (grupo de suplementación prenatal)[68]. La colonización intestinal con LGG se observó únicamente en las madres y no en la descendencia; sin embargo, se observó una reducción de la expresión de TNF (Tumor necrosis factor alpha), IFNγ, IL-5 e IL-10 en las crías de madres suplementadas en el período perinatal, mientras que la expresión de IL-13 y IL-4 se mantuvo sin cambios. Los autores concluyen que la suplementación con LGG tendría efectos beneficiosos sobre el desarrollo de alergia cuando se aplica en una fase muy temprana de la vida, postulando que los efectos inmunológicos son, al menos en parte, mediados a través de la placenta probablemente por inducción de señales de células pro-inflamatorias[68]. En un estudio de intervención, 159 mujeres gestantes recibieron un suplemento con LGG, antes del parto y por los primeros 6 meses de vida si el lactante recibía lactancia materna (LM) o bien se suplementó a los lactantes si no recibían pecho materno[69]; se observó que el eczema a los 2 años de edad se redujo en 50% en el grupo intervenido, y este efecto protector persistió hasta los 7 años de edad; sin embargo, la prevalencia de eczema en la muestra fue muy baja y no mostró diferencias con el grupo tratado con probióticos[69,70].

Lamentablemente existe amplia variabilidad en los métodos de estudio, cepas utilizadas y protocolos usados, lo que lleva a la considerable heterogeneidad observada en los resultados. Los efectos encontrados dependen de la cepa usada, de factores ambientales y de características del huésped.

Por otro lado, existe especial interés en el uso de prebióticos (oligosacáridos fermentables, no digeribles), que puedan estimular selectivamente el crecimiento y actividad de las bacterias en el colon y así mejorar, indirectamente, la salud del huésped. En niños de alto riesgo de desarrollar alergia, la suplementación con prebióticos demostró una menor incidencia acumulativa de dermatitis atópica, sibilancias recurrentes y urti-

caria en comparación al grupo placebo[71,72]. Esta disminución de la frecuencia de eczema asociada a la ingesta de prebióticos también se ha demostrado en niños con bajo riesgo de desarrollar alergia[73]. Aunque los resultados en esta área son interesantes, actualmente se considera que estudios acerca de la acción de prebióticos son todavía insuficientes para establecer recomendaciones de uso.

Prácticas alimentarias del lactante y desordenes alérgicos

Uno de los principales cambios en el tratamiento de la AA en pediatría ha sido su enfoque en la prevención en etapas tempranas (fig. 1). Históricamente, el tratamiento se basaba en restringir la mayoría de los alérgenos alimentarios desde el nacimiento, hasta alcanzar la maduración del sistema inmune y digestivo; de esta manera se prevenía la sensibilización alérgica temprana o al menos se la reducía significativamente. En la práctica, la indicación de introducción de alérgenos alimentarios comunes era "mientras más tarde mejor". Sin embargo, la evidencia acumulada en las últimas décadas sugieren que la exposición a alérgenos en etapas tempranas podría promover la tolerancia del sistema inmune del lactante y prevenir la sensibilización a alimentos, especialmente si el primer contacto ocurre mientras el lactante aún recibe leche materna[74]. La nueva mirada requiere definir los grupos de riesgo que deberían usarse para hacer la evaluación, ya que hay evidencia que muestra que los niños con alto riesgo de desarrollar reacciones alérgicas responden distinto si se les compara con grupos sin riesgo. La incidencia de alergia en niños de alto riesgo es significativamente mayor que en niños no atópicos; se estima que los factores genéticos darían cuenta de 50-70% de los desórdenes alérgicos y del asma[75]. La sensibilización a alérgenos alimentarios ocurre principalmente en el primer año de vida y la alergia a la proteína de la leche de vaca (APLV) es a menudo la primera AA en lactantes susceptibles[76].

Al analizar la evolución de AA, otro concepto relevante es la duración de estos cuadros. Actualmente se sugiere que la AA no sería autolimitada y de duración corta y que también puede tener una evolución lenta y permanecer durante buena parte de la infancia y adolescencia. Estudios de Savage y cols.[77] y Skripak y cols.[78] muestran que a los 4 años de edad sólo el 11% de las alergias al huevo y 19% de la alergia a la leche que cursan con IgE altas se han resuelto; de éstas, el 80% desaparece a los 16 años. Algunos autores han propuesto que la AA habría cambiado su patrón de evolución debido a varios factores, por ejemplo cambios de la dieta (edad de introducción de sólidos, sólidos cocinados o crudos, sólidos entregados cuando el niño es aún amamantado), o uso de antiácidos (que aumentan la exposición a proteínas más complejas). Un estudio de niños judíos de 8-14 meses que habitaban en Israel o en Inglaterra, mostró que la alergia al cacahuete era 0,2% en los primeros y 10 veces mayor en los segundos, mientras que el consumo de cacahuete era de 7,1g en Israel en comparación a los niños ingleses que no consumían cacahuete a esas edades[79].

Lactancia materna

La leche humana entrega una nutrición ideal para el recién nacido desde el punto de vista inmunológico, fisiológico y nutricional, potenciando las defensas naturales del lactante y promoviendo la maduración del sistema inmune[80]. En vista de la amplia evidencia que respalda el rol de la LM en promover el bienestar de todos los lactantes, la OMS[81] y ESPGHAN[82] recomiendan que los lactantes sean alimentados con LM exclusiva hasta los 6 meses de vida, comenzando con la alimentación complementaria a partir de entonces.

Sin embargo, el efecto de la LM en el desarrollo de enfermedad alérgica del lactante es aún controversial[83,84]. En lactantes con lactancia exclusiva y eliminación de alimentos altamente alergénicos de su dieta, hay estudios que han reportado que la leche humana protegería contra la alergia, con mejoría definitiva en lactantes con eczema y malestar gastrointestinal asociado, así como también una reducción del riesgo de asma en los primeros 2 años[85]. Una investigación realizada en lactantes menores de dos años con y sin alergia alimentaria, mostró que la introducción temprana (3 meses de edad) de fórmulas lácteas (FL) artificiales fue más frecuente en el grupo de niños alérgicos que en aquellos sin alergia[86]. Recientemente, se ha reportado que complejos inmunes IgG presentes en la leche humana, son potentes inductores de tolerancia a aeroalérgenos para los cuales las madres estaban sensibilizadas, entregando protección antígeno-específica para el desarrollo de asma en sus hijos[87]. Sin embargo, otros estudios muestran que la LM no tiene efecto en los síntomas de alergia del lactante, asociándose más bien con un aumento en la prevalencia de eczema atópico[83,84].

Una de las explicaciones propuestas para esta contradicción es que habría diferencias en la composición de la leche de madres atópicas respecto de aquellas no atópicas[88,89]. La leche de madres atópicas presenta altos niveles de citoquinas y quimioquinas asociadas con alergias y menor concentración de TGF-β1, esta última, molécula que promovería la tolerancia a componentes alimentarios en la respuesta inmune intestinal[90]. La evidencia disponible actualmente sugiere que la LM protege contra la alergia cuando la madre no es atópica, pero que hijos de madres alérgicas podrían tener riesgo de desarrollar alergias (especialmente alimentaria) durante esta etapa de lactancia[91]. En el caso específico de la APLV, se recomienda que la madre que continua amamantando debiera eliminar toda proteína de leche de vaca de su dieta. Cuando el cuadro es sugerente de APLV pero el diagnóstico no se ha demostrado, algunos autores consideran que esta indicación es innecesa-

ria. La consulta nutricional resulta esencial para la madre que mantiene una dieta de eliminación para alérgenos alimentarios, la organización y el reemplazo de alimentos que permita cumplir con los requerimientos diarios de macro y micronutrientes es una meta importante de alcanzar, focalizando particularmente la atención en una adecuada ingesta de calcio y proteínas[92].

Fórmulas Lácteas (FL)

Existe evidencia que sugiere que cuando un lactante de riesgo deja de recibir leche materna debiera recibir una FL parcialmente hidrolizadas, o sea una FL donde las proteínas han sido modificadas mediante hidrolización[93,94]. Se ha observado que la alimentación con una FL de proteína de suero parcialmente hidrolizada (y no con proteína de leche de vaca intacta) reduce el riesgo de dermatitis atópica en lactantes, particularmente en aquellos con historia familiar de alergia[95]. Dependiendo del grado de modificación de la proteínas, las FL son diferenciadas en parcial o extensamente hidrolizadas, ya sea partiendo de proteína de suero o caseína[94]. Estudios comparativos de varias FL hidrolizadas indican que no todas tienen el mismo efecto protector[22,96]. En este sentido, las FL parcialmente hidrolizadas pueden ser usadas para prevención primaria de alergia en lactantes de riesgo atópico, mientras que solamente aquellas extensamente hidrolizadas son indicadas para la prevención secundaria en pacientes con APLV[97]. El rol de estas FL en la prevención de enfermedad atópica ha sido motivo de estudios tanto en lactantes alimentados con FL como en aquellos alimentados con LM[22]. Un estudio alemán mostró que la incidencia de dermatitis atópica se redujo sustancialmente en lactantes que consumieron FL con caseína parcial y extensamente hidrolizadas, pero no ocurrió lo mismo en aquellos que recibieron FL que contenían proteína de suero extensamente hidrolizadas[96]. Por otra parte, las FL de soja, han sido ampliamente usadas en lactantes con enfermedad atópica. Sin embargo, un reciente meta-análisis de 5 estudios randomizados y cuasi randomizados, concluyó que la alimentación a base de FL de soja podría no ser recomendable para la prevención de atopia en lactantes de alto riesgo de desarrollar alergia[22].

En resumen, la LM exclusiva debe ser el alimento de elección desde el nacimiento. Sin embargo, en lactantes de alto riesgo para desarrollar alergia que no puedan recibir LM exclusiva, una FL parcialmente hidrolizada puede ser considerada una medida efectiva para reducir potencialmente el riesgo de desarrollar alergia. En cambio, un lactante con AA ya diagnosticada debe recibir una FL extensamente hidrolizada o una FL basada en aminoácidos[98].

Alimentación complementaria

A pesar de las escasas publicaciones existentes, en la práctica diaria es evidente que en los últimos 40 años las edades a las cuales se introducen los primeros alimentos sólidos en el lactante han cambiado considerablemente. En la década del '60, la introducción de alimentos sólidos era recomendada a los 4 meses de edad. Una década más tarde, se recomendaba la introducción de sólidos después de los 4 meses. Para la década del '90, el consenso fue retardar la introducción de sólidos hasta los 6 meses[99]. Hasta hace poco, las guías alimentarias recomendaban retardar la introducción de alérgenos alimentarios (retardando la introducción de huevo hasta los 2 años y nueces hasta los 3 años) en lactantes con historia familiar de alergia; también se aconsejaba retardar la alimentación sólida hasta los 6 meses y continuar con LM hasta el año de vida[13]. Estas recomendaciones han sido reevaluadas en estudios poblacionales recientes, sustentando que la práctica de atrasar la introducción de ciertos alérgenos aumenta más que disminuye el riesgo de alergia.

Al respecto, un estudio realizado en lactantes chilenos, que evaluó la relación entre el patrón alimentario y la presencia de manifestaciones alérgicas, no encontró ninguna diferencia en la temporalidad de inclusión de los alimentos sólidos entre lactantes alérgicos y controles sanos, con un cumplimiento considerable de los tiempos de inclusión recomendados (después de los 6 meses de edad) en ambos grupos[86]. En el 2004, Zutavern y cols., en un estudio prospectivo de cohorte de nacimiento mostraron un aumento del riesgo de eczema relacionado con la introducción tardía de huevos y leche[100]. La introducción tardía de huevo mostró una tendencia a aumentar el riesgo de sibilancias en la edad preescolar[100]. Por otro lado, un reciente estudio que evaluó la exposición temprana y regular al huevo (4 meses) en lactantes con eczema atópico, mostró que al año de edad el grupo que recibió huevo tempranamente tuvo una menor frecuencia de diagnóstico de alergia mediada por IgE que el grupo control[101].

En este sentido otros autores han demostrado que los niños expuestos al trigo por primera vez después de los seis meses de vida tuvieron mayor riesgo de alergia que los niños que recibieron trigo antes de los seis meses de edad[102]. Otro estudio que evaluó una cohorte de 2.073 niños de seis años de edad, demostró que la introducción tardía de sólidos (después de los 6 meses) no se asoció con una disminución en el riesgo para asma, rinitis alérgica o sensibilización frente a alérgenos alimentarios o aero-alérgenos, evaluado a los cinco años de edad[103]. Por el contrario, la sensibilización a alimentos fue más frecuente en niños que introdujeron los sólidos más tardíamente.

El consumo de pescado durante la infancia ha sido considerado un factor de riesgo para la enfermedad alérgica, sin embargo un estudio que incorporó a 4.089 recién nacidos que fueron seguidos por 4 años demostró que el consumo regular de pescado antes del año de vida es asociado con un menor riesgo de enfermedad alérgica y sensibilización a alimentos y a aero-alérgenos durante los primeros 4 años de vida[104].

No es posible aún proponer un modelo de cómo opera la ingesta de los alérgenos y la falla de la tolerancia

en los sujetos alérgicos. La tolerancia a los alérgenos alimentarios, parece estar impulsada por la exposición regular y temprana a las proteínas durante una "ventana crítica" inicial del desarrollo[105]. Esta ventana de vulnerabilidad en la primera infancia, sería el período óptimo para dirigir las estrategias que permitan reducir la incidencia de enfermedades alérgicas[22]. Aunque la temporalidad de este período no es del todo claro, la evidencia actual sugiere que es más probable que se distribuya entre el cuarto y el sexto mes de vida, y que la exposición muy retrasada a los alimentos sólidos, más allá del sétimo mes, puede aumentar el riesgo de alergia a los alimentos, a la enfermedad celíaca y a enfermedades autoinmunes[105].

Por otro lado, la introducción muy temprana de alimentos sólidos puede causar sensibilización alérgica a algunos alérgenos alimentarios, debido a que la barrera de mucosa intestinal del lactante es inmadura[8]. No obstante existe evidencia de que el riesgo para desarrollar AA en niños prematuros o con bajo peso de nacimiento es similar en relación a un grupo control[106].

Conclusiones

El impacto de factores alimentarios en el desarrollo y mantención de la tolerancia oral es un área de investigación emergente en la cual los mecanismos moleculares involucrados no son del todo conocidos. Sin embargo, es claro que el efecto beneficioso en la modulación del sistema inmune del lactante guarda estrecha relación con el momento en el cual son incorporados en la dieta, tanto materna como infantil. Por tanto, las prácticas alimentarias durante el período perinatal y los primeros meses de la vida parecen ser relevantes en el desenlace futuro de un desorden alérgico. Factores tales como AGPICL ω-3, probióticos y prebióticos aparecen como candidatos prometedores para futuras investigaciones. Los primeros meses de vida representan una fase crítica en el desarrollo de la tolerancia oral, momento en el cual la microbiota no está completamente establecida y la barrera epitelial aun está en desarrollo. La alimentación láctea, ya sea como LM o FL artificiales y el momento en el cual son incorporados los alimentos sólidos en la dieta del lactante, representan importantes factores ambientales posibles de ser modulados y que podrían contribuir a la mantención de una respuesta inmune adecuada.

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Revisión

Beneficios del entrenamiento de fuerza para la prevención y tratamiento de la sarcopenia

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Resumen

La sarcopenia es un síndrome que se caracteriza por una pérdida gradual y generalizada de la masa muscular esquelética y la fuerza, con riesgo de presentar resultados adversos como discapacidad física, calidad de vida deficiente y mortalidad. Existen varios factores que contribuyen: el proceso de envejecimiento a lo largo de la vida, influencias sobre el desarrollo en las etapas iniciales de la vida, una alimentación inadecuada, el reposo en cama o sedentarismo, enfermedades crónicas y determinados tratamientos farmacológicos. La sarcopenia representa un deterioro del estado de salud con un costo personal elevado: trastornos de la movilidad, mayor riesgo de caídas y fracturas, deterioro de la capacidad de realizar actividades cotidianas, discapacidad, perdida de independencia y mayor riesgo de muerte. El entrenamiento de la fuerza es actualmente uno de los métodos más eficaces para combatir la sarcopenia mediante la estimulación de la hipertrofia e incremento de la fuerza. Los programas de entrenamiento de fuerza en personas mayores probablemente constituyen, por sí mismos, una de las medidas preventivas más eficaces para retrasar la aparición de sarcopenia. En la presente revisión bibliográfica se analizarán diferentes factores relacionados con la sarcopenia y el entrenamiento de la fuerza como método preventivo.

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Palabras clave: *Entrenamiento de fuerza. Sarcopenia. Personas mayores.*

BENEFITS OF STRENGTH TRAINING FOR THE PREVENTION AND TREATMENT OF SARCOPENIA

Abstract

Sarcopenia is a syndrome characterized by a gradual loss and generalized skeletal muscle mass and strength at risk for adverse outcomes such as physical disability, poor quality of life and mortality. It has several contributing factors: the aging process throughout life, influences on development in the early stages of life, eating sub optimal, bed rest or sedentary lifestyle, chronic diseases and certain drug treatments. Sarcopenia represents a deterioration of health status with a high personal cost: mobility disorders, increased risk of falls and fractures, impaired ability to perform everyday activities, disability, loss of independence and increased risk of death. The strength training is currently one of the most effective methods for combating sarcopenia by stimulating hypertrophy and increase strength. The strength training programs in older people themselves are probably one of the most effective preventive measures to delay the onset of sarcopenia. In this literature review different factors related sarcopenia and strength training as a preventive method is analyzed.

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Key words: *Strength training. Sarcopenia. Elderly.*

Abreviaturas

ADN: Ácido desoxirribonucleico.
ADNmt: Genoma mitocondrial (ADN mitocondrial).
CNTF: Factor neurotrófico ciliar.
GH: Hormona de crecimiento.
IGF-1: Factor de crecimiento insulínico tipo 1.
IL-1: Interleuquina-1.
IL-6 : Interleuquina-6.
IL-15: Interleuquina-15.
MicroARN: Micro ácido ribonucleico.
1RM: 1 Repetición máxima.
TNF-α: Factor de necrosis tumoral-α.

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Introducción

El envejecimiento es el producto de diferentes cambios funcionales que conducen al ser humano a una reducción sustancial de todas sus capacidades. La estructura corporal compuesta de huesos y músculos también es susceptible a ser vulnerable, por lo que su deterioro suele ocasionar una discapacidad relativa. Algunas funciones pueden verse afectadas aún antes del envejecimiento. El hecho de no haber experimentado un óptimo desarrollo durante la plenitud de la vida (como por ejemplo tener poca masa ósea o escaso volumen muscular) puede favorecer el deterioro más temprano[1]. Dentro de las complicaciones asociadas al envejecimiento esta la sarcopenia, la cual es el resultado de múltiples variables, lo que hace compleja su fisiopatología, diagnóstico, prevención y tratamiento[1]. La sarcopenia, según Cruz y cols.[2], es un síndrome que se caracteriza por una pérdida gradual y generalizada de la masa muscular esquelética y la fuerza con riesgo de provocar resultados adversos como discapacidad física, calidad de vida deficiente y mortalidad[3,4].

Dentro de los tratamientos encontrados para prevenir o retrasar la sarcopenia encontramos el entrenamiento de la fuerza. No obstante, es importante destacar que la fuerza muscular no solo depende de la masa muscular y la relación entre fuerza y masa no es lineal[4,5]. Por este motivo no podemos definir la sarcopenia solamente en relación con la masa muscular ya que no sería totalmente correcto y su utilidad clínica sería muy limitada. De hecho, diversos autores sostienen que el termino dinapenia resulta más idóneo para describir la pérdida de fuerza y función muscular asociada a la edad[6]. En la sarcopenia se une la reducción del volumen de los músculos con una menor capacidad funcional de los mismos. En general, se solapan situaciones como: menor actividad física de la requerida, sedentarismo y nutrición inadecuada. A estos factores se suman otros elementos, tales como: cambios hormonales, participación de citoquinas y cambios neuromusculares. Además, no se debe olvidar que existen factores genéticos y nutricionales de base (es decir, la conformación del cuerpo humano de la niñez a la edad adulta puede dar una base de músculos gruesos, o por el contrario, delgados)[7].

Los músculos se adaptan a todas las circunstancias que deben afrontarse durante la vida. Uno de los principales puntos de regulación se encuentra a nivel de las células satélites que, finalmente, determinan la síntesis de las proteínas musculares, en especial la miosina. La capacidad del músculo, determinada por factores genéticos y nutricionales, puede verse influenciada y afectada por hormonas, como el factor de crecimiento insulínico tipo 1 (IGF-1), la testosterona, agentes anabólicos[8] y reducción de fibras musculares (tipo I y II, especialmente las fibras de tipo II) que impiden la función muscular mecánica[9].

La fuerza muscular disminuye gradualmente desde los 30 a los 50 años, siendo mayor en los hombres que en las mujeres[10]. En la sexta década de vida, se produce una fuerte disminución no lineal de un 15%, que puede alcanzar hasta un 30% cerca de los 80 años. El resultado es la pérdida de fuerza y equilibrio. Todo ello aumenta el riesgo de problemas graves debido a las caídas, lesiones crónicas y recurrentes y enfermedades degenerativas[11]. Diversos estudios han demostrado que el ejercicio de fuerza puede contrarrestar estas deficiencias relacionadas con la edad[9,12]. Pese a la idea obsoleta de que el entrenamiento de la fuerza es innecesario o ineficaz para las personas mayores, existen evidencias que indican con claridad que estas personas tienen una posibilidad importante de beneficiarse con este tipo de ejercicios. De hecho, se ha puesto de manifiesto que incluso individuos mayores de 90 años pueden aumentar su acondicionamiento muscular mediante el entrenamiento de la fuerza[13].

Sarcopenia

Definición de la sarcopenia

El término Sarcopenia fue acuñado por el doctor Rosenberg[14] director del Research Center on Aging de la Universidad de Tufts (Boston, Estados Unidos). Rosenberg utilizó el concepto de sarcopenia para referirse a la pérdida involuntaria del músculo esquelético (del griego sarcos-carne y penia-carencia)[15-18]. Esta pérdida de masa muscular es la principal causa de la disminución de la fuerza.

Mecanismos de la sarcopenia

Toda condición en el ser humano tiene un comienzo y la sarcopenia no es la excepción. Dentro de los mecanismos que podrían intervenir en el inicio y la progresión de la sarcopenia cabe destacar la síntesis proteica, proteólisis, integridad neuromuscular y contenido de grasa muscular[2]. En un sujeto con la condición de sarcopenia pueden intervenir varios factores y las contribuciones relativas de éstos pueden variar con el tiempo (fig. 1). Por tanto, es esperable que la identificación de estos mecanismos y sus causas subyacentes facilite el diseño de ensayos de intervención en los que se actúe sobre uno o más de los factores implicados en el origen y desarrollo de la sarcopenia[2].

Etiología de la sarcopenia

La etiología de la sarcopenia es multifactorial, y su progresión se atribuye generalmente a cambios relacionados con la edad en el músculo esquelético: un aumento de la pérdida, o la resistencia a los factores anabólicos[19]. Diferentes estudios longitudinales sobre la calidad muscular han puesto de manifiesto una disminución importante en la capacidad para producir la fuer-

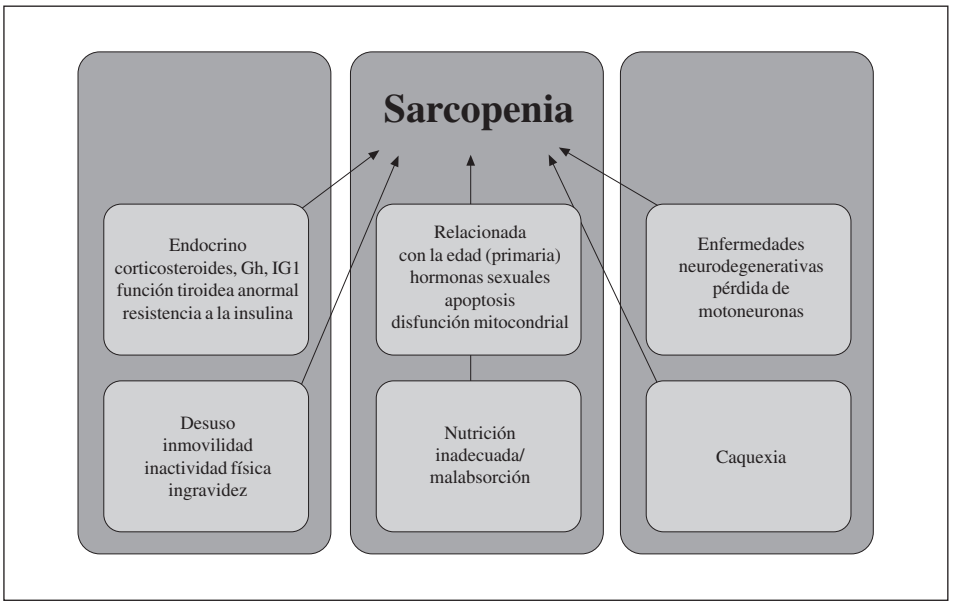


Fig. 1.—Mecanismos de la sarcopenia (modificado de Cruz y cols.[2]).

za por unidad de músculo durante el envejecimiento[20-22]. La disminución muscular en las extremidades inferiores tiene mayor importancia ya que produce un descenso grave en la capacidad funcional de las personas[23]. La sarcopenia puede depender del proceso de inflamación crónico que afecta a la mayor parte de las personas mayores[24], agravada por la infiltración de grasa en el músculo y la obesidad sarcopénica[25-27]. Además, el aumento drástico de alimentos altos en calorías promueve a una mayor disminución de masa muscular[28].

Sin embargo, la heredabilidad de la masa muscular y fuerza puede ser tan alta como del 50 al 60%[29,30], lo que indica que, desde el punto de vista genético, el desarrollo de la sarcopenia puede ser controlable. En efecto, determinados genes han sido identificados como posibles mediadores de la sarcopenia[31]. Así, situaciones e influencias tempranas de la vida pueden determinar la progresión de la sarcopenia en una edad posterior.

La incapacidad funcional aparece como consecuencia de la disminución de la producción de la fuerza rápida (fibras rápidas o fibras tipo II)[26,32]. Esto puede ser debido a una menor resistencia de este tipo de fibras, a la denervación[25,33], deficiencias en la expresión génica de la miosina tipo II[33] y a una menor resistencia de estas fibras al estrés oxidativo[34,35]. También se ha indicado que estos mecanismos podrían estar relacionados con la deficiencia de testosterona encontrada en las personas mayores[32,35].

La reducción de fibras en la masa muscular también se produce por factores intrínsecos en los miocitos. Este efecto perjudicial es causado por la acumulación de daño del ADNmt que afecta negativamente a la tasa metabólica, la síntesis de proteínas y la producción de ATP. Como resultado esto produce la muerte de las fibras musculares[25,35].

Por otra parte, los mecanismos de regeneración y reparación de fibras musculares también están comprometidos en las personas mayores, debido a una menor actividad de las células satélite[26,36], estrés oxidativo[33,37], respuesta anormal del microARN[38] y una regulación inadecuada de los procesos de reparación de fibras musculares dañadas.

Otras causas y factores relacionados con la etiología de la sarcopenia son las siguientes:

- *Causa neurológica*. Esta causa se asocia con la pérdida del tono neurotrófico vital para mantener el tono muscular, la pérdida de unidades motoras alfa y fibras nerviosas de conducción rápida de la médula espinal. Estas fibras nerviosas son indispensables para conducir el impulso nervioso a aquellas fibras musculares de contracción rápida tipo 2 que corrigen posición y actitudes corporales y que ayudan a evitar caídas, mantener la estación bípeda, así como moverse con destreza y habilidad[39,40].
- *Causa muscular*. A partir de los 30 años se pierde hueso y masa muscular. Las fibras musculares sufren una disminución en el número de proteínas de contracción, se hacen más delgadas y son reemplazadas por tejido conjuntivo y colágeno. Finalmente, se atrofian y desaparecen[41].
- *Causa hormonal*. La edad está asociada con la reducción de hormonas anabólicas como andrógenos (testosterona), estrógenos y hormonas del crecimiento, IGF-1 (factor de crecimiento similar a la insulina). También se asocia con el aumento de citoquinas antiinflamatorias y proinflamatorias como las interleuquinas IL-1 (interleuquina-1), IL-6 (interleuquina -6), TNF-α (factor de necrosis tumoral-α), IL-15 (interleuquina-15) y CNTF (factor neurotrófico ciliar), que tienen una fuerte influencia en el equilibrio entre la síntesis proteica y la degradación muscular[42] y llevan al deterioro de la fibra muscular[43].

– *Causa nutricional*. La disminución de la ingesta de alimentos en personas mayores conlleva serias consecuencias que podrían reflejarse en la pérdida de peso y masa muscular y fuerza[44,45]. Además, ya que las personas mayores consumen cantidades más pequeñas de alimento, puede ser más difícil para ellos el satisfacer sus necesidades de nutrientes, especialmente de micronutrientes. Aunque la importancia de una nutrición adecuada se conoce desde hace mucho tiempo, su contribución a la masa muscular y la fuerza no se ha estudiado ampliamente y gran parte de la investigación en esta área es relativamente nueva[46]. Se han realizado diversas intervenciones que van desde el apoyo nutricional[47] hasta la suplementación con nutrientes específicos[48-50], y se ha encontrado que, los nutrientes que han sido más consistentemente ligados a la sarcopenia y fragilidad en adultos mayores son: la vitamina D, proteínas, y una serie de nutrientes antioxidantes, que incluyen carotenoides, selenio y vitaminas E y C[46]. Sin embargo, también hay cierta evidencia de que las variaciones en el consumo de ácidos grasos polinsaturados pueden tener importantes efectos en la fuerza muscular en personas de edad avanzada[49].
– *Estilo de vida sedentario*. La condición de la sarcopenia empeora con el desuso y una vida sedentaria, lo que produce una mayor y más rápida pérdida de músculo que una vida activa[20]. El estilo de vida sedentario está relacionado con un nivel bajo de actividad física. Una de las causas más importantes, y que todo ser humano tiene, son las alteraciones de la marcha y el equilibrio. Así, con la edad y el paso del tiempo se va perdiendo fuerza y la percepción de las cosas y esto se exacerba con un estilo de vida sedentario[51].
– *Caquexia*. Reconocida como una condición asociada con un número de enfermedades crónicas y agudas, la caquexia fue definida por Evans y cols.[52] como un síndrome metabólico complejo asociado con la enfermedad subyacente y caracterizado por la pérdida de músculo con o sin pérdida de masa grasa. Esta pérdida exagerada de masa músculo esquelética distingue la caquexia de la pérdida de peso que se debe únicamente a la reducción de ingesta de energía.
– *Estrés oxidativo*. Es un estado en el que se altera el control normal y equilibrado de la producción de oxidantes y la capacidad antioxidante[53]. A niveles fisiológicos, estas moléculas oxidantes cumplen importantes tareas de señalización, pero cuando la concentración se eleva, se produce el fenómeno conocido como estrés oxidativo, el cual provoca efectos adversos tales como alteraciones de los lípidos, proteínas y el ADN. Está ampliamente demostrado en la literatura que el estrés oxidativo se asocia con enfermedades crónicas y con el proceso de envejecimiento[54], y supone que un aumento de estrés oxidativo dirige a las células del músculo a un estado catabólico que lleva a pérdida de masa muscular[55]. Existen múltiples estudios que prueban que el estrés oxidativo se asocia con enfermedades crónicas Además, el estrés oxidativo es un potente inductor de la apoptosis, una forma de muerte celular programada que está regulada genéticamente[56].
– *Células satélites*. Aunque los mecanismos exactos que causan la sarcopenia no se han dilucidado, la hipótesis de que las células satélites podrían desempeñar un papel importante en la pérdida de masa muscular esquelética relacionada con la edad ha ganado recientemente mucho interés. Las células satélites, o células madre del músculo, son la única fuente para la generación de mionúcleos nuevos *in vivo* en el músculo esquelético[57]. Las células satélites son esenciales para la reparación e hipertrofia del tejido muscular. Normalmente, estas células se encuentran en reposo entre la lámina basal y la membrana plasmática de fibras musculares. En la proliferación y activación subsiguiente, la mayoría de las células satélites se diferencian para formar mionúcleos nuevos, o bien se fusionan con las fibras existentes para generar nuevas fibras, mientras que una pequeña proporción vuelve a quiescencia[58,59]. Debido a que las células satélites son responsables del mantenimiento de la masa muscular esquelética, una disminución en el número de estas células, o en su capacidad para activarse y proliferar en respuesta a estímulos anabólico, es probable que resulte en una alteración estructural del musculo y su función[58,60,61].
– *Composición corporal*. A través de la historia se ha relacionado la pérdida de peso con el aumento en la edad. También, la disminución de la masa muscular en la población de edad avanzada es un factor importante de debilidad muscular[62]. Los hombres mientras van envejeciendo aumentan la masa grasa y disminuye la masa muscular pero, posteriormente, la masa grasa disminuye[63]. Por su parte, las mujeres tienen un patrón semejante[63], aumento de la grasa intramuscular y visceral con el envejecimiento al tiempo que disminuye la grasa subcutánea[64,65].
– *Fragilidad*. Se le conoce como un síndrome geriátrico que se caracteriza por deterioros acumulativos, relacionados con la edad, de varios sistemas fisiológicos, con alteración de la reserva homeostática y disminución de la capacidad del organismo de soportar el estrés. Todo ello tiende a aumentar la vulnerabilidad dando lugar a efectos no deseados como caídas, hospitalización, institucionalización y mortalidad[2,66,67]. Fried y cols.[67] crearon una definición fenotípica de la fragilidad basada en aspectos físicos fácilmente identificables. Tres o más de las características siguientes respaldan un diagnostico de fragilidad: pérdida de peso involuntaria, agotamiento, debilidad, velocidad lenta de la marcha y baja actividad física[2,67]. La fragilidad y la sar-

copenia se superponen; y de esta forma gran cantidad de ancianos frágiles presentan sarcopenia y algunas personas de edad avanzada con sarcopenia también son frágiles[2]. El concepto general de fragilidad, sin embargo, va mas allá de los factores físicos, de modo que también abarca dimensiones psicológicas y sociales, como estado cognitivo, apoyo social y otros factores ambientales[66].

- *Inmovilidad y cama*. Son lamentablemente consecuencias comunes de ingreso hospitalario por enfermedad o trauma. Diversos estudios han demostrado que, en pacientes ancianos sanos en cama durante 10 días, existe una reducción en la síntesis de proteínas, y una significativa pérdida de masa muscular sin cambios significativos en la masa grasa, mientras que en los jóvenes tales efectos sólo se observan después de 28 días de estar en cama[68,69]. Esto demuestra que la persona de edad avanzada es especialmente propensa a la pérdida de masa muscular cuando está en cama. En pacientes sometidos a cirugía, el aumento de los niveles de cortisol tiene efectos graves sobre el metabolismo de las proteínas del músculo esquelético, causando más proteólisis y afectando los niveles de insulina[70]. Los efectos de la suplementación de aminoácidos durante el período de inactividad post-traumático pueden mejorar los efectos inducidos por altos niveles de cortisol[70].
- *Pérdida de neuronas por medio del envejecimiento neuromuscular*. Es un proceso progresivo e irreversible que aumenta con la edad. Entre las causas que contribuyen a la pérdida de resistencia observada en la sarcopenia, debemos mencionar los cambios en el sistema nervioso debido a la edad, que provocan la pérdida de unidades motoras. Una unidad motora se compone de una motoneurona alfa y todas las fibras musculares conectadas con ella. Si las motoneuronas alfa se pierden, las fibras del músculo denervado se conectan para sobrevivir a las motoneuronas alfa. Ésto determina que una motoneurona alfa puede conectarse con más fibras musculares y constituir grandes unidades motoras[33]. Todo ello conduce a la pérdida de eficacia y podría ser la causa del temblor típico y fatiga en el anciano, dando como resultado la pérdida de precisión motor y la mala coordinación relacionada con la edad[71]. También se produce la desaceleración del pico de contracción, dando lugar a una reducción en la fuerza producida y la proporción en la fuerza-velocidad. Estos efectos son secundarios a los cambios en dos proteínas esenciales para el control de la contracción: (1) el receptor ryanodine y (2) la Ca-ATPasa.

Tratamiento de la sarcopenia

Dentro de los tratamientos para combatir la sarcopenia y sus efectos a través del tiempo se ha encontrado que el entrenamiento de la fuerza es uno de los más utilizados y que a su vez arroja resultados muy positivos y beneficiosos para esta población.

Entrenamiento de la fuerza

El entrenamiento de fuerza consiste en la utilización de la fuerza para lograr la contracción muscular, y así incrementar la resistencia anaeróbica, la fuerza muscular y el tamaño de los músculos. El entrenamiento con pesas puede proporcionar beneficios funcionales significativos, incrementos en las capacidades cognitivas, volitivas y una mejora en la salud general y el bienestar[13].

Ejercicios de fuerza

Como se ha comentado con anterioridad la sarcopenia está mediada por múltiples mecanismos, incluyendo estilos de vida sedentarios, la malnutrición, muerte de las neuronas alfa, concentraciones alteradas de hormonas y aumento de la inflamación[33,72]. Actualmente, el entrenamiento de la fuerza es uno de los métodos más eficaces para combatir la sarcopenia (mediante la estimulación de la hipertrofia), incrementar la masa muscular y la fuerza[69] y mejorar la adaptación neuromuscular[25,33,74-82].

Por tanto, dentro de un programa de ejercicios se debería incluir el entrenamiento de la fuerza. Típicamente, los incrementos de fuerza asociados con el entrenamiento han sido mucho más grandes que la respuesta hipertrófica. Además, el entrenamiento de fuerza parece ser relativamente seguro, incluso en los participantes con múltiples comorbilidades[83,84]. Como resultado, se obtiene una mayor capacidad para realizar las actividades de la vida diaria, la prevención del deterioro funcional y la discapacidad. Por otra parte, es importante destacar que se han reportado escasos efectos secundarios asociados a este tipo de tratamiento, y que únicamente habría que limitarlo en pacientes con insuficiencia cardíaca congestiva[70].

Entrenamiento de la fuerza en personas mayores

Revisiones sistemáticas han demostrado que incluso en los ancianos más viejos el entrenamiento de fuerza aumenta la masa muscular, la potencia y la fuerza muscular[82], además de mejorar parámetros objetivos del síndrome de fragilidad tales como la velocidad de la marcha y el tiempo de levantarse de una silla[82]. Aunque inicialmente estos resultados sobre la mejoría de la función física no eran claros, los estudios de Liu y Latham[82], han demostrado que es una intervención eficaz para mejorar la función física en ancianos y retrasar por lo tanto la discapacidad. Otros estudios experimentales han demostrado, en grupos de personas de edad avanzada, diferencias significativas en el área de la sección

transversal muscular del grupo muscular cuádriceps femoral, medida antes y después de sólo 2-3 meses de un entrenamiento de fuerza[85,86]. Sin embargo, los efectos del entrenamiento sobre el área de la sección transversal muscular se tiene que interpretar con cautela debido a que la hipertrofia muscular inducida por el entrenamiento de fuerza puede no ser un proceso uniforme a lo largo de todo el paquete muscular[87]. Así, en un estudio realizado en mujeres de edad avanzada por Häkkinen y cols.[87] se puso de manifiesto que los cambios inducidos tras 21 semanas de entrenamiento de fuerza en el área de sección transversal, determinada por resonancia magnética nuclear, no eran uniformes a lo largo de grupo muscular cuádriceps femoral, de tal forma que los aumentos fueron superiores en las regiones con más sección transversal, en las porciones proximales del vasto lateral y en las porciones distales del vasto medial. Sin embargo, estos hallazgos no se observaron en el músculo vasto intermedio ni en el recto femoral.

Por otro lado, al analizar la influencia que tiene la proporción de fibras rápidas y lentas sobre los incrementos en la fuerza muscular y el área de sección transversal, se observaron mayores incrementos en el área de sección transversal de los músculos entrenados que aquellos sujetos que tenían una menor proporción de fibras rápidas[88]. Esto podría ser de gran importancia si la pérdida de fibras musculares que se produce con el envejecimiento realmente afectara en mayor medida a las fibras musculares de contracción rápida, tal y como han sugerido algunos estudios. La explicación podría encontrarse en los cambios producidos a nivel del sistema nervioso y por pequeñas modificaciones en las propiedades contráctiles de las fibras con el entrenamiento. Así, un anciano vigoroso con funcionalidad conservada, sin comorbilidad y con un nivel de actividad física previa elevado, necesitará un tipo de entrenamiento más exigente que aquel que sea frágil y presente patologías asociadas que afecten a su función y que deberá comenzar el programa con un estímulo menor.

Está claro, conforme a lo establecido por Seguin y Miriam[89], que a partir de una variedad de programas de entrenamiento de fuerza controlado y supervisado, incluso en el propio domicilio, se pueden reportar beneficios significativos en la salud de los adultos mayores. Los principales retos de este campo del ejercicio serían identificar las mejores recomendaciones para los adultos mayores y aumentar, en gran medida, el acceso a métodos seguros y eficaces en programas de entrenamiento de fuerza.

Frischknecht[90] concluyó que el entrenamiento de fuerza en personas de edad avanzada produce hipertrofia de las fibras musculares y mejora los factores neurales implicados en la producción de fuerza. La fuerza a su vez mejora el rendimiento físico y permite una vida más activa e independiente hacia el final de la misma. Frontera y Bigard[91] indicaron que el entrenamiento de fuerza ha demostrado invertir parcialmente las pérdidas relacionadas con la edad en la función muscular. El progreso en los resultados del entrenamiento de fuerza aumenta de forma espectacular la fuerza muscular, hipertrofia (aunque en menor medida), aumento en la síntesis de proteínas, aumento en la fuerza de la fibra muscular específica, y cambios en pruebas funcionales, tales como caminar y poder subir escaleras. Todas estas afirmaciones refuerzan la hipótesis de que el entrenamiento de la fuerza progresivo podría ser una herramienta eficaz y segura contra la sarcopenia también en los pacientes geriátricos. Por lo tanto, desde un punto de vista preventivo, todos los sujetos de edad avanzada deben ser advertidos para iniciar este tipo de programa de ejercicio y continuar tanto tiempo como sea posible[92,93]. De hecho, si realizamos una comparación con personas jóvenes, los ejercicios de fuerza en ancianos producen un incremento en la fuerza muscular menor en términos absolutos pero similares en términos relativos[70].

Componentes del entrenamiento de la fuerza

Diferentes combinaciones de las variables que componen el entrenamiento, como por ejemplo el número de repeticiones por serie, número de series y descanso entre series, originan diferentes respuestas fisiológicas. De manera general, todos los programas de entrenamiento inducen ciertas mejoras de la fuerza máxima, hipertrofia o potencia muscular. Sin embargo, determinadas combinaciones tendrán un especial énfasis de adaptación en unas o en otras manifestaciones de la fuerza[94]. Estos ejercicios de fuerza deben ser realizados en la modalidad de circuitos con intensidades del 70-90% de (1RM) y enfatizando el movimiento excéntrico por lo menos dos días a la semana no consecutivos[25,33,76,78,95]. Las personas mayores retienen la capacidad de mejorar su fuerza muscular después de participar en un programa de entrenamiento sistemático de fuerza máxima siempre y cuando la intensidad y duración del periodo de entrenamiento sean suficientes[96]. Estos programas deberán seguir los mismos principios básicos de entrenamiento que los diseñados para jóvenes o deportistas: 1) principio de sobrecarga, 2) progresión, 3) especificidad e individualidad del entrenamiento, y 4) desentrenamiento o reversibilidad[97]. Así, este tipo de programa de entrenamiento deberá producir un estímulo lo suficientemente intenso, por encima del que suponen las actividades regulares de la vida diaria, como para obtener la respuesta de adaptación deseada (principio de sobrecarga), pero sin llegar a producir agotamiento o esfuerzo indebido[94]. Una vez que el organismo se adapte a este estímulo será necesario que se modifique y/o incremente, para que se continúe progresando (principio de la progresión). Si las cargas de entrenamiento no se incrementan progresivamente (entrenamiento de fuerza progresivo), los músculos se adaptarán al nivel de fuerza solicitado y se mantendrán los mismos niveles de fuerza hasta que no se someta al sistema neuromuscular a un estímulo mayor[94]. Cuando una persona deja de entrenar, se producirá la regresión de las adaptaciones conseguidas. Además, el entrena-

miento de fuerza deberá ser específico para los grupos musculares más utilizados y con transferencia directa (principio de especificidad) a actividades de la vida diaria como, por ejemplo, sostener una bolsa de la compra o subir escaleras.

No obstante, las adaptaciones producidas por un programa de entrenamiento de fuerza serán diferentes entre las personas y vendrán determinadas por su nivel de entrenamiento previo y edad. Una persona que se encuentre en buen estado físico necesitará un tipo de entrenamiento más exigente que aquel que sea inactivo y deba comenzar el programa de entrenamiento con un estímulo menor. Por ello, los programas de entrenamiento de fuerza suelen variar en función de su intensidad, número de repeticiones y series, así como la duración y la frecuencia de las unidades según el objetivo del entrenamiento (tabla I).

El entrenamiento de fuerza muscular progresiva requiere instrucciones precisas acerca de la carga externa, principalmente según la intensidad. La carga a levantar por cada sujeto está definida por los equipos tradicionales de entrenamiento: pesas, bandas de resistencia, propio peso corporal entre otros. La forma en que se realizan los ejercicios contribuye a la transferencia de la fuerza muscular en las actividades de la vida cotidiana como por ejemplo, levantarse de una posición sentada o llevar las compras[98].

Existe la opinión generalizada de que, a una edad avanzada, la intensidad de la carga debe reducirse a fin de evitar lesiones y uso excesivo crónico. Sin embargo, este efecto no se apoya en la evidencia actual, y varios grupos de trabajo han señalado la necesidad de una mayor intensidad para ancianos y jóvenes. En varios estudios controlados aleatoriamente que incluyeron un total de 1,313 sujetos mayores de 65 años, Steib y cols.[99] demostraron una dependencia notable de la capacidad de fuerza a la mejora de la intensidad del entrenamiento de fuerza (> 75% de la capacidad de la fuerza máxima)[99]. Ciolac y cols.[100] realizaron un estudio combinado durante 13 semanas de un entrenamiento de alta intensidad en dos grupos (mujeres entre 29 y 65 años) y registraron aumentos en la fuerza en ambos grupos, sin

Tabla I

Efectos y ejemplos de las dosis recomendadas en el entrenamiento de fuerza y los posibles enfoques organizativos para diferentes formas de entrenamiento en las personas mayores (modificado de Mayer y cols.[98])

Objetivos	*Posibles efectos del entrenamiento*	*Dosis*	*Posibles enfoques organizativos*
Aumento de la fuerza muscular	Incremento de la masa muscular	8-12 repeticiones por grupo muscular de un 70-85% de una repetición máxima, 3 sets; 2-3 unidades de entrenamiento por semana, por lo menos 8 a 12 semanas.	Ejercicios en estudio, gimnasio, programa en el hogar, inicialmente bajo la instrucción, luego de forma independiente.
	Entrenamiento de la coordinación intramuscular	Hasta 8 repeticiones por grupo muscular con intensidades de más del 80% de una repetición máxima, 3-5 series, 3 unidades de entrenamiento por semana, varias semanas.	Ejercicio en estudio, gimnasio, programa en el hogar, bajo instrucción.
	Entrenamiento de la coordinación intermuscular	Varias repeticiones, mas unidades de entrenamiento diario, de alta velocidad de movimiento, entre otros.	Entrenamiento sobre superficies irregulares, con o sin pesos adicionales; bajo instrucción, luego de forma independiente.
Reducción de la sarcopenia	Incremento de la masa muscular	8-12 repeticiones por grupo muscular de un 60-80% de una repetición máxima, 3 series, 3 unidades de entrenamiento por semana, por lo menos 8-12 semanas	Ejercicios en estudio, gimnasio, programa en el hogar, inicialmente bajo la instrucción, luego de forma independiente.
Adaptación a tendones y huesos	Aumento de la síntesis neta de colágeno, reducción en la pérdida de densidad ósea	Intensidades medias a elevadas (> 60-80% de una repetición máxima, > peso corporal), varias unidades de entrenamiento por semana, semanas o meses.	Ejercicio en estudio, gimnasio, bajo instrucción.
Prevención de caídas y lesiones	Optimizar el control postural, la formación de la coordinación intermuscular	Varias repeticiones, mas unidades de entrenamiento diario, de alta velocidad de movimiento.	Entrenamiento sobre superficies irregulares, con o sin pesos adicionales; bajo instrucción, luego de forma independiente.
	Entrenamiento de la coordinación intramuscular	Hasta 8 repeticiones por grupo muscular en las intensidades de más de 80% de una repetición máxima; 3-5 series; 3 unidades de entrenamiento por semana; varias semanas.	Ejercicio en estudio, gimnasio, programa en el hogar, bajo instrucción.

diferencias entre los grupos y sin efectos adversos. En otro estudio de seguimiento, hombres (con edades comprendidas entre 65 y 72 años) también se sometieron a 13 semanas de entrenamiento de fuerza. Los resultados también pusieron de manifiesto aumentos relevantes en la fuerza como una adaptación al entrenamiento con pesos[101]. Por lo tanto, en las personas de edad avanzada, la fuerza de alta intensidad progresiva es efectiva y no son de esperar efectos adversos importantes.

Junto al componente de la intensidad es importante recalcar la importancia del tiempo de duración y el volumen de ejercicios en el entrenamiento de fuerza para esta población. Strasser y cols.[102] demostraron que después de 6 meses de entrenamiento de fuerza 3 veces por semana como máximo, la fuerza se incrementó un promedio del 15% para el press de pierna ($P < ,01$), 25% para el press de banca ($P < 0,01$), 30% para jalón al pecho ($P < ,001$), y la masa corporal magra se incrementó en un $1,0 \pm 0,5$ kg en los adultos de edad avanzada. Sobre la base de este ensayo controlado aleatoriamente, concluyeron que la intensidad de carga para promover la hipertrofia con el entrenamiento de la fuerza debe acercarse a un 60-80% de una repetición máxima (1RM), con un volumen de ejercicio de 3 a 6 series por grupo muscular por semana y de 10 a 15 repeticiones por ejercicio. Binder y cols.[103], en un ensayo aleatorio y controlado, estudiaron los efectos del entrenamiento de la fuerza en 91 sujetos con el síndrome de fragilidad (≥ 78 años) residentes de una comunidad. Tres meses de entrenamiento de fuerza supervisado provocó un aumento en la fuerza máxima voluntaria y la masa libre de grasa en el cuerpo de las mujeres y hombres que participaron en el estudio, principalmente en el área de las piernas. En general, las mejorías significativas (hasta > 50% de aumento de la fuerza) se puede esperar hasta después de 6 semanas del entrenamiento de fuerza a un ritmo de 2 a 3 sesiones por semana. Por el contrario, Vincent y cols.[104] realizaron un estudio en adultos mayores sanos con una duración de 26 semanas, en un programa de ejercicios de fuerza de baja y alta intensidad y sólo encontraron una mejora modesta en la fuerza muscular del muslo en el entrenamiento de alta intensidad. Por otra parte, Roth y cols.[105] demostraron que 6 meses de entrenamiento de fuerza en las personas mayores de 65-75 años, produce beneficios en la fuerza muscular similares a los obtenidos en individuos más jóvenes de 20 a 30 años. El tiempo de tratamiento necesario para observar efectos positivos es de 10 a 12 semanas, aunque en algunos estudios se observan efectos positivos con 2 semanas de entrenamiento[106].

Además del objetivo de la hipertrofia muscular, el entrenamiento de la fuerza tiene como fin aumentar la fuerza muscular mediante la mejora de la adquisición, la frecuencia y sincronización de las unidades de motoras[9]. Este entrenamiento de la coordinación intramuscular como regla de oro debe realizarse en personas de edad avanzada con mayor peso y con un menor número de repeticiones por serie.

Conclusión

La realización de entrenamiento físico, de forma más específica el entrenamiento de la fuerza, es una de las intervenciones más eficaces para retrasar la sarcopenia y los eventos relacionados que se asocian habitualmente con esta condición. Cada vez se confirman más resultados beneficiosos del entrenamiento de fuerza en la población de personas mayores y sus efectos se extienden a otras situaciones como lo son las caídas y el deterioro cognitivo. En la actualidad se necesitan más estudios que continúen aportando una visión más clara sobre la utilización e integración del entrenamiento fuerza a condiciones como la sarcopenia, así como a otras patologías relacionadas con el deterioro funcional de las personas mayores.

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Revisión

Adherence to Mediterranean diet and bone health

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Abstract

Introduction: **Several studies have concluded that incidences of osteoporosis and osteoporosis-related fractures vary across the European Union, the lowest incidence being reported in the Mediterranean area. The beneficial effect is mainly attributed to a specific eating pattern. The Mediterranean diet contain a complex array of naturally occurring bioactive molecules with antioxidant, anti-inflammatory and alkalinising properties that may contribute to the bone-sparing effect of the Mediterranean diet.**

Objective: **The purpose of this review is to examine the evidence to date on the effects of Mediterranean diet on bone health.**

Methods: **The search for articles came from extensive research in the following databases: PubMed, Scopus and Web of Science. We used the search terms "Mediterranean diet", "adherence", "fruit and vegetable", "olive oil", "fish" "legume", "cereal" "alcohol", "bone", "osteoporosis", "fracture", and combinations, such as "Mediterranean diet and bone" or "Mediterranean diet and fracture".**

Results: **A limited number of studies have examined the relationship between Mediterranean Diet and bone health, and they have reported conflicting results. On the one hand, adherence to a traditional MeDi has been associated with higher bone mineral density and lower fracture risk. The results of these studies could be attributed to the combined beneficial effects of individual components of the Mediterranean diet. On the contrary, several studies failed to show any association between adherence to the MeDi and indices of bone mass.**

Conclusions: **Further large-scale studies are required to clarify the effect of Mediterranean diet on bone health, in order to establish the role of this diet in the prevention of osteoporosis.**

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Key words: *Mediterranean diet. Osteoporosis. Bone.*

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ADHERENCIA A LA DIETA MEDITERRÁNEA Y SALUD ÓSEA

Resumen

Introducción: **Se han encontrado diferencias en los valores de incidencia de osteoporosis y fracturas relacionadas entre los países de la Unión Europea, siendo menor en los países de la zona mediterránea. Este hecho se atribuye principalmente a un patrón de alimentación específica común. La dieta mediterránea contiene un complejo conjunto de componentes bioactivos con propiedades antioxidantes, anti-inflamatorias y alcalinizantes que pueden contribuir al efecto de esta dieta en la salud ósea.**

Objetivo: **El propósito de esta revisión es examinar la evidencia hasta la fecha sobre los efectos de la dieta mediterránea sobre la salud ósea.**

Métodos: **Se realizó una búsqueda en la literatura científica utilizando las siguientes base de datos: PubMed, Scopus and Web of Science. Utilizamos los términos de búsqueda "Dieta Mediterránea", "adhesión", "frutas y verduras", "aceite de oliva", "pescado" "legumbres", "cereal", "alcohol", "hueso", "osteoporosis","fractura", y combinaciones, como "Dieta Mediterránea y el hueso" o "Dieta mediterránea y fracturas".**

Resultados: **Existe un número limitado de estudios que analicen la relación entre el seguimiento de la Dieta Mediterránea y la salud ósea, mostrando resultados contradictorios. Diversos trabajos han mostrado que la adherencia a una dieta mediterránea tradicional se asociado con una mayor densidad mineral ósea y un menor riesgo de fractura en población adulta. Los resultados de estos estudios podrían atribuirse a un efecto beneficioso combinado de los componentes individuales de la dieta mediterránea. Por el contrario, en otros trabajos no se ha encontrado ninguna asociación entre la adherencia a la dieta mediterránea y los índices de masa ósea.**

Conclusiones: **Se requieren más estudios a gran escala para aclarar el efecto de la dieta mediterránea sobre la salud ósea, con el fin de establecer el papel de la dieta en la prevención de la osteoporosis.**

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Palabras clave: *Dieta mediterránea. Osteoporosis. Hueso.*

Introduction

Osteoporosis (OP) is an important worldwide public health concern[1] that affects many millions of people around the world and that will take on increasing significance as people live longer and the world s population continues to increase in number[2]. In addition, osteoporosis related fractures are one of the leading causes of significant morbidity and disability in elderly patients and increases the economic burden on the health care system.The mechanisms involved in osteoporosis pathogenesis are not fully understood[3]. A reduction in bone density in earlier life is likely to increase the risk of OP and its sequelae in adulthood. It is therefore important to raise awareness among the general population on the need to form and maintain good bone health from childhood through the adoption of healthy habits. OP development is influenced by multiple factors. Bone modelling and remodelling processes are governed not only by heritable traits but also by nutritional, mechanical and hormonal factors[4]. Besides the aging process, an inadequate diet and sedentary lifestyle can reduce mineralization.

Although nutrition is only one of the many factors that influence bone mass and fragility fractures, it is of particular importance to bone health because it is modifiable. Diet can be modified for the maintenance and development of bone mass. Proper nutrient intake has a crucial role in both prevention and treatment of osteoporosis[5]. The most relevant nutrients to bone health are calcium and phosphorus because they compose roughly 80% to 90% of the mineral content of bone hydroxyapatite; protein is essential because it is incorporated into the organic matrix of bone for collagen structure upon which mineralization occurs; trace elements, and vitamins (e.g., vitamins D and K) are also crucial in carrying out metabolic processes and reactions in bone[6,7]. Other benefits on bone metabolism derives from bioactive components found basically in vegetables but also some herbs and fruit. Phytochemicals, antioxidants, and other bioactive compounds influence bone metabolism through a variety of mechanisms mainly in reducing oxidative stress and inflammation[8].

To date, the most consistently followed approach to examine the potential relation between dietary factors and skeletal health was based on particular nutrients such as calcium and vitamin D[3]. However, people do not eat isolated nutrients but meals consisting of a variety of foods with complex combinations of nutrients and bioactive components. 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 compounds contained in food. For this reason, there is an increasing interest in the study of dietary patterns that could answer some questions and promote the development of appropriate recommendations for overall dietary habits[9] .

Several studies have concluded that incidences of osteoporosis and osteoporosis-related fractures vary across the European Union. Conspicuous differences are encountered in the severity of osteoporosis, the lowest incidence being reported in the Mediterranean area[10]. The beneficial effect is mainly attributed to a specific eating pattern. The Mediterranean diet (MeDi) key characteristics are high intake of vegetables, legumes, fruits and cereals; moderate to high intake of fish; low intake of saturated lipids and high intake of unsaturated lipids, particulary olive oil; low to moderate intake of dairy products, low intake of meat; and modest intake of ethanol, mostly in the form of wine[11,12]. The Mediterranean diet was introduced to the scientific community by the classic Seven Countries study. Since then data on the association between this diet and cardiovascular disease[13,14], cancer and other chronic diseases have been accumulating[15,16]. However, a limited number of cross-sectional studies have examined the relationship between Mediterranean diet adherence and bone health, and they have reported conflicting results. Therefore, the purpose of this review is to examine the evidence to date on the effects of Mediterranean diet on bone health.

Methods

The search for articles came from extensive research in the following databases: PubMed, Scopus and Web of Science. We used the search terms “Mediterranean diet”, “adherence”, “fruit and vegetable“, “olive oil“, “fish” “legume”, “cereal” “alcohol”, “bone”, “osteoporosis”, “fracture”, and combinations, such as “Mediterranean diet and bone” or “Mediterranean diet and fracture”. The titles and abstracts of the located documents were initially reviewed and the reference lists of selected papers were searched to identify additional articles. We narrowed the search to studies published in English. Additional publications were identified from references provided in original papers.

Results and discussion

Adherence to Mediterranean diet and bone health

The Mediterranean diet is characterized by a high intake of olive oil, plant products, fish and seafood; a low intake of dairies, meat and meat products; and a moderate ethanol intake[15]. These food items contain a complex array of naturally occurring bioactive molecules with antioxidant, anti-inflammatory and alkalinising properties that may contribute to the bone-sparing effect of the Mediterranean diet[10].

Adherence to a dietary pattern close to the Mediterranean diet, have shown to prevent bone disease. Eating habits based on fruit, vegetables, milk, and cereals –that is, similar to those of the Mediterranean

diet– were proven by the Framingham study to be significantly associated with greater bone mass[17]. Nakashima and Takayanagi[18] studied associations between dietary patterns and bone mineral density in Japanese farmwomen and showed that a "healthy" pattern, described by high intakes of green and dark yellow vegetables, mushrooms, fish and shellfish, and fruit, was positively related to bone mineral density. Furthermore, the effect of vegetarian dietary patterns on skeletal health has been studied; lacto-ovo vegetarians appear to have normal bone mass when compared with omnivores. However, a more recent study reported that the scientific findings support the hypothesis that vegans do have lower bone mineral density than their nonvegan counterparts[19].

There are few studies that have assessed the effect of the Mediterranean diet on bone health. Besides, the impact of MeDi adherence on bone health remains unclear. In table I are summarized the characteristics of these studies included in relation to where the work was conducted, the number of participants in each study, the methods used to evaluate Mediterranean diet adherence, and the main results. Kontogianni et al.[20] described that adherence to a Mediterranean diet evaluated through a Mediterranean Diet Score was not associated with bone mass rates in a sample of adult Greek women, whereas adherence to a dietary pattern close to the Mediterranean diet, i.e., high consumption of fish and olive oil and low red meat intakes, was positively related to bone mass, suggesting the potential bone-preserving properties of this pattern through adult life. An interventional study conducted in Spain[21], concluded that a Mediterranean dietary pattern enriched with mixed nuts, does not seem to have any significant effect on bone metabolism in elderly subjects. However the authors pointed out that the sample selection criteria could limit the extrapolation of the findings, as the endpoint of the study was cardiovascular mortality, so the study focused on subjects with a high risk of cardiovascular disease and had already been eating a reasonably good Mediterranean diet pattern for a long time before randomization into the trial[21]. Recently, Rivas and coworkers[22] hypothesized that adherence to the Mediterranean diet measured as a Mediterranean diet score (MDS) has a beneficial effect on bone mineral density in the calcaneus measured by a dual energy X-ray absorptiometry. For the purposes of this study, a sample of healthy women from Southern Spain was chosen. Subjects were grouped into two major groups: a first group consisted of women of reproductive age, and a second group consisted of postmenopausal women. Significant linear trends between the MDS and bone mineral density were observed in all subjects studied. The authors concluded that a varied diet based on Mediterranean diet patterns may be beneficial in the prevention of osteoporosis. Fernandez-Real et al.[23] compared the effects of a virgin olive oil enriched Mediterranean diet, a walnut-enriched Mediterranean diet, and a low-fat diet for two years on osteocalcin and bone formation markers in the blood of men at high risk of cardiovascular disease. The virgin olive oil enriched Mediterranean diet alone was associated with increased serum levels of osteocalcin and the bone remodelling marker procollagen amino-terminal propeptide, suggesting a protective role for this diet in bone health.

The potential protective effect of the MeDi against the risk of hip fractures has been evaluated in several studies. Recently, in a large cohort of adults from eight European countries, Benetou et al[11] reported an inverse association between adherence to a Mediterranean-type diet and the risk of hip fracture in European older persons. Indeed, in this large cohort of adults enrolled in the EPIC study (N = 188,795 participants, 802 incident hip fractures), higher adherence to the MeDi was associated with a 7% decrease in hip fracture incidence, notably among participants aged 60 years or older and among men in the model adjusted only. On the contrary Feart and coworkers[24] showed that greater MeDi adherence was not associated with a decreased risk of fractures in French older persons.

There is evidence that specific components of Mediterranean diet may prevent the prevention of osteoporosis and/or hip fracture occurrence. In this context, a summary of the studies that demonstrate this association is shown below.

Olive oil and bone

Scarce epidemiological literature is available about the association between fat intake and the bone health. Saturated fat (SFA) intake has been reported to be associated with a higher risk of bone loss and osteoporotic fractures[25]. On the contrary, monounsaturated fat (MUFA) has been reported to have a beneficial effect on bone health[25,26]. Various epidemiological studies have associated the intake of the monounsaturated fatty acids of olive oil with bone health. A study of male and female adults in Greece[26] reported a positive association between the intake of monounsaturated fats and mineral bone density; the authors highlighted the substantially lower incidence of fractures in Greece, where there is high olive oil consumption, than in the USA or North European countries. Rivas et al.[4] described in female adults in Spain a significant correlation between the consumption of monounsaturated fatty acids and the mineral density of the heel bone (calcaneus).

Besides triglycerides, olive oil contains a wide variety of so-called minor compounds that are of major importance from a chemical and organoleptic standpoint. These include phenolic compounds, which constitute a highly complex fraction formed by numerous substances, some of which are yet to be identified. The known substances include simple phenols, e.g., hydroxytyrosol, tyrosol, caffeic acid, vanillic acid, *p*-coumaric acid, ferulic acid, and vanillin; flavonoids,

Tabla I

Description of the studies that have assessed the effect of the Mediterranean diet on bone health

Reference	*Country*	*Subjects*	*Method for measuring bone mass/fracture risk*	*Method used to evaluate MeDi adherence*	*Results*	*Conclusions*
Kontogani *et al*. (2010)[20]	Greece.	Adult women (N=300)	Lumbar spine and total BMD by DEXA.	Mediterranean Diet Score (Trichopoulou et al., 2003)[22].	Adherence to MedDi was not associated with indices of bone mass. Consumption of fish, olive oil and low intake of red meat was associated with lumbar spine BMD (p = 0.017) and total body BMD (p = 0.048)	Adherence to a MedDi was not associated with indices of bone mass.
Bullo *et al*. (2009)[21]	Spain.	Adult aged 60 to 80 at high risk for CVdisease (N=230).	Bone formation and resorption markers Bone mass by ultrasound scanning.	Three interventional groups: low-fat diet, a MedDi supplemented with VOO, or MedDi supplemented with nuts.	Subjects in MedDi with nuts group had nonsignificantly higher urine free deoxypyridoxine:creatinine ratio (p=0.14).	A Mediterranean dietary pattern does not seem to have a much greater effect on bone metabolism biomarker.
Fernández-real *et al*. (2012)[23]	Spain.	Adult aged 60 to 80 years at high risk for CVdisease (N=230).	Total circulating osteocalcin Bone markers N-terminal propeptide (P1NP).	Three interventional groups: low-fat diet, a MedDi supplemented with VOO, or MedDi supplemented with nuts.	Total osteocalcin increased in the MedDiet+VOO group (p=0.007) in parallel to increased P1NP levels (p=0.01) but not in subjects on the MedDiet+nuts (p=0.32).	Consumption of a Mediterranean diet enriched with virgin olive oil for 2 years is associated with increased serum osteocalcin and P1NP concentrations, suggesting protective effects on bone.
Rivas *et al*. (2013)[22]	Spain.	Adult women aged 18-65 years (N=200).	Calcaneous BMD by DEXA.	Mediterranean Diet Score (Trichopoulou et al., 2003)[22].	Significant linear trends between MeDi adherence and BMD were observed (p= 0.001).	MedDi pattern is associated with higher BMD.
Benetou et al. (2013)[11]	European countries participants in the EPIC study.	Adults aged 35-70 years (N= 188,795).	Incident hip fracture was reported by hip and radius fracture registries for a median of 9 years.	Mediterranean Diet Score (Trichopoulou et al., 2003)[22].	Adherence to MeDi was associated with a 7% decrease in hip fracture incidence. Association was more evident among men and older individuals.	Increased adherence to MeDi appears to protect against hip fracture occurrence, particularly among men.
Feart et al. (2013)[24]	France	Adult aged 67 years or older (N=1,482).	Incidence of hip, vertebral and wrist fractures were self-reported every 2 years over 8 years.	Mediterranean Diet Score (Trichopoulou et al., 2003)[22].	Higher MeDi adherence was associated with a non-significant increased risk of fractures at any site.	Greater MeDi adherence was not associated with a decreased risk of fractures in French older persons.

MeDi: Mediterranean diet. BMD: bone mineral density. DEXA: Dual-energy X-ray absorptiometry. CV: cardiovascular. VOO: Virgin olive oil.

e.g., luteolin and apigenin; and other more complex compounds such as those derived from oleuropein, ligstroside, ligustaloside[27]. Numerous potential health benefits of the phenolic compounds of olive oil have been reported, but their role in the prevention of bone diseases (e.g., osteoporosis) has been less well studied. Researchers have shown the phenolic compounds in different vegetables species can modulate the functions of osteoblastic cells, including their proliferative capacity and maturation, by increasing alkaline phosphatase activity and the deposit of calcium ions in the extracellular matrix[28-30]. Oleuropein, the main phenolic compound in olive-tree leaves, together with virgin olive oil and olives, was proved to be effective in a rat model of senile osteoporosis with a dosage of 150 mg/kg diet. In addition oleuropein shifts the differentiation of mesenchymal stromal cells in favour of osteoblastogenesis suggesting that oleuropein intake might have preventive effects against the bone loss associated with osteoporosis and aging[31]. The main phenolic compounds in virgin olive oil are tyrosol and hydroxytyrosol. Their administration in the diet at doses of 0.017% prevented the inflammation-induced bone mass loss in ovariectomized rats in a model of senile osteoporosis and increased their osteoblast activity, as evidenced by their elevated plasma osteocalcin levels[32,33]. Finally, luteolin, a flavonoid present in VOO, lessens bone mass loss in postmenopausal osteoporosis by reducing osteoclast differentiation and function[34].

Intake of fruits and vegetables: implications for bone health

Fruit and vegetable consumption is a common feature of the Mediterranean diet. Recent studies have focused on the effects of fruit and vegetable intakes on bone health[35,36]. Fruit and vegetable intake has been associated with increased bone mineral density or reduced fracture risk[37]. Larger bone size in early pubertal children and adolescents[38-40], and better bone mass in adult men and women have been associated with fruit and vegetable consumption[41,42]. In addition, it has been demonstrated that a dietary intervention based on low fat and increased fruit, vegetable, and grain intake reduced moderately the risk of multiple falls and slightly lower hip BMD[43].

The mechanism whereby fruit and vegetables may affect bone is not clear and may be multifactorial[44]. Fruits and vegetables might affect bone health via the effects of several components in these foods, such as minerals (e.g., calcium, potassium, and magnesium), vitamins (e.g., vitamin K and C), phytochemicals (e.g., phytoestrogens), and oligosaccharides (especially inulin-type fructans), either through their effect on calcium absorption or their involvement in the bone remodeling sequence, could mediate this association[11,45]. In addition, fruits and vegetables contain many different antioxidant components. 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[12,46]. Recently, Rivas et al.[3] demonstrated that the overall dietary antioxidant intake was significantly associated with bone mineral density in adult women.

It should be taken into account that a higher dietary acid load is believed to result in bone mineral dissolution and greater bone resorption, and a diet rich in fruit and vegetables may result in a more alkaline environment, which has been proven to reduce urinary calcium excretion[43]. The low grade metabolic acidosis induced by the modern diet is exacerbated during ageing when renal function begins to decline requiring the body's skeletal reserves to be called upon to relinquish bicarbonate to produce alkaline buffers needed to continuously balance the acid load.Typical diets are acidic because predominantly acid (hydrogen ions) rather than base (bicarbonate) is created during the metabolism of the daily food intake. Acid forming grains and high protein food derived from animal origin (meat, fish, and eggs) contain sulphur-based amino acids, methionine, and cysteine which create acid when metabolized. Alkaline forming foods contain potassium salts which can be broken down to make alkaline buffers[47]. Fruit/vegetables influence on acid-base balance is crucial, being the unique dietary source of alkaline precursor constituents, so it is important reason to increase consumption to avoid bone loss during ageing[8,48,49]. Vegetables and fruit are considered alkaline because of their high mineral content in the form of salts of organic acids. The salts, predominantly potassium based but also calcium and magnesium, generate bicarbonate to balance the acid produced from the rest of the diet[20].

Consumption of legumes and cereal and bone health

Legume and cereal consumption is high in Mediterranean areas. These foods are highly rich in vitamin B, calcium, phytoestrogens and other phytochemicals. Thus, an adequate intake of these foods has been associated with higher bone mineral density, decreased bone loss with ageing, or reduced risk of fracture[22]. There are data showing that legumes and grains may protect bone metabolism in humans[50]. It has been showed that the consumption of legumes decreased bone turnover in ovariectomized rats. In a recent study, Park et al.[51] showed that a diet containing legumes significantly increased the bone mineral density of the femur and spine, and bone volume of the femur in ovariectomized rats. On the contrary, Rivas and coworkers[22] did not find any significant association between legume and cereal intake and bone mineral density in a sample of healthy women from Southern Spain. One explanation could be that the consumption

of this food group was similar in all the subjects studied, so it may be difficult to find any significant differences. In addition non-refined cereals and legumes are acid-producing foods, which may alter the acid-base balance that is associated with negative impact on bone health[20].

Alcohol effects on bone

Alcohol and more specifically wine, is an essential component of the Mediterranean diet. There is inconsistent evidence regarding the association between alcohol consumption and bone mineral density (BMD). Tucker et al.[52] showed that moderate consumption of alcohol may be beneficial to bone in men and postmenopausal women. However, in men, high liquor intakes (> 2 drinks/d) were associated with significantly lower BMD. The authors concluded that the tendency toward stronger associations between BMD and beer or wine, relative to liquor, suggests that constituents other than ethanol may contribute to bone health. Ying et al.[53] describe the associations between total and beverage-specific alcohol intake and bone loss in older men and women. Their data showed that alcohol intake especially red wine might prevent bone loss in older men. However, women consuming excessive alcohol amount, were found to be at higher risk for hip fracture incidence compared to those consuming moderate amounts. This finding is in agreement with results from other relevant investigations in which moderate intake of alcohol was found to increase bone mineral density[54]. Nevertheless, over and beyond bone mineral density, one cannot oversee the effect of high alcohol consumption on the risk of falling, as well as its association with low body mass index, which is a risk factor for hip fractures.

Fish bone health benefits

A moderate consumption of fish is recommended for a healthy diet and is also a feature of the Mediterranean diet. Fish is a source of high quality protein; omega-3 fatty acids; vitamins, such as A and D; and minerals, such as selenium, calcium, iodine and zinc[55]. Many of these nutrients have positive effects on bone health. The positive effects of calcium and vitamin D, which are the most important nutrients for bone health, have long been established. In Spain, fish consumption accounts for 87% of total dietary vitamin D intake. Several studies have shown a potentially beneficial effect of fish intake[56,57] against osteoporosis and fracture occurrence. Recently, omega-3 fatty acids, especially eicosapentaenoic acid and docosahexaenoic acid, have been shown to have a beneficial effect on bone health. Several mechanisms have been proposed (affecting bone formation, bone resorption, serum calcium and vitamin D, oxidative stress, and inflammatory mediators). However, neither the exact benefit nor the exact mechanism of action of fatty acids has been determined yet. Therefore, although there are some clinical evidences linking bone metabolism and dietary lipids, more clinical trials are necessary to prove whether dietary changes or omega-3 supplementation play a major role in bone health and turnover[8].

Conclusion

In conclusion, a limited number of studies have examined the relationship between Mediterranean Diet and bone health, and they have reported conflicting results. On the one hand, adherence to a traditional MeDi has been associated with higher bone mineral density and lower fracture risk. The results of these studies could be attributed to the combined beneficial effects of individual components of the Mediterranean diet. On the contrary, several studies failed to show any association between adherence to the MeDi and indices of bone mass. There is evidence that specific components of this diet may play a role in the prevention of osteoporosis and/or hip fracture occurrence. In this context, an association has been showed between individual key characteristics of MeDi, such as high consumption of fruits, vegetables, and olive oil, as well as moderate to high consumption of fish, and moderate intake of alcohol with reduced incidence of osteoporosis, or reduced fracture occurrence. Further large-scale studies are required to clarify the effect of Mediterranean diet on bone health, in order to establish the role of this diet in the prevention of osteoporosis.

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Revisión

Efecto de la desnutrición pre y posnatal sobre componentes del síndrome metabólico sobre etapas posteriores de la vida; revisión sistemática

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Resumen

Antecedentes: **Un entorno intrauterino o una infancia temprana con desnutrición, pueden convertirse en factores de riesgo que aumentan la susceptibilidad de enfermedades crónicas degenerativas en etapas posteriores de la vida. La programación fetal significa que durante la etapa embrionaria pueden presentarse condiciones adversas del entorno que generan cambios en los parámetros fisiológicos que a su vez aumentan la susceptibilidad a cambios metabólicos en etapas posteriores de la vida.**

Objetivo: **El propósito de este estudio fue analizar el efecto de la desnutrición pre y post natal en la presentación de obesidad y componentes del síndrome metabólico (SM) en etapas posteriores de la vida.**

Metodología: **Se realizó una búsqueda electrónica de la literatura en las bases de datos de PubMed y EBSCO con el siguiente término: "Undernutrition in early life and obesity" de artículos publicados de noviembre de 1997 a enero del 2014. Se identificaron siete estudios y se anexaron seis obtenidos de otras referencias.**

Resultados: **Se analizaron trece publicaciones de seis estudios realizados en seis países de Asia, África, Europa y Latinoamérica. Diez de los trece estudios fueron de tipo retrospectivo y la edad de la población que participó al final del estudio osciló de los 11 a los 70 años. En todos los estudios se observó una asociación entre la desnutrición pre y postnatal y la aparición de varios componentes del SM.**

Conclusión: **En esta revisión se observó una consistente asociación entre la desnutrición pre y post natal con algún componente del SM en etapas posteriores de la vida.**

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Palabras clave: *Desnutrición. Síndrome metabólico. Factores prenatales. Factores postnatales. Revisión sistemática.*

EFFECT OF PRE AND POST NATAL UNDERNUTRITION ON COMPONENTS OF METABOLIC SYNDROME LATER IN LIFE; SYSTEMATIC REVIEW

Abstract

Background: **A fetal environment or postnatal undernutrition, might become risk factors that increase susceptibility for chronic-degenerative diseases later in life. Fetal programming means that during prenatal period adverse environment might increase the susceptibility for metabolic changes later in life.**

Objective: **The purpose of this study was to analyze the effect of pre-and postnatal malnutrition in the presentation of obesity and components of metabolic syndrome (MS) later in life.**

Methods: **A literature electronic search on PubMed and EBSCO was conducted. The following term was searched: "Undernutrition in early life and obesity", from studies published from November 1997 through January 2014. Seven studies were identified, and six more were included from other references.**

Results: **We analyzed thirteen publications form six studies conducted in six countries from Asia, Africa, Europe and Latin America. Ten of the studies were retrospectives and the age ranged from 11 to 70 years old. In all studies an association of pre or postnatal undernutrition with components of MS later in life was observed.**

Conclusion: **This review shows a consistent association between prenatal and postnatal undernutrition with one or more MS components later in life.**

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Key words: *Undernutrition. Metabolic syndrome. Prenatal factors. Postnatal factors. Systematic review.*

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Introducción

Una de las hipótesis del desarrollo de las enfermedades crónicas propone que la desnutrición durante los períodos importantes de crecimiento y desarrollo como son: la etapa fetal, la infancia temprana y la niñez, daría como resultado una serie de adaptaciones en la estructura y funcionamiento del organismo, las cuales serían importantes para sobrevivir, pero a largo plazo ocasionarían un incremento en el riesgo de presentar diversas patologías[1]. La susceptibilidad para padecer ciertas enfermedades crónico-degenerativas como la hipertensión arterial y la diabetes mellitus tipo 2, pudiera estar programada o determinada por una deficiencia nutricional en etapas tempranas de la vida[2,3]. Así mismo la etapa fetal parece ser un periodo crítico para el desarrollo de la obesidad[4]. Algunos investigadores han observado asociaciones entre el bajo peso al nacer con el riesgo de presentar enfermedad coronaria [5] y bajos niveles de colesterol HDL o concentraciones altas de triglicéridos[6-8]. Otros estudios observaron que la combinación entre el bajo peso al nacer y el período de recuperación rápida de crecimiento (catch-up growth) posterior, pudieran estar relacionados con un incremento en el depósito de grasa central (abdominal) y resistencia a la insulina[9]. En el estudio realizado por Martins y cols., 2004, mencionan que sus hallazgos son similares a los de varios estudios de cohorte, que investigaron el efecto de la malnutrición intrauterina, los cuales mostraron evidencia de que el retardo en el crecimiento intrauterino resulta en una proporción menor de masa magra en la etapa adulta, lo que indica una asociación positiva del peso al nacer con la masa magra, pero no con la masa grasa corporal[11-14].

Los riesgos de la exposición a la desnutrición en etapas tempranas de la vida, pudieran aumentar al estar en contacto con un ambiente nutricional de sobreabundancia en etapas posteriores de la vida[15,16].

Objetivo

El propósito de este estudio fue analizar el efecto de la desnutrición pre y post natal en la presentación de componentes del síndrome metabólico (SM) en etapas posteriores de la vida.

Metodología

Se realizó una búsqueda electrónica de la literatura en base de datos de PubMed y EBSCO con las palabras claves "Undernutrition in early life and obesity", de artículos publicados de noviembre del 1997 a enero del 2014. Se identificaron siete estudios y se anexaron seis más obtenidos de las referencias bibliográficas de los mismos.

Resultados

Se analizaron trece publicaciones de seis estudios, uno realizado en China[17,18], 2011), uno en Biafra[19], uno en Brasil[10], uno en México[20,21], 2003) y uno en Rusia[22] y uno en Holanda[23-28].

Wang y cols., 2012 realizaron un estudio retrospectivo de cohorte en 12.065 adultos de 46 a 53 años de edad, expuestos a desnutrición intrauterina y durante la infancia (dos primeros años de vida, 1959-1961) para valorar el riesgo de presentar hipertensión, estatura baja y obesidad en la etapa adulta. Se observó que el riesgo de presentar hipertensión arterial no se elevó significativamente en los sujetos expuestos a desnutrición, durante el desarrollo fetal en general, comparados con los no expuestos. En los niños expuestos a desnutrición calórica (DCP) durante el primer trimestre del embarazo fue 36% más (OR: 1,36 (95% CI 1,03 a 1,79); los expuestos a DCP durante la infancia fue de 83% más (OR: 1,83 95% CI 1,61 a 2,08) y en aquellos expuestos en la etapa intrauterina y en la infancia fue de 31% más (OR: 1,31, 95% CI 1,14 a 1,51). Además se observó que la exposición a la desnutrición durante la infancia incrementó el riesgo de estatura baja, sin aumentar el riesgo de obesidad. Del mismo estudio, Li y cols., 2011, analizaron una cohorte de 7, 874 adultos nacidos entre 1954 y 1964. Utilizaron los criterios de ATP III para clasificar el síndrome metabólico (tres o más de los siguientes criterios: niveles elevados de triglicéridos en ayunas, baja concentración de colesterol- HDL, concentración elevada de glucosa en ayunas, circunferencia de cintura elevada e hipertensión arterial). Se observó que los adultos expuestos a desnutrición durante la etapa fetal tenían un riesgo elevado de presentar síndrome metabólico, comparado con los no expuestos (OR: 3,13, 95% CI 1,24 a 7,89, p = 0,016). Efectos similares se observaron en adultos expuestos a desnutrición en la etapa temprana de la infancia (OR: 2,85, 95% CI 1,19-6,83, p = ,0,019), pero no durante la etapa media, (OR: 2,07, 95% CI 0,77-5,53) o tardía de la infancia (OR: 2,21, 95% CI 0,91-5,40).

Hult y cols., 2010, realizaron un estudio de cohorte en Nigeria, en 1, 339 adultos nacidos antes de (1965-67), durante (1968-enero 1970), o después de (1971-73), los años de la hambruna se incluyeron, para ver la relación entre la desnutrición y el riesgo de presentar hipertensión arterial, intolerancia a la glucosa y sobrepeso. Se midieron los siguientes parámetros: presión arterial, niveles plasmáticos de glucosa medidas antropométricas, así como prevalencia de hipertensión arterial (> 140/90 mm Hg), intolerancia a la glucosa (7,8-11,0 mmol/l), sobrepeso (IMC ≥ 25 kg/m^2). Se observó que la desnutrición en etapas fetales estaba asociada a una presión sistólica elevada (+7 mm Hg; p < 0,001), y diastólica (+5 mm Hg; p < 0,001), una glucosa plasmática elevada (+0,3 mmol/l; p < 0,05), y circunferencia de cintura (+3 cm, p < 0,001), los riesgos para hipertensión sistólica (OR 2,87; 95% CI 1,90 a 4,34), intolerancia a la glucosa (OR 1,65; 95% CI 1,02 a 2,69) y sobre-

peso (OR 1,41; 95% 1,03 a 1,93) fueron elevados con respecto a los no expuestos.

En otro estudio realizado por Martins y cols., 2004 en Brasil, se analizó la composición corporal de niños desnutridos, durante un periodo de tres años, para probar la hipótesis de la tendencia de acumular grasa corporal, como consecuencia de desnutrición en etapas tempranas de la vida. Se seleccionaron 50 niños y niñas entre los 11 y 15 años de edad; de los cuales 20 estaban desnutridos con baja talla y 30 normales. Para determinar la composición corporal de los niños se realizaron mediciones antropométricas y absorciometría de rayos X de energía-dual al inicio del estudio y después de tres años (final), así mismo se calcularon los porcentajes de masa magra (%) y masa grasa (%). Se observó que los niños desnutridos acumularon un mayor porcentaje de masa grasa (p = 0,003), y ganaron menos masa magra (p = 0,004). Las niñas desnutridas ganaron menos masa magra (p = 0,032), y tuvieron una ganacia de masa grasa mayor en su seguimiento con respecto al inicio (p = 0,008).

En otro estudio de cohorte reportado en seis publicaciones[23-28] realizado en Holanda, en sujetos expuestos a desnutrición intrauterina y durante la infancia, analizaron diferentes efectos: van Abeelen y cols., 2012, estudiaron la asociación entre la desnutrición en etapas tempranas de la vida y el riesgo de presentar diabetes tipo 2. Se estudiaron a 7, 837 mujeres de 49 a 70 años expuestas a desnutrición entre las edades de 0 a 21 años. Se encontró que en aquellas mujeres expuestas a desnutrición moderada el HR para diabetes tipo 2 fue de 1,36 (95% CI 1,09 a 1,70) y en aquellas expuestas a desnutrición severa fue de 1,64 (95% CI 1,26 a 2,14). Además evaluaron, la asociación entre la desnutrición durante el periodo postnatal y el riesgo de presentar sobrepeso en la etapa adulta (tabla I). van Abeelen y cols., 2012, estudiaron a 8, 091 mujeres expuestas a desnutrición entre los 0 a 21 años de edad, fueron reclutadas para el estudio entre las edades de 49 a 70 años. Se observó que en general la exposición a desnutrición postnatal se asoció con un mayor IMC y circunferencia de cintura en forma gradiente dosis-respuesta (p < 0,01); el grupo de edad de 0-9 años que fue expuesto a desnutrición severa tuvo un 25% (95% CI 1,05 a 1,50) más de riesgo comparado con el no expuesto. Painter y cols., 2005, estudiaron a 741 individuos con una edad promedio de 50 años (48-53), nacidos a término. Se encontró que los niños expuestos a desnutrición en etapa temprana de la gestación fueron ligeramente más pesados que los no expuestos (p = 0,02). Los expuestos en etapas tardías de la gestación presentaron mayor intolerancia a la glucosa comparados con los no expuestos. Así mismo, los expuestos a desnutrición en la etapa media del embarazo presentaron un incremento en el riesgo de enfermedad obstructiva respiratoria (OR 1,7, 95% CI 1,1 a 2,6) y en la prevalencia de microalbuminuria (OR 2,1)% CI 1,0 a 4,3). Se triplicó el riesgo de presentar enfermedad coronaria (OR 3,0 (95% CI 1,1 a 8,1), un mayor perfil aterogénico, mayor obesidad, así como niveles elevados de fibrinógeno y disminución en el factor VII, en los expuestos a desnutrición en etapas tempranas de la gestación. También se encontró una relación entre talla baja al nacer e incremento en la presión arterial en la etapa adulta, por cada kg menos al nacer se encontró un incremento en la presión arterial sistólica de 2,7 mm Hg; más que a la desnutrición, se relacionó al incremento en la relación proteína/carbohidrato (consumo) durante el tercer trimestre del embarazo. Roseboom y cols., 2000, estudiaron a 736 individuos expuestos a desnutrición materna durante el embarazo con la prevalencia de enfermedad coronaria en etapa adulta. Encontraron que la prevalencia de enfermedad coronaria fue más alta en aquellos expuestos en etapas tempranas de la gestación comparados con los no expuestos (8.8% *vs* 3,2%; OR ajustados para sexo 3,0 95% CI 1,1 a 1,8). La prevalencia no se incrementó en los expuestos a desnutrición en la mitad del embarazo (0,9%) o tardía (2,5%). Los individuos adultos con enfermedad coronaria tuvieron un peso más bajo al nacer (3,215 g *vs* 3,352 g) (p = 0,13) y una menor circunferencia de cabeza (32,2 cm *vs* 32,8 cm) (p = 0,05), pero el efecto de la exposición a la desnutrición en etapa temprana de la gestación fue independiente del peso al nacer (3,2 95% CI 1,2 a 8,8). Roseboom y cols., 2000, en la misma población observó que en los individuos expuestos a desnutrición en etapas tempranas de la gestación tuvieron un mayor perfil aterogénico, comparados con los no expuestos y la relación de LDL-HDL (lipoproteínas de baja densidad-lipoproteínas de alta densidad por sus siglas en inglés) fue significativamente más alta 13,9% (95% CI 2,6 a 26,4%).

En otro análisis realizado por Ravelli y cols., 1999, en la misma población, en mujeres y hombres de 50 años de edad, observaron mayor peso corporal (p < 0,05) en los sujetos expuestos a desnutrición durante el primer trimestre del embarazo, con respecto a los no expuestos, así mismo el índice de masa corporal (IMC) en las mujeres expuestas a desnutrición intrauterina en etapas tempranas de la gestación fue significativamente más alto 7,4% (95% CI: 0,7%, 14,5%) comparado con el de las no expuestas.

En el estudio realizado en la ciudad de México, González-Barranco, y cols., (2013), observaron que los individuos con desnutrición en etapas tempranas de la vida, tenían la glucosa (p = ,012) y la insulina (p < ,002) más altas, independientemente del peso al nacer, el IMC o la edad. El IMC se relacionó positivamente con la insulina plasmática en ayunas, los triglicéridos, las lipoproteínas de alta densidad y el colesterol total. En la misma población, se observó que una correlación negativa entre el área total de tejido adiposo abdominal y la sensibilidad a la insulina en los individuos malnutridos (r^2 = 0,65 y 0,35, p < 0,01)[20].

Stanner y cols., en 1997, realizaron un estudio en San Petersburgo, en individuos expuestos a desnutrición intrauterina e infantil, para valorar la relación de ésta, con los factores de riesgo de enfermedad coronaria en la etapa adulta. Observaron en las mujeres expuestas a desnutrición intrauterina una correlación entre la obesidad y la elevación de la presión arterial

Tabla I
Estudios retrospectivos de cohorte y prospectivos del efecto de la desnutrición pre y post natal sobre componentes del síndrome metabólico

Autor, año	*Edad en años*	*n*	*Tipo de estudio*	*Tipo de exposición*	*Resultados*
Wang, 2012 China	46-53	12,065	R. Cohorte	Desnutrición: primer trimestre del embarazo infancia etapa fetal e infancia	OR para hipertensión: 1.36 (IC 95% 1.03-1.79). OR para hipertensión: 1.83 (IC 95% (1.61-2.08). OR para hipertensión: 1.31 IC 95% (1.14-1.51) En ningún período la desnutrición incrementó el riesgo de obesidad.
van Abeelen, 2012, Holanda	49-70	7,837	R. Cohorte	Exposición a desnutrición intrauterina: total severa	HR para diabetes tipo 2: 1,36 (95% CI 1,09-1,70) 1,64 (95% CI 1,26-2,14)
van Abeelen, 2012	49-70	8,091	R. Cohorte	Exposición a desnutrición intrauterina: moderada	OR para sobrepeso: 1,10 (95% CI: 1,00 a 1,22) en todos los grupos de edad 0-9 años: 1,1 (95% CI: 0,96 a 1,26) 10-17 años: 1,13 (95% CI: 0,96 a 1,33) ≥ 18 años: 1,15 (95% CI: 0,75 a 1,78) Asociación entre edad de inicio de desnutrición e IMC a los 50 años, p = 0,02 (todos los grupos)
				severa	OR de sobrepeso: 1,15 (95% CI: 1,01 a 1,31) en todos los grupos de edad 0-9 años: 1,25% (95% CI: 1,05 a 1,50) p = 0,002 10-17 años: 1,01 (95% CI: 0,82 a 1,25) ≥ 18 años: 1,60 (95% CI: 0,89 a 2,87)
Painter, 2005 Holanda	48-53	741	R. Cohorte	Desnutrición intrauterina: etapa temprana etapa tardía	Mayor LDL/HDL colesterol (p < 0,05) Mayor enfermedad coronaria (p < 0,05) Mayor glucosa e insulina postprandial (p < 0,05)
Roseboom, 2000 (1) Holanda	50	736	R. Cohorte	Exposición a desnutrición intrauterina: etapa temprana etapa media etapa tardía	OR para enfermedad coronaria: 3,0 (95% CI 1,1 a 8,1) OR para hipertensión arterial: 3,2 (95% CI 1,2 a 8,6) OR para glucosa plasmática postprandial : 2,5 (95% CI 0,8 a 7,2) OR para relación LDL-HDL: 2,6, (95% CI 1,0 a 7,2). OR para enfermedad coronaria: 0,3 (95% CI 0,0 a 2,2) OR para enfermedad coronaria: 0,8 (95% CI 0,2 a 2,8).
Roseboom, 2000 (2) Holanda	50	704	R. Cohorte	Exposición a desnutrición intrauterina: no expuestos etapa temprana etapa media etapa tardía	Relación LDL-HDL: 2,91 2,82 2,69 3,26
Ravelli, 1999 Holanda	50	741	R. Cohorte	Desnutrición en mujeres: primer trimestre del embarazo segundo y tercer trimestre	Mayor peso corporal (p<0.05) que los no expuestos No diferencias
Li, 2011	49-53	7874	R. Cohorte	Desnutrición: etapa fetal infancia temprana infancia media infancia tardía	OR para prevalencia de síndrome metabólico: 3,13 [95% CI 1,24-7,89, p = 0,016) 2,85 (95% CI 1,19-6,83, p = 0,019) 2,07 (95% CI 0,77-5,53) 2,21 (95% CI 0,91-5,40)

Tabla I *(cont.)*
Estudios retrospectivos de cohorte y prospectivos del efecto de la desnutrición pre y post natal sobre componentes del síndrome metabólico

Autor, año	*Edad en años*	*n*	*Tipo de estudio*	*Tipo de exposición*	*Resultados*
Hult, 2010 *Biafra*	36-44	1339	R. Cohorte	Desnutrición : fetal infancia fetal infancia fetal infancia fetal infancia fetal infancia	OR para HTA sistólica (95% CI): 3,02 (2,01-4,52) 1,78 (1,19-2,68) OR para HTA diastólica (95% CI) 2,49 (1,72-3,62) 1,35 (0,93-1,97) OR para HTA severa (95% CI) 2,68 (1,31-5,46) 1,36 (0,63-2,93) OR para Intolerancia a la glucosa (95% CI) 1,76 (1,09-2,85) 1,15 (0,70-1,86) OR para Diabetes (95% CI) 3,11 (1,14-8,51) 1,88 (0,66-5,33)
Martins, 2004 *Brasil*	11-15	50	Prospectivo (3 años)	Desnutrición en etapa temprana de la infancia niños niñas	Menor peso corporal e IMC que los no desnutridos ($p < 0,001$). Mayor porcentaje de grasa corporal ($p = 0,004$) que al inicio del estudio. Menor masa magra ($p = 0,001$) que los no desnutridos Menor peso corporal que las no desnutridas ($p < 0,05$) Mayor porcentaje de masa grasa corporal ($p = 0,008$) Menor porcentaje de masa magra ($p = 0,007$)
González-Barranco, *2003 México*	20,2 ± 3,6 23,3 ± 1,8	102	R. Cohorte	Desnutrición en el primer año de vida Grupo con desnutrición	La glucosa e insulina fueron significativamente más altas ($p = 0,012$ y $< 0,002$, respectivamente) independientemente del peso al nacer, el IMC o la edad. El IMC estaba relacionado significativamente con el nivel de insulina plasmática en ayunas, el índice de sensibilidad a la insulina, nivel de triglicéridos, LAD, concentraciones de colesterol en el grupo 1, pero no en el grupo control.
Boulé, 2003 *Mexico*	20,2 ± 3,6 23,3 ± 1,8	53	R. Cohorte	Desnutrición en el primer año de vida Grupo con desnutrición	Hubo una correlación negativa entre el área grasa abdominal total y la sensibilidad a la insulina en los sujetos con antecedentes de desnutrición y en el grupo control ($r^2 = 0,65$ y $0,35$, $p < 0,01$, respectivamente). Cuando se relacionó con bajo contenido de grasa abdominal ($114\ cm^2$), los participantes con y sin antecedentes de desnutrición tuvieron un valor similar para la sensibilidad a la insulina (9,03 *vs* 8,88 mg/ kg (-1) × min (-1). Cuando se compararon con niveles altos de grasa abdominal ($310\ cm^2$) los participantes que tuvieron desnutrición durante el primer año de vida, tuvieron un nivel menor de sensibilidad a la insulina (4,74 *vs* 6,85 mg × kg (-1), $p < 0,05$).
Stanner, 1997 *Rusia*	52-53	361	R. Cohorte	Desnutrición (campos de concentración): Intrauterina e infancia	Mayor presión sistólica ($p = 0,01$) y diastólica ($p = 0,04$)

R = Retrospectivo.

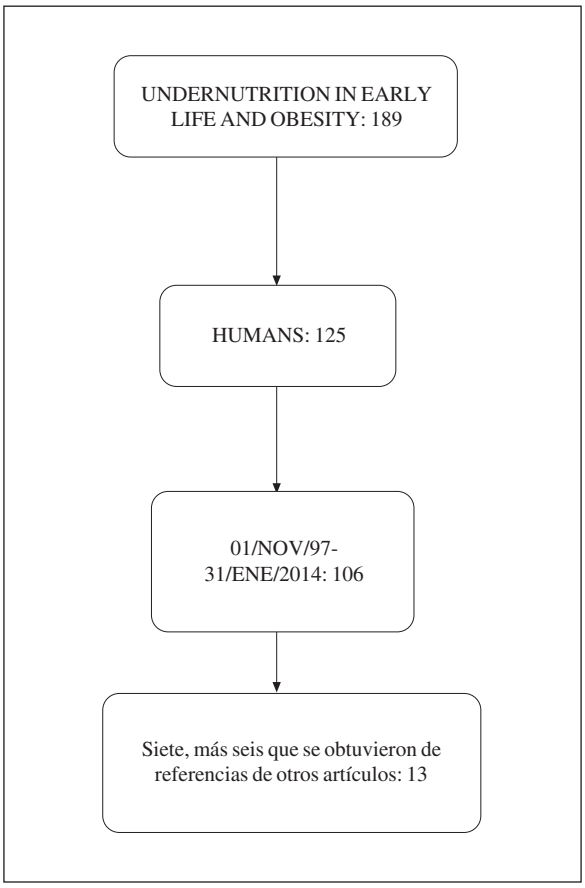


Fig. 1.—Flujograma para la selección de los estudios (Fecha: febrero 2014).

(sistólica p = 0,01) y (diastólica p = 0,04), con respecto a las expuestas durante la infancia.

Discusión

Se revisaron trece publicaciones de seis estudios; el número de participantes en los estudios osciló desde 50 hasta 12,065, con un rango de edad de 11 a 70 años. Esta revisión demostró de manera consistente que existió una asociación entre la DCP pre y postnatal con algún componente del síndrome metabólico en adolescentes y adultos. Entre los que se incluyen aumento del sobrepeso[24,28], obesidad, adiposidad abdominal[10,20], hipertensión arterial[17,22,27], enfermedad coronaria[25,27], intolerancia a la glucosa, diabetes tipo 2, disminución de la sensibilidad a la insulina[19-21, 23,25,26], alteración del perfil lipídico y colesterol total[21,25,26] . Estos resultados son consistentes con la recuperación rápida de peso que se ha observado en niños mexicanos con desnutrición moderada, de menos de 24 meses, quienes transitaron en breve tiempo al sobrepeso y obesidad[29].

Los resultados observados son congruentes con la teoría de la programación de enfermedades crónico-degenerativas durante el embarazo y el período postnatal. Lucas (1992), definió la programación fetal como una respuesta a un estímulo o agresión experimentada durante un periodo crítico del desarrollo fetal, dando como resultado cambios a largo plazo en la morfología de los órganos y en las funciones metabólicas y endócrinas. Baker y cols. (1994), mencionan que la influencia primaria para la programación fetal podría ser a través de la nutrición materna. Estudios realizados en modelos experimentales en animales (ratas) han reportado que la dieta materna tiene una influencia sobre la programación de la función cardiovascular del feto, lo que podría ocasionar resistencia vascular e hipertensión[32]. Se ha observado que el "catch-up growth" que se presenta en etapas tempranas de la vida después de un retraso en el crecimiento, fetal, neonatal o infantil, representa un riesgo mayor para desarrollar: obesidad, diabetes tipo 2 y enfermedades cardiovasculares en etapas posteriores de la vida[32,33]. Este riesgo podría ser el resultado de factores ambientales en etapas tempranas de la vida, debido a una programación de "mecanismos ahorradores". Durante el período de recuperación del crecimiento aumenta de manera desproporcionada la acumulación de tejido graso en relación al tejido magro. Probablemente resultante o debido a mecanismos de conservación de energía mediante la supresión de la termogénesis[34-36].

Una de las fortalezas de esta revisión es que incluye poblaciones de distintas regiones geográficas, culturales y que el número de casos analizados es en la mayoría de los casos muy alto.

Debido a la heterogeneidad en los grupos de edad y en las variables dependientes analizadas no fue posible realizar un meta-análisis. Entre las limitaciones de esta revisión se incluye que la mayoría de los estudios fueron retrospectivos de cohorte, que varias publicaciones corresponden a la misma población, lo que reduce el número a cinco estudios retrospectivos de cohorte y un estudio prospectivo de tres años de seguimiento.

En esta revisión se demuestra que la desnutrición intrauterina durante el primer trimestre del embarazo y en el período postnatal son factores de riesgo de distintos componentes del síndrome metabólico en etapas posteriores de la vida. A estos resultados deben añadirse el alto riesgo que la diabetes gestacional produce sobre los mismos componentes en etapas posteriores de la vida[38]. Estos hallazgos podrían tener implicaciones importantes en la salud pública. Indican la necesidad de establecer acciones de prevención en población de alto riesgo de desnutrición durante el embarazo y los primeros dos años de vida. Un sistema de detección atención de la desnutrición en las mujeres embarazadas y en niños en los primeros años de vida podría tener una gran efectividad para la prevención de la obesidad y otros componentes del síndrome metabólico en etapas posteriores de la vida.

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Original / *Obesidad*

Pilot nutrition and physical activity intervention for preschool children attending daycare centres (JUNJI); primary and secondary outcomes

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Abstract

Introduction: **A pilot intervention was conducted to promote physical activity and nutrition in public preschool education (near half a million children in Chile), in order to prevent obesity.**

Objective: **To assess the primary (body fat) and secondary outcomes (physical activity and energy intake) of a nutrition and physical activity pilot intervention for preschool children, attending day care centres.**

Methods: **A pilot intervention in six day care centres selected at random (n = 530), in 4-5 years old preschool children, Santiago, Chile intending to: provide nutritional and physical activity education to educators and health promotion activities for the family, which in turn, will affect the primary (body fat), and secondary outcomes (physical activity pattern and energy food intake) were measured in a representative subsample of 120 intervened and 145 controls children.**

Results: **In relation to secondary outcomes monitoring, moderate-vigorous activity was duplicated in the intervention group (+5.4% and +4.7%, respectively), in both obese and eutrophic children. Energy intake decreased in 11.7% in obese and 7.5% in eutrophic children. Dietary fat intake was reduced (-11 g in obese and -8.4 g in eutrophic children). Intervened obese children reduced body fat in 1.5%, meanwhile in control obese children, b*ody fat increased 1.3% (p < 0.01).***

Conclusions: **The pilot intervention demonstrated the feasibility to influence dietary risk factors and physical activity at the day care centres and families. Therefore, the implementation of the validated intervention program will be tested in different weather conditions, to prevent unhealthy habits in preschool children and their families.**

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INTERVENCIÓN PILOTO EN NUTRICIÓN Y ACTIVIDAD FÍSICA PARA PREESCOLARES ASISTENTES A JARDINES INFANTILES (JUNJI); RESULTADOS PRIMARIOS Y SECUNDARIOS

Resumen

Introducción: **Intervención piloto en nutrición y actividad física para prevenir obesidad en la educación preescolar (cerca de medio millón de niños en Chile).**

Objetivo: **Evaluar los resultados primarios (grasa corporal) y secundarios (actividad física e ingesta energética) de una intervención piloto para niños/as asistentes a guarderías infantiles.**

Métodos: **Intervención piloto en seis guarderías seleccionadas al azar (n = 530 preescolares), 4-5 años en Santiago de Chile, con el objeto de: a) proporcionar educación en nutrición y actividad física para los educadores; b) actividades de promoción de la salud para la familia.**

El objetivo primario (grasa corporal), y los resultados secundarios (patrón de actividad física y la ingesta energética) se midieron en 265 preescolares (120 intervenidos y 145 niños controles).

Resultados: **La actividad física moderada- intensa se duplicó en los intervenidos (+5,4% y +4,7%, respectivamente), tanto en niños obesos y eutróficos. La ingesta energética se redujo en 11,7% en obesos y 7,5% en los eutróficos y la de grasa en (-11 g en obesos y -8,4 g en niños eutróficos). Los niños obesos intervenidos redujeron la grasa corporal en 1,5%, mientras que en los niños controles obesos, se incrementó 1,3% (p < 0,01).**

Conclusiones: **La intervención piloto demostró la viabilidad de influir en los factores de riesgo dietarios y de actividad física en las guarderías y en las familias. Por lo tanto, la ejecución del proyecto piloto se pondrá a prueba en diferentes condiciones climáticas, para prevenir hábitos no saludables en los preescolares y sus familias.**

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Palabras clave: *Intervención. Resultados. Preescolares. Actividad física. Nutrición.*

Abbreviations

JUNJI: National Day Care Centres.
DCC: Day Care Centres.
BMI: Body Mass Index.
FMI: Fat-Mass Index.
FFMI: Fat-Free Mass Index.

Introduction

Obesity prevalence in Chilean children and women from low socio-economic status has increased steadily[1-3], and weight excess is over 30% in three-to-five year old preschool children[3].

Obesity prevention should be done from intrauterine life, infancy and preschool years, physiological states in which long-term regulation of energy balance may be regulated[4]. Weight excess in children and adolescents has increased in alarming proportion worldwide, reaching 20% in many European countries[5,6].

This progression from a normal nutritional status to obesity, is due to adverse environmental factors, genetic predisposition and lifestyle, all which modulate the risk of developing obesity or later on cardiovascular risk factors[7,8]. The imbalance between the energy spent by physical activity and food and on the other hand, energy intake, is in the roots of obesity[9]. The preschool age has been identified as a crucial period to prevent obesity, as it is not only the time when nutritional habits and physical activity settle down, but also a it is the period previous to the rise of the body mass index and the adiposity rebound[10,11]. Numerous studies have demonstrated that a precocious adiposity rebound is later associated to an obesity increased risk, during adolescence and adulthood[12,13].

Evidence-based interventions aimed at the prevention of preschool obesity are important. Several works have aimed to improve diet, increase physical activity, achieve behavioural change, but only a few studies have been successful, either in improving quality of diet or increasing physical activity[14].

In Chile, pre-schoolers under six years, beneficiaries of the public health system, have an overweight prevalence of 22.6% and 9.6% obesity prevalence[3]. Preschool attendants to the JUNJI have a prevalence of 29.0% of overweight and 13.0% of obesity[15].

The fast and dramatic increase of obesity prevalence in preschool children in Chile is associated to an insufficient physical activity and unhealthy energy intake. Some studies have observed an energy intake far superior to the child needs, a surplus coming especially from the consumption of food high in fat and sugar[16,17]. Obese children attending day-care centres were in energy balance during the week (6,873 ± 1,005 kJ/d) while at the weekend excess energy intake energy reached 25% (8,814 ± 1,817 kJ/d), During the eight hours permanence n the day-care centre the average consumption of fat was 22 grams while in the 4-5 when at home, the child ingested 26 grams and this consumption reached 70 grams over the he weekend[18].

Kain et. al, compared children attending day-care centres with the non assistants, measured through a daily record of activities. Sedentary activities, such as sleeping, being sat and watching reached 18.3 hours duration, independently of the nutritional state and the child's sex[19]. A more precise evaluation was done with movement sensors, being the result similar as normal and obese preschool dedicated 70-80% of daily activities to minimum activity and sedentary activity[18]. Additionally, obese boys had only 50% of the moderate/vigorous activity of their eutrophic pairs. Preschool girls had similar quantity of physical activity time in both nutritional states, thus being equally sedentary[20,21]. Being sedentary at early age, affects the appropriate and opportune motor development and physical aptitude, and contributing to the rising of cardiovascular risk factors, that increases the risk of later morbidity and mortality[22].

In a previous work conducted at the JUNJI, total body fat was evaluated by means of isotopic dilution in 250 normal children, overweight and obese. The range for this variable in normal children stretched from 12% to 34% and from 20% to 38% in obese children[23]. The excess of body fat and inactivity in preschool children urgently need the development and testing of strategies for reverting this situation. This fact, plus an altered energy balance and energy intake, led to the decision of conducting a multistage intervention in JUNJI, firstly in the Metropolitan region boroughs, which had the biggest prevalence of overweight and obesity in the metropolitan area. The main objectives in the pilot study, was to assess the primary and secondary outcomes of a designed intervention in Nutrition and Physical activity for 4 to 5 years old, aiming to increase moderate-vigorous physical activity, reduce the amount of energy-dense food and consequently their body fat content.

Materials and methods

Subjects

The study was conducted in 4-5 year old children (n = 530), attending four JUNJI DCC (two intervened and two control), located in the south-east zone of Santiago, Chile, in the largest boroughs in Santiago (La Florida, Peñalolen y Ñuñoa) where most of the low socioeconomic population lived, thus with a high obesity prevalence. Evaluation was performed on a representative sample of 85 normal nutritional status and 35 obese children. The control group (n = 145), was composed of 40 obese and 105 eutrophic children. Inclusion criteria included: none undernourished children[24], no impediments to enrol in physical activity and ethical consent of parents, to participate in the study. Exclusion criteria considered medical diagnosis of psy-

chomotor disorder, use of drugs that could alter body composition, physical activity or biochemical parameters. This research was approved by the Ethics Committee of University of Chile.

Educational Methodology Design[25,26]

a) The educational intervention in Nutrition and Physical activity in preschool children, was built according to the theory of the "Social Cognitive Learning" and the Ecological model. The sub model of Community organization was selected, as it able to develop community capacities to contribute to the solutions of problems.
b) The project included a multidisciplinary team: nutritionists, physical education teachers, anthropologists, evaluation experts and medical doctors.
c) The control group received no intervention and continued as usual.

In the Pilot year, the *validation of the educational methodology* considered the following activities:

a) Educational material, designed to target the involved community, plus questionnaires to evidence the quality and comprehension of educative materials for educators. The material was based on the new curricula of the national Preschool Education. Educative Guidelines in Nutrition and Physical Activity were firstly designed and validated during the implementation of the project, May to September. Further counselling was carried on weekly by nutritionists and physical education teachers to clarify doubts during the intervention.
*b) After testing, f*urther design and validation of Manuals and Didactic Guide in Nutrition and Physical activity for the educators was done, in terms of materials comprehension and the process of transference of educative contents to the preschool children.
c) Specific training program for educators and parents, using designed Didactic Guides for Physical Activity and Nutrition. An anthropologist conducted perceptions and attitudes of educators and parents, relevant to changes in lifestyle and feasibility of the intervention.
d) Educational, playful *motivational strategy* for the parents and families, called "Healthy Days", conducted once/twice a month, especially at Saturday morning or Friday evenings, when parents were prone to attend. Educational leaflets containing information on growth, nutritional factors and physical activity needs, were designed and provided to parents, in order to minimise additional consumption of energy dense food to the normal pattern (breakfast, lunch, milk and bread plus dinner) and to avoid excess TV time (> one hour daily), and encouraging daily play time.
e) Educative process follow-up. Advances were registered by the educator at every play school, using and adhoc questionnaire and supervised by the intervening team.

First stage (pilot) measurements

Primary outcome in boy intervened and control DCC. *Total body fat*; with the validated equation, derived from the measurement of total body water. Body fat measurements, obtained[27]:

Body fat (kg) = [-1,524 + (0.371 * weight, kg) + 0.114 * (triceps + subscapular, mm) - (0.238* age, years) + (0.378 * sex) - (0.105 * calf circumference, cm)]
(Sex: 1 Boys, 2 Girls)

Secondary outcomes (intervened children)

– *Energy Intake in the* day *care-centre*, food intake measured during the eight hours of stay in DCC (twice a week), on non-consecutive days. Food intake was weighed before each meal, and data was obtained by subtracting the weight of the food leftover on the tray. The food components of each preparation were known in advance and its chemical composition was provided by the food suppliers. All children ate the same menu; hence, there were no differences in the type of foods served, but only in the amount eaten by each child. The children were discretely supervised during the mealtime.
– *Week days food intake measurement at home:* the same day of the measurement at the day care centre, home food intake was measured by providing the mother a questionnaire, on which to record all week foods eaten by the child from 16:30 until bedtime and the next day breakfast. The following day, the mother came to the centre, to review the information regarding the types of preparations, amount or portions consumed, and name brand foods eaten by the child. A trained nutritionist, who also weighed the food intake at the day care centre, checked with the mother, the information on home intake in the immediate next day of the measurement. Dietary information on energy and macronutrient composition during the week was obtained via an ad-hoc computational program based on the Chilean Food Composition table[28].
– *Weekend food intake*. Mothers were provided with a 24 h recall questionnaire to record all food intakes at home on one weekend day. The mother was interviewed the following Monday in order to review with her the portion sizes, food types, in-

gredients of food preparations and name brand foods. This information was utilised to quantify energy intake during the week and weekend. The measurement of energy intake as described above had a 7.3% difference, compared to doubly-labelled water (sent to publication).

– *Physical Activity*. A triaxial movement sensor was used (TRITRAC-R3D RESEARCH ERGOMETER, Professional Products, Division of Reining International, Madison, Wisconsin, USA). This sensor collected information on three-dimensional movement (lateral, vertical and horizontal) every minute and this information is stored as a Vector of Magnitude, which is the square root of the sum of each vector in directions X, Y, Z elevated to the square power. The information was collected during three days (two during the week and one day at weekend). Results were downloaded to a computer where it could be analyzed as needed.

Preschool children require setting distinct activity cut-off points for this group. Children's activities were categorized into four ranges after direct observation of 20 children of normal nutritional status (table I). The cut-off counts for moderate and moderate-vigorous activity in our group is similar to three Mets activities (around 1,000 counts) as found in Rowland et al[29]. The Tritrac motion monitors were used during three full days (two weekdays and one weekend day). The monitor was placed immediately after waking up and disconnected once asleep; the mother or caretaker was asked to register those times, as well as any other moment of disconnection of the equipment (i.e., shower, swimming) in an ad-hoc questionnaire.

The movement sensor was firmly attached to the child's chest within a stitched pocket. This fact ensured the monitor's tight positioning, avoiding the possibility of shifting, to reflect the child's real activity but allowing freedom of movement**.** Positioning the monitor at the hip was either not accepted by the children, due to their stature or had the risk of being easily manipulated. The position in the chest was used as a proxy, (8-10 centimetres away from the hip in 4-5 year old children).

Table I
Cut-off points used to classify physical activity levels based on Tritrac measurements

Activities	*Activity counts (Vector of Magnitude)*
Resting and minimal movements	< 188
Sedentary activities in the classroom	188-349
Light effort activities in the playground	350-1,074
Moderate and intense activities in the playground	> 1,074

Data analysis

Descriptive statistics were performed on the data, including minimums, maximums, and frequency tables. Below we provide a description of the variables utilised. For continuous variables the Shapiro Wilk goodness of fit and the homogeneity of variance tests were used. Descriptive statistics was performed according to the nature of the variables. For those that complied with the assumption of normality, the population mean and standard deviation were used; for those that did not, the median and interquartile range were preferred. A Student or Wilcoxon test was used to assess statistical significant differences according to data distribution. Statistical significance was set at $p < 0.05$. Data was analysed using the STATA program version 12.0 (StataCorp. 2011 Stata Statistical Software: Release 12. College Station, TX: StataCorp LP).

Results

Table II shows the baseline anthropometrical data for obese and eutrophic children. The expected differences are presented for weight, Z Weight for Age, Z Height for Age and Z Weight for Height ($p < 0.05$), as well as arm circumferences, calf circumferences, triceps, subscapular, suprailiac and then, the two, four and five sum of skinfold thickness, body fat, FMI and FFMI.

Table III, shows the changes produced by the Pilot intervention in energy intake (kcal), physical activity pattern and body fat (k), for intervened (obese and eutrophic), preschool children. The intervention produced a significant reduction in the energy intake of both obese and eutrophic children (-745 kJ and -447 kJ respectively). A significant reduction in fat intake -23.9% (-11 g) for obese and eutrophic children -18,5% (-8,4 g) was observed.

Physical activity, significantly decreased in minimal activity (12.5% in obese children (57.6 minutes) and 12,1% in normal nutritional status children (58.1 minutes). The intervention produced an increase in moderate-vigorous activity, in obese preschool children with 5.4% (25.9 minutes) and 4,7% (22.6 minutes), in eutrophic preschool children ($p < 0.01$). A reduction in the energy intake in -11.8% (-712 kJ, $p < 0.05$) and -6.3% (-372 kJ) in obese and eutrophic children, respectively. Fat intake decreased in -20.3% (-9.2 g, $p < 0.05$) in obese and -16.9% (-7.5 g, $p < 0.01$) in eutrophic children. Minimal physical activity decreased 20.8% in obese (99.8 minutes) and -18.2% (92.2 minutes in eutrophic preschool children). Moderate-vigorous activity, increased significantly in obese preschool children, from 1.7% to 7.5% (31.7 minutes increase) and 5.8% in sedentary eutrophic (19.7 minutes).

According to the positive results in food and physical activity, a reduction was observed in the sum of skinfold thickness, of 8.2 mm and 2.8 mm, in obese and eutrophic children, respectively ($p < 0.01$). Table IV,

Table II
Anthropometrical baseline data for intervened obese and eutrophic children

Variable	*Obese Group (n = 13 M, 22 F)*	*Eutrophic Group (n = 52 M, 33 F)*
Age (years)	4.4 ± 0.4	4.4 ± 0.4
Weight (kg)	22.3 ± 2.5*	17.2 ± 1.7*
Height (cm)	107.2 ± 4.5	104.7 ± 4.7
Weight for Age Z-score	2.2 ± 1.0*	-0.1 ± 0.7*
Height for Age Z-score	0.3 ± 0.8*	-0.3 ± 0.9*
Weight for Height Z-score	2.7 ± 0.8*	0.1 ± 0.5*
Circumferences (cm)		
Arm	19.6 ± 1.3*	16.7 ± 0.8*
Calf	25.1 ± 1.5	21.7 ± 2.7*
Skinfold thickness (mm)		
Triceps (T)	14.6 ± 3.1*	9.6 ± 2.3*
Biceps (B)	8.9 ± 2.5	8.3 ± 2.9
Subscapular (SB)	10.9 ± 4.6*	6.6 ± 1.6*
Suprailiac (SP)	14.6 ± 6.1*	7.5 ± 3.3*
Calf (C)	16.4 ± 4.4*	12.9 ± 3.3*
T + SB	25.5 ± 7.1*	16.1 ± 3.3*
Σ 4 (T+B+SB+SP)	49.1 ± 14.0*	32.1 ± 6.9*
Σ 5 (T+B+SB+SP+C)	65.5 ± 17.3*	45.0 ± 9.3*
Body Fat (%)	29.4 ± 3.7*	21.7 ± 3.1*
FMI (kg/m²)	5.7 ± 1.0*	2.4 ± 0.5*
FFMI (kg/m²)	15.7 ± 1.6*	13.4 ± 1.3*

Mean ± SD FMI; Fat-Mass Index. FFMI; Fat-free Mass Index. *p < 0.05.

Table III
Changes of intake (kJ), physical activity (%) and body fat in obese (O) and eutrophic (E) in intervened preschool children

Variable	*Group*	*Baseline*	*Follow-up*	*Change*
Energy intake (kJ)	O	6,347 ± 1,086	5,602 ± 904	-745.0*
	E	5,991 ± 820	5,544 ± 946	-447.0*
Fat intake (g)	O	46.1 ± 9.2	35.1 ± 7.8	-11.0*
	E	45.4 ± 11.9	37.0 ± 10.3	-8.4*
Minimal Activity (%)	O	60.5 ± 13.6	48.0 ± 9.4	-12.5*
	E	58.3 ± 10.5	46.2 ± 10.7	-12.1*
Vigorous Activity (%)	O	2.8 ± 3.2	8.2 ± 4.5	+5.4*
	E	3.8 ± 3.5	8.5 ± 5.1	+4.7*
Σ 4 (T+B+SB+SP) (mm)	O	48.5 ± 14.0	40.3 ± 11.5	-8.2*
	E	26.4 ± 5.4	23.6 ± 4.2	-2.8*
Body fat (%)	O	30.7 ± 5.7	29.7 ± 6.6	-1.0
	E	20.4 ± 6.2	19.4 ± 5.0	-1.0

Mean ± SD. *p < 0,01.

describes the effect of the intervention, on sedentary obese and eutrophic preschool children (who had a minimal weekly physical activity > 50%, at baseline level). The intervention program was more efficacious in this *sedentary* group (obese and eutrophic children), producing a higher reduction of the skinfold thickness sum (-6.1 mm ± 14.3, p < 0.05) and greater reduction in body fat in obese children (-3.1% ± 4.4).

Results in the primary outcome. In the control group, two skinfolds sum increased in 3.3 mm, four skinfolds (+7.0 mm) or five skinfold thickness (+7.8 mm). In respect to body fat (%) a small reduction was observed in obese preschool children (from 30.7 ± 5.7 to 29.7 ± 6.6), and also in eutrophic preschool children (20.4 ± 6.2 to 19.4 ± 5.0).

Thus, the intervention pilot project was able to produce favourable changes in preschool children, to-

Table IV
Changes of intake and fat intake, physical activity and body fat in the baseline inactive obese (O) and eutrophic (E) children

Variable	*Group*	*Baseline*	*Follow-up*	*Change*
Energy intake (kJ)	O	6,021 ± 858	5,309 ± 797	-712*
	E	5,899 ± 907	5,527 ± 1051	-372
Fat intake (g)	O	45.3 ± 12.1	36.1 ± 8.0	-9.2*
	E	44.3 ± 13.5	36.8 ± 10.5	-7.5**
Minimal activity (%)	O	68.0 ± 8.0	47.2 ± 9.2	-20.8**
	E	66.1 ± 5.8	47.9 ± 10.3	-18.2**
Vigorous activity (%)	O	0.9 ± 0.9	8.4 ± 5.8	+7.5**
	E	1.7 ± 1.9	7.5 ± 4.0	+5.8**
Σ 4 (T+B+SB+SP) (mm)	O	49.9 ± 15.0	43.8 ± 13.5	-6.1*
	E	26.6 ± 5.5	24.1 ± 4.4	-2.5**
Body fat (%)	O	31.7 ± 4.7	28.6 ± 4.1	-3.1*
	E	20.6 ± 6.2	20.0 ± 5.3	-0.6

Mean ± SD. T: triceps. B; Biceps. SB, subscapular. SP: Suprailiac. *p < 0.05. **p < 0.01.

Table V
Intervention and control group comparison in change of anthropometrial data in obese and eutrophic children

	Obese children			*Europhic children*		
Variable	*Intervention group*	*Control group*	*p*	*Intervention group*	*Control group*	*p*
Weight (kg)	+1.4 ± 1.0	+0.9 ± 2.3	0.18	+1.1 ± 0.6	+0.9 ± 1.5	0.31
Height (cm)	+3.6 ± 1.5	+2.8 ± 4.7	0.21	+3.3 ± 1.5	+3.4 ± 4.4	0.88
Weight for Age Z-score	- 0.03 ± 0.4	-0.2 ± 1.0	0.43	-0.00 ± 0.4	0.08 ± 1.0	0.45
Height for Age Z-score	+0.1 ± 0.6	-0.09 ± 1.0	0.22	-0.07 ± 0.5	+0.04 ± 0.9	0.31
Weight for Height Z-score	-0.1 ± 0.5	-0.1 ± 0.7	0.64	-0.02 ± 0.4	-0.05 ± 0.4	0.56
T + SB	-3.2 ± 2.1	+ 3.3 ± 3.5	< 0.01	1.0 ± 2.3	+2.0 ± 2.8	< 0.01
Σ 4 (T+B+SB+SP)	-8.2 ± 5.1	+7.0 ± 4.9	< 0.01	-2.8 ± 4.8	+3.8 ± 3.8	< 0.01
Σ 5 (T+B+SB+SP+C)	-10.9 ± 7.6	+7.8 ± 5.1	< 0.01	-5.0 ± 7.3	+4.8 ± 4.3	< 0.01
Body fat (%)	-1.5 ± 1.8	+1.3 ± 2.0	< 0.01	-0.7± 2.2	+1.0 ± 2.1	< 0.01
FMI (kg/m^2)	-0.3 ± 0.4	+0.2 ± 0.5	< 0.01	-0.1 ± 0.3	+0.1 ± 0.3	< 0.01
FFMI (kg/m^2)	+1.4 ± 0.7	+0.3 ± 1.5	< 0.01	+ 1.0 ± 0.5	+0.5 ± 1.0	< 0.01

Mean ± SD. T: Triceps. B: Biceps. SB: Subscapular. SP: Suprailiac.

wards a healthier nutritional status and physical activity. Additionally, the intervention was able to affect positively the most inactive children found at baseline. As Chile is 4,000 km long, in the following stage, the validated guides and educational methodology for educators and parents, will be applied to preschool children living different weather conditions (dry, Mediterranean and cold).

Discussion

An intervention in California which lasted for six months, produced a statistically significant reduction in BMI (intervention versus control change: 18.38 to 18.67 kg/m^2 *versus* 18.10 to 18.81 kg/m^2, respectively; adjusted difference -0.45 kg/m^2 [95% confidence interval, -0.73 to -0.17]; p = 0.002)[30]. Another intervention for two years in Massachusetts reduced watching television in children and found that each hour of reduction in television viewing, predicted reduced obesity prevalence (odds ratio, 0.85; 95% confidence interval, 0.75-0.97; p = 0.02)[31]. These results are similar to the ones obtained in an investigation in 66 obese Austrian children, participating in a similar intervention, aimed for the reduction of weight and improvement of metabolic own factors of risk of obesity[32].

Other studies in preschool children and teenagers in Thailand and Greece, also showed significant reduc-

tion of skinfold thickness, due to the intervention[33,34]. Previous studies in Chilean children have shown a high consumption of energetic food, with a contribution higher than their requirements, excess coming from ingestion of rich food in saturated fats, cholesterol, sucrose and sodium, which added to intake of sweet, salt, tipsy delicacies and juices, contribute to the excess of calories[18,21].

In the present intervention, obese girls, achieved a significant decrease in the energy intake, of proteins, fat and carbohydrates ($p < 0.05$), although in boys, only a significant decrease in the ingestion of carbohydrates was obtained ($p = 0.01$). In the eutrophic girls and boys, the intervention also produced a significant reduction in fat and carbohydrates intake ($p < 0.05$). During weekend, obese boys and girls, reduced the energy intake ($p = 0.04$), as carbohydrates in girls ($p = 0.02$) and lipids in boys ($p = 0.03$). The intervention generated at home, the reduction of energy intake and fat; this reduction is very important, as home contributes with a higher energy and fat intake in children, mainly during the weekend, as seen in another study, whereas obese children were at energy balance during the week, due to the attendance to play schools.

Parents and caregivers are important role models and their food choices influence those made by their children. In Chile, day care centres are centrally regulated in respect to the quality and quantity of food delivered to the children covering 65% of their needs. Additionally no kiosks are allowed within the play centre, although vendors outside, may pose a problem, as well as additional food the child may bring into the day care centre[15].

Energy intake at home together with the sedentary time at the day-care centre, were the main risk factor for obesity[18,21]. Another positive change, product of the intervention, was the significant increase of fruits and vegetables intake (of 124.1 g to 190,4 g; $p < 0.05$) and the ingestion of sweet and salty snacks (of 63.1 g to 36.8 g; $p < 0.05$).

In the main outcome, we verified an absolute difference of 2.5% in body fat intervened obese compared to control preschool children (1.5% decrease in the intervened children and 1% increase in body fat in control group).

An intervention in North American students, increased in the consumption of fruits, vegetables and a reduction in the energetic ingestion of fat during 7, 9 and 24 months[35,36]. It is important to emphasize the efficiency of an early intervention, so that changes in diet take place, which are often difficult to obtain at greater ages.

Physical activity interventions are attractive to attempt in preschool children, as children are prone to play at this age, and thus easier to incorporate in the daily routine of educators. This study was able to reduce minimum physical activity, and encourage its moderate-vigorous counterpart, which is cleared in the most inactive children at baseline.

The role of parents has been visualised in a recent paper, with successful results in the promotion of vigorous physical activity[37], an aspect which was strongly considered in our intervention. Physical activity is also a key component of the energy balance in children, being also one of the factors promoting an ideal growth and development, as well as a healthier life[38]. Diverse authors highlight the fact that passive education, the availability of computers, video games, plus other cultural aspects and environmental ones, combine to reduce active physical activity and therefore, the energy expenditure, constituting a risk for childhood obesity[39,40].

The information gathered with movement sensors suggested that obese and eutrophic children (boys and girls), initially had characteristics of a sedentary population, during most of the day. During the week, the intervention was able to decrease minimal activity ($p = 0.04$) and increased, especially moderate to moderate-vigorous activity ($p = 0.01$) in obese preschool children. At weekend, this increase occurred only in moderate-vigorous activity ($p = 0.04$), which reflects in children having more time to run, jump or playing active games.

Over the week and weekend, minimal activity decreased ($p < 0.00001$) and moderate-vigorous activity ($p < 0.0001$), increased in eutrophic boys, a result that shows that intervention was able to counteract the environmental leaning to sedentary habits. On the week days, a similar trend is observed in obese girls: reduction in the minimal activity ($p = 0.04$) and an increase of moderate-vigorous activity one ($p = 0.02$). At the weekend, minimal activity also diminished the ($p = 0.01$) and the moderate-vigorous category was increased ($p = 0.03$).

In eutrophic girls, similar results were observed during the week and weekend, adding the reduction of sedentary activity ($p = 0.02$). The intervention produced a significant increase in the physical activities of a major energy demand, both in the week and the weekend. In the eight hours period, that preschool children attended JUNJI day care centres, the majority of the time was dedicated to the fulfilment of educative aspects (children sat most of the time)[16].

Studies have demonstrated the viability of increasing physical activity in the educational environment[41,42], as involves the educational system, rather than producing changes in dietary intake, which involves mainly family habits. The quantity of time spent in sedentary activities (watching television, play computer games, sat or lying down), suggests that the consistent reduction in time for sedentary activities, can be as important than increasing short periods of vigorous activity, to support daily energy balance. Other studies which have explored the effect of watching television, although to produce an obesity prevalence reduction, there is a need of a multistage intervention, given the difficulty to produce significant and sustainable changes in a short time.

The association between the time spent on sedentary activity and the obesity was firstly investigated by Dietz and Gortmaker in the 1980s[30], and later confirmed[31,43]. In our study, minimum activity was reduced in 20.2% during the eight hours of permanence (equivalent to 96 minutes) and vigorous physical activity increased 5.4% (26 minutes), a goal achieved in five months of intervention. Our investigation has also been effective in decreasing energy dense intake and body fat in intervened children. The main outcome demonstrated a significant reduction in subcutaneous and total body fat, compared to the control group. In Scottish day care centres, Reilly et al increased 30 minutes of vigorous physical activity, significantly higher performance in movement skills tests than control children at six month follow-up ($p < 0.0027$), but no change was obtained in BMI, which could be due to a higher energy intake[44]. In our experience, physical activity and exercise are more easily incorporated in the preschool and school settings, but should be accompanied by nutrition workshops for parents and educators, and if needed, changes made in the food received at canteens. Additionally, it may be not possible to reduce obesity prevalence in one year intervention, so a multistage intervention should be considered since start, to assure sustainable changes in a school or day-care centre settings.

The results of this work have shown that the intervention was effective in controlling excess fat intake, energy intake and inactivity. These results are similar to interventions including diet and physical exercise, conducted in children from Europe and Asia[32-34]. The contribution of the child's home is reflected in the diet and physical activity changes, which supports that parents can positively influence healthy habits in children at this age, as socialization of many behaviors occurs within the family, related to parents' beliefs, attitudes, and behaviors substantially affecting children's health[45,46].

Results in the more inactive group of preschool children, reinforce that this intervention was able to significantly increase moderate-vigorous physical activity, reduce consumption of fat and sugar, all resulting in a higher reduction of body fat compared to the whole group. Thus, interventions should be addressed to all day care centres children, instead of only choosing overweight ones.

Lastly and quite important has been the role of public planning officers (Ministries of Health, Education and Sports), as the DCC's Nutrition officer, that have been part of the planning and implementation of the intervention, facilitating the process, financial issues and eventually, sustainability.

Several stages of the intervention will be implemented during the next three years, in different geographical settings in Chile (north, centre and south), in order to propose an effective educational intervention methodology, able to reduce cardiovascular risk factors in preschool children living in different weather conditions.

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Conflict of interest

The authors declare no conflict of interest.

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Super obese behave different from simple and morbid obese patients in the changes of body composition after tailored one anastomosis gastric bypass (BAGUA)

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Abstract

Introduction: **Super obese patients behave different from simple and morbid obese patients when they reach final changes of body composition (BC) after bariatric surgery. This has led us to tailor One Anastomosis Gastric Bypass (BAGUA) to achieve better results in this group of patients.**

Patients and Methods: **We studied 83 (37 diabetic and 46 non-diabetic BMI 30 and up) patients who completed all evaluation appointment (preoperative, 10 days, 1, 3, 6 and 12 months) after tailored BAGUA for diabesity. We used the Tanita body composition analyzer BC-420 MA by the method of single frequency impedance to analyze the evolution of BC in patients classified by BMI 30 - 34,9, 35 - 50, and >50.**

Results: **While preoperative excess weight presented dramatic decreases after tailored BAGUA in all the groups, super obese have different final BC. Diabetics retained more fat mass and visceral fat, where super obese have double (14 kg) that simple obese patients (6 kg), they lost more muscle mass, and have higher basal metabolism. The final BC is altered in all parameters if diabetes is added.**

Conclusions: **The reduction of the preoperative excess weight is motivated largely by the tailored effect of BAGUA. Patients BMI 30-50 behaved homogeneous in BC after surgery while patients BMI >50 behave different. Super obese lose less weight, retained more fat mass, visceral fat, bone mass, and total water. This effect should be treated by more aggressive surgery by measuring the entire small intestine to make a proper exclusion (tailored) to achieve homogeneous effects.**

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LOS SÚPER OBESOS SE COMPORTAN DE FORMA DIFERENTE A LOS PACIENTES CON OBESIDAD SIMPLE U OBESIDAD MÓRBIDA CON RESPECTO A LOS CAMBIOS EN LA COMPOSICIÓN CORPORAL TRAS LA CIRUGÍA PERSONALIZADA DE DERIVACIÓN GÁSTRICA DE UNA ÚNICA ANASTOMOSIS (BAGUA)

Resumen

Introducción: **Los pacientes súper obesos se comportan de manera distinta a los pacientes con obesidad simple y obesidad mórbida cuando alcanzan los cambios finales de la composición corporal (CC) tras la cirugía bariátrica. Esto nos condujo a individualizar la anastomosis única de derivación gástrica (BAGUA) para conseguir mejores resultados en estos pacientes.**

Pacientes y métodos: **Estudiamos a 83 pacientes (37 diabéticos y 46 no diabéticos, con IMC ≥ 30) que completaron todos las visitas de evaluación (preoperatorio, 10 días, 1, 3, 6 y 12 meses) tras la cirugía personalizada BAGUA para la obesidad. Empleamos el analizador de la composición corporal Tanita CC-420 MA mediante el método de impedancia de un única frecuencia para analizar la evolución de la CC en pacientes clasificados por el IMC 30 - 34,9, 35 - 50, y > 50.**

Resultados: **Mientras que el exceso de peso preoperatorio mostró unas reducciones drásticas tras la cirugía BAGUA personalizada en todos los grupos, los súper obesos tuvieron una CC final diferente. Los diabéticos retuvieron más masa grasa y grasa visceral, mientras que los súper obesos mostraban el doble (14 kg) que los pacientes con obesidad simple (6 kg), perdieron más masa muscular y tuvieron un mayor metabolismo basal. La CC final se altera en todos sus parámetros si se añade la diabetes.**

Conclusiones: **La reducción del exceso de peso preoperatorio está motivada en gran medida por el efecto de la cirugía BAGUA personalizada. Los pacientes con un IMC entre 30-50 se comportan de forma homogénea en la CC tras la cirugía mientras que los pacientes con un IMC > 50 se comportan diferentemente. Los súper obsesos pierden menos peso, retienen más masa grasa, grasa visceral, masa ósea y agua total. Este efecto debería tratarse con una cirugía más agresiva midiendo todo el intestino delgado para realizar una exclusión adecuada (personalizada) para conseguir unos efectos homogéneos.**

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Palabras clave: *Composición corporal. Diabetes. BAGUA. IMC. Personalizada.*

Introduction

The study of body composition (BC) is the measurements of the different components and compartments of the body and the quantitative relationships among them. The knowledge of these parameters are important for all surgeons performing bariatric surgery.

The measurement of BC began in the 1940s in the laboratory of Behnke[1]. Since then, BC has been introduced in different methods of clinical and research field, where the study of BC has emerged as a new field within biomedical disciplines.

In the 1960s, Siri[2] measured different body compartments especially total body fat, and developed the two-compartment model, where the body is divided of two compartments: fat mass (FM) and fat-free mass (FFM). The fat mass compartment is relatively homogeneous in composition, but the FFM compartment is a heterogeneous mixture in protein-mineral and watery, causing variability between individuals and even within the same individual in different pathophysiological states such as obesity or diabetes, and considering differences of age, sex and race.

Therefore, total body mass is composed by FFM and FM[3]. Lean body mass not only includes FFM but water, muscle, bone, connective tissue and viscera, and also have small amounts of essential fats[4]. FM has non-essential and essential fats[5]. Hence, BC is influenced for total water (TW) in FFM when evaluating.

Kelley et al[6] found that obesity is associated with increased adipose tissue and density reduction of lean tissue. Obesity increases selectively of low-density lean tissue without altering the volume of tissue from normal density. Therefore, the average density of muscle tissue decreased reciprocally to obesity.

When there is weight lost through caloric restriction, loss is only about 75% of fat and 25% of FFM. However, if caloric restriction is associated with an exercise program, the loss of lean tissue can be reduced to approximately 5% of the overall body mass loss. The true effectiveness of an intervention depends not only on the prescription of exercise (mode, frequency, duration, intensity, progression), but also for compliance by the patient. Has also been shown that repeated cycles of weight loss and regain is detrimental to health because weight is recovered disproportionately compound for grease[7]. Therefore, the ultimate goal of any weight loss program is to get long-term weight control, while immediate weight loss is achieved by bariatric surgery.

Once bariatric surgery is performed, the reduction in energy metabolism after weight loss can be attributed to the reduced mass of the body after weight reduction, especially loss of FFM, low power consumption after slimming, therefore, there is a reduction in the thermogenic response to food, and decrease in energy expenditure of physical activity for the same level of activity[8].

Nevertheless, 10% of weight loss was associated with changes in organ weights with high metabolic activity (liver, heart and kidneys); however, there is no change in cerebral mass. Nevertheless, it is known that the brain mass decreases after severe weight loss in patients with anorexia nervosa, predominantly gray matter, which is reversible after nutritional recovery[9]).

The search for the pathogenesis of obesity-related diseases have shown a close relationship between excess nutrients and alterations in cellular and molecular mediators of immunity and inflammation. This has led to the concept of metainflammation to describe the inflammatory response of low-grade in obesity. Inflammation is a coordinated response to noxious stimuli in order to return the system to a normal baseline. The metainflammation in obesity is unique compared with other inflammatory diseases. The chronic nature of obesity causes a low-grade activation of the innate immune system that affects metabolic homeostasis over time. Furthermore, the involvement of multiple organs in inflammation induced by obesity is unique and presents a challenge for researchers trying to unravel the mechanisms of obesity in complex metabolic systems. Multiple inputs contribute to inflammatory metabolic dysfunction that allows a patient to reach the super obesity and they respond differently than expected when faced with weight loss induced by surgery[10].

The tailored One Anastomosis Gastric Bypass (BAGUA) performed in our patients was according to BMI. In super obese patients, the gastric pouch was always smaller size than for morbid obese patients[11]; because of super obese patients behave different in weight loss and final changes in BC from simple and morbid obese patients. For this situation, it is important to tailor the BAGUA surgery, looking for an optimal grade of feeding and malabsorption, proportional to excess preoperative weight, BMI, age and total small intestine length[12].

Bariatric surgery is gaining acceptance as an effective treatment modality in the long-term for obese patients, but it is necessary to have accurate explanations of the effects of bariatric surgery on BC and fat distribution that are still limited, and its complete knowledge give us the opportunity to provide better control of complications in postoperative outcomes.

The aim of the present study is to show that super obese patient (BMI > 50) behave different on postoperative changes of BC from simple (BMI 30-34.9) and morbid obese (BMI 35-49.9) patients undergoing to tailored BAGUA.

Patients and methods

Patients

The study group consisted in 83 (37 diabetic and 46 non-diabetic) patients, distributed by BMI groups: BMI 30-34.9 (12 non-diabetics and 16 diabetics), BMI 35-50 (25 non-diabetics and 17 diabetics) and BMI > 50 (9 non-diabetics and 4 diabetics). They had undergone tailored One Anastomosis Gastric Bypass (BAGUA) for obesity, diabetes or diabesity, and completed all evalua-

tion appointment (preoperative, 10 days, 1, 3, 6 and 12 months), during the first postoperative year.

The distribution of the patients was performed according to the presence or absence of diabetes and BMI ranges (BMI 30 -34.9, BMI 35-50, and BMI > 50).

Preoperative evaluation

In all patients, a preoperative study were conducted following the indications of the Clinical Practice Guideline (CPG) of the European Association for Endoscopic Surgery (EAES)[13].

Body composition analysis

The analysis of BC was performed using a single frequency impedance BC analyzer (TANITA brand, model BC-420MA). This equipment provides estimated values for FM, MM, bone mass, VF, BM and TW calculated by passing an alternating current through the patient to measure the water content, where approximately 73% corresponds to MM. The FM is obtained by subtracting to the weight of FFM to the TBW. The other components are calculated using validated mathematical formula[14]. PEW was calculated subtracting the ideal weight given by the impedance analyzer to the preoperative weight of the patient. All our patients were evaluated in the morning after breakfast. This analysis was performed preoperatively and in the next evaluation follow up appointment after surgery.

Surgical procedure

Before surgery, all patients eat only liquid diet during 5 (BMI 34-34.9) to 7 days (BMI 35-50) depending of preoperative BMI, received antibiotic and antithrombotic prophylaxis. Tailored BAGUA consisted in the construction of a gastric pouch from the gastroesophageal junction to the end of the minor gastric curvature at the lower level of the cisura angularis. The stapler line of the gastric pouch was fixed approximately 12 cm to the intestinal loop (first layer of the anti-reflux mechanism of BAGUA), and it was anastomosed in a laterolateral position to the mesenteric border of a small bowel loop 120 cm (BMI 30-32), 150 cm (BMI 33-34.9), 200 cm (BMI 35-40), 250 cm (BMI 40-44.9), and 280 cm distal (BMI 45-50) to the treitz ligament when the total length of small intestine is 6-7 m. If the total length was more than that measure, we excluded proportionally. The anti-reflux mechanism is completed fixing the afferent loop to the gastric remnant and the efferent loop to the antrum.

The size of the gastric pouch depends on the BMI of the patient. In BMI 30-34.9 we performed a floppy 36 French bougie pouch, while in BMI > 33 a narrow 36 French bougie one s is performed. We left systematically a drainage during the 48 h of hospital stay. After surgery, they eat liquid diet in the 1st week, semifluids in 2nd week, purée in 3-4th weeks and normal diet after one month of surgery. The patient were reviewed at 10 days, 1, 3, 6 and 12 months.

Follow up

The data were collected prospectively according with the protocol, including a baseline evaluation preoperatively that analyzed parameters related to the evaluation of the BC, comorbidities, weight and BMI. After tailored BAGUA surgery, according to the protocol outline, the follow up was performed analyzing BMI and BC in the next 10 days, 1, 3, 6 and 12 months.

Statistical analysis

We used descriptive statistics (mean, median and standard deviation). To test possible significant differences of these parameters between the different study groups we used Student's T test for independent samples. The differences less than 5% were considered significant.

Analyses were performed using SPSS (version 21 for Windows, SPSS, Chicago IL) and Excel 2013.

Results

The results were evaluated by BMI range, presence or not of diabetes, and changes in BC (FM, MM, bone mass, VF, BM, and TW) in the different evaluation appointments.

Preoperative body composition in the study groups

Differences in BC (table I) in the preoperative status of patients, clearly shows some aspects: the relationship among greater BMI with higher levels of all parameters of BC except MM. We also found a correlation between increased both BMI and FM, and higher BM especially in diabetic patients.

Bone mass shows a linear increase especially in non-diabetic patients. Preoperative over-weight ranges between 92 to 159 kg. Levels of VF, BM and TW also show an increment in higher BMI. VF is predominant in all groups of diabetics.

Body composition changes in patients after tailored BAGUA

One month after surgery

Table II shows greater changes over time in BC in regards to FM with respect to other parameters, especially

Table I
Body composition in the six preoperative study groups

	Weight (kg)		BMI		FM (kg)		MM (kg)		Bone M (kg)		VF (kg)		BM (kcal/day)		TW (kg)	
BMI	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Non-diabetics 30-34.9	92	15	32	1	35	14	55	10	2.8	0.6	11	2	1,785	353	44	9
Diabetics 30-34.9	95	17	33	2	37	14	62	11	3.1	0.7	14	3	1,841	360	47	9
Non-diabetics 35-50	110	14	41	4	52	10	55	6	2.9	0.4	18	4	1,852	232	44	6
Diabetics 35-50	115	14	42	3	50	10	61	13	3.1	0.7	22	2	1,998	368	48	11
Non-diabetics > 50	150	23	53	3	80	14	69	17	3.5	0.7	26	2	2,612	547	56	14
Diabetics > 50	159	26	52	2	86	20	63	7	3.3	0.3	25	1	1,795	601	61	9

This data represent mean values (Mean) and standard deviation (SD) of the weight, body mass index (BMI), fat mass (FM), muscle mass (MM), bone mass (Bone M), visceral fat level (VF), basal metabolism (BM) and total water (TW) patients in the preoperative period.

Table II
Changes in body composition in all study groups one month after tailored BAGUA

	Weight (kg)		BMI		FM (kg)		MM (kg)		Bone M (kg)		VF (kg)		BM (kcal/day)		TW (kg)	
BMI Ranges	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Non-diabetics 30-34.9	79	14	28	2	24	9	55	9	2.8	0.5	8	2	1,641	313	40	8
Diabetics 30-34.9	83	16	29	3	26	9	58	11	3.0	0.7	10	3	1,677	329	42	8
Non-diabetics 35-50	94	14	35	5	37	9	54	9	2.8	0.4	13	3	1,688	209	40	7
Diabetics 35-50	98	14	36	4	35	8	59	11	3.0	0.7	17	2	1,795	326	42	9
Non-diabetics > 50	125	19	44	3	55	12	65	15	3.4	0.7	21	1	2,297	444	52	13
Diabetics > 50	130	13	43	4	61	11	66	12	3.4	0.4	20	2	2,400	390	54	6

Data represent mean values (Mean) and standard deviation (SD) of the weight, body mass index (BMI), fat mass (FM), muscle mass (MM), bone mass (Bone M), visceral fat level (VF), basal metabolism (BM) and total water (TW) of patients at one month after surgery.

in patients with a BMI > 50 were the largest decreases achieved, especially in non-diabetic patients. VF, BM and TW continued down continuously but without major changes. MM in this group (diabetic BMI > 50) continued to show a proportional increase of MM compared to preoperative status a month after surgery.

3 months after surgery

FM has the highest percentage of registered decline (table III). Values were less decline in MM and TW. In MM diabetics BMI > 50 had less decline after a month of surgery. In total, values decline ratio of preoperative excess weight (PEW) is proportional to initial BMI: higher preoperative BMI greater decrease in PEW. Patients with BMI > 50, showed declines of 46 kg (diabetic) and 37 kg (non-diabetic) group respectively.

6 months after surgery

In table IV, FM continued to decline but at a slower rate, with a mean decrease in the overall group, repre-

Table III
Changes in body composition in all study groups at 3 months after tailored BAGUA

	Weight (kg)		BMI		FM (kg)		MM (kg)		Bone M (kg)		VF (kg)		BM (kcal/day)		TW (kg)	
BMI Ranges	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Non-diabetics 30-34.9	73	14	26	2	17	6	53	9	2.8	0.5	5	2	1,576	312	39	7
Diabetics 30-34.9	77	16	27	3	19	8	56	12	3.0	0.7	9	2	1,603	316	41	9
Non-diabetics 35-50	82	12	31	4	29	7	51	8	2.7	0.5	11	2	1,574	184	39	6
Diabetics 35-50	88	12	32	3	28	7	56	10	3.0	0.7	15	2	1,683	291	40	9
Non-diabetics > 50	113	19	40	4	45	13	61	14	3.4	0.8	18	2	2,152	418	50	12
Diabetics > 50	113	10	37	5	47	9	65	11	3.4	0.4	18	3	2,176	311	50	6

Data represent mean values (Mean) and standard deviation (SD) of the weight, body mass index (BMI), fat mass (FM), muscle mass (MM), bone mass (Bone M), visceral fat level (VF), basal metabolism (BM) and total water (TW) of patients at 3 moths after surgery.

Table IV
Changes in body composition in all study groups at 6 months after surgery

	Weight (kg)		BMI		FM (kg)		MM (kg)		Bone M (kg)		VF (kg)		BM (kcal/day)		TW (kg)	
BMI Ranges	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Non-diabetics 30-34.9	69	15	24	2	13	5	52	9	2.8	0.5	5	2	1,529	307	36	7
Diabetics 30-34.9	73	14	25	2	15	8	54	11	3.0	0.7	7	2	1,549	291	40	9
Non-diabetics 35-50	74	11	28	4	22	6	49	7	2.7	0.5	9	2	1,486	164	38	6
Diabetics 35-50	79	11	29	3	22	5	53	9	3.0	0.7	13	2	1,581	264	39	8
Non-diabetics > 50	101	15	36	4	36	11	58	12	3.4	0.8	17	2	2,000	340	46	11
Diabetics > 50	104	11	34	4	37	8	62	10	3.4	0.4	16	2	2,058	312	48	7

This data represent mean values (Mean) and standard deviation (SD) of the weight, body mass index (BMI), fat mass (FM), muscle mass (MM), bone mass (Bone M), visceral fat level (VF), basal metabolism (BM) and total water (TW) of patients at within 6 months after surgery.

Table V
Postoperative body composition a year after tailored BAGUA in the six groups

	Weight (kg)		BMI		FM (kg)		MM (kg)		Bone M (kg)		VF (kg)		BM (kcal/day)		TW (kg)	
BMI Ranges	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Non-diabetics 30-34.9	65	14	23	2	10	4	49	9	2.8	0.5	5	2	1484	296	34	6
Diabetics 30-34.9	68	14	24	2	12	8	53	11	3.0	0.7	6	2	1488	278	38	8
Non-diabetics 35-50	68	12	26	4	19	7	47	7	2.8	0.5	8	2	1430	152	36	6
Diabetics 35-50	73	11	27	3	18	6	51	9	3.0	0.7	11	2	1513	244	36	8
Non-diabetics > 50	92	13	33	5	30	9	55	11	3.3	0.7	14	2	1884	285	43	10
Diabetics > 50	90	10	29	3	28	5	57	9	3.4	0.4	14	2	1880	285	45	7

They represent mean values (Mean) and standard deviation (SD) of the weight, body mass index (BMI), fat mass (FM), muscle mass (MM), bone mass (Bone M), visceral fat level (VF), basal metabolism (BM) and total water (TW) of patients one year after surgery.

senting a reduction with respect to preoperative value. In the case of TW, diabetic patients BMI >50 reported greater proportional decrease in this measure. MM continued to show the same trend as the above measures.

One year after surgery

In the last measure (table B), FM presented impressive descent levels in BMI > 50 (non-diabetics and diabetics patients). The TW ended up showing a direct relationship between preoperative BMI and evolution of this value. MM had more random changes in comparison to other groups, as initial values.

The biggest decline corresponds to non-diabetic patients BMI > 50 a difference of patients with diabetes BMI > 50 which showed smaller decrease.

In absolute terms, the group of diabetic patients lost 10 kg in mean, compared to 9 kg of MM loss in non-diabetic patients. Although the biggest decline all parameters was BMI > 50 patients, the way to get the last changes was different.

Discussion

The BC analysis has been used for decades to study possible changes in activities or situations that could cause major alteration of one or more body components in sports[15,16]. Soon it began to be used to control different weight loss diets[17].

Nevertheless, surgeons not measure the BC routinely to monitor their patients. While it is true that some anthropometric measures are used to control the use of clinical nutrition diets enteral or parenteral, with former plicometers still in use. However, consultations neither have bio-impedance devices easy to use nor trained surgeons to understand the clinical significance of changes in FM, FFM, VF, resting energy expenditure (metabolic rate), total energy expenditure, and other BC components in the short, medium and long term after bariatric surgery. The next step is to understand the biological and clinical significance of each of the components of the BC.

However, it is surprising that there is no systematic use of BC analysis after bariatric surgery to analyze if the weight loss is healthy because of loss of excess fat and no other components. In fact, our group used to measure BC before and after BAGUA routinely to ensure that weight loss is proper and correct.

The loss of excess of fat and body weight is the result of the reversal of obesity and expected result of any type of bariatric surgery. Gastric bypass (GB) is one of the most effective surgical procedures to get a large weight loss sustained over time in obese subjects[18,19]. It is important to note that super obese patients behave

different from the others groups, with less weight loss than the other group using the same technique. Although super-obesity is a selection criterion for prioritizing the surgery in the waiting list, there are insufficient studies to demonstrate why super obese behave differently after bariatric surgery[20]. Large patient studies show that super-obese patients overall required longer operating room times and longer hospital length of stay[21].

Therefore, it is important to improve the surgery making it a more aggressive technique. In our group, surgery is tailored according to each patient for best results, first by measuring the total length of the small intestine and make the bypass and limb length according to BMI to lose enough weight[11,12]. However, there are studies like Sarhan et al[22] which mention that the sustained weight loss long-term of patients with super obesity is just obtained by standard bariatric surgery.

Weight loss after bariatric surgery has three phases. An initial phase of rapid weight loss mainly due to severe reduction in energy intake, in part caused by nonspecific effects of surgery. A second phase of slower weight loss after intake has returned to near normal levels. Third phase characterized by stable body weight or slow regain[23]. Our results have followed this pattern.

Body weight loss in our patients are mainly due to the loss of FM, with a proportionally lower loss of MM. However, the meta-analysis of Chaston et al[24] shows that the relative loss of FFM through dietary restriction, behavior modification, and several types of bariatric surgery, is correlated positively with the degree of caloric restriction.

After one month of tailored BAGUA, changes in BC are greater in the preoperative BMI ≥ 50, where had the greatest decrease, especially in non-diabetics. In this phase, diabetic group BMI ≥ 50 have an increment of MM (mean 4 kg).

At 3 months after surgery, FM decreased, but not the TW and MM, except for diabetic patients BMI ≥ 50. At this time, it is more noticeable the decrease in both body weight and BMI. On the other hand, 6 months postoperatively, fat decreases but at a slower pace, but in proportion to the preoperative BMI, not the TW. However, one year after surgery, it is appreciated spectacular data regarding the preoperative, where non-diabetic patients with higher BMI were the most favored. At this point, the TW is already about the new weight. As for MM loss, diabetic are more affected than non-diabetic patients are. BM decreases but remains higher in diabetics and patients BMI > 50.

In this sense, the loss of MM is a challenge for the physician and a real problem for the patient, so that Savastano et al[25] suggest the use of growth hormone for 6 months (P = 0.000) after bariatric surgery to reduce loss of lean body mass. With our tailored BAGUA, the loss of MM is around 15%, but up to 30% is considered healthy. Therefore, the surgery demonstrated a good protein absorption without malnutrition effects.

Christou et al[26], in their study of 1,035 patients undergoing bariatric surgery were followed for five years, finding that since the first quarter, up to 2 years, weight loss is progressive, and that depending on the characteristics of the patient, it can be achieved to surgery successful if it reaches at least BMI 35. In their data, after reviewing the two years, some patients had weight loss, but they did not measure BC to know which parameters were modified. Nevertheless, Strain et al[27] demonstrates that changes in body composition after bariatric surgery in super obese patients are different; they lost less body fat than the morbid obese patients did.

This data show us that in the overall assessment of BC changes over time, certain groups with particular characteristics had changes in the loss of any parameter studied. Date et al[20] mentions that morbid obese patients are more benefited than super obese patients in the aspects of health, quality of life, and employment outcomes after bariatric surgery.

Logically, the most notorious change was in FM loss due to tailored surgery performed. Some of the important features found in our study are that patients that had little weight loss, had more total water (p = 0.005).

Over time, BM is higher in the diabetic patients (p = 0.003). Furthermore, after tailored BAGUA, BM (p = 0.001) and MM (p = 0,000) remains higher in diabetic patients.

Although super obese patients are considered higher risk than other types of obesity, bariatric surgery is considered safe in super obese and super-super obese patients[28].

We are aware that the main limitation of our study was the number of patients analyzed, however the resultant data are troubling and require study of a larger number of patients and longer-term studies. However, this study is a watershed in the ideas importance of conducting BC in all patients undergoing surgery for obesity, diabetes, diabesity.

These results have motivated us to continue with the tailored One Anastomosis Gastric Bypass (BAGUA) to achieve better results in this group of patients, unlike other techniques that do not.

Conclusions

To achieve better outcomes after bariatric surgery, it is important to both measure the total length of the gut and tailor the BAGUA surgery according to patient's BMI. The systematic measurement of BC in patients undergoing bariatric surgery should be routinely in all patients to operate since it has proven to be a vital parameter for metabolic control and nutrition of patients after GB.

The behavior of the BC (FM, VF, MM and BM) are different between patients BMI > 50 and BMI 30-50. After tailored BAGUA, patients with BMI 30-50 behave homogeneous in final body composition. Patients BMI > 50 behave different. They lose less weight, retain more fat mass, visceral fat, bone mass and total wa-

ter. This effect should be treated by more aggressive surgery, having to measure the entire small intestine to make a proper exclusion (tailored effect) to achieve homogeneous effects. Besides, bearing diabetes alter the finally result of body composition.

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Original / *Obesidad*

Despistaje rutinario de Síndrome de Cushing en pacientes con obesidad mórbida; ¿es realmente necesario?

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Resumen

Introducción: **El síndrome de Cushing (SC) es más frecuente en pacientes con síndrome metabólico. Estudios previos han sugerido que es necesario realizar un despistaje de SC en pacientes obesos; sin embargo, estudios más recientes sólo recomiendan el despistaje en pacientes con hipertensión o diabetes mal controlados, a pesar de tratamiento.**

Objetivo: **Evaluar la prevalencia de SC oculto en pacientes con obesidad mórbida.**

Pacientes y métodos: **Estudio observacional retrospectivo en el que se incluyeron 399 pacientes que iban a someterse a cirugía bariátrica. A todos los pacientes se les realizó una historia clínica completa, incluyendo exploración física y test de Nugent, como parte del protocolo precirugía.**

Resultados: **399 pacientes (308 mujeres, edad media 41,9 ± 10,5 años; IMC medio 51,5 ± 8,4 kg/m^2). El 10,3% de los pacientes presentaban prediabetes y el 27,8% diabetes. En 21 de los 399 pacientes, el despistaje fue anormal. En 8 pacientes, medimos cortisol libre en orina de 24 horas (CLU), siendo en todos normal al menos en dos ocasiones (CLU < 150 mcg/24 h), lo que descartaba SC. En 13 pacientes, repetimos el test de Nugent; sólo en 3, el test resultó patológico. Dos de los pacientes estaban en tratamiento con carbamacepina, lo que se consideró un falso positivo. El otro paciente se diagnosticó de Enfermedad de Cushing.**

Conclusión: **La prevalencia de SC fue muy baja en pacientes con obesidad mórbida. Nuestros datos sugieren que no se debería realizarse un despistaje de SC de forma rutinaria.**

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Palabras clave: *Cushing. Obesidad mórbida. Despistaje. Nugent.*

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SCREEENING FOR CUSHING'S SYNDROME IN OBESE PATIENTS: IS IT REALLY NECESSARY?

Abstract

Background: **Cushing's syndrome (CS) is considered to be more frequent among patients with metabolic syndrome. Previous studies have suggested to perform a routine screening for CS in obese patients; however, more recent reports only recommend a case-finding approach in patients with uncontrolled diabetes and hypertension, despite appropriate treatment.**

Objective: **The aim of this study was to evaluate the prevalence of unsuspected CS in morbidly obese patients in an outpatient's clinic.**

Patients and methods: **Retrospective case-note study. We reviewed the medical records of morbidly obese patients referred to our clinic prior to bariatric surgery between january 2001 and december 2011. All patients had a complete medical history including physical examination, and 399 underwent screening for CS as part of our pre-surgical protocol. As screening for autonomous cortisol secretion, we performed an overnight 1 mg Dexamethasone Suppression Test (DST). Serum cortisol < 1.8 µg/dl was the cut-off point for normal suppression.**

Results: **399 patients (308 female; mean age 41.9 ± 10.5 years; mean BMI 51.5 ± 8.4 kg/m2). In the retrospective analysis, prediabetes and diabetes mellitus were observed in 10.3% and 27.8% respectively. In 21 of 399 patients, screening was considered to be abnormal. Eight of these 21 patients had subsequent normal 24h Urinary Free Cortisol (UFC) levels (150 µg/24h). In 13 of 20 patients, we repeated an overnight 1mg DST, on suspicion of failing to take the dexamethasone correctly. Three patients failed to suppress their cortisol levels, two of them were on carbamazepine, which was considered to be a false positive result. The other patient with abnormal UFC levels was diagnosed with CS (0.26%), whose cause was a pituitary microadenoma.**

C*onclusion:* **A low proportion of patients with morbid obesity were found to have CS. Our findings suggest that morbidly obese patients should not be routinely screened for CS.**

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Key words: *Cushing. Obesity. Screening. Nugent.*

Introducción

La obesidad es el problema metabólico más frecuente en países industrializados. Datos del estudio Enrica realizado en España entre 2008 y 2010 revelaron que el 23% de los adultos presentaba obesidad (IMC ≥ 30 kg/m²), lo cual convierte a esta patología en un problema de salud de primer orden.

El Síndrome de Cushing (SC) endógeno es, por el contrario, una entidad mucho menos frecuente. No obstante, hay pocos datos disponibles sobre la verdadera incidencia de esta enfermedad. Un estudio realizado en el País Vasco entre 1975 y 1992[1], le atribuye una incidencia de 2-3 casos por millón de habitantes por año. Sin embargo, algunos autores defienden que la prevalencia podría ser más alta si se realizara una búsqueda prospectiva de casos en pacientes sin signos ni síntomas específicos de SC, pero con algunas características que se presentan más en pacientes con exceso crónico de cortisol, tales como la obesidad, la intolerancia a la glucosa o la HTA.

Tiryakioglu y cols. hallaron una proporción muy significativa (9,33%) de pacientes con SC asintomático al realizar despistaje rutinario en enfermos con obesidad[2] y recomiendan evaluar sistemáticamente a los enfermos obesos para despistaje de SC. Sin embargo, un estudio más reciente realizado en 369 pacientes con sobrepeso y obesidad no confirma estos hallazgos[3]. Asimismo, Terzolo y cols. en un estudio prospectivo con 813 pacientes con diabetes tipo 2 e IMC ≥ 25 Kg/m², sólo recomiendan la búsqueda activa de casos en pacientes con diabetes e hipertensión no controlada a pesar de tratamiento adecuado[4].

El objetivo de nuestro estudio fue evaluar la presencia no sospechada de SC en pacientes con obesidad mórbida pre-cirugía bariátrica en consultas externas de un Hospital de tercer nivel.

Material y métodos

Estudio observacional retrospectivo en el que se incluyó una muestra aleatoria de 399 pacientes de los pacientes que iban a someterse a cirugía bariátrica en la unidad de Endocrinología y Nutrición del Hospital Universitario Reina Sofía (Córdoba) desde enero de 2001 a diciembre de 2011.

Los criterios de inclusión fueron tener entre 18 y 60 años, índice de masa corporal (IMC) ≥ a 35 kg/m² y estar en lista de espera de cirugía bariátrica. Los criterios de exclusión fueron la presencia de características específicas de SC (plétora facial, miopatía proximal, estrías rojo vinosas o fragilidad capilar[5]), enfermedad aguda grave, síndrome depresivo, tratamiento con fármacos que afecten al eje hipotálamo-hipófisis-suprarrenal o embarazo. Se clasificaron como hipertensos, aquellos pacientes en tratamiento farmacológico con tensión arterial sistólica mayor de 140 mmHg o diastólica mayor de 90 mmHg. La dislipemia se definió como hipercolesterolemia si el colesterol total era superior a 200 mg/dl, con triglicéridos normales; hipertrigliceridemia si los niveles séricos de triglicéridos eran superiores a 150 mg/dl, con colesterol normal; y dislipemia mixta, si niveles de colesterol y triglicéridos estaban elevados. En cuanto a la intolerancia hidrocarbonada, se definió siguiendo la guía ADA 2011, se consideró diabético a todo paciente con tratamiento antidiabético, hemoglobina glicosilada (HbA1c) ≥ 6,5% o glucemia en ayunas ≥ 126 mg/dl en dos determinaciones distintas. La prediabetes se definió como HbA1c entre 5,8 y 6,5% o glucemias en ayunas entre 100 y 126 mg/dl. Los dolores articulares se definieron como limitantes, si disminuían su capacidad de movimiento o su calidad de vida.

Se recogieron variables demográficas (edad y sexo), comorbilidades asociadas a la obesidad, así como datos de exploración física (peso, talla, tensión arterial). En nuestro hospital, como protocolo, antes de la cirugía de la obesidad se realiza un estudio hormonal que incluye la realización de un test de Nugent (cortisol plasmático a las 8.00 h tras supresión con 1 miligramo de dexametasona tomado a las 23.00 horas), tomando como punto de corte normal 1,8 mcg/dl. En aquellos pacientes que el test dio un resultado patológico, se continuó el estudio para confirmar o descartar la presencia de SC.

Para el análisis descriptivo de variables cualitativas se emplearon las frecuencias absolutas y el porcentaje para cada categoría. Las variables cuantitativas se expresaron con su media ± desviación estándar (m ± DE) y se comprobó la normalidad de las mismas mediante el test de Shapiro-Wilk. Cuando las variables no fueron normales se utilizaron test no paramétricos en función de las características de las mismas. Para la asociación de variables cualitativas se empleó el test de chi cuadrado. Para la comparación de medias se emplearon los test de Student o la U de Mann Whitney en función de si eran variables paramétricas o no. En todo momento se trabajó con significación estadística del 5% y se empleó el programa estadístico SPSS para Windows versión 15.0 (licencia del Hospital Universitario Reina Sofía).

Resultados

Se incluyeron 399 pacientes, el 77,2% eran mujeres (308 pacientes) con una edad media de 41,95 ± 10,53 años (Rango 20-67). Entre las características de la exploración física destaca un IMC medio de 51,51 ± 8,38 kg/m² antes de la cirugía, una tensión arterial sistólica de 128,02 ± 17,27 mmHg y diastólica de 76,20 ± 12,52 mmHg. En cuanto a los datos de la analítica basal, cabe destacar un colesterol total medio de 165,97 ± 35,95 mg/dl (LDL 115,89 ± 35,95 mg/dl; HDL 46,75 ± 11,60 mg/dl) y unos triglicéridos de 116,42 ± 63,52 mg/dl.

Las comorbilidades asociadas a la obesidad se muestran en la tabla I. Destaca la hipertensión, presente en el 40,4% de los pacientes, la dislipemia mixta en el 11,8% o la presencia de dolores articulares limitantes para la

Tabla I
Comorbilidades asociadas a la obesidad

Comorbilidad	*Frecuencia*	*Porcentaje*
Hipertensión arterial	**161**	**40,4%**
Intolerancia hidrocarbonada		
– Diabetes Mellitus	111	27,8%
– Prediabetes	41	10,3%
Síndrome de apnea obstructiva del sueño	**49**	**12,3%**
Dislipemia		
– Dislipemia mixta	47	11,8%
– Hipercolesterolemia	25	8,3%
– Hipertrigliceridemia	16	4%
Dolores articulares		
– Limitantes	**41**	**10,3%**
– No limitantes	**37**	**9,3%**
Hipertiroidismo	6	1,5%

vida diaria en el 10,3%. En cuanto al metabolismo hidrocarbonado, el 27,8% de los pacientes son diabéticos tipo. El 21,9% de los pacientes eran diabéticos conocidos, el resto se diagnosticaron en el ingreso.

En 21 de los 399 pacientes (5,3%) el test de Nugent resultó patológico (Cortisol tras 1 mg de dexametasona >1,8 mcg/dl). En 8 pacientes, medimos cortisol libre en orina de 24 horas (CLU), siendo en todos normal al menos en dos ocasiones (CLU < 150 mcg/24 h), lo que descartaba SC. En 13 pacientes, repetimos el test de supresión con 1 mg de dexametasona, por la sospecha de que no se habían tomado la dexametasona o lo habían hecho antes del horario determinado. Sólo en 3, el test resultó patológico. Dos de los pacientes estaban en tratamiento con carbamacepina, lo que se consideró un falso positivo. En el otro paciente, con dos test patológicos, se realizó un CLU y un cortisol nocturno, siendo ambas pruebas patológicas. Se continuó el estudio y fue diagnosticado de Enfermedad de Cushing por un microadenoma hipofisario (fig. 1).

Discusión

En nuestra serie, el despistaje sistemático de SC en pacientes con obesidad mórbida no está justificado. Sólo un paciente (0,25%) de 399 presentó esta enfermedad.

La prevalencia del SC en nuestra serie, es menor a la descrita en estudios anteriores, que usan un método de cribado similar, y esto se puede explicar porque en nuestro estudio, la detección se realizó en una población

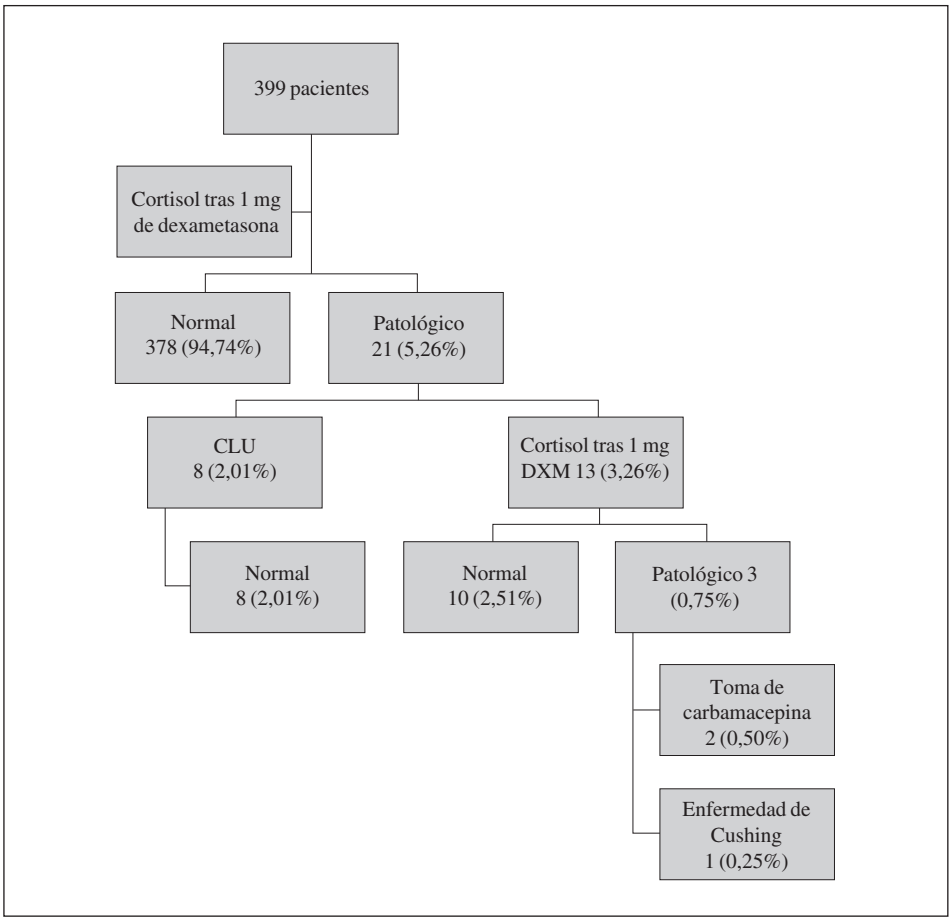


Fig. 1.—Algoritmo de seguimiento.

no seleccionada, y no en pacientes con alto riesgo de hipercortisolismo, es decir, con signos o síntomas que hiciesen sospechar un SC. Además, nuestra población presenta una obesidad grado IV o extrema de media, y la obesidad asociada al SC es una obesidad grado I-II.

Para el despistaje de SC usamos, el punto de corte más sensible (1,8 µg/dl) para cortisol en el test de Nugent. Este punto de cortes es el más usado, con una sensibilidad diagnóstica del 95% y una especificidad del 80%[5]. Ello nos obligó a repetir la prueba o a realizar una prueba adicional en el 5,26% de los pacientes. Sin embargo, la posibilidad de haber perdido a pacientes con hipercortisolismo es muy baja. En otros estudios se ha utilizado el punto 5 µg/dl[4], que es más específico, y un claro indicador de hipercortisolismo, aunque no pueden excluir la pérdida de pacientes con hipercortisolismo subclínico.

Según la Endocrine Society[6] la detección de SC se recomienda en pacientes con características clínicas típicas (plétora facial, fragilidad capilar, estrías rojo-vinosas y miopatía proximal), con patología inusual para su edad (por ejemplo, la osteoporosis, la hipertensión y la diabetes tipo 2), y en aquellos con incidentalomas adrenales.

El diagnóstico precoz de los pacientes con SC es importante para prevenir las comorbilidades a largo plazo y el aumento de la mortalidad. En nuestro estudio hemos incluido pacientes obesos para el despistaje de SC que no tienen un claro fenotipo Cushing, jóvenes y con alta prevalencia de alteración del metabolismo hidrocarbonado e hipertensión. La prevalencia de SC entre los pacientes obesos varía ampliamente entre los diferentes estudios, oscila entre 0,6% y 9,4%[2-4,7,8]. Esta heterogeneidad puede ser debida a los diferentes criterios de inclusión, y a los distintos puntos de corte para definir la supresión de cortisol tras 1mg de dexametasona.

En conclusión, los resultados del presente estudio no apoyan la aplicación de un cribado universal de SC en pacientes con obesidad mórbida, a menos que tengan características específicas de esta enfermedad.

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High-oleic peanuts increase diet-induced thermogenesis in overweight and obese men

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Abstract

Background: **Evidences suggest that nuts consumption can improve energy metabolism.**

Purpose: **This study aimed to compare the effects of acute ingestion of high-oleic and conventional peanuts on appetite, food intake, and energy metabolism in overweight and obese men.**

Methods: **Seventy one subjects (29.8 ± 2.4 kg/m²) were assigned to the groups: control (CT, n = 24); conventional peanuts (CVP, n = 23); high-oleic peanuts (HOP, n = 24). Subjects consumed 56 g of peanuts (CVP and HOP) or control biscuits (CT) after overnight fasting. Thereafter, energy metabolism was evaluated over 200 minutes, during which diet-induced thermogenesis (DIT) and substrate oxidation were analyzed. Appetite sensation was recorded for 3 hours. Statistical analyses were performed using the SAS software considering 5% as the significance level.**

Results: **Postprandial energy expenditure and DIT were significantly higher in HOP than in CVP. Substrate oxidation did not differ between groups. Only HOP presented score below 100 indicating incomplete compensation. CT and CVP showed a complete caloric compensation (scores > 100). Regarding appetite sensation, CVP group felt less "full" than HOP and CT. After 3 hours, satiety score of CVP returned to baseline, whereas HOP and CT remained significantly higher. Hunger scores returned to baseline in CVP and CT and they were maintained significantly lowered in HOP.**

Conclusion: **High-oleic peanuts contributed to higher DIT, higher sensation of fullness and incomplete compensation for energy intake compared to conventional peanuts and may be useful to dietary intervention to reduce body weight.**

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CACAHUETE ALTO-OLEICO AUMENTA LA TERMOGÉNESIS INDUCIDA POR LA DIETA EN HOMBRES CON SOBREPESO Y OBESIDAD

Resumen

Antecedentes: **Las pruebas sugieren que el consumo de frutos secos puede mejorar el metabolismo energético.**

Propósito: **Este estudio tenía por finalidad comparar los efectos de la ingesta aguda de cacahuetes con alto contenido en oleico y cacahuetes convencionales sobre el apetito, el consumo de alimentos y el metabolismo energético in hombres con sobrepeso y obesos.**

Métodos: **Se distribuyó a 71 individuos (29,8 ± 2,4 kg/m²) a los grupos: control (CT, n = 24); cacahuetes convencionales (CVP, n = 23); cacahuetes con alto contenido en oleico (HOP, n = 24). Los individuos consumieron 56 g de cacahuetes (CVP y HOP) o control (CT) tras un ayuno nocturno. Posteriormente, se evaluó el metabolismo energético a lo largo de 200 minutes, durante los cuales se analizaron la termogénesis inducida por la dieta (TID) y la oxidación de sustratos. La sensación de apetito se registró durante 3 horas. Se realizaron los análisis estadísticos con el programa SAS considerando un nivel de significación del 5%.**

Resultados: **El consumo de energía posprandial y la TID fueron significativamente superiores en el HOP que el CVP. La oxidación de sustratos no difirió entre los grupos. Sólo el HOP presentó una puntuación por debajo de 100, lo que indicaba una compensación incompleta. El CT y el CVP mostraron una compensación calórica completa (puntuaciones > 100). Con respecto a la sensación de apetito, el grupo CVP se mostró menos "lleno" que los grupos HOP y CT. A las 3 horas, la puntuación de saciedad del CVP volvió a la situación basal, mientras que en los grupos HOP y CT permanecía significativamente superior. Las puntuaciones de hambre volvieron a la situación basal in los grupos CVP y CT y se mantuvieron significativamente por debajo a las del grupo HOP.**

Conclusión: **Los cacahuetes con alto contenido en oleico contribuyen a una mayor TID, mayor sensación de plenitud y una compensation incompleta del consumo de energía en comparación con los cacahuetes convencionales y pueden ser de ayuda como intervention dietética para disminuir el peso corporal.**

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Palabras clave: *Obesidad. Metabolismo energético. Oxidación de sustrato. Apetito. Ácido graso oleico.*

Abbreviations

ANOVA: Analyses of variance.
BMI: Body mass index.
CHO: Carbohydrate.
CT: Control group.
CVP: Conventional peanuts group.
DIT: Diet-induced thermogenesis.
HOP: High-oleic peanuts group.
MUFA: Monounsaturated fatty acids.
piAUC: Positive incremental area under the curve.
REE: Resting energy expenditure.
rm-ANOVA: Repeated measure analyses of variance.
SEM: Standard error of the means.
SFA: Saturated fatty acids.

Introduction

Obesity represents one of the major risk factors for the development of other metabolic disease. Its appropriate treatment is essential for the maintenance of good health status[1,2]. Therefore, many studies have been conducting to verify the metabolic effects of seed on overweight individuals[3-11].

Evidences suggest that peanuts ingestion may favor body weight control by reducing food intake and by modulating energy metabolism and substrate oxidation[5,6]. Nuts satiating and thermogenic proprieties can be attributed to their high contents of dietary fiber, protein, and unsaturated fatty acids[7,12].

There is general agreement that protein has greater effect on diet-induced thermogenesis (DIT) than carbohydrate and fat[1,13-17]. Besides, dietary fiber improves satiety and reduces hunger sensation[15,18-21]. Since peanuts is one of the highest protein contents nuts (≈24%), and it also has ≈8% of dietary fiber, its consumption may contribute to appetite control and to increase DIT[3,5].

Energy metabolism improvement of overweigh individuals after peanuts oil ingestion has been reported[6]. The authors attributed the results to the peanuts fatty acids profile. It is known that monounsaturated fatty acids (MUFA) increase body fat oxidation while saturated fatty acids (SFA) contribute for lower DIT and are prone to be stored in adipose tissue[6,22-26]. Despite its high energy density (≈6 kcal/g) and high-fat content (≈50%), peanuts is an excellent source of MUFA[3,5].

Oleic acid is the major MUFA of peanuts. There is a great interest in producing high-oleic peanuts since this fatty acid preserves the sensory and antioxidant proprieties by decreasing lipid peroxidation during storage[27-30]. However, there is a lack of knowledge about the effects of high-oleic peanuts in human metabolism[11]. Thus, this trial aimed at comparing the effects of acute intake of high-oleic and conventional peanuts on appetite, food intake, and energy metabolism in overweight and obese men.

Subjects and methods

Subjects

One hundred fifty potential men were recruited by public advertisements and posted flyers. Subjects underwent a brief nutritional screening, which included measurement of body weight and height, and filling out a questionnaire about medical, sports, and nutritional history. They were required to be aged between 18 and 50 years, with body mass index (BMI) ranging from 26 to 35 kg/m^2 and stable weight (± 3 kg) during the previous 3 months. Subjects presenting any chronic/acute diseases were not included. Other exclusion criteria were the use of any medication that might affect the results of the study, and/or be under weight-loss diets over 3-months prior to the study; drinking more than 168 g of alcohol/week. The study was approved by the ethical committee in human research of the Federal University of Viçosa, MG, Brazil (protocol: 185/2011). The study procedures were conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All participants signed a written informed consent and received no financial compensation or gifts for their cooperation.

Study Design

This was a one-day intervention randomized trial. After successfully completing the screening, seventy one subjects were randomly assigned to the experimental groups: Control (CT; n = 24); Conventional peanuts (CVP; n = 23); High-oleic peanuts (HOP; n = 24). They were explained about the protocol (fig. 1). Subjects received a standard dinner to be consumed the night prior to the assessments (see *Test meal* section). After an overnight fasting, subjects consumed the test meal, which included 56 g of conventional or high-oleic peanuts (CVP and HOP) or control biscuits. The analysis included measurements of anthropometry, body composition, appetite subjective sensation, food intake, resting energy expenditure (REE), DIT, and substrate oxidation.

Test meal

The night prior to the assessments, subjects were required to eat a standard dinner which consisted of 109 g of a instant plain noodles (Nissin®) with 5 g of parmesan cheese, and 200 mL of grape juice (731 kcal; 65.1% from carbohydrate, 7.6% from protein, and 28.3% from fat). This meal was intended to reduce DIT and substrate oxidation during fasting conditions since the thermic effect of protein may remain longer than 7 hours[1].

On the test day, subject consumed within 15 minutes one of the three test meals according to the experimen-

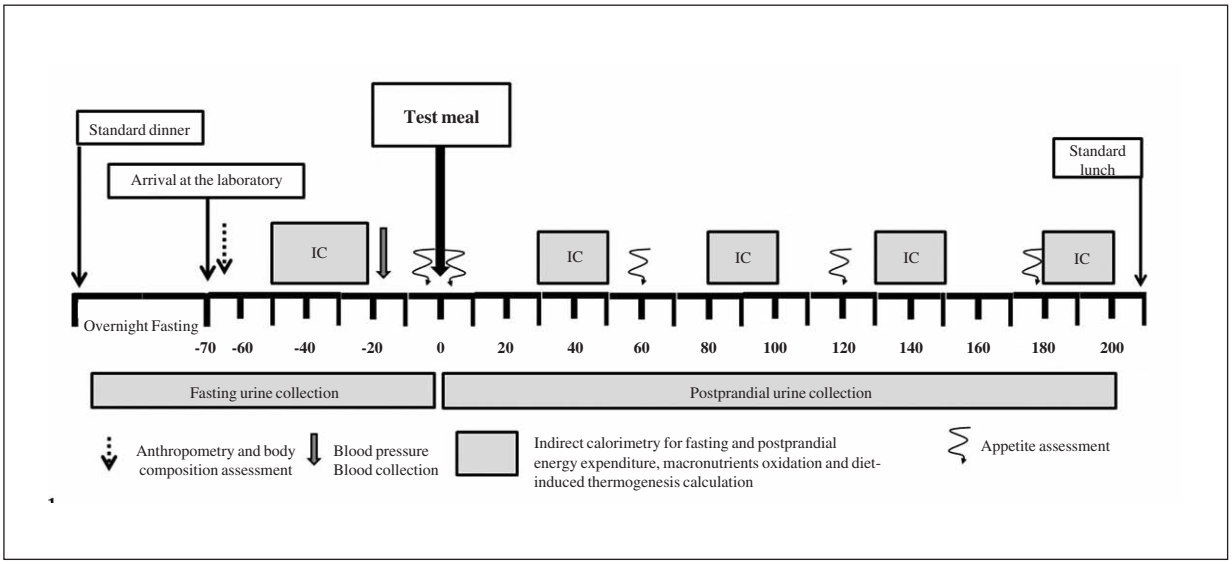


Fig. 1.—Experimental protocol.

tal group. Each test meal was calculated to provide 25% of each subject's daily energy requirement (706 ± 73 kcal). They had the same energy density and provided 35% of the calories from carbohydrate, 16% from protein, and 49% from fat. They consisted of a strawberry flavored milk shake and 56 g of unpeeled roasted peanuts (conventional or high-oleic) or control biscuits.

Conventional (IAC-886) and high-oleic (IAC-505) peanuts were prepared in dry heat for 25 minutes at 180 ºC being revolved every 5 minutes. After cooling, 56 g of peanuts were packed in vacuum and stored at -20°C for further use. Samples were analyzed for macronutrients and dietary fiber contents according to validated methods[31,32]. This portion of conventional and high-oleic peanuts contains, respectively, 13.6 and 12.8 g of carbohydrates, 16.8 and 16.3 g of proteins, 24.0 and 24.7 g of fat, and 5.0 and 5.5 g of dietary fiber (0.2 and 0.7g of soluble; 4.8 and 4.8 g of insoluble). Oleic fatty acid represents 51.0% of total fat in conventional peanuts and 81.5% in high-oleic peanuts.

Control biscuits were developed in the laboratory to offer similar amount of macronutrients and fiber, and energy density of the mean composition of both peanuts types. Its ingredients, in each portion, consisted of egg (30 g), whey protein supplement (13.8 g), whole wheat flour (11.6 g), margarine (9.6), hydrogenated vegetable shortening (8.6 g), soybean oil (7.2 g), dietary fiber supplement (1.6 g), sesame seed (1.5 g), wheat bran (1.2 g), salt (0.7 g), and powder yeast (0.3 g). It was prepared 1-2 days before each test day. The centesimal composition of control biscuits were also analyzed[31,32]. One portion of 56g contains 12.2 g of carbohydrates, 16.4 g of proteins, 24.6 g of fat, and 4.7 g of dietary fiber (0.4 g of soluble; 4.3 g of insoluble). Oleic fatty acid represents 35.2% of total fat.

The milk shake was prepared right before its consumption and consisted of whole milk powder, whey protein supplement, Nesquik® strawberry powder, soybean oil, water, and ice. The proportion of ingredients varied since it was prepared to complete the calories and macronutrients content respecting the macronutrient proportion previously described in this section. Besides, in order to control the volume of 500 mL/meal, additional water was given to subjects.

After completing all the study protocol, a 750 kcal meal was offered. It consisted of a sandwich, fruit juice (250 mL), and apple (130 g).

Dietary intake assessment

Subjects provided 3-days food records (two non-consecutive week days and one weekend day) filled out the week before the assessments. On test-day, subjects were also required to fill out a food record until bed time. A dietitian reviewed the food records with the subjects to check for errors or omissions. All the food records were analyzed by the same dietitian using a specific computer software system (Dietpro 5.2i, 2007. Agromídia Software Sistemas-Universidade Federal de Viçosa) based on Brazilian food composition tables[33,34].

Dietary compensation for the test meal calories consumed was calculated as described by Kirkmeyer and Mattes[35] using the equation: (energy intake from the self-selected diet + energy from the test meals) minus (actual energy intake from the self-selected diet + energy from test meals) divided by the energy value of the test meals. Results were expressed as percentage. A value of 100 represents an adjustment of free-feeding intake that exactly offsets the energy contributed by the peanuts. Values below 100 indicate incomplete compensation.

Appetite assessment

One hundred millimeter visual analog scales were used for appetite assessment. These scales include words anchored at each end, expressing the most positive and negative rating, to assess hunger, satiety, fullness, and prospective food consumption[36]. Subjects were carefully trained to use the questionnaire prior the test. The questionnaires were made as small booklets showing one question at a time. Subjects were instructed to rate the appetite dimensions by marking the scale at the point that was most appropriate to their feeling at that time and they could not refer to their previous ratings when marking the questionnaire. Appetite ratings were recorded immediately before and after the test meal consumption, and hourly for three hours (fig. 1). The results were expressed as the positive incremental area under the curve ($_{pi}$AUC) of the scores.

Measurements and calculations

Subjects were instructed not to consume caffeine and alcohol, to refrain from heavy physical activity and to maintain a regular sleep-wake schedule (8 hours/night) during 72-hours before test day. They were also instructed to fast overnight prior to the assessments and to minimize activity in the morning of the measurements. Body weight, height, and waist and hip circumferences were taken with subjects standing straight, barefoot and wearing only light shorts. Body weight and composition were assessed by a bioelectrical impedance analysis device (Tanita, model TBF-300, Tanita Corporation) in full compliance with the manufacturer guidelines. After at least 10 minutes of resting, blood pressure was measured with the use of a sphygmomanometer by trained specialists.

Respiratory gas exchange was measured by indirect calorimetry using a ventilated respiratory canopy (Deltatrac II, MBM-200; Datex Instrumentarium Corporation) in full compliance with the manufacturer guidelines. The volume of oxygen consumption and carbon dioxide production were measured over 30 minutes under fasting conditions. Then, the REE was obtained from the device. To evaluate DIT and substrate oxidation, the gas exchange was measured four times over 200 minutes after test meal ingestion during 20 minutes within 30 minutes intervals (fig 1). Subjects were asked to be awake and minimize motion during measurements. DIT was calculated as the incremental increase in energy expenditure above REE, expressed as percentage of the meal calories[13]. Cumulative energy expenditure (kcal x 200 minutes) was expressed as $_{pi}$AUC[13,37]. To calculate carbohydrate and fat oxidation, the urinary nitrogen was analyzed by Kjeldahl method in timed urine samples, which were collected during fasting period and over 200 minutes after meal consumption (fig 1). Fasting and postprandial substrate oxidation were calculated using the equations propose by Frayn[38] and expressed as mg/min and as its $_{pi}$AUC.

Subjects' daily energy requirements were calculated by multiplying the measured REE by a physical activity coefficient. This coefficient depended on the physical activity level of each subject, which was evaluated by using the *International Physical activity Questionnaire* and classified according to FAO/WHO/UNU (2001)[39-41].

In order to preserve subjects' health, peanut samples were analyzed for aflatoxin content. Briefly, immunoaffinity columns were used (Aflatest®, Vicam) for sample purification. The toxin was quantified by using a high-performance liquid chromatography with fluorescence detection. The post-column derivatization was done using a Kobra cell® electrochemical cell.

Statistical analysis

The $_{pi}$AUCs were calculated using GraphPad Prism (Version 5; GraphPad software Inc) using the trapezoidal method. The statistical analyses were performed using the SAS statistical package (Version 9.2; SAS Institute Inc). Normality and homogeneity of variance were evaluated by Shapiro-Wilk and Levene tests, respectively. Accordingly, parametric or nonparametric tests were performed.

Variables were compared between groups using One-way analyses of variance (ANOVA) followed by Tukey's test or using the Kruskal-Wallis test followed by Dunn's test, as appropriate. Two-way repeated-measures ANOVA were applied to test the differences between groups throughout the test day for energy metabolism variables and appetite sensation with treatment and time as repeated factors. Paired t-tests or Wilcoxon test were performed to compare habitual dietary intake with the test day intake. Power analysis was calculated using the analyst procedures of the SAS software. It indicated that a sample of 23 per group would permit detection of a treatment effects with more than 99% of power. The rejection level of significance used was 5%. Results are presented as mean ± SEM.

Results

Seventy one subjects were randomized to the trial. Subjects' characteristics at baseline (fasting condition), including anthropometry, body composition, blood pressure, and energy metabolism variables did not differ between groups (table I). Physical activity level (1.57 ± 0.01) was not significantly different between groups nor did the habitual food intake (*data not shown*).

Fasting resting metabolic rates were not different between groups (0.95 ± 0.02 kcal/min; p = 0.7621) and increased after the consumption of all test meals (p <

Table I
Subjects characteristics at baseline (fasting conditions)

	Overall (n = 71)	*CT (n = 24)*	*CVP (n = 23)*	*HOP (n = 24)*
Age (years)	27.1 ± 0.9	26.3 ± 1.6	27.6 ± 1.5	27.4 ± 1.7
Body weight (kg)	94.1 ± 1.3	94.2 ± 2.5	93.1 ± 2.0	94.9 ± 2.1
BMI (kg/m^2)	29.8 ± 0.3	29.8 ± 0.6	29.5 ± 0.4	30.1 ± 0.5
Waist (cm)	101.5 ± 0.9	101.9 ± 1.8	100.7 ± 1.2	101.8 ±1.6
Hip (cm)	108.7 ± 0.6	109.2 ± 1.1	108.1 ± 1.2	108.9 ± 1.1
Fat mass (kg)	25.3 ± 0.7	25.6 ± 1.5	24.2 ± 1.1	26.1 ± 1.2
Body fat percentage (%)	26.7 ± 0.5	26.8 ± 0.9	25.8 ± 0.8	27.3 ± 0.8
Fat free mass (kg)	68.8 ± 0.8	68.7 ± 1.4	68.9 ± 1.3	68.8 ± 1.3
Total body water (kg)	50.4 ± 0.6	50.3 ± 1.0	50.4 ± 1.0	50.4 ± 1.0
Systolic BP (mmHg)	119.0 ± 1.6	121.0 ± 4.0	118.0 ± 1.7	118.0 ± 2.2
Diastolic BP (mmHg)	69.0 ± 1.5	73.0 ± 2.8	67.0 ± 2.0	70.0 ± 2.6
REE(kcal/day)	1954 ± 22.3	1930 ± 41.2	1964 ± 43.9	1968 ± 31.3
CHO oxidation (mg/min)	173.2 ± 6.8	178.7 ± 14.3	173.8 ± 11.5	167.2 ± 9.5
Fat oxidation (mg/min)	49.2 ±2.5	47.8 ± 4.7	50.1 ± 3.6	49.7 ± 4.7

Values are mean ± SEM. There was no difference between groups (ANOVA; $p > 0.05$). *CT*: control group. *CVP:* conventional peanut group. *HOP:* high-oleic peanut group. *BMI:* body mass index. *REE*: resting energy expenditure. *CHO*: carbohydrate.

0.001). Energy expenditure increased significantly after the consumption of test meals (fig. 2). It is remarkable that at 200 minutes, the HOP postprandial energy expenditure was 9.25% higher than the resting energy expenditure in fasting state, which was similar to the value found for CT (9.04%), and both values were significantly higher than CVP value (6.46%). There was no group-time interaction in rm-ANOVA ($p > 0.05$). Energy expenditure expressed as $_{pi}$AUC was significantly higher in HOP (636.6 ± 43.7) than in CVP (492.9 ± 35.1), yet, peanuts meals did not differ significantly from CT meal (582.7 ± 37.7) (fig. 2A).

DIT after each meal ingestion is illustrated in figure 2B. Since test meals were isocaloric, the thermic effect reflected the $_{pi}$AUC of energy expenditure for each meal. The DIT of high-oleic peanut (3.43 ± 0.24%) was significantly higher than the DIT of conventional peanut (2.63 ± 0.17%) but did not differ significantly from the control meal (3.19 ± 0.23%). The DIT from CT was similar to the CVP ($p > 0.05$).

Carbohydrate and fat oxidation in fasting resting state did not differ between groups (table I). Figure 2C-D illustrates the changes in substrate oxidation after test meal intake. Overall, carbohydrate oxidation increased but returned close to baseline values after 200 minutes (172.4 ± 9.8 mg/min). Conversely, fat oxidation increased significantly in all groups at 200 minutes compared to fasting state (66.7 ± 3.7 mg/min). The $_{pi}$AUC for carbohydrate (179.9 ± 12.7; overall) and fat oxidation (47.3 ± 5.0; overall) did not differ between groups ($p > 0.05$).

The food record filled out at the assessments day showed that dietary intake did not differ between groups neither from habitual dietary intake ($p > 0.05$). Besides, the difference between dietary intake at the assessment day and habitual diet (Delta-Δ) was not significantly difference between groups (*data not shown*).

There was no significant difference between groups for energy compensation score. However, an important clinical result of this study must be highlighted. Only HOP showed a mean score below 100 (84.0 ± 23.2), which indicates incomplete compensation for caloric intake. CT (102.3 ± 19.9) and CVP (134.2 ± 22.7) meals contributed to a complete compensation for meal test calories.

Concerning the $_{pi}$AUC of fullness sensation score (fig. 3), the subjects felt significantly less "full" after the CVP meal (105.1 ± 15.8) than did those from HOP (158.6 ± 15.5) and CT (155.8 ± 15.52) ($p = 0.0384$). Satiety did not differ significantly between groups after test meal intake (CT: 143.6 ± 16.9; CVP: 126.8 ± 15.1; HOP: 136.8 ± 16.7). Regarding prospective food consumption and hunger sensation, it must be noticed that their analyses represents the opposite of the preceding questions. Therefore, the higher $_{pi}$AUC is the lower the subjective sensation is. The CT subjects were significantly less prone to eat something else (54.8 ± 9.9) than did subjects from CVP (33.9 ± 16.5) and HOP (31.2 ± 10.3). For hunger sensation no significant difference between groups was verified after test meal ingestion (CT: 99.5 ± 15.7; CVP: 93.9 ± 13.9; HOP: 113.4 ± 16.8).

There were no group-time interaction in rm-ANOVA for appetite scores ($p > 0.05$). Interestingly, all groups increased the "fullness" sensation ($p < 0.001$), yet, while CT and HOP maintained their scores significantly higher during the 3 hours ($p < 0.001$), at the third hour the "fullness" score of CVP was similar to baseline ($p = 0.9925$). All of the meals increased significantly the subjects' satiety ($p < 0.001$) and its score remain higher for all groups until the second hour after meal intake ($p < 0.01$). However, at the third hour the

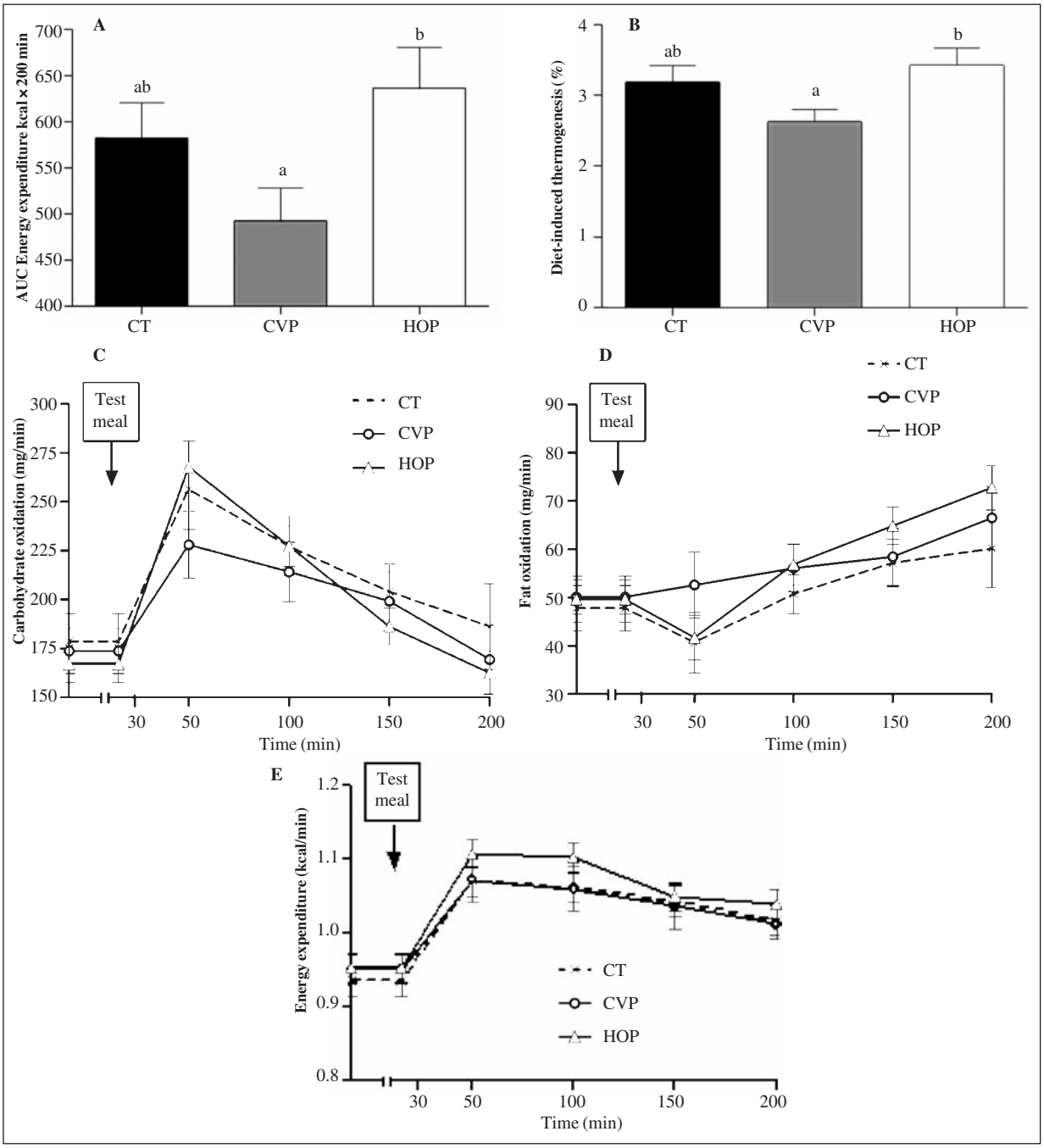


Fig. 2.—Mean (± SEM) changes in cumulative energy expenditure (A), diet-induced thermogenesis expressed as the percentage of each meal calories (B), carbohydrate oxidation (C), fat oxidation (D) and resting energy expenditure (E) during 200 min after test meal intake. Bars with different letters are significantly different (ANOVA; $p < 0.05$). A mixed model with "meal" as a fixed effect and "subject" as a random effect was used to estimate each meal effect on cumulative substrate oxidation. There was no group-time interaction for substrate oxidation (rm-ANOVA/ $p > 0.05$). CT, control group; CVP, conventional peanut group; HOP, high-oleic peanut group; piAUC, positive incremental area under the curve.

satiety score in CVP did not differ from baseline ($p = 0.0857$), while the HOP ($p = 0.0243$) and CT ($p = 0.0037$) did. For hunger sensation score, all groups showed significant reduction after meal intake, but after 2 hours CVP and CT scores returned to baseline values ($p = 0.2009$; $p = 0.1683$, respectively), while HOP maintained it lower than at baseline ($p = 0.0177$).

Discussion

DIT and fat oxidation are important key elements on energy balance regulation, thus, a decrease in these elements could result in body fat accumulation[42,43]. On the other hand, an increase in DIT and fat oxidation may lead to body fat reduction. This trial showed that

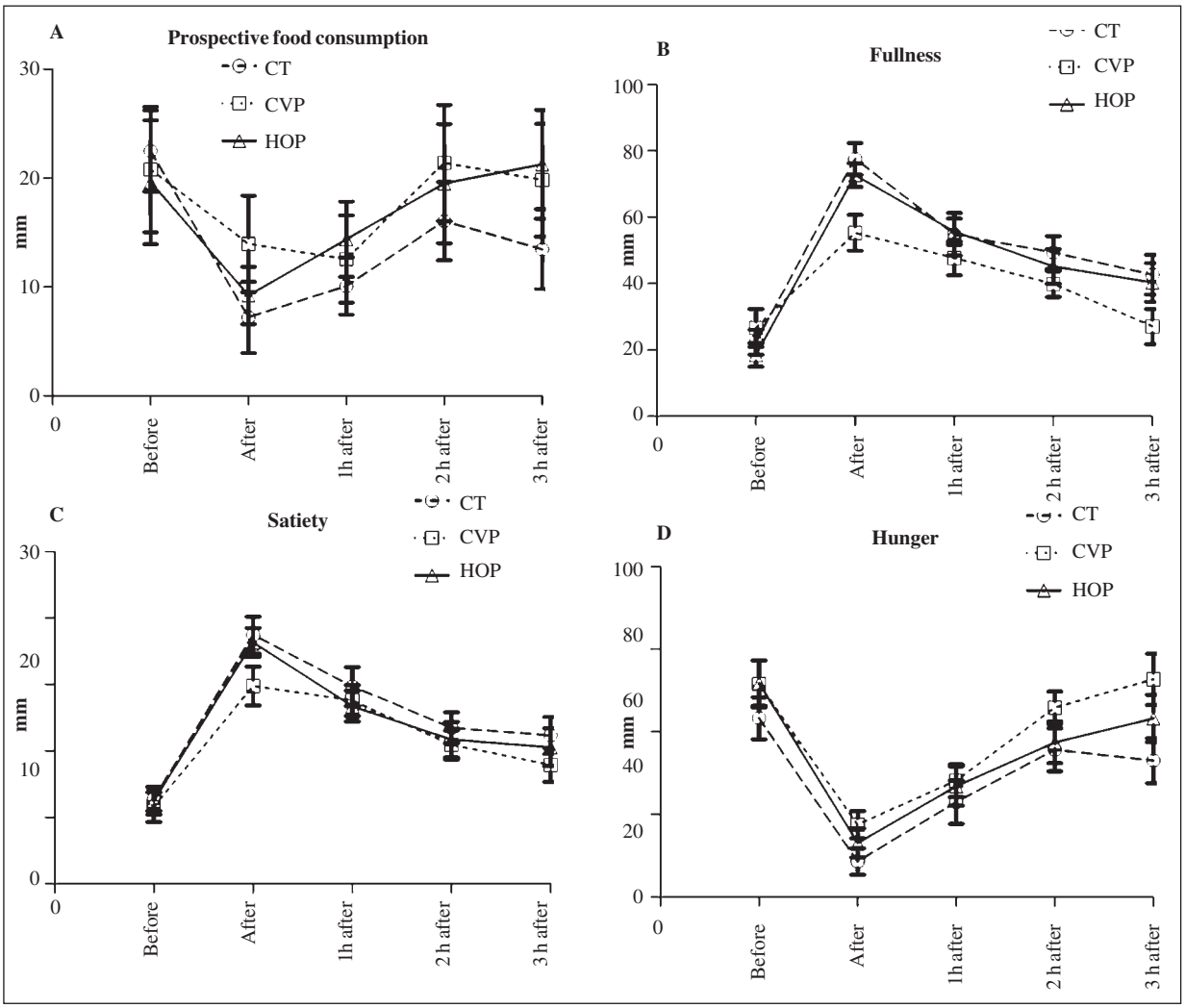


Fig. 3.—Mean (± SEM) changes in scores for prospective food consumption (A), fullness (B), satiety (C) and Hunger (D) after test meals intake. A mixed model with "meal" as a fixed effect and "subject" as a random effect was used to estimate each meal effect on scores over the time. Adjustments on p values were done by using Tukey-Kramer's multiple group comparison procedures. CT, control group; CVP, conventional peanut group; HOP, high-oleic peanut group.

high-oleic peanuts contribute for greater increment on DIT (%) and on cumulative energy expenditure ($_{pi}$AUC) compared to conventional peanuts. It is well documented that carbohydrate and fat lead to lower DIT than do protein since high-protein food/meal induces body protein synthesis and also increases the cost of deamination and convertion to glucose[13,17]. However, in our study the difference in DIT can not be attributed to peanuts' protein contents since both have similar amount of protein (30.0 and 29.1%, respectively).

The fatty acids structure including number, position, and configuration of double bonds influences metabolic rate [5,23]. Therefore, it can be inferred that the difference in DIT, as well as in $_{pi}$AUC of energy expenditure reported in this trial may be due to the fatty acid profile of the tested peanuts. Oleic acid represents the major fatty acid of high-oleic type (81.5%), which means 59.8% more oleic acid than the conventional type.

It is well known that unsaturated fatty acids contribute for higher DIT and fat oxidation compared to SFA[24,26,42]. Besides, SFA have higher propensity to be stored in adipose tissue than unsaturated fatty acids, which are preferable oxidized and stimulates body fat oxidation[6,22-24,26]. The authors of studies in which MUFA intake increased DIT and fat oxidation, suggested that this occurs due to a higher stimulation of the sympathetic nervous system by the MUFA than by other fatty acids[23,44].

Few studies have evaluated the effects of peanuts on energy metabolism. Moreover, we did not find studies in which the effects of high-oleic peanuts in energy metabolism were tested. Alper and Mattes[5] designed a crossover trial with 15 lean subjects that consumed conventional peanuts (≈ 505 kcal/day). In their study it was verified an increment of 11% ($p < 0.01$) in REE without changing the DIT ($p > 0.05$) after 19-weeks[5]. However, in an 8-week intervention clinical trial, con-

ventional peanuts oil intake promoted a significant increment (5%) in REE in overweight subjects (n = 24)[6]. In that study, overweight subjects (n = 24) the consumption of the peanut oil contributed for an increment of 5% in REE ($p < 0.01$), while an increment of 11% ($p < 0.01$) was verified when only men were included in analysis (n = 12).

Although, there were no significant differences between groups for dietary data after the assessments, including in dietary compensation score, an incomplete compensation for caloric intake was verifyed only in HOP. If the findings of this acute trial, persists for chronic consumption of high-oleic peanuts, it could be inferred that this type of peanuts do not pose a risk for weight gain. Besides, as described by Kirkmeyer and Mattes, there are great evidences that nuts consumers are not heavier than subjects those who do not eat nuts frequently[35].

According to Acheson et al, foods that contribute to higher DIT, also increase satiety[13]. The results for DIT showed that HOP had higher DIT than CVP ($p < 0.05$), which is consistent with the incomplete compensation for caloric intake found in HOP group. The composition of the test peanuts may have influenced the appetite, which contributed for this clinical difference found for caloric intake compensation. However, the difference in fatty acids profile of test food, including conventional peanut, may not be the only factor for this compensation since, according to Kirkmeyer and Mattes,the degree of fatty acid saturation is not an important factor for appetite sensation[35].

There is general agreement that food rich in protein and dieatry fiber are more satiating[13,19]. The foods tested in this trial had similar amount of protein, as described before. The total dietary fiber contents of test foods were also similar since the high-oleic peanuts have 9.8% of dietary fiber while the conventional peanuts have 8.9% and the control biscuits have 8.3%. However, high-oleic peanuts have more soluble fiber (1.17%) than conventional peanuts (0.32%) and control biscuits (0.62%). Thus, soluble fiber contents may partially explain the results described below for appetite subjective sensation.

The type of protein used to prepare the control biscuits may be one limitation of the present study since it may have influenced the subjective appetite sensation and the DIT results in the CT group. There are evidences that different protein sources can modulate the energy metabolism and appetite[13,17]. The main protein source of the control biscuits was whey protein, while main one used on HOP and CVP meals came from the peanuts. According to Acheson at al., animal protein rather than vegetable protein improve protein turnover and favor protein synthesis, which contributes to increase DIT, indirectly influencing appetite[13]. Yet, how different protein source influences satiety is less clear.

To our knowledge, this is the first study that evaluates the effects of high-oleic peanuts on energy metabolism and appetite. A study conducted by O'Byrne et al evaluated the long-term effect of a low-fat diet containing high-oleic peanuts on serum lipoprotein profiles[11]. They found that high-oleic peanuts improved serum lipid profile[11]. Thus, high-oleic peanuts seem to have other beneficial metabolic effects also. Yet, further investigations are necessary to evaluate the effects of a chronic intake of high-oleic peanut on metabolism, including the variables of the present study, as well as other variables such as body weight and composition, and biochemical parameters. Regular consumption of high-oleic peanut probably will increase DIT, which in turns would increase total energy expenditure contributing to negative energy balance, since peanuts may also lead to lower caloric intake by reducing hunger and caloric compensation, and increasing satiety.

Conclusion

The results of the present study showed that high-oleic peanuts increased DIT compared to conventional peanuts in overweight and obese men. Furthermore, high-oleic peanuts contributed to interesting effects on appetite sensation. The fatty acids profile of the high-oleic peanuts seem to be the main factor responsible for these effects. A long-term clinical trial is necessary to elucidate the potential of high-oleic peanuts within a dietary intervention in modulating appetite and energy metabolism and as an outcome in controling obesity.

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Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Original / *Obesidad*

Prevalence of overweight and obesity among a university faculty and staffs from 2004 to 2010, China

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Abstract

Background: **Overweight and obesity are epidemic worldwide. Our present study was to examine the prevalence of overweight and obesity in a university faculty and staffs using two references [Working Group on Obesity references in China (2004) and World Health Organization (WHO) criteria 2000].**

Objective: **The purpose of this study was to estimate the prevalence of overweight and obesity among university faculty and staffs in China.**

Methods: **A cross-sectional study was designed to collect the routine health screening data for a university faculty and staffs from 2004 to 2010(2004, 2006, 2008 and 2010); the subjects aged 22-94 years.**

Results: **Depending on the references used (China and WHO, respectively), the overall prevalence of overweight, including obesity of the subjects was 36.1% and 25.5%, the prevalence of obesity was 5.3%, and 1.5%, respectively, the prevalence of overweight, including obesity among the male subjects was 46% and 32.5%, respectively, the prevalence of overweight, including obesity among the female subjects was 21% and 14.1%, respectively, An interesting observation made was that the overall prevalence of overweight was increased with age.**

Conclusions: **Regarding the harmful of overweight and obesity, it is encourage reducing liberal food environment and increasing physical activity among university faculty and staffs, especially for male faculty.**

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Key words: *Body mass index. Faculty. Obesity. Overweight. China.*

PREVALENCIA DE SOBREPESO Y OBESIDAD ENTRE UNA UNIVERSIDAD, FACULTAD Y PERSONAL, DE 2004 A 2010, CHINA

Resumen

Antecedentes: **El sobrepeso y la obesidad son epidemia en todo el mundo. El presente estudio fue examinar la prevalencia de sobrepeso y obesidad en una universidad, Facultad y personal utilizando dos referencias [Grupo de trabajo sobre la obesidad referencias en China (2004) y la Organización Mundial de la salud (OMS) criterios (2000)].**

Objetivo: **El objetivo de este estudio fue estimar la prevalencia del sobrepeso y la obesidad entre la facultad y personal de la Universidad en China.**

Métodos: **Un estudio transversal fue diseñado para recoger los exámenes de salud de rutina los datos para una universidad la facultad y personal de 2004 a 2010 (2004, 2006, 2008 y 2010); los sujetos de 22-94 años.**

Resultados: **Dependiendo de las referencias utilizadas (China y la OMS, respectivamente), la prevalencia de sobrepeso, incluyendo la obesidad de los sujetos fue un 36,1% y 25,5%, la prevalencia de obesidad fue del 5,3% y 1,5%, respectivamente, la prevalencia de sobrepeso, incluyendo la obesidad entre los sujetos varones, fue de 46% y 32,5%, respectivamente la prevalencia de sobrepeso, incluyendo la obesidad entre las mujeres fue de 21% y 14,1%, respectivamente, de una observación interesante es que la prevalencia global de sobrepeso aumentó con la edad.**

Conclusiones: **Respecto a los daños del sobrepeso y la obesidad, es alentar la reducción de alimentos ambiente liberal y aumentar la actividad física entre universidad, Facultad y personal, especialmente para hombre facultad.**

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Palabras clave: *Índice de masa corporal. Facultad. Obesidad. Sobrepeso. China.*

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Introduction

In recent decades, the prevalence of obesity in children and adult has risen steeply world wide[1-6]. Some researcher documented that employees have less self-efficacy and consume less healthful diets than their normal weight colleagues[7]. A high prevalence of adults obesity and overweight cases has been reported in developing countries undergoing nutritional transition[8]. These are also emerging as a major public health problem in China[9,10].

Obesity is associated with significant comorbidities and health problems such as breast cancer[11], diabetes mellitus[12,13], hypertension[14], coronary artery disease[15], and occupational injuries[16]. Some researcher showed that the prevalence of obesity was higher among middle-aged adults[17,18]. In China, the prevalence of overweight, general obesity and abdominal obesity among Chinese adults has increased greatly during the past 17 years. However, there is a paucity of data on prevalence of overweight and obesity in university faculty and staffs[19].

In this study, the Center for Working Group on Obesity references in China[20] and World Health Organization (WHO) criteria[21] was used to assess the prevalence of overweight, obesity in a university faculty and staffs in Wuhu area of south Anhui, China.

Methods

Subjects and Methods

Participants

Routine health screening was preformed among a university faculty and staffs every two years, in this study a total of 9,979 person-years (6,038 male and 3,941 female) data was collected between 2004 to 2010 (2004, 2006, 2008 and 2010), aged 22-94 years. All subjects agreed to provide their personal information regarding the purpose and the procedures of our study. This study was approved by local committee.

Anthropometric measurements

Height was measured using a standard stadiometer following study protocols, and weight in kilograms was measured on an electronic scales. BMI was computed using the following standard equation: BMI = Weight in kg/height squared in meter.

Definitions

Overweight and obesity were defined on BMI cutoff points, which are gender and age specific. 1 Working Group on Obesity references in China, the BMI cut-off points are 24 and 28 for overweight and obesity respectively; 2 the WHO reference is based on the BMI of 25 and 30 at the age of 18 for classification of childhood and adolescent overweight and obesity, respectively.

Ethical consideration

Faculty and staffs in the selected university were well-informed on the scope and extent of the survey and consent of the parents were also obtained.

Statistical analysis

R software programming language[22] was performed to describe the prevalence of overweight/obesity ,A line graph was draw by Excel software.

Results

In this study a total of 9,979 person-years (6,038 male and 3,941 female)data was collected between 2004 to 2010 (2004, 2006, 2008 and 2010), aged 22-94 years. The mean values (± SD) of weight, height, and calculated BMI are shown in table I. An interesting observation made was that the mean of BMI and weight was increased with year in male but not in female (fig.1).

The prevalence of overweight and obesity for university faculty and staffs are shown in table II. Depending on the references used (China and WHO, respectively), the overall prevalence of overweight, including obesity of the subjects was 36.1% and 25.5%, the prevalence of obesity was 5.3%, and 1.5%, respectively, the prevalence of overweight, including obesity among the male subjects was 46% and 32.5%, respectively, the prevalence of overweight, including obesity among the female subjects was 21% and 14.1%, respectively, An interesting observation made was that the overall prevalence of overweight was increased with age. The higher prevalence of overweight and obesity observed in our subjects using the WHO reference and working group on obesity references in China.

Discussion

In the present study, we use two references to compare the overweight and obesity. The results revealed that overall prevalence of overweight, including obesity of the subjects was 36.1% and 25.5%, the prevalence of obesity was 5.3%, and 1.5%, respectively, depending on the references used (China and WHO, respectively). An interesting observation made was that the mean of BMI and weight was increased with year in male but not in female, these data provide an indication that university male faculty and staffs should be taken more attention.

Table I
Mean (± SD) of height, weight and BMI of university faculty and staffs from 2004 to 2010

		2004	2006	2008	2010
male	n	1,436	1,646	1,673	1,627
	Age(years)	51.20 ± 16.80	50.82 ± 16.56	50.53 ± 17.11	51.46 ± 17.36
	Height(m)	1.69 ± 0.06	1.69 ± 0.06	1.70 ± 0.06	1.71 ± 0.06
	Weight(kg)	67.03 ± 17.36	67.60 ± 9.85	68.49 ± 9.65	70.03 ± 9.87
	BMI(kg/m^2)	23.31 ± 3.09	23.50 ± 2.94	23.72 ± 2.86	24.04 ± 2.93
Female	n	892	1,100	1,185	1,190
	Age(years)	47.58 ± 16.59	47.05 ± 16.27	45.39 ± 17.59	46.20 ± 18.08
	Height(m)	1.59 ± 0.12	1.59 ± 0.06	1.59 ± 0.06	1.60 ± 0.07
	Weight(kg)	54.76 ± 8.08	55.25 ± 8.09	55.22 ± 7.83	55.69 ± 7.74
	BMI(kg/m^2)	21.76 ± 3.11	21.94 ± 3.11	21.89 ± 2.97	21.83 ± 2.84

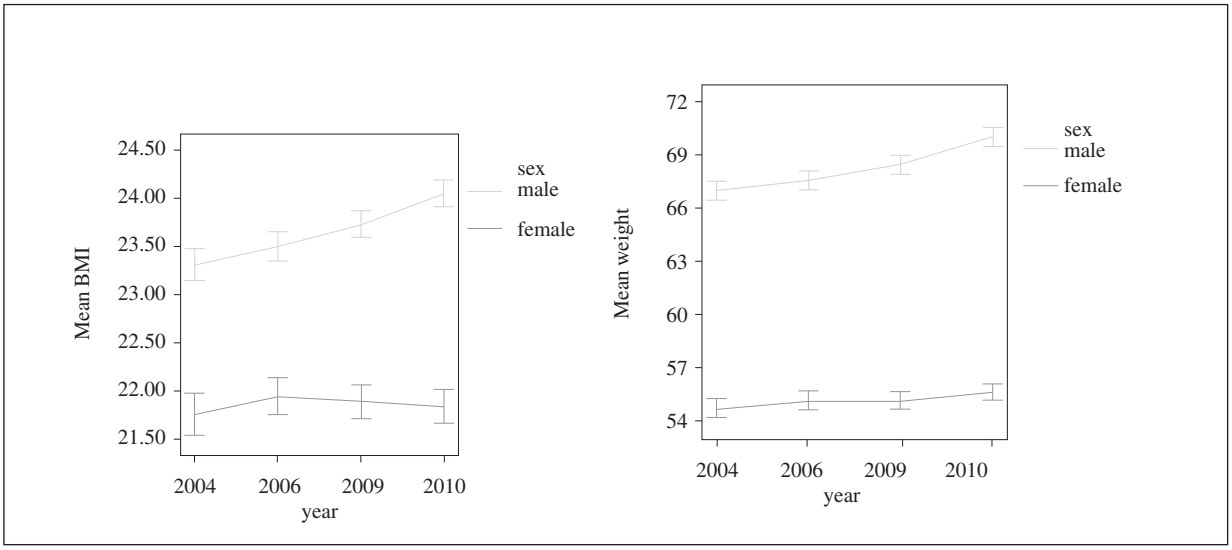


Fig. 1.—Trend of BMI and weight according to sex from 2004 to 2010.

Table II
The prevalence of obesity for university faculty and staffs according to age

		Reference	*Prevalence (%)*						
male	Age(years)		22-30	31-40	41-50	51-60	61-70	older 70	overall
	n		607	1375	1259	946	760	1091	6038
	Overweighta	China##	31.5	44.8	54.8	53.4	46.2	39.0	46.0
	obesity	China##	4.6	5.9	7.1	7.7	5.7	5.9	6.3
	Overweighta	WHO#	19.4	30.4	39.6	39.0	33.4	27.8	32.5
	obesity	WHO#	1.3	1.7	1	1.6	1.1	2.2	1.5
Female	n		693	1047	734	568	455	444	3941
	Overweighta	China##	8.4	12.2	18.5	32.2	32.1	39.9	21.0
	obesity	China##	1.0	0.9	2.5	7.0	8.8	9.0	3.9
	Overweighta	WHO#	5.6	7.4	11.9	22.4	23.5	26.4	14.1
	obesity	WHO#	0.1	0.2	0.8	2.6	3.5	3.2	1.4
All	n		1300	1673	1993	1514	1215	1535	9979
	Overweighta	China##	19.2	30.7	41.4	45.4	40.9	39.2	36.1
	obesity	China##	2.7	3.7	5.4	7.5	6.8	6.8	5.3
	Overweighta	WHO#	12.1	20.4	29.4	32.8	29.7	27.4	25.2
	obesity	WHO#	0.7	1.1	0.9	2.0	2.0	2.5	1.5

Working Group on Obesity references in China. # The WHO reference. Overweighta: Overweight including obesity.

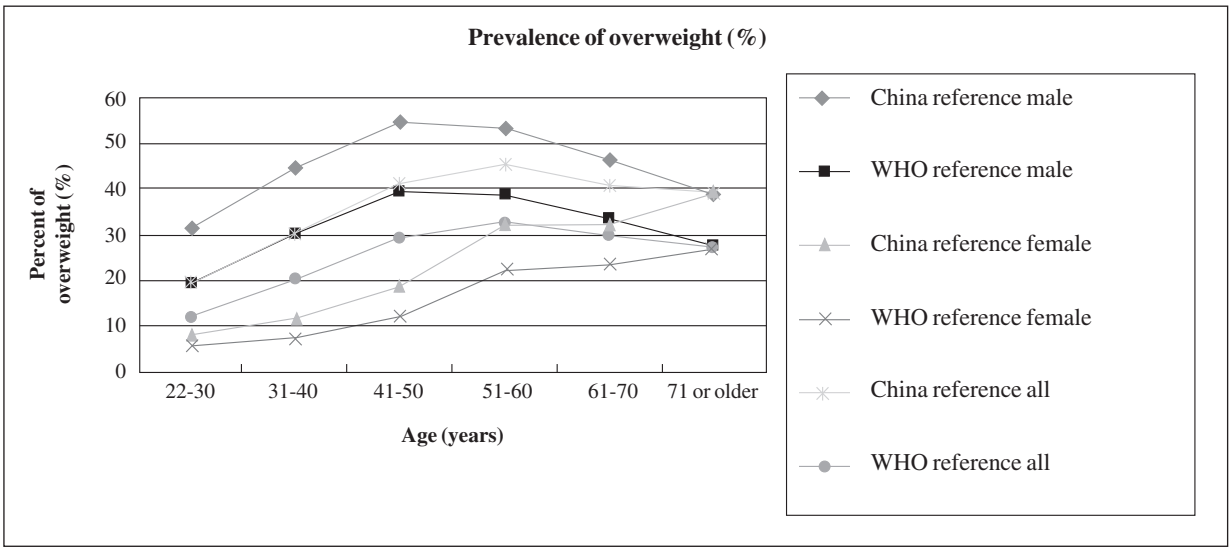


Fig. 2.—The prevalence of overweight for university faculty and staffs according to different reverence in different age.

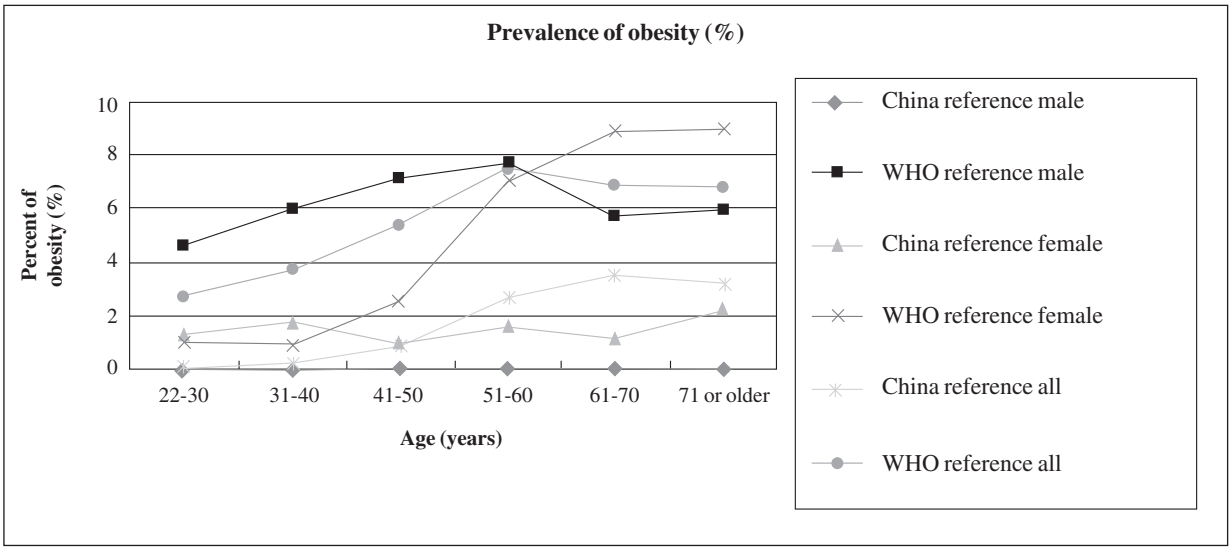


Fig. 3.—The prevalence of obesity for university faculty and staffs according to different reverence in different age.

Recent evidence suggests that the nutrition transition is accelerating and the outcome of this trend is a rapid increase in obesity and chronic diseases[23]. Lifestyle transition and socio-economic improvement have contributed enormously to the escalating problem in developing countries. Especially, lifestyle[24] and food variety[25] may have an influence on obesity. Meanwhile, obesity also is associated with reduced sleeping hours and long working hours[26], Lack of health awareness to male university faculty may also be linked to its high prevalence.

The references used in this study produce different estimates for overweight and obesity. However, future research is needed to identify more accurate defining criteria for overweight and obesity using the BMI cut-offs in adults.

Conclusions

The study showed that the prevalence of overweight in early adolescence school girls in small town of our country is a critical health issue. The study suggests that greater risk of overweight among university faculty and staffs for targeted intervention that promotes increased physical activity and decreased consumption of energy dense foods to control the escalating prevalence.

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Conflict of Interest

None declared.

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Original / *Obesidad*

A comparison of dual energy X- ray absorptiometry and two bioelectrical impedance analyzers to measure body fat percentage and fat-free mass index in a group of Mexican young women

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Abstract

Introduction: **Studies of obesity require the estimation of fat mass (FM) and fat-free mass (FFM); therefore it is important to validate methods that evaluate these measurements.**

Objective: **We sought to compare two different bioelectrical impedance analysis systems (BIAs) to estimate FM and FFM using dual-energy X-ray absorptiometry (DXA) as reference.**

Methods: **We used a cross-sectional design. We evaluated FM and FFM using DXA and two types of BIA equipment: a foot-foot system (FFS) and a hand-foot-system (HFS). We conducted paired analysis (paired t-test). We used Bland-Altman plots to assess the relationships between FM and FFMI, limits of agreement were constructed (CL)**

Results: **A total of 175 female students (22.9 ± 2.2 years-old) participated in the study. The paired analysis showed significant differences between the mean value of body fat percentage (BF%) estimated by BIA equipment compared to DXA (FFS = 28.7%, HFS= 34.4% and DXA= 35.3%). The mean difference between the HFS and DXA of BF% was -0.96, ((CL -5.29, 7.20). For the FFS, the mean difference was -6.69, (CL -0.29, -13.09). The paired analysis revealed significant differences between the estimates of FFMI by BIA compared to DXA (FFS =16.29, HFS =14.95, DXA =14.18). The mean difference between HFS and DXA was 0.78, and (CL -2.27, 0.72) whereas the FFS mean difference was -2.11 (CL -3.73 -0.49).**

Conclusion: **A different magnitude of bias was observed between the BIA equipment arrays. The HFS appears to be more reliable than the FFS used, particularly in obtaining FFMI in young women.**

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Key words: *Body composition. Body fat. Fat-free mass index. BIA. DXA. Validation*

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COMPARACIÓN DE LA ABSORCIOMETRÍA DE RAYOS X DE ENERGIA DUAL Y DOS ANALIZADORES DE IMPEDANCIA BIOELÉCTRICA PARA MEDIR EL PORCENTAJE DE GRASA CORPORAL Y EL ÍNDICE DE MASA LIBRE DE GRASA EN UN GRUPO DE MUJERES JÓVENES MEXICANAS

Resumen

Introducción: **Los estudios de obesidad requieren estimación de masa grasa (FM) y masa libre de grasa (FFM).**

Objetivo: **Comparar dos equipos de impedancia bioeléctrica (BIA) para estimar FM y FFM usando absorciometría de rayos X de energía dual (DXA) como referencia.**

Métodos: **Estudio transversal. FM y FFM fueron evaluados por DXA y BIA: sistema pie-pie (FFS) y sistema mano-pie (HFS). Se realizaron pruebas t pareadas, coeficientes de correlación y análisis de Bland y Altman. Límites de acuerdo fueron calculados (CL).**

Resultados: **Fueron estudiadas 175 mujeres (22,9 ± 2,2 años). Hubo diferencias significativas entre el promedio del porcentaje de grasa estimado por los equipos de BIA en comparación con DXA (FFS = 28,7%, HFS = 34,4% y DXA = 35,3%). La diferencia de medias del porcentaje de grasa entre HFS y DXA fue -0.96, (CL -5,29, 7,21). La diferencia de medias para FFS fue de -6,69,(CL -0,29, -13.09) Hubo diferencias significativas entre las estimaciones de FFMI por BIA y DXA (FFS = 16,29, HFS = 14,95, DXA = 14,18). La diferencia de medias entre HFS y DXA fue = 0,78, (CL -2,27, 0,72) y la diferencia de medias de FFS fue -2,11: (CL -3,73 , -0,49).**

Conclusiones: **Niveles diferentes de sesgo se observaron entre los equipos de BIA. El HFS parece ser más confiable que el FFS, sobre todo en la obtención de FFMI en mujeres jóvenes.**

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Palabras clave: *Composición corporal. Grasa corporal. DXA impedancia bioeléctrica. Validación.*

Abbreviations

BIA: Bioelectrical impedance analysis.
BMI: Body mass Index.
BF%: Body fat percentage.
DXA: Dual-energy X-ray absorptiometry.
HFS: Hand-to-foot system.
FFM: Fat-free mass.
FFMI: Fat-free mass index.
FM: Fat mass.
FFS: Foot-to-foot system.

Introduction

The prevalence and incidence of obesity have rapidly increased in both developed and underdeveloped countries; the National Survey of Health and Nutrition 2012 in Mexico showed that the prevalence of obesity was 35.8% in young women[1]. The obesity trends in young adults should be monitored to avoid health problems in their future[2]. The increase in body fat could promote the development of chronic diseases such as hypertension, dyslipidemia, disturbed glucose tolerance, diabetes mellitus, and coronary heart disease[3-4]. Body fat mass should be assessed to develop preventive programs at a young age.

In the clinical and epidemiological field to study obesity it is important to assess not only the anthropometric measurements such as body weight, body mass index (BMI), waist circumference, and waist-to-hip ratio, because these measurements do not reflect body fat mass[5]. For this reason, researchers have developed different methods to estimate body composition, including magnetic resonance imaging (MRI), dual-energy absorptiometry X-ray (DXA), air-displacement plethysmography and bioelectrical impedance analysis (BIA)[6].

The fat-free mass index (FFMI) offers better specificity, because this index is based on fat-free mass and not body weight, which is composed of both fat and lean mass[7]. DXA is an accepted method to measure body composition, using a three-compartment model: fat mass, fat-free mass, and total mineral content[8]. This technique has been validated against other direct methods such as neutron activation in vivo, total body potassium, and hydrodensitometry[9-10]. This technique is highly recommended by *The European Society of Clinical Nutrition and Metabolism* as a reference method in studies to determine body composition[11]. However, the use of this method is limited due to its high cost and the fear of radiation emitted in the course of a DXA study, although the radiation is low –even lower than a standard chest X-ray.

By contrast, the BIA method is widely used in clinics, sports medicine, and weight-reduction programs; it is accessible, minimally invasive, and does not require extensive clinical training[12]. BIA evaluates the resistance of an electric current exerted across the fat-free mass due to its high water and electrolytes (sodium and potassium) content. BIA techniques are based on the notion that tissues rich in water and electrolytes are less resistant to the passage of electricity than adipose tissue[12]; it is therefore based on a single body-resistance parameter and not on a direct measure of body components such fat mass or fat-free mass.

It is thus a doubly indirect technique that requires the use of equations to estimate the body fat. The validity and reliability of the equations depends on the population characteristics and the reference method used. Ideally, the reliability of the methods should be tested before being used on a different sample.

Some reports have compared the percentage of body fat obtained by BIA with those obtained through other methods of reference, but the results are contradictory[13-15]. Several studies showed that the percentage of body fat is overestimated[16], whereas others suggested that BIA underestimates body fat percentage[17-18]. Additionally, other reports have compared body composition data between BIA and DXA and have shown different limits of agreement[19-20].

In Mexico there is a lack of information on body composition on young groups. There are no published works that show the results of BIA validation in this population group. The aim of this study was to compare two different BIA equipments to estimate FM and FFMI, using DXA as the method of reference in a group of Mexican young women.

Materials and Methods

Participants

We performed a cross-sectional study on a convenience sample of 188 students aged 18 to 30 years old enrolled in their last year of undergraduate nutrition sciences at Universidad Autonoma Metropolitana-Xochimilco. Each participant signed an informed consent form. We excluded 13 students because their data were incomplete.

Anthropometry

We asked all participants to fast for twelve hours before being measured. We weighed the subjects in standardized light clothes and without shoes. We measured the participants' height in centimeters using a stadimeter (SECA) and their weight using an integrated scale in the BIA equipment *(Tanita BC-418)*.

Body composition

Measurements by dual energy x-ray absorptiometry (DXA)

We used DXA equipment (Lunar Prodigy Advance®; GE Medical Systems, Madison WI) to analyze

body composition: fat mass, fat-free mass and bone mineral densities; we obtained the FFMI using the formula: FFM/height^2. We asked the participants to remove all metal objects to the ensure accuracy of the measurements, and the students lay in a supine position during DXA assessments. Whole body composition analysis provided data of different anatomical regions of interest. We calibrated the equipment each day according to the manufacturer's instructions[21].

Measurements by bioelectrical impedance analysis

We used a *foot-to-foot BIA system* (FFS) *(Tanita BC-418, Tanita Corp., Tokyo, Japan™)* immediately after the DXA study. The subjects followed the standard BIA guidelines: light clothes, standing erect and barefooted on the analyzer's footpads, which were previously cleaned with isopropyl alcohol. The electric current was then supplied from the electrodes on the tips of toes and fingers and the machine measured the voltage on the heels of both feet and the near sides of both hands. Before the valuation, the participants were to fast for 12 hours and avoid vigorous physical exercise and alcohol intake. Measurements began when the subjects placed their hands on the grips after wiping their feet and standing on the weighing platform. Body resistance was reported in Ohms.

Hand to foot BIA system (HFS) (RJL Quantum III, Detroit Michigan, USA). The electrodes in this system are placed on the hand and foot on the same side of body. Measurements were carried out with the subject lying in a supine position on a flat surface. One of the electrode's edges is placed on the right hand on an imaginary line bisecting the ulnar head, proximal to the third metacarpophalangeal joint (positive); the second electrode edge is placed on the right foot on an imaginary line bisecting the medial malleolus (negative). Before the valuation, the participants were to fast for 12 hours and avoid vigorous physical exercise and alcohol intake.

Body composition data included FM (kg), BF%, and FFMI (kg) measures obtained by DXA and by BIA. All participants were assessed at the Unit of Body Composition and Energy Expenditure located within the facilities of the campus.

Statistical analysis

We used a paired Student's t-test to compare the results of the BIA with DXA for body fat percentage and fat-free mass index and applied the Pearson correlation coefficient between the BIA and DXA results. We constructed a Bland and Altman plot to detected bias in body composition measurements. To detect a possible trend in the differences between methods, we constructed another plot applying a linear relationship in the paired difference between DXA and BIA and paired means of methods for body fat percentage. We also obtained 95% confidence limits of agreement (CL). P-values < 0.05 were statistically significant. We performed the data analysis using the STATA V12 statistical package (StataCorp LP).

Results

A total of 175 female college students with a mean age of 22.9 (± 2.2) years old participated in the study. The mean values of weight and height were 58.06 (± 11.4) kg (range: 41.2-119.2) and 1.58 (± 0.06) m (range: 1.44-1.74 m), respectively. The mean value of BMI (kg/m^2) was 23.1 (± 4.2) with a range from 16.9 to 47.8 kg/m^2. According to WHO classification, 66.2% were in a normal BMI category, 8.0% presented low weight, 20.0% were overweight and 5.7% were obese. The results of the body composition measurements with the different methods applied are shown in table I.

Fat mass

Body fat mass percentage by DXA analysis was 35.36% (± 7.0); the mean body fat mass was 20.3 kg (± 8.6) (table I). The paired comparison of BF% between DXA and HFS showed that this percentage was slightly underestimated by HFS, (35.36% DXA *vs* 34.40% BIA-HFS), ($p < 0.001$) and the correlation was $r = 0.90$. No significant difference was detected in the mean fat mass (kg) between DXA and HFS results, ($p = 0.08$). Figure 1 (A) depicts the Bland Altman plot of body fat

Table I
Mean of the body fat percentage, body fat mass and fat free mass index obtained by DXA, hand to foot and foot to foot BIA analyzers

	DXA		*BIA Hand to foot*			*BIA Foot to foot*		
	Mean	*(SD)*	*Mean*	*(SD)*	*P**	*Mean*	*(SD)*	*P**
Fat mass (%)	35.36	(7.0)	34.40	(6.0)	0.0001	28.66	(6.7)	0.0001
Fat mass (kg)	20.30	(8.6)	21.00	(8.8)	0.0800	17.30	(7.5)	0.0001
Fat free mass index (kg/m^2)	14.18	(1.5)	14.95	(1.4)	0.0001	16.29	(1.5)	0.0001

[1]SD: Standar Deviation. *P value between DXA and BIA analyzers using paired Student' t- test.

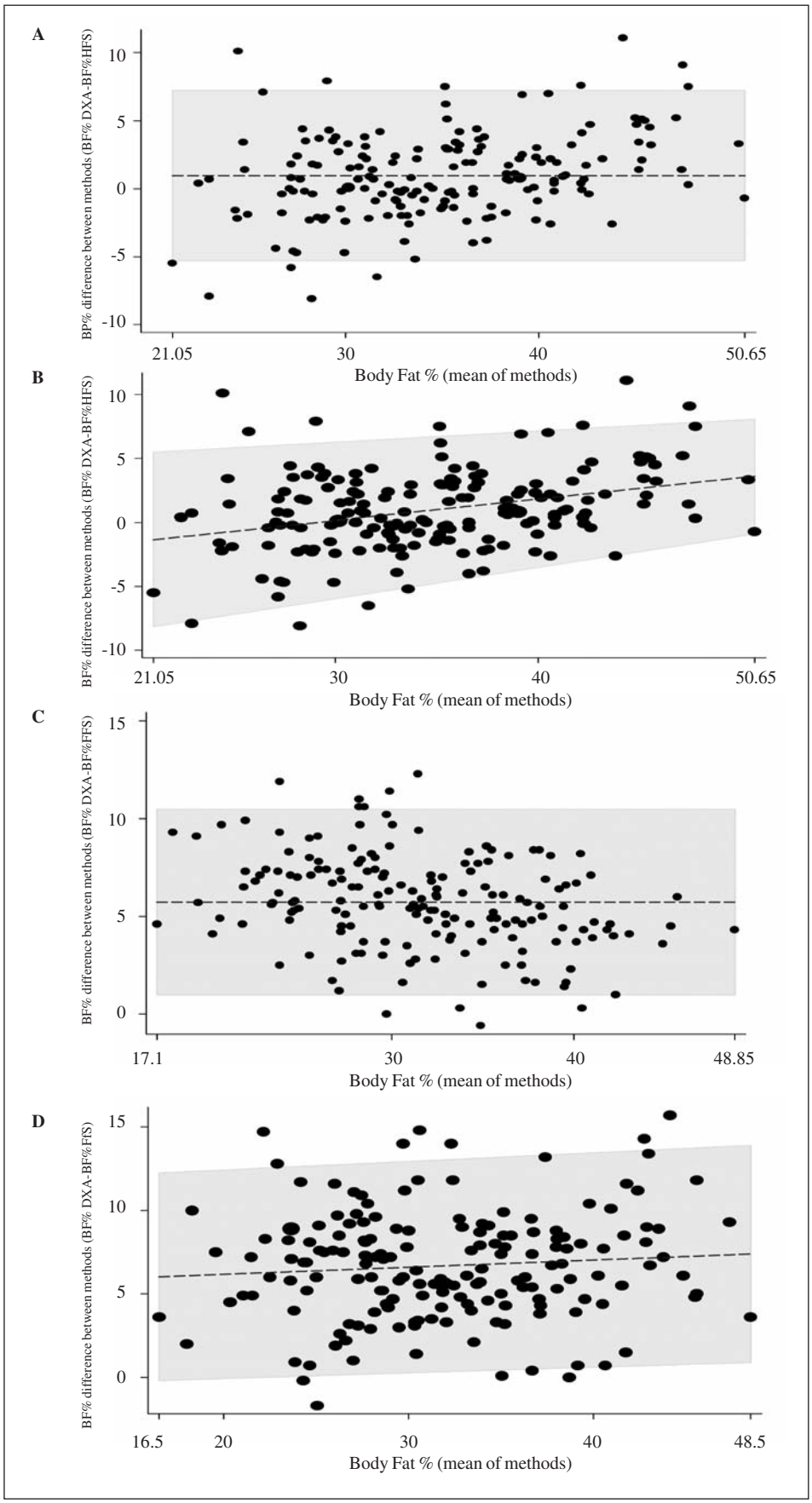


*Fig. 1.—**(A)** Bland Altman plot of Body Fat percentage (BF%) with mean difference (-0.96) and 95% limits of agreement (-5.29, 7.21) between DXA and BIA Hand-Foot system (HFS). **(B)** Linear relationship between the paired BF% difference and paired BF% average of DXA and HFS, and 95% limits of agreement). The positive slop indicates that the difference between methods was larger with higher BF% values (mean difference = -4.85 +0.17* mean BF%). **(C)** Bland Altman plot of BF% with mean difference (-6.69) and 95% limits of agreement (-0.29, -13.09) between DXA and FFS. **(D)** Linear relationship between the paired Body Fat percentage (BF%) difference and paired body fat percentage and average of DXA and FFS, and 95% limits of agreement. The positive slop indicates that the difference between methods was larger with higher BF% values (mean difference = 5.32 + 0.04* mean BF%).*

percentage (BF%) between DXA and BIA HFS, with a mean difference of -0.96 and 95% limits of agreement (CL -5.29, 7.21). Figure 1 (B) presents the regression line between the paired difference and the paired mean of body fat percentage (BF%) between DXA and BIA HSF 6.9% of the measurements were outside the limits of agreement.

The matched paired comparison of BF% between DXA and BIA-FFS showed a significant difference of -6.69 (35.36% DXA *vs* 28.66% BIA FFS), ($p < 0.001$), and the $r = 0.89$. Figure 1 (C) presents the Bland Altman plot between DXA BF% and BIA FFS BF%; the mean difference close to -6,69% indicated an underestimation of the BIA-FFS equipment in this percentage and wide limits of agreement (CL -0.29, -13.09). Figure 1 (D) presents the regression line obtained between the paired difference and the paired mean of body fat percentage (BF%) between the DXA and BIA FFS 6.7% of the measurements were outside the limits of agreement.

The comparison of BF% of the two BIA systems studied showed a significant difference (34.40% *vs* 28.66% BIA FFS), ($p < 0.001$), and the $r = 0.93$. The FFS showed lower values (mean difference = -5.73), (CL -0.94, -10.48), and 5.71% of the observations were outside of the limits of agreement, figure 2 (A). Figure 2 (B) shows the regression line obtained between the paired difference and the paired mean of body fat percentage (BF%) between BIA HFS and 95% limits (± 2.46*(2.35 + -0.02*mean), and 5.7% of the measurements were outside the limits of agreement.

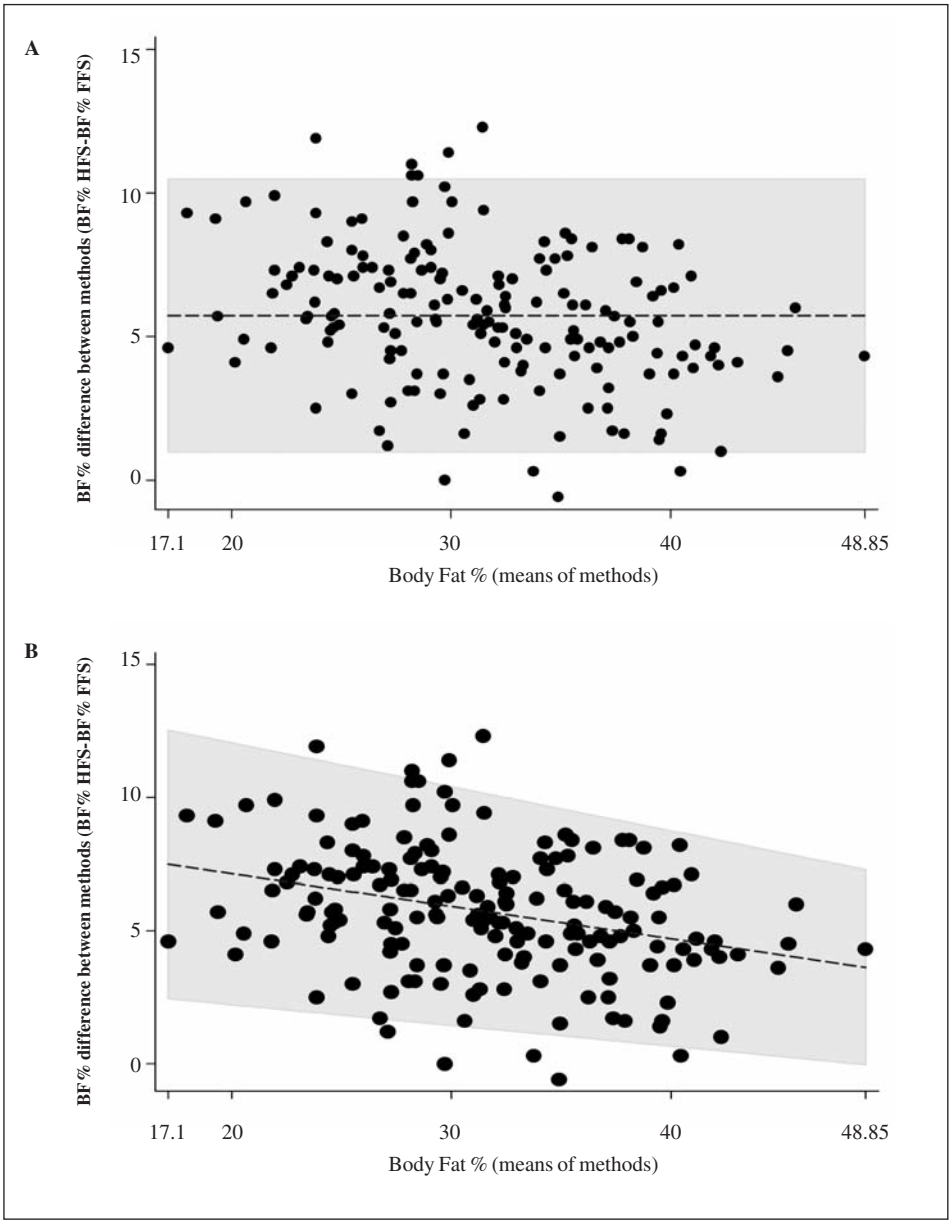


*Fig. 2.—**(A)** Bland Altman plot of Body Fat percentage (BF%) with mean difference (5.73) and 95% limits of agreement (0.97, 10.48) between BIA Hand-Foot system (HFS) and BIA Foot-Foot system (FFS). **(B)** Linear relationship between the paired BF% difference and paired BF% average of HFS and FFS, and 95% limits of agreement. The negative slop indicates that the difference between methods were lower as BF% increased (mean difference = 9.56 + -0.12* mean BF%).*

Fat Free Mass Index

The matched pair difference between DXA and BIA HFS was statistically significant (14.18 kg/m^2 DXA *vs* 14.95 kg/m^2 BIA HFS), ($p < 0.001$), (table I); however, this difference was small (mean difference = 0.78), and the correlation was r = 0.85. Figure 3 (A) presents the Bland Altman plot of the FFMI comparing the DXA and BIA HFS results; the limits of agreement were between (-2.27, 0.72), and 5.7% of the observations were outside of the limits of agreement.

The mean difference between DXA and BIA FFS showed a significant difference (14.18 kg/m^2 DXA *vs* 16.29 kg/m^2 BIA FFS), ($p < 0.0001$); higher values were obtained using the BIA FFS (mean difference = 2.11) than with DXA; and the correlation was r = 0.83.

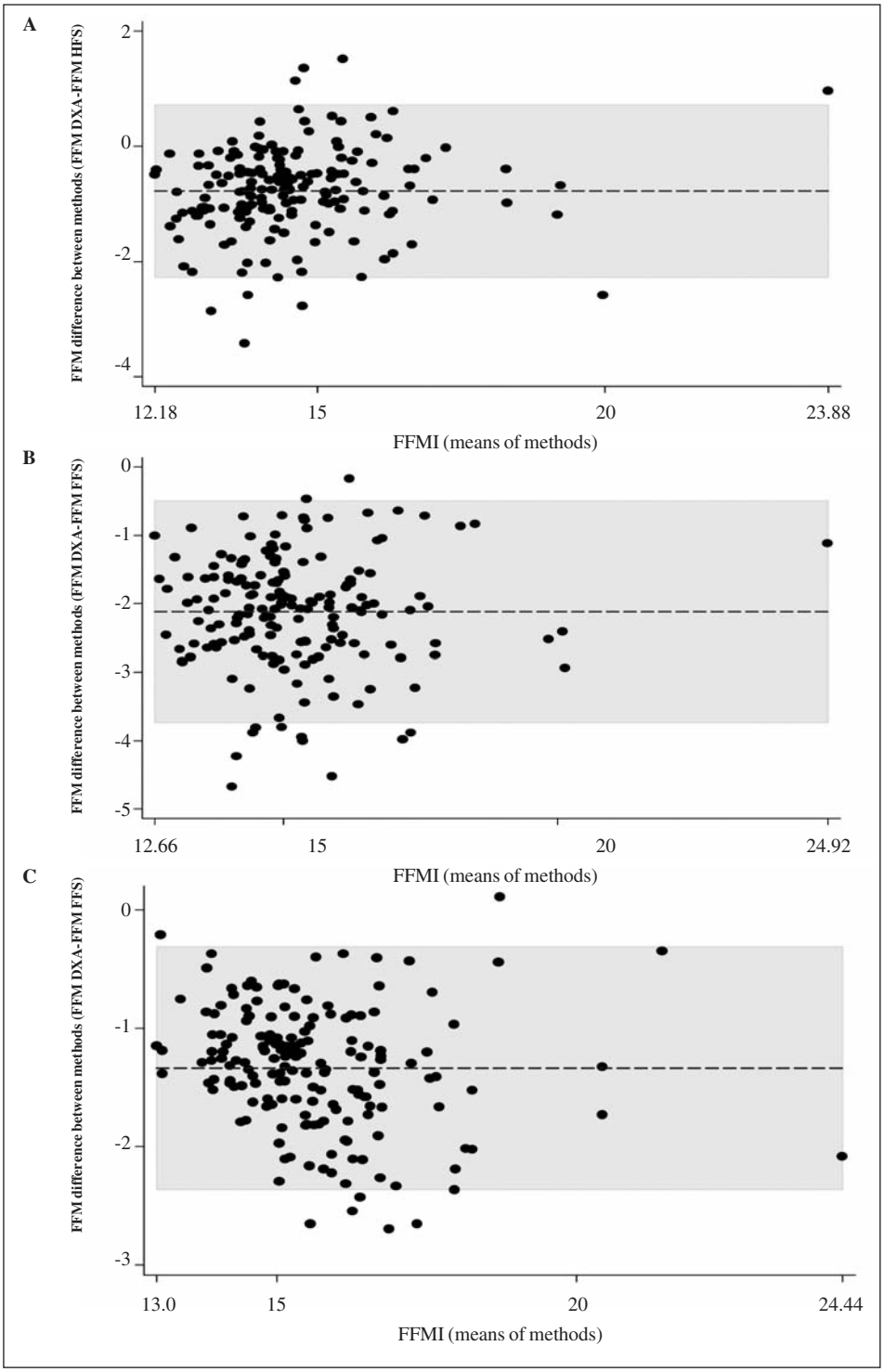


*Fig. 3.—**(A)** Bland Altman plot of Fat Free Mass index (FFMI (kg/m^2)) with mean difference (-0.78) and 95% limits of agreement (-2.27, 0.72) between DXA (FFMI DXA) and BIA Hand-Foot system (FFMI HFS), **(B)** Bland Altman plot of FFMI) with mean difference (-2.12) and 95% limits of agreement (-3.74,- 0.49) between DXA (FFMI DXA) and BIA Foot-Foot system DXA (FFMI DXA), **(C) (A)** Bland Altman plot of Fat Free Mass index (FFMI (kg/m^2)) with mean difference (-1.33) and 95% limits of agreement (-2.36 -0.31) between BIA Hand-Foot system (HFMI FFS) and BIA Foot-Foot system (FFMI FFS).*

Figure 3 (B) presents the Bland and Altman plot of the FFMI comparing the DXA and BIA FFS results. The limits of agreement were between (-3.73,-0.49), and 6.86% of the observations were outside of the limits of agreement. Figure 3 (C) depicts the Bland Altman plot of the two BIA systems. The mean difference was 1.33, and the 95% limits of agreement were (0.31, 2.36). The matched pair difference was significant (14.95 kg/m^2 BIA HFS *vs* 16.29 kg/m^2 BIA FFS), ($p < 0.001$).The percentage of observations outside the limits of agreement was 4.57%. The correlation was 0.90.

Discussion

In the present study, we assessed the validity of two types of BIA (HFS and FFS) systems. We compared the estimates of body fat percentage and fat-free mass index with DXA results as the reference method. The HFS and the FFS equipment showed biases of different magnitude.

Body fat percentage

The values of body fat percentage obtained by BIA HFS equipment and DXA were close to each other. We found significant statistical differences in the paired comparisons. However, the mean difference between DXA vs. HFS was approximately one percentage point; clinically, this difference is small, although significant in statistical analysis.

However, the limits of agreement between DXA and HFS were wide; therefore, the bias could be large and the methods cannot be considered equivalent for a given patient. The limits of agreement showed a higher bias as the BF% increased; this bias was slightly different at diverse levels of BF%; and the limits tended to be narrower at higher values of BF%. Similar data were reported in a group of adult women aged 18-39 years[22].

DXA discrepancies vs. BIA probably are due to various factors, such as the characteristics of the equipment used, equations applied, electrical frequency, and the number of electrodes of each device, as well as the hydration status of the participants. The results can be affected by fluid retention or the state of hydration because the BIA technique is based on the conduction of electric current across the body's water by electrolytes, which are good conductors, and the opposition of electrical flow is used to estimate total body water and lean mass, assuming that the lean body mass contains nearly about 73% of water[23].

In this study, we found that body fat could be underestimated by 6.7%, comparing FFS with DXA. This is relevant from a clinical point of view, because the patients would be informed of having a lower BF% than they really had. In addition, the regression analysis showed higher variation with higher BF% values.

The underestimation of the FFS BIA could be attributed to a technique that is doubly indirect in relation to DXA, which is an indirect technique based on two X-ray beams with different energy levels. BIA systems have several advantages for the assessment of body composition in clinical settings: the equipment is portable and less expensive than DXA, easy and simple to use, and quick; but it needs to be used with caution, especially for the assessment of patients who are overweight or obese[24]. When using bioelectrical impedance analysis, clinicians should consider various factors such as their biophysical principles, methodological foundations, previous validation studies in the population (according to ethnic origin), measurement conditions, and intra- and inter-individual variability. In addition, it is important to consider other factors associated with the characteristics of the study population: obesity, weight loss, menstrual cycle, racial variations, among others[25].

The mean difference between the BIA equipment studied (HFS *vs* FFS) was statistically significant and of clinical importance: the BIA FFS underestimated BF% by almost six percentage points, which in daily medical or nutritional counseling is relevant. The limits of agreement were wide but narrower than those found between DXA and both BIA systems. The results of BF% of the HFS were closer to those of DXA than the results obtained by the FFS studied.

Fat-Free Mass Index

The results of the comparisons of the FFMI agreed with the findings of the BF%: the FFMI results of the HFS device were close to those found by DXA; however, the limits of agreement were wide. The FFS had a larger difference than the HFS results and also showed wide limits of agreement. The results of both BIA systems studied were closer to DXA than the results found regarding the BF%.

The fat-free mass index is not a new concept. VanItallie et al. were the first to define it nearly 20 years ago to overcome some of the limitations related to the simple expressions of FM and FFM in absolute terms[26]. There are new ranges of standard normality for BMI and recommended percentage of fat[27], but this does not mean these constitute a normal or healthy amount of FFM. Just as BMI is a useful tool to compare body weight in individuals who differ in height, the FFMI has proven a useful measurement to compare body composition in subjects who differ in height and content of FFM[28]. FMI seems to be a better indicator to provide information about body compartments than measurements that do not take height into account.

Body composition results evaluated by HFS BIA were similar to the values obtained by DXA on average. This could suggest that the HFS method used is reliable for evaluating young Mexican women. Body composition measurements obtained by the HFS were closer to the results estimated by DXA than the values

obtained by the FFS equipment used in the present study. The results of the FFS equipment showed a considerable underestimation of BF% and an overestimation of the FFMI. In addition, the limits of agreement were wide in both BIA systems and they showed an increase in bias as in the case of the BF% and FFMI when the values were larger.

Clinicians should be aware of the accuracy of their patients' body composition assessments, that different types of BIA equipment had different levels of bias, and that the results of different BIA systems may not be interchangeable. It is important to consider these aspects in helping their patients achieve healthy weight. Clinicians should pay close attention when interpreting the values of fat mass percentage obtained by BIA in clinical practice, particularly in obese or overweight patients.

Finally, the BMI values of 84.3% of the students were within the normal standard range, which was higher than the national prevalence for women of the same age group (42.1%) according to the results obtained in the Mexican National Health and Nutrition Survey for 2012[1]. This may affect the external validity of the study. The low prevalence of the overweight and obese conditions could be due to the fact that the participants were students of human nutrition science, and they were interested in healthy lifestyles.

Similarly, a high prevalence of normal weight was observed in other studies with young women: for example, Ledo Varela et al. in Spain found a prevalence of over 85.0%[29], and Vanessa Mealha et al. registered prevalence of over 90.0% in a sample of university students in Portugal[30]. The mean value of the fat mass percentage was higher in the Mexican students compared with the findings of a similar study published by Alburquerque–Sendin et al. about Spanish young women (35.36% *vs* 28.1%)[31] and in another study from Irish women with similar ages (35.36% *vs* 29.9%)[32]. The high body fat percentage found in the Mexican women studied is of concern and nutritional counseling is in order.

Limitations of the study

The study group was restricted to Mexican women from 20 to 30 years of age. Most were within a normal range of BMI. The results probably are not valid for other population groups.

Conclusion

Although BIA systems are used in clinical practice, not all BIA equipments are reliable in different population groups. In this study we compared two different tools: a hand-to-foot system and a foot-to-foot system. The HTF appears more reliable than the FTF system to evaluate body fat percentage and fat-free mass index in young Mexican women.

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Length of residence and risk of eating disorders in immigrant adolescents living in Madrid; the AFINOS study

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Abstract

Objectives: **This study was designed to compare the risk of having an eating disorder (ED) among immigrant and native adolescents living in Madrid and to determine the possible influence of length of residence (LOR) on the risk of the immigrants.**

Methods: **A cross-sectional survey was conducted from november 2007 to february 2008 in a representative sample of adolescents aged 13 to 17 years (n = 2,077, 1,052 girls) living in the Madrid region. Data were collected using the Spanish version of the SCOFF Eating Disorders Questionnaire. Further factors considered were country of birth, LOR and several biological, socio-demographic, lifestyle and health-related variables.**

Results: **According to the three logistic regression models constructed, female immigrant adolescents on the whole showed a greater ED risk (OR = 1.95; 95%CI 1.29-2.95; p = 0.001) than native adolescents. Moreover, the likelihood of ED was higher among female immigrants living in Spain for <6 years than for Spanish native females (OR = 2.44; 95%CI 1.42-4.18; p = 0.001), while no significant differences were found when female natives were compared with female immigrants living in this country for ≥ 6 years. Similarly, no differences were observed in the ED risk recorded for male native and immigrant adolescents, both as a whole and by length of residence in Spain.**

Conclusions: **The immigrant status and the length of Spanish residence are relevant factors in regard to the ED risk in adolescents living in Madrid.**

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TIEMPO DE RESIDENCIA Y RIESGO DE TRASTORNOS DE CONDUCTA ALIMENTARIA EN ADOLESCENTES INMIGRANTES RESIDENTES EN MADRID; ESTUDIO AFINOS

Resumen

Objetivos: **Este estudio fue diseñado para comparar el riesgo de trastornos de conducta alimentaria (TCA) entre adolescentes nativos e inmigrantes residentes en Madrid, así como para determinar la posible influencia del tiempo de residencia en el riesgo de los inmigrantes.**

Métodos: **Se llevó a cabo un estudio transversal durante el periodo comprendido entre noviembre 2007 y febrero 2008 sobre una muestra representativa de adolescentes residentes en Madrid, con edades de entre 13 y 17 años (n = 2.077, 1.052 mujeres). Los datos se recogieron usando la versión española del cuestionario SCOFF para la detección de trastornos alimentarios. Otros factores considerados fueron el país de nacimiento, el tiempo de residencia y diversas variables biológicas, socio-demográficas, relativas a estilo de vida y la salud.**

Resultados: **Según los tres modelos de regresión logística construidos, las mujeres adolescentes inmigrantes en conjunto mostraron un mayor riesgo de TCA (OR = 1,95; 95%CI 1,29-2,95; p = 0,001) que las nativas. Además, la probabilidad de sufrir TCA fue mayor entre las adolescentes inmigrantes con una residencia en España < 6 años que en las nativas (OR = 2,44; 95%CI 1,42-4,18; p = 0,001), mientras que no se encontraron diferencias entre las adolescentes nativas y las inmigrantes con un tiempo de residencia ≥ 6 años. No se observaron diferencias en el riesgo de TCA entre los adolescentes varones nativos y los inmigrantes, tanto en conjunto como según tiempo de residencia.**

Conclusiones: **La condición de inmigrante y el tiempo de residencia son factores relevantes a la hora de considerar el riesgo de TCA en adolescentes residentes en Madrid.**

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Palabras clave: *Inmigración. Trastornos alimentarios. Tiempo de residencia. Aculturación. España.*

Introduction

Eating disorders (ED) are a growing concern linked to a wide range of gastrointestinal, neurological and endocrine conditions[1]. In immigrant populations, the appearance of ED has also been related to socio-cultural factors such as ethnicity and acculturation[2,3].

Acculturation is the multi-component process whereby immigrant populations change their original lifestyle to adopt behaviors and habits of the dominant culture[4]. Length of residence can be understood as an indirect measure of acculturation[5], as confirmed in another study[6].

Unlike the situation in other countries, immigration is a very recent phenomenon in Spain, which has substantially increased in some areas. For instance, in the Madrid region, the immigrant population grew from 2.3% in 1998 to 16.7% in 2010[7].

Only a few studies have examined differences in the frequency or risk of ED between native and immigrant populations, and most have focused on female subjects. For this reason, in contextualizing this study, we have also considered those studies comparing the presence of ED among different ethnic groups as well as those carried out in adult populations. In one such study, increased bulimic behavior was observed in Greek adolescents of both sexes living in Greece compared with Greek migrants to Germany in the 1980s, yet no significant difference in this behavior was detected two decades later[8]. In contrast, numerous studies have addressed ethnic differences related to ED. For instance, among female adolescents, several studies have established that, certain ethnic groups are more vulnerable to ED[2,3,9]. However, the results of two further studies indicate that young adult Asian and Caucasian women are equally susceptible to ED[10,11].

Further research efforts have addressed the issue of acculturation according to language proficiency and use, using indirect measures of this variable such as LOR or generation, but also using different acculturation scales based on cultural orientation and self-identification[5]. In effect, positive relationship was detected in adult women between the likelihood of suffering ED and acculturation[12] and this relationship was also observed for certain ED in both men and women[13]. In another study, a longer length of residence in young women was related to a higher rate of weight-related concerns and behaviors (weight dissatisfaction, binge eating or dieting)[6]. Similarly, a greater identification with the western culture has been associated with a greater likelihood of disordered eating behavior in children of both sexes[14], yet the opposite was also observed in that less acculturated female adolescents were found to be more vulnerable to ED[3]. However, in adult women, no differences have been observed between acculturation and eating behavior[15], or between acculturation and ED symptoms[16].

Given the lack of Spanish studies examining this issue, the aim of our study was: 1) to establish differences in ED risk between male and female immigrant and Spanish adolescents living in Madrid, and 2) to assess the effect of LOR, as an indirect measure of acculturation, on the ED risk.

Methods

Study design and participants

The participants for this study were recruited from the AFINOS (*La Actividad Física como Agente Preventivo del Desarrollo de Sobrepeso, Obesidad, Alergias, Infecciones y Factores de Riesgo Cardiovascular en Adolescentes*-Physical Activity as a Preventive Agent for the Development of Overweight, Obesity, Infections, Allergies and Cardiovascular Risk Factors in Adolescents) study. The rationale and methods of the AFINOS study have been described in detail elsewhere[17]. Briefly, it is a cross-sectional survey conducted in 2007-2008 designed to obtain data on lifestyle and health indicators through a questionnaire administered to a representative sample of adolescents (*N*~2,000) aged 13 to 17 years from the Madrid region. Data were collected at randomly selected secondary schools (grades 8th to 11th). The final sample comprised 2,077 subjects (1,052 girls), around 15% (n = 335; 186 girls) of whom were born in a foreign country [263 in a Latin American country (South and Central America) and 72 in a European country, mostly (around 85%) of Eastern Europe]. This figure of 15% is in line with the estimated pattern for the immigrant population of Madrid (around 16%) based on data from the National Institute of Statistics for 2010[7]. The countries of origin also coincide with the two largest immigrant groups (Europeans and Latin-Americans) living in the Madrid region according to the National Survey of Immigrants 2007[18]. Of the 335 immigrants enrolled, only 318 provided LOR data for our analysis of the influence of this variable on the ED risk. The study protocol was approved by the Review Board of the *Puerta de Hierro* Hospital (Madrid, Spain) and the Bioethics Committee of the Spanish National Research Council (CSIC, Madrid, Spain). All parents or guardians and adolescents gave their written informed consent for participation.

Dependent variables

All the variables used in this study were collected by questionnaire. The dependent variable, having a risk of ED, was estimated according to the Spanish version of the SCOFF Eating Disorders Questionnaire[19]. This is a screening tool originally designed for routine use to detect individuals considered to be at risk for ED and consists of five questions designed to assess deliberate vomiting, inability to control eating, weight loss, body image distortion and the impact of food on life. Two or

more positive answers to the questions were taken to indicate being at risk of disordered eating behavior[20].

Independent variables

The independent variables in this study were immigrant status and LOR in Spain. For the analysis of LOR, two categories were defined for girls and boys separately: adolescents who had lived in Spain for fewer than 6 years (n = 182) and those who had spent 6 years or more in this country (n = 136), which is the only measure of acculturation available in the AFINOS study. Given that LOR has not been well defined in studies performed on immigrant adolescents, we selected a cut-off value that would divide our subjects into two similar-sized groups. The cut-off of 6 years used also seems reasonable for the average age of the adolescents (14.7-9+1.2 years).

Co-variables

Some variables were considered co-variables in the analysis. These were: age, as a biological variable with a proven effect on ED[21], socio-demographic variables that were available for all subjects such as family structure (two categories, both parents living at home, one or neither parent living at home) and large family (defined as ≥ 3 children by the Spanish government), also previously related to ED[22]; type of school (state versus private) and area of residence (Madrid center/suburbs versus rural areas). These last two variables have been related to socioeconomic status[23,24], which has been considered in another study examining ED[21]. It should be noted that we lacked information on socioeconomic status (SES) for most of the AFINOS study sample owing to a low response rate of parents to the questionnaire.

Also included as co-variables were factors related to lifestyle: smoking (daily or occasionally) or non smoking (subjects who had never smoked or had given up smoking); daily consumption of fruit (at least one piece per day); dieting (currently on a restrictive diet to lose weight) and physical activity (active or non-active according to the PACE Program recommendation for adolescents of at least 60 min of moderate to vigorous exercise five days or more per week)[25], given that several lifestyle factors have been considered as risk factors for ED[26].

Finally, we considered the following health-related variables: the presence of overweight or obese (estimated as the self-reported body mass index or weight/height squared (kg/m^2) using the BMI age- and gender-specific cut-offs proposed by Cole et al.)[27], self-reported medical diagnosis of depression and self-reported school performance (poor/adequate, good or very good), which has also been linked to health behaviors, due to the confirmed relationship between health condition and ED[13, 26].

Data analysis

The characteristics of the sample and output results of the study are provided as frequencies (percentages). Data for the male and female immigrant and native adolescents were compared by the Chi-squared test. Significance was two-sided ($p < 0.05$).

The relationship between ED risk and LOR was assessed by binary logistic regression using three different regression models for boys and girls separately, with the Spanish subjects as the reference group (calculating odds ratios and 95% confidence intervals). In the first model, we adjusted for age as a biological variable, in the second model we adjusted also for socio-demographic and lifestyle variables and in the third model we added the health state variables. These three models were used to evaluate the potential impacts as confounders of all co-variables on the relationship between LOR and ED risk. All statistical tests were performed using the SPSS package (v 15.0) for Windows XP.

Results

The characteristics of the male/female native and immigrant adolescents, overall and by LOR, are provided in table I. Risk prevalence for ED in the Spanish native and immigrant adolescent populations by sex are provided in figure 1. The female immigrant adolescents showed a higher prevalence than the female Spanish ($P < 0.001$). Significant differences also emerged in ED risk when we compared female native and immigrant females with a LOR < 6 years ($P < 0.001$) yet these differences were no longer significant for female adolescents in the group LOR ≥ 6 years ($P = 0.173$). No significant differences were observed when comparing male natives with male immigrants as a whole, or in the groups LOR < 6 years ($P = 0.460$) and LOR ≥ 6 years ($P = 0.893$).

The logistic regression models constructed are shown in table II. Using the native female adolescents as the reference group, the ED risk adjusted for age was greater in immigrants (Model 1) (OR = 1.84; 95%CI 1.32-2.57; $p = 0.002$). After adjusting also for socio-demographic and lifestyle variables (Model 2) the ED risk of the female immigrants was slightly higher (OR = 2.01; 95%CI 1.36-2.98; $p < 0.001$). When factors related to health state were added as co-variables (Model 3), the ED risk was also higher among the female immigrant adolescents (OR = 1.95; 95%CI 1.29-2.95; $p = 0.001$).

When the female natives (reference group) were compared with the female immigrants according to LOR, those whose LOR was < 6 years showed a higher ED risk according to the three models (OR = 2.29; 95%CI 1.49-3.50; $p < 0.001$, OR = 2.40; 95%CI 1.44-3.99; $p = 0.001$, OR = 2.44; 95%CI 1.42-4.18; $p = 0.001$, respectively), however these differences in the

Table I
Characteristics of the Spanish native and immigrant adolescents examined, overall and by length of residence in the Madrid region, Spain. Sample comprised of 2,077 subjects aged 13-17 years

				Immigrants		
				Length of residence		
	Spanish	*Immigrants*	*P**	*< 6 years*	*≥ 6 years*	*P**
Girls						
n	866	186		101	77	
Age [mean, (SD)]	14.7 (1.2)	14.9 (1.2)	0.113	14.8 (1.2)	15.1 (1.2)	0.088
Age 13-14 years (%)	41.9	43.0	0.784	43.5	36.4	0.173
Age 15-17 years (%)	58.1	57.0		53.5	63.6	
Living with both parents (%)	79.7	64.5	**< 0.001**	70.3	57.1	0.069
Large family (%)	8.2	23.6	**< 0.001**	19.6	29.7	0.128
Public school (%)	85.3	83.9	0.611	88.1	77.9	0.068
Residing in metropolitan area + suburbs (%)	62.4	67.6	0.187	60.8	75.3	**0.042**
Curently dieting (%)	12.3	15.8	0.205	20.8	9.1	**0.034**
Overweight and obesity (%)	9.9	13.6	0.144	14.6	10.8	0.468
Smokers (%)	21.7	13.4	**0.013**	12.0	15.3	0.536
Physically active (%)	16.4	13.0	0.257	12.9	14.3	0.784
Daily fruit consumption (%)	45.0	44.1	0.834	37.8	50.9	0.089
Reported medical diagnosis of depression (%)	2.4	6.0	**0.010**	6.1	5.3	0.838
Poor school performance (%)	5.2	7.6	0.212	8.0	6.5	0.703
Boys						
n	876	149		81	59	
Age [mean, (SD)]	14.7 (1.2)	14.9 (1.2)	0.113	14.9 (1.2)	14.7 (1.2)	0.493
Age 13-14 years (%)	44.2	44.3		42.0	49.2	0.399
Age 15-17 years (%)	55.8	55.7		58.0	50.8	
Living with both parents (%)	81.7	69.9	**0.001**	69.6	69.0	0.935
Large family (%)	7.0	16.3	**< 0.001**	20.0	10.5	0.140
Public school (%)	83.6	86.6	0.928	90.1	81.4	0.135
Residing in metropolitan area + suburbs (%)	65.5	67.9	0.931	64.1	75.9	0.142
Curently dieting (%)	7.0	7.0	0.994	9.2	1.7	0.067
Overweight and obesity (%)	24.1	27.8	0.338	32.1	19.3	0.098
Smokers (%)	12.9	11.8	0.709	13.9	10.7	0.580
Physically active (%)	28.8	28.9	0.982	35.8	20.3	**0.047**
Daily fruit consumption (%)	40.9	36.1	0.279	32.1	40.4	0.320
Reported medical diagnosis of depression (%)	1.0	2.1	0.288	3.8	0.0	0.136
Poor school performance (%)	7.4	8.1	0.773	9.6	5.5	0.388

*Pearson's χ^2 test (Student's t-test for age and BMI as a continuous variables).

three models were not detected for those whose LOR was ≥ 6 years.

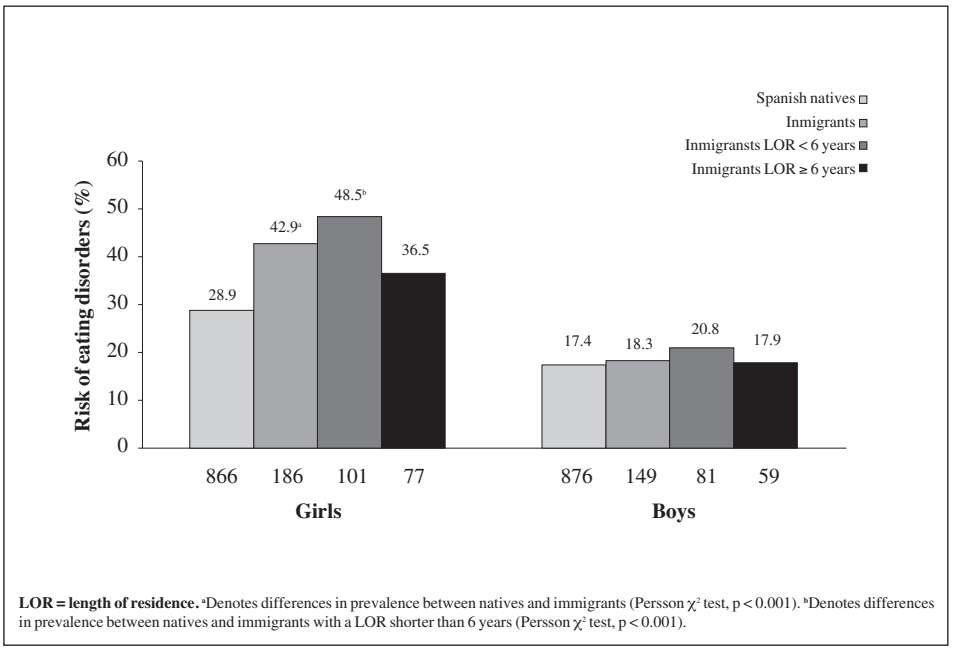
For the adolescent boys, no differences were observed in ED risk between natives and immigrants as a whole, or when comparing natives with the two immigrant LOR groups.

Discussion

Results related to ethnicity

The findings of this study indicate that female immigrant adolescents carry a greater risk of having an ED than their Spanish counterparts, while no differences were detected in the ED risk between male native and immigrant adolescents. To our knowledge this risk has not been previously examined in Spain. The only research found with any similitude at all is a study performed in Ceuta (a Spanish city in North Africa) a higher prevalence of ED was observed in Muslim adolescents of both sexes (12-20 years) than in Christian adolescents, probably due to the common cultural ties of these subjects with the neighboring country Morocco[28].

Very few studies outside Spain have compared ED risks in immigrant and native populations. We therefore consider of interest studies that have addressed related issues including those assessing the influence of ethnicity on ED. The findings of many of these investigations are partially consistent with the present results obtained in female adolescents. For example, the frequency of unhealthy eating behaviors was reported higher among Asian than Caucasian adolescents living in the UK[2]. In Croatia, restrained eating behavior seems to be more common among immigrant adolescents of both sexes compared to natives[29]. Asian ado-



LOR = length of residence. [a]Denotes differences in prevalence between natives and immigrants (Persson χ^2 test, $p < 0.001$). [b]Denotes differences in prevalence between natives and immigrants with a LOR shorter than 6 years (Persson χ^2 test, $p < 0.001$).

Fig. 1.—Eating disroder risk prevalences according to SCOFF scores recorded in Spanish and immigrant adolescents living in the Madrid region, Spain (surveyed 2007-8).

Table II

Logistic regression models for the risk of having an eating disorder in Spanish native and immigrant adolescents (13-17 years), overall and by length of residence (LOR) in the Madrid region, Spain. Sample comprised of 2,077 subjects

	Model 1			*Model 2*			*Model 3*		
	OR	*95% CI*	*P*	*OR*	*95% CI*	*P*	*OR*	*95% CI*	*P*
Boys									
Spanish	1.00			1.00			1.00		
Immigrants	1.06	0.66-1.68	0.802	1.12	0.68-1.85	0.647	1.13	0.66-1.94	0.634
Length of residence									
Spanish	1.00			1.00			1.00		
Immigrants < 6 years	1.24	0.69-2.22	0.458	1.23	0.64-2.33	0.525	1.16	0.59-2.29	0.657
Immigrants ≥ 6 years	1.02	0.50-2.07	0.949	1.24	0.59-2.61	0.558	1.37	0.61-3.10	0.441
Girls									
Spanish	1.00			1.00			1.00		
Immigrants	1.84	1.32-2.57	**< 0.001**	2.01	1.36-2.98	**< 0.001**	1.95	1.29-2.95	**0.001**
Length of residence									
Spanish	1.00			1.00			1.00		
Immigrants < 6 years	2.29	1.49-3.50	**< 0.001**	2.40	1.44-3.99	**0.001**	2.44	1.42-4.18	**0.001**
Immigrants ≥ 6 years	1.42	0.86-2.33	0.164	1.65	0.94-2.91	0.079	1.66	0.92-2.99	0.091

Model 1, adjusted by age.
Model 2, adjusted by age, cohabiting with parents, family size, school, area of residence, smoking, dieting, physical activity and daily fruit consumption.
Model 3, adjusted by age, cohabiting with parents, family size, school, area of residence, smoking, currently dieting, physical activity, daily fruit consumption, overweight or obese, school performance and depression.

lescent girls in Australia showed higher scores in attitudes to and psychopathology of ED than their Caucasian counterparts[3].

Moreover, several authors have reported results indicating a higher vulnerability to ED or related issues among native subjects compared with immigrants, or among Caucasian subjects compared with other ethnicities (those with a more likely migrant background) while other investigations have detected no such differences. Thus, in two studies carried out in the UK, Caucasian mothers and daughters reported higher levels of restrained eating than Asian mothers and daughters[15], although there were no differences between young British and Asian girls (mean age 21-22 years) in terms of having ED[10].

In the United States, female Caucasian and Latino adolescents have shown a higher ED risk than their African counterparts[9]. However among adults, no differences were observed between native Americans and other ethnicities in ED symptoms[30], which is in line

with the lack of differences observed among women belonging to different ethnic groups[12].

Results related to acculturation

The findings of the present study also reveal a greater risk of ED in female immigrants living in Spain for < 6 years compared to female natives, but this difference disappears when these girls have lived for ≥ 6 years in this country. This outcome suggests that a longer time of residence is slightly protective against ED in adolescent girls. However, no differences were detected when we compared our two length of residence groups of male immigrants and male native adolescents.

Few studies have addressed the relationship between acculturation or length of residence and ED in adolescents. In agreement with our results, a study carried out in Australia revealed that less acculturated Asian adolescent girls aged 14-17 years scored higher in attitudes to and psychopathology of ED than those who were more acculturated[3]. Partially in line with our results, in children of both sexes living in the US, length of residence was not correlated with ED, while stronger identification with the host culture was associated with a greater likelihood of ED[14]. To the best of our knowledge, no Spanish study exists with which to compare our results. In Europe, a single study examining this issue among Asian mothers and daughters, all adults living in London, concluded that acculturation was not associated with eating behaviors (restrained eating and calorie concerns)[15], contradicting what we observed in girls.

Much of the information from the US and Australia conflicts with our observations in adolescents and studies performed in adults have provided inconsistent results. For example, in a study comparing Hispanic, Asian, Black and White adult women aged 18-44 years in the US, more acculturated subjects were more prone to suffer from ED[12], which is in disagreement with our results. Similarly, positive correlation was noted between LOR and the risk of certain ED among males and females aged 18 years or older[13].

In Australia, identifying with the western culture (indicating greater acculturation) was positively associated with disordered eating, and a negative relationship was detected between identification with the culture of origin and disordered eating in Muslim-Australian women aged 18-44[4]. Besides, a longer LOR in Australia was linked to more weight dissatisfaction in young women aged 18-23 years, despite a shorter time of residence being correlated with more dieting and binging[6].

Possible causes of ED risk

The main reason for a female immigrant adolescent showing a higher ED risk than a female native adolescent could be stress during the course of acculturation[31]. In the US, acculturation stress and body dissatisfaction combined have been shown to make female students from different ethnic groups more vulnerable to bulimic symptoms. Specifically, those who reported body dissatisfaction combined with a low level of acculturation stress were less vulnerable to these bulimic symptoms[32]. Further, a higher level of acculturation stress was linked to higher rates of ED symptoms in Black and Latino women living in the US[16]. However, according to other authors, stress could diminish with a greater LOR[33], which would be in agreement with our results.

Otherwise, it is possible that immigrants from non-western countries adopt the social standards of western societies, given that the acculturation process implies an adaptation of values and behaviors as a result of interaction with the host culture[5]. This could be extended to eating attitudes and behaviors. Accordingly, female immigrant adolescents would be pressured to adopt a thin model of beauty as the cultural stereotype, especially the western ideal of a slim female body. In this regard, Mexican-American women with an Anglo orientation showed a greater preference for a thinner body and less tolerance for overweight figures than those with a Mexican orientation[34]. This pressure and the internalization of the thin ideal present in western countries, have been identified as risk factors for the body dissatisfaction and body image problems associated with ED[35].

Conclusions and limitations of the study

Based on our results, we may conclude that: 1) female immigrant adolescents living in the Madrid region carry a greater ED risk than their female Spanish peers. We were able to detect this link independently of the model used to adjust for several co-variables; 2) female immigrant adolescents living in Spain for fewer than 6 years are more prone to develop an ED than female native adolescents, while female immigrants living for 6 years or longer in the country show a similar risk to their female native peers; and 3) length of residence could be an independent factor affecting ED risk.

Our study has several limitations. The first is that variables were self-reported, which compromises the quality of data. In addition, the group of immigrants was multiethnic and it is possible that different countries of origin could determine a different response when individuals come into contact with another culture. Another limitation is that we have used the length of residence as an indirect measure of acculturation, which could be incomplete; unfortunately, no other measure was available in the AFINOS study. Also, information on socioeconomic status (e.g., family income, work activities or level of parent studies) was not available because of the low completion rate of the questionnaire by parents (under 40%) in the AFINOS study. Consequently, we could not enter this informa-

tion as a co-variable in the regression models. Lastly, the cross-sectional design of our study precludes establishing cause-effect relationships. Despite these limitations, the lack of research assessing ED risk in immigrant adolescent populations makes this a pioneer study performed on a wide representative epidemiological sample of adolescents from the Madrid region.

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Evaluando la aceptación de alimentos en escolares; registro visual cualitativo frente a análisis de residuos de alimentos

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Resumen

Introducción: **Los comedores escolares cuentan con normativa de gestión y supervisión de menús, sin embargo no se ha valorado si son consumidos en su totalidad.**

Objetivo: **Valorar la aceptación de alimentos mediante pesado de restos y validación de una metodología visual para su estimación en comedores escolares de Murcia.**

Metodología: **Participaron escolares de segundo y tercer ciclo de educación primaria, de 8-12 años. La estimación de restos se realizó mediante pesado de alimentos de 765 bandejas. La valoración visual (300 bandejas) se realizó con escala categórica: 1 = 0-25%; 2 = 26-50%; 3 = 51-75% y 4 = 76-100%, por dos dietistas y se valoró la fiabilidad con respecto al pesado de alimentos. La concordancia entre ambos métodos fue evaluada en dos muestras estratificadas por la presencia/ausencia de cocina en la escuela.**

Resultados: **Los primeros platos con más restos fueron pasta, arroz y purés de verduras siendo mayor en aquellos colegios sin cocina en el centro ($p < 0,05$). También los segundos platos a base de legumbres, ave y pescado y ensaladas de guarnición. Las frutas y el total de restos son superiores en colegios sin cocina ($p < 0,05$). La concordancia entre evaluadoras fue alta en platos a base de carnes y en ensaladas, y considerable en legumbres, precocinados, tortilla de huevo, pasta, pescado y arroz.**

Conclusiones: **Los restos son elevados y existieron diferencias en la aceptación de ciertos alimentos acorde al tipo de menú ofertado. La escala visual es una herramienta confiable para medir la aceptación de forma indirecta, pero necesita capacitación y entrenamiento del personal implicado.**

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Palabras clave: *Comedores escolares. Aceptación alimentos. Residuos. Escolares.*

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ASSESSING FOOD ACCEPTANCE IN SCHOOLAR CHILDREN; QUALITATIVE VISUAL RECORD VERSUS FOOD WASTE ANALYSIS

Abstract

Introduction: **School canteens have rules of management and supervision of menus, however has not been assessed if they are totally consumed.**

Objective: **To assess the acceptance of food by weigh food leftovers and validation of a methodology for visual estimation in school canteens of Murcia.**

Methodology: **Participated pupils in the second and third cycle of primary education, between 8 and 12 years. The estimate of leftovers was performed by 765 food trays. Visual estimation of 300 trays was based on a categorical scale as follow: 1 (0-25%), 2 (26-50%), 3 (51-75%), 4 (76-100%) by two dietitians and reliability was assessed with respect to the weighed food. The reliability between both methods was assessed in two samples stratified by presence or absence of school kitchen.**

Results: **The first dishes with leftovers were pasta, rice and vegetable purees and was higher in those schools without kitchen ($p < 0.05$). Also, the second dishes poultry and fish salads and vegetables garnish. Fruit and the total sum of leftovers was higher in schools without dining menus ($p < 0.05$). The agreement between evaluators was high in meat dishes and salads, and substantial in vegetables, pre-cooked, omelet, pasta, fish and rice.**

Conclusions: **The leftlovers are high and there are differences in the acceptance of certain foods according to the type of menu offered. The visual scale is a reliable to measure acceptance indirectly, but training to catering staff is needed.**

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Key words: *School canteen. Food acceptance. Leftovers. Qualitative assessment. School children.*

Introducción

El análisis de restos de alimentos ha sido tradicionalmente utilizado para evaluar la aceptación, sin embargo en los comedores escolares pesar los restos de cada comensal individualmente requiere mucho tiempo y a menudo es poco práctico. Por lo que se plantea como alternativa la medición indirecta a través de la estimación visual, ya que correlaciona altamente con los restos, aunque sea menos precisa que un registro pesado de alimentos. La más utilizada es la clasificación de Comstock y cols., (1981), que señala 6 puntos de corte: plato lleno, plato casi lleno, ¾ partes del plato, ½ plato, una cuarta parte del plato, plato vacío[1]. En España esta metodología se ha empleado para evaluar la aceptación en otros tipos de servicios de alimentos como los hospitales, con el propósito de mejorar la calidad del servicio, prevenir complicaciones de la nutrición incorrecta y mejorar la estancia hospitalaria[2]. Se ha reportado que tiene una buena correlación con el método de pesada de alimentos, sobre todo de primeros y segundos platos servidos[3]. Al parecer, el tipo de menú y el grupo de alimento de los platos, pueden tener una influencia sobre el nivel de aceptación[4].

También se ha probado que el método visual es válido para evaluar los programas de alimentación escolar[5]. Debido a que la evaluación visual es fácil de aplicar y puede ser realizada durante el período de la comida escolar (requiriendo un mínimo de personal), además, es un medio conveniente y discreto de evaluar el consumo de elementos específicos del menú escolar. Por lo que este método es ideal para las evaluaciones de los programas de educación nutricional y la vigilancia general de los hábitos alimentarios de los escolares[6]. Otro método probado, es el uso de la fotografía digital para la valoración visual de los alimentos que los estudiantes seleccionan y realmente consumen del menú escolar, lo que sugiere que se trata de un método preciso y fiable, para medir el consumo real de las comidas escolares[7].

Los diferentes estudios llevados a cabo mediante la estimación visual de los restos de alimento, han puesto de manifiesto que la cantidad consumida de los platos es menor a la recomendada, ya que los restos pueden alcanzar un 26% de la cantidad total servida. Estos resultados son importantes no sólo por el costo económico del desperdicio de alimentos, sino también por las pérdidas en energía, vitaminas, minerales y fibra[8].

Resultados de otras investigaciones indican que en niños de tercero a sexto curso, los alimentos con mayor cantidad de restos fueron las ensaladas (34,5%), hortalizas –excepto patatas– (54,3%) y el pan (54,2%). Los restos fueron ligeramente menor en los grados 3° y 4° que en 5° y 6° y las chicas dejan más hortalizas que los niños[9]. Los restos de vegetales son muy elevados (ensaladas y purés), a pesar de las estrategias para fomentar su consumo[5]. Con respecto a las frutas, se observó que cuando se sirve en pieza entera presentan mayor proporción de restos comparados con su versión modificada (puré)[10].

En España, los resultados de la confederación de cooperativas de consumidores y usuarios indican que los alimentos en los hogares con mayor cantidad de desperdicios son el pan, frutas, verduras, lácteos, pastas, arroz y legumbres[11]. Datos estimados de los residuos de alimentos en la restauración colectiva indicaron que van desde 4%[12] hasta 14%[13]. Sin embargo, hasta el momento poco se conoce sobre cuánto y cómo se desperdicia la comida en los comedores escolares. Esta debería ser una prioridad para los gestores de los centros educativos, las empresas de catering involucradas y sobretodo de los servicios municipales o estatales que financian las comidas escolares. Además, otra estrategia dentro del marco escolar, no sólo desde el nivel nutricional sino formativo, debería incluir la promoción del consumo de la totalidad de los menús bien planificados y así evitar los restos de alimentos. Actualmente la evaluación del consumo real de comidas mediante métodos exactos como el pesado de alimentos en los comedores escolares presenta desafíos, teniendo en cuenta los problemas de organización de los diferentes turnos de comida de los niños, el escaso tiempo disponible de los monitores y las limitaciones de tiempo en la organización del personal docente involucrado.

Objetivos

Debido a lo anterior y a la importancia de conocer los restos de alimentos ofertados en los comedores escolares, el objetivo de nuestro trabajo fue valorar el grado de aceptación de alimentos mediante análisis de restos por pesado de alimentos y validar una metodología visual para su estimación considerando el tipo de gestión de los comedores.

Métodos

Diseño del estudio

La empresa de catering participante, presta el servicio en 24 colegios de la ciudad, y sobre ésta lista, se solicitó la participación durante el periodo de febrero-junio de 2012. Sin embargo, respondieron a la invitación únicamente 5 colegios de la ciudad, 2 concertados y 3 públicos. En vista de la poca respuesta por parte de los centros educativos, se solicitó la participación en el ciclo 2012/2013, a la que respondieron 6 colegios más, 5 de ellos públicos y 1 concertado. El principal motivo de la poca participación de los centros educativos fue que en el momento de la solicitud, ya desarrollaban otras investigaciones en el marco escolar que no permitían atender a las necesidades de nuestro proyecto. Otro aspecto importante es que de los 11 colegios participantes, 9 no contaban con un responsable de comedor, y las gestiones dependían únicamente del director. Previa autorización de los centros educativos participantes y la empresa de catering participante, se realizó la prime-

ra valoración en los meses de abril a junio de 2012 y la segunda entre octubre de 2012 y enero de 2013.

En la dinámica de los comedores, el catering sirve dos tipos de menús, uno denominado "línea fría" donde se elaboran los alimentos en una cocina central y se trasladan los alimentos al colegio, donde sólo se calienta previo al servicio. El otro tipo de menú los alimentos se elaboran en su totalidad en los comedores. Se evaluaron 51 menús, de las cuales se evaluó 15 bandejas en promedio por menú, haciendo un total de 765 bandejas. Los primeros y segundos platos servidos han sido clasificados por grupo de alimento en base a su componente principal. En todos los menús, lo postres se clasificaron en 3: fruta fresca, lácteo (leche o yogur) y otros como helado, natillas y flanes. El pan se clasificó en dos, integral y blanco.

Participantes

Usuarios de comedores escolares voluntarios, elegidos de forma aleatoria que cursaban segundo ciclo (3º y 4º curso) y tercer ciclo (5º y 6º curso) de educación primaria, con edades comprendidas entre 8 y 12 años. Se solicitó la autorización de la dirección y consejo escolar de cada uno de los centros seleccionados. El protocolo y diseño del estudio cumple las normas de investigación en humanos, y se obtuvo consentimiento informado de los padres o tutores.

Instrumentos y procedimientos

Registro pesado de alimentos

Antes de iniciar la comida, dos dietistas entrenadas pesó cada uno de los alimentos, utilizando una balanza digital de precisión (TOPCOM 200). El tiempo estimado en el pesado de alimentos fue mínimo procurando no afectar el horario normal de la comida para los usuarios. Durante la comida se realizó observación directa, a fin de identificar que los niños no intercambiaran alimentos o los desecharan antes de registrar los restos. Posterior a la comida, se pesaron los restos de cada alimento de cada bandeja para calcular la cantidad neta consumida, considerando las porciones no consumibles de alimentos.

Análisis de restos

Se calculó la proporción restos de alimentos ajustando las porciones no consumibles de alimentos como pollo con piel y huesos y desechos de frutas. Se consideró para el cálculo únicamente aquellos alimentos que presentaron restos; se valoró a un alimento como aceptado cuando fue consumido en el 75% de la porción servida.

Validación de una herramienta visual para estimación de restos

Se realizó en la primera prueba con la participación de 5 colegios. Para la validación visual de los restos se tomó fotografía a 300 bandejas antes y después de la comida, con los alimentos no consumidos. Las estimaciones visuales fueron realizadas por dos dietistas entrenadas a tal fin apoyándose en unas tarjetas de registro (fig. 1). En vista de que la bandeja contiene espacios en forma triangular se definieron cuatro puntos de corte: 1 = 0-25% hasta 1/4 parte (casi vacío, vacío); 2 = 26-50% hasta 2/4 partes; 3 = 51-75% hasta 3/4 partes; 4 = 76-100% (casi lleno, lleno). Para la validación del método se contrastó la valoración visual basándose en las fotografías digitales con el porcentaje de restos calculado mediante el pesado de cada alimento de cada bandeja.

Análisis estadístico

Se utilizó el análisis de proporciones y las diferencias entre grupos se realizaron mediante la prueba no paramétrica χ^2. Para la validación de la escala visual se usó el análisis de concordancia de la evaluación visual

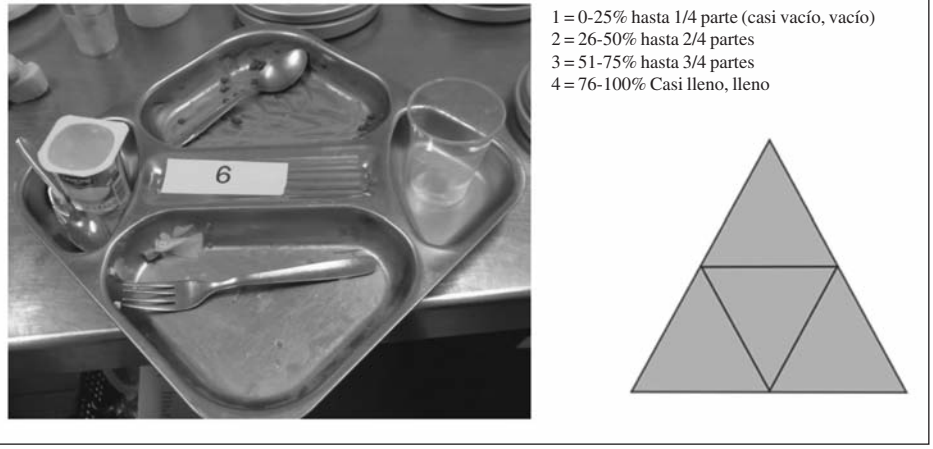


Fig. 1.—Escala visual para identificación de residuos de alimentos en bandejas.

entre ambas dietistas evaluadoras y entre cada dietista con el método de pesado de alimentos, mediante el coeficiente Kappa[14]. Todos los análisis han considerado la probabilidad de 95% de confianza, mediante el paquete estadístico SPSS versión 21.0.

Resultados

Participaron escolares (8-12 años), con proporciones iguales de segundo y tercer ciclo de educación primaria, de los cuales 40% fueron niñas y 60% niños. Los alimentos que formaban parte de los dos tipos de menús se muestran en la tabla I. Se aprecia que en el menú de línea fría no se sirven guisos con pescado como primer o segundo plato, así como otros alimentos listos para consumir como queso y fiambres. Ensaladas y legumbres son los primeros platos más comunes en la línea fría y purés y ensaladas en la línea caliente. Por otro lado legumbres y pastas son los segundos platos más comunes en la línea fría y ave y carne en la línea caliente.

En la tabla II se presentan los restos de alimentos de acuerdo al tipo de menú y gestión del comedor. Se apreció que de los primeros platos a base de pasta, arroz, legumbres, ensaladas y purés presentaron más restos en comedores con línea fría. Además los platos de pasta, arroz y puré de verduras en la línea fría tuvieron mayor proporción de restos por encima del 25% de la porción servida. Sobre los segundos platos, se encontró que los platos de ave tuvieron más restos en la línea caliente que la fría, pero los platos a base de legumbres fueron al contrario. No se encontraron diferencias en la proporción de restos superior al 25% en los segundos platos entre los tipos de menús.

El 84% y 79% de ensaladas de guarnición presentaron restos en el menú de línea fría y caliente respectivamente. Con respecto a los postres, no se encontraron diferencias entre el número de porciones de frutas que presentaron restos pero si entre la proporción de restos, ya que en el menú de línea fría presentaron cifras superiores de > 25%. Estas diferencias no se apreciaron en los lácteos, ya que son consumidos casi en su totalidad.

Las porciones de pan blanco servidas en el menú de línea caliente presentaron más restos, sin diferencias en la proporción en ambos tipos de pan. A pesar de no existir diferencias significativas, se observó que el pan integral tuvo más restos que el blanco.

Se calcularon los gramos totales de restos de todos los alimentos de los menús evaluados, encontrándose que es mayor en los de línea fría que la caliente (164 ± 68 *vs* 106 ± 96; $p < 0,05$). Con esto se determinó la proporción global de restos con respecto a lo servido siendo superior en menús de línea fría que en menús de línea caliente (34% y 22%, respectivamente; $p < 0,05$).

Validación método visual

Los resultados de la evaluación visual, –asumiendo que, las dos dietistas realizaron un entrenamiento previo–, indicaron que existe muy buena concordancia entre ambas para carnes y ensaladas; considerable para

Tabla I
Tipos de platos servidos de acuerdo al tipo de gestión del comedor

	Línea fría (N = 283)		*Línea caliente (N = 478)*	
Alimento	*N*	*%*	*N*	*%*
Primeros platos				
Pasta	59	21,0	51	10,7
Arroz	25	8,8	40	8,5
Legumbres	70	24,7	70	14,7
Ensalada	115	40,5	110	23,0
Puré de verduras	14	5,0	161	33,6
Guiso de patatas con pescado	—	—	45	9,5
Segundos platos				
Ave	52	18,5	102	21,3
Pescado	44	15,7	21	4,3
Huevo (tortillas)	37	13,1	32	6,7
Precocinado	10	3,5	38	7,8
Carne	24	8,6	94	19,6
Legumbres	60	21,2	33	6,8
Pasta	55	19,4	—	—
Arroz	—	—	21	4,5
Queso	—	—	30	6,2
Fiambre	—	—	41	8,6
Guiso de patatas con pescado	—	—	68	14,1

Tabla II
Residuos de alimentos de acuerdo al tipo de gestión del comedor

	Línea fría	*Línea caliente*	*Línea fría*	*Línea caliente*
Alimento	*% de platos con residuos*		*≥ 25% de la porción servida*	
Primeros platos				
Pasta	90,1[a]	63,4[b]	64,3[a]	32,4[b]
Arroz	100,0[a]	73,2[b]	88,0[a]	57,9[b]
Legumbres	97,8[a]	87,7[b]	76,3	73,0
Ensalada	95,7[a]	79,8[b]	93,9	85,8
Puré de verduras	80,0[a]	57,3[b]	100,0[a]	47,2[b]
Guiso de patatas con pescado*		76,1		74,0
Segundos platos				
Ave	70,9[a]	98,6[b]	95,9	93,3
Pescado	59,8	48,6	70,7	76,4
Huevo (tortillas)	28,2	15,8	35,2	57,0
Precocinado	0	6,1	0	100,0
Carne	38,2	25,7	46,2	49,2
Legumbres	91,7[a]	77,7[b]	81,3	61,9
Pasta§	93,9		76,7	
Arroz*		80,0		72,7
Queso*		4,9		100,0
Fiambre*		8,8		80,0
Guiso de patatas con pescado*		87,0		57,7
Ensaladas (guarniciones)	84,5	79,1	92,7[a]	85,6[b]
Postres				
Frutas	66,3	64,8	90,6[a]	81,4[b]
Lácteos	3,6	7,7	44,8	,0
Otros (helados, natillas…)*		10,8		60,6
Pan				
Blanco	13,4[a]	26,2[b]	84,7	88,1
Integral	21,4	34,7	92,4	95,1

[a-b] Indican diferencias significativas entre grupos; $p < 0,05$; Estadístico χ^2. *No servido en línea fría; §No servido en línea caliente.

platos como pasta, legumbres, huevos, precocinados y carne y moderada para purés de verduras, guisos de patatas con pescado y platos a base de ave (tabla III).

Posteriormente se evaluó el índice de concordancia entre cada evaluadora y el método de referencia, es importante resaltar que las pastas se separaron entre secas y caldosas y los platos de ave con (muslo y contra-muslo) y sin huesos (filetes). Los resultados mostraron que la concordancia fue aceptable en ambas evaluadoras para alimentos como ave con piel y huesos, moderada para arroz y ave (general), considerable para ensaladas, legumbres y pasta seca. Se apreció menor concordancia en aquellos platos con sobrantes naturales, como el caso de ave, cuando llevan piel y huesos; o aquellos cuya densidad dificulta la estimación como el puré de verduras. Algo similar ocurrió con las pastas, donde las secas tuvieron mayor concordancia que las caldosas (tabla IV).

Discusión

Debido a la importancia que tiene el consumo de alimentos en los comedores escolares, existe una normativa clara sobre las condiciones de funcionamiento y gestión de los mismos. Además se han realizado múltiples esfuerzos por obtener un consenso de las recomendaciones nutricionales que deben cubrir los menús[15]. Recientemente la Ley de Seguridad Alimentaria[16] ha indicado que los menús deben ser supervisados por un especialista de la nutrición, sin embargo, de acuerdo con nuestros resultados, la correcta planificación de los menús, no garantiza una adecuada alimentación de los escolares. Los restos de alimentos, modifican sustancialmente el aporte de energía y nutrientes, lo cual coincide con lo reportado en otros comedores escolares[17].

En este grupo de usuarios, el resto total de alimentos fue de 34% en menús de línea fría y 22% en caliente, ci-

Tabla III
Índice de concordancia entre evaluadoras

Alimento	*N*	*Kappa*	*p*
Carne	20	1	0,000
Ensaladas	218	0,832	0,000
Legumbres	59	0,778	0,000
Precocinado	24	0,733	0,000
Huevo (tortilla)	29	0,651	0,000
Pasta	87	0,607	0,000
Pescado (filete)	49	0,58	0,000
Arroz	15	0,575	0,002
Puré de verduras	20	0,485	0,001
Guiso de patatas con pescado	11	0,482	0,008
Ave	52	0,473	0,000

Tabla III
Índice de concordancia entre evaluadoras

		Evaluadora 1		*Evaluadora 2*	
Alimento	*N*	*Kappa*	*p*	*Kappa*	*p*
Pasta	80	,690	,000	,501	,000
Pasta seca	57	,720	,000	,682	,000
Pasta caldosa	23	,586	,001	,105	ns
Arroz	15	,450	,007	,409	,023
Legumbres	55	,618	,000	,721	,000
Lentejas	28	,489	,002	,625	,000
Garbanzos	27	,721	,000	,885	,000
Puré de verduras	20	,487	,000	,337	,020
Guisos de patatas	11	,476	,006	,185	ns
Ave	52	,438	,000	,496	,000
Pollo con piel y hueso	25	,255	,009	,229	,043
Filete de pollo sin huesos	27	,580	,000	,716	,000
Pescado	48	,353	,003	,631	,000
Huevo	29	-,048	ns	,463	,013
Precocinado	24	-,091	ns	-,067	ns
Carne	20	,048	ns	,048	ns
Ensaladas	218	,687	,000	,692	,000

ns = no significativo. Índice de concordancia de Kappa; $p < 0,05$.

fra que es muy superior a lo reportado por otros estudios realizados en comidas escolares[5], estos resultados son importantes si además del costo económico de las pérdidas de alimentos, se suman las pérdidas en calorías, vitaminas, minerales y fibra[8]. Por lo anterior, es necesario resaltar la necesidad de que los menús escolares deben ser complementados en el hogar, a fin de lograr una teórica pauta de alimentación adecuada.

Alimentos como pasta y arroz tuvieron muchos restos, debido probablemente a la forma de preparación ya que, en encuestas de preferencias son de los preferidos por los niños[18]. Las preparaciones de pasta suelen incluir tomate y atún y se identificó que tuvieron más restos que los de línea caliente, debido posiblemente a modificaciones organolépticas, por cocción excesiva durante el calentamiento previo al servicio. Otro aspecto a considerar es la cantidad en que se empaquetan estos alimentos, por lo que se podría mejorar si los paquetes de pastas y arroz incluyeran menor cantidad y así requerir menor tiempo de exposición a calor previo al servicio y evitar texturas desagradables para los escolares.

En los primeros platos de la línea caliente los alimentos con mayor proporción de restos fueron legumbres, ensaladas y guisos con pescado; en los segundos platos a base de ave, legumbres y pescado. Es conocido que el pescado y las legumbres, han sido identificados previamente como los menos preferidos en esta población[18-20]. En el caso del pescado otro aspecto que puede jugar un papel primordial es el método de preparación, ya que los evaluados en este trabajo, fueron elaborados principalmente al horno, método que difiere de lo reportado en una encuesta de comedores escolares, donde el más común fue la fritura o rebozado[21].

Los motivos de la proporción excesiva de los restos de las ensaladas, pueden ser debido a la estructura del menú, que los alimentos se sirven al mismo tiempo, –ya que el usuario elige qué comer entre todos los alimentos–, o bien al rechazo por los vegetales que es común en este colectivo[18, 22]. Cabe mencionar que la supervisión de la correcta planificación de los menús escolares (como integrar vegetales diariamente) y la monitorización de los alimentos, tampoco garantiza una adecuada alimentación si no se cuenta con el apoyo familiar, sobre todo de alimentos de menor consumo como los vegetales.

Los platos a base de ave presentaron muchos restos, sobre todo en aquellos que se sirvieron con piel y huesos, –después de ajustar la porción comestible–, por lo cual la presentación parece tener un efecto importante. Quizá la opción más viable son aquellos de fácil manipulación por los niños como los filetes y cortes magros.

En ambos tipos de menús las porciones de frutas ofrecidas presentaron muchos restos siendo mayor en los de línea caliente, debido probablemente a que la cantidad total de alimentos consumidos es mayor y la capacidad gástrica de los escolares no les permite ingerir estos alimentos en el postre. Otro aspecto que puede influir en su bajo consumo es probablemente porque se sirven en pieza y éstas son menos atractivas; en muchas ocasiones los niños solicitaron al monitor que les pelaran la fruta, lo cual va en contra de las recomendaciones de consumo.

Al parecer, si los niños son presionados a comer ciertos alimentos pueden mostrar disminución de la preferencia por los alimentos en el futuro[23]. Por esto, no debe forzarse al consumo de frutas como postre, así que futuras investigaciones deberán considerar aspectos como el grado de apetito al momento de la comida o la capacidad gástrica del niño, ya que esto puede afectar el consumo del postre en su totalidad. También se requiere mayor investigación sobre el índice de saciedad de los diferentes platos servidos a fin de asegurar el consumo de la fruta y el menú completo.

El pan como un integrante del menú, es relevante por su aporte de hidratos de carbono y en el equilibrio energético. Similar a otras investigaciones[24], el pan fue bien aceptado, sobre todo en menús de línea fría, y en general se evaluó mejor el pan blanco que el integral. La

proporción de restos en el menú de línea caliente puede deberse a varios aspectos como, los hábitos alimentarios, ya que de acuerdo con el panel de consumo alimentario, el consumo de pan ha descendido[25]. Estos resultados coinciden con el bajo consumo en este grupo de población reportado en escolares de 5 regiones de la península, donde además se identificó que los niños que consumen más pan, tienen un mejor perfil calórico y nutricional[26]. También puede deberse a que no existe una correcta distribución de las cantidades servidas de los platos principales conforme a la edad, o bien por la combinación que se hace de los alimentos que integran los platos principales. Futuras investigaciones deberán considerar el consumo de pan durante las horas previas a la comida, ya que la ingesta de bocadillos es bastante común en los escolares[19].

Es importante resaltar las limitaciones de este trabajo, ya que se realizó bajo condiciones reales del servicio de comedores, por lo que las cantidades de restos se refieren a la proporción de la cantidad servida, sin considerar si ésta es adecuada o no. Además, futuros estudios deberán analizar porque los escolares dejan tantos residuos, así como si son recompensados en casa cuando se quedan con hambre y por último, las características de las cenas y su contribución a la alimentación saludable.

Hemos probado una herramienta de evaluación visual de restos ya que puede ser útil para optimizar la calidad y el tipo de menús ofertados[2-4]. Nuestros resultados revelaron que éste método es útil para identificar los restos en los comedores escolares, principalmente de aquellos platos como pasta seca, arroz, ensaladas, ave (filetes) y legumbres. Se apreció una mayor concordancia entre las dietistas evaluadoras con alimentos servidos en pieza como la carne, o raciones homogéneas de alimentos como ensaladas, tortilla y pasta; se identificó una concordancia menor en algunos platos con caldo y modificación de la textura, como los purés ya que, el cambio en la textura afecta la identificación de los restos[27].

En este trabajo se usó una escala visual con 4 puntos de corte, ya que se sirve en bandejas con cuatro espacios de forma triangular y donde la escala de Comstock.,1981[1] es poco viable ya que se ha usado para evaluar alimentos en platos redondos. La estimación visual puede ser una herramienta aplicable dentro del marco escolar a fin de identificar de forma práctica por parte del personal de catering, los platos con mayor proporción de restos y adecuar la cantidad servida, así como analizar aspectos organolépticos que generan rechazo. Además esto facilitaría identificar que alimentos necesitan mayor promoción para favorecer su consumo.

Conclusión

Existen diferencias en la aceptación de ciertos alimentos acorde al tipo de menú ofertado, ya que de los primeros platos los de mayor proporción de restos fueron a base de vegetales como purés y ensaladas, pasta y arroz (línea fría) y legumbres, ensaladas y guisos con pescado (línea caliente). Los segundos platos son mejor valorados que los primeros platos y, de éstos, los de mayor proporción de restos fueron a base de legumbres, ave y pescado. Las frutas como postre presentaron gran proporción de restos y el pan, sobre todo el integral. Debido a lo anterior es necesario dentro del marco escolar un programa de educación a los escolares sobre la cantidad recomendada de alimentos, y concienciar el consumo del 100% de la porción servida. Así como también se deberían reforzar otros aspectos que contribuyen al resultado final de la alimentación como, la presentación de las comidas, las habilidades del escolar en la mesa, sus actitudes, etc. Por otro lado, a pesar de la variabilidad de algunos platos sobre todo aquellos caldosos, (que indican una necesidad de estandarización), la escala visual es una herramienta viable para medir la aceptación de forma indirecta, por parte del personal del catering que supervisa la comida (monitores).

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Original / *Pediatría*

Herramienta de educación nutricional para alergicos a huevo y proteína de leche de vaca de edad pediátrica®

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Resumen

Introducción: **La alergia alimentaria afecta a gran parte de la población y sus cifras siguen aumentando. Aunque, se esta avanzando en el conocimiento de la patología, los alérgicos encuentran grandes dificultades para llevar una vida normal, especialmente en lo relativo a su alimentación. Hasta ahora el colectivo no contaba con herramientas prácticas que les ayudasen en la elaboración diaria de una dieta equilibrada, como existen para la población en general, en forma de pirámides y guías alimentarias. Con este trabajo se ha cubierto esta necesidad para dos de las alergias más prevalentes en los primeros años de vida.**

Objetivos: **Recopilar información sobre la alergia a la proteína de leche de vaca (APLV) y huevo, para diseñar una pirámide alimenticia para estos pacientes, basada en los consensos, recomendaciones y guías científicas.**

Resultados: **Tras comprobar la inexistencia de un trabajo similar, se diseñaron pirámides alimenticias para alérgicos a huevo y APLV, adaptadas a cada uno de ellos, así como una pirámide conjunta a ambas alergias. Además se incluyeron recomendaciones basicas para la alimentación saludable en general y, en particular, con interés especial para el colectivo (higiene alimentaria, aditivos alimentarios, productos de cosmética, medicamentos, etc).**

Conclusiones: **Debido a la importancia que la nutrición adquiere en la infancia y las dificultades subyacentes a este colectivo, poder planificar adecuadamente la alimentación es muy importante pues puede prevenir accidentes y carencias nutricionales a largo plazo. Por ello, facilitar herramientas gráficas y prácticas para este fin, es de gran importancia comunitaria y medico-científico, y es el resultado de este trabajo.**

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Palabras clave: *Pirámide para alergias alimentarias. Alergia a huevo. Alergia a leche. Alergia alimentaria.*

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TOOL OF NUTRITION EDUCATION FOR ALLERGIC TO EGG AND COW'S MILK PROTEIN IN PEDIATRIC AGE®

Abstract

I*ntroduction:* Food allergy affects a large part of the population and their numbers are increasing. Although the knowing of this pathology is growing, allergic patients have really difficulties to lead a normal life, especially with food. Until now,this group hadn t practical tools that would help them in the development of a balanced daily diet, as there are for the general population in the form of pyramids and dietary guidelines . This work has covered this need for two of the most prevalent allergies in early life.

Aims: **gather information on the allergy of cow's milk protein and egg, to design a food pyramid for these patients, based on the consensus, recommendations and scientific guidance.**

Results: **After confirming the absence of a similar work, food pyramids allergy to egg and cow's milk protein, adapted to each, and a joint pyramid is designed to both allergies. Besides basic recommendations for healthy eating were included in general and in particular individuals, with special interest for the collective (food hygiene, food additives, cosmetics, medicines, etc).**

Conclusions: **Due to the importance of nutrition in childhood and acquires the underlying difficulties this group, to properly plan the diet is very important as it can prevent accidents and long-term nutritional deficiencies. Therefore provide graphical tools and practices to this goal, is importance for population and medical and scientific community, and is the result of this work.**

(*Nutr Hosp.* 2014;29:1062-1069)

DOI:10.3305/nh.2014.29.5.7215

Key words: *Pyramid of food allergies. Egg allergy. Milk allergy. Food allergy.*

Abreviaturas

AA: Alergia a alimentos.
APLV: Alergia a proteina de leche de vaca.
IgE: Inmunoglobulina E
RDA: Recomendación diaria recomendada.

Introducción

Alergia a alimentos es una respuesta anormal tras la ingesta de un alérgeno de un alimento, donde existe un mecanismo inmunológico comprobado, conduciendo a la aparición de efectos nocivos e indeseados. Siendo el principal mecanismo, una respuesta en la producción de inmunoglobulina E (IgE). Según la Organización Mundial de la Alergia, la alergia alimentaria afecta al 6-8% de los niños menores de 3 años y entre el 2 y el 3% de la población general. En España, hay que destacar el aumento de prevalencia de las enfermedades alérgicas en los últimos años. En concreto se ha duplicado en poco más de un decenio, y ha pasado de una prevalencia del 3,6% en 1992 al 7,4% en 2005[1]. Pese a la mejora de las técnicas diagnósticas, cada vez con mayor aproximación molecular; el avance en los abordajes terapéuticos como la inmunuterapia o mayor conocimiento de los factores influyentes en la aparición de esta patología (contaminantes ambientales, alimentación, programación nutricional, predisposición genética, etc), no consiguen establecer recomendaciones prácticas en el día a día para el colectivo. Mientras afloran estudios y opiniones al respecto, el colectivo sigue preocupado y sin herramientas prácticas que les ayuden en la elaboración diaria de una dieta equilibrada, como existen disponibles para la población general en forma de pirámides y guías alimentarias[2-5]. Con este trabajo queremos cubrir esta necesidad para las dos alergias más prevalentes en niños con una edad comprendida entre uno y cinco años de edad: alergia a proteina de leche de vaca, personas que producen IgE específica frente a las proteinas de la leche tras su ingesta, contacto, o en menor medida inhalación; y alergia a proteina de huevo de gallina, personas que sufren la misma alteración que en el caso anterior, pero con los huevos en lugar de la leche. Además de la reacción inmunológica, las alergias alimentarias pueden causar diversos síntomas que cursan con una pequeña rojez o picor o con shock anafiláctico en su versión más grave. Estos pueden aparecer inmediatamente, normalmente entre los primeros minutos y las dos horas tras la ingesta de los alergenos que continen los alimentos o bien de forma tardía. La prevalencia de la APLV en países desarrollados se situa en un 2-3 % en niños menores de 1 año, que suele remitir a partir de los 3 años, y mayoritariamemte a los 5 años[6]. La alergia al huevo se situa entre 0,5-2,7 en niños mayores de 12 meses, siendo poco habitual la aparción a partir de los 2 años. La evolución y tolerancia de la misma va desde el 20 % a los 24 meses hasta el 60-75 % a los 9 años. Además esta última alergia representa el 44 % de las consultas de alergia alimentaria en menores de 5 años[7].

Objetivos

Recopilar información de las principales características de la alimentación de pacientes con alergia a proteína a leche de vaca y huevo, así como las guías y pirámides alimenticias. Además de tener en cuenta sus implicaciones y restricciones nutricionales, para determinar alimentos de sustitución que cubran, en cada caso, las Recomendación diaria recomendada (RDA) de forma segura.

Diseño de una pirámide alimenticia para APLV, alérgicos a huevo, APLV y huevo conjuntamente para niños de 1 a 5 años de edad.

Material y métodos

Al inicio del proyecto se comprobó la inexistencia de un trabajo similar. Para ello, se revisaron distintas bases de datos científicas (PubMed, Elsevier, Excelenciaclinica.net, Scielo, Scirus, ScienceDirect). La estrategia de búsqueda en Pubmed fue: “food allergy pyramid”, “pyramid of food allergy”, “food allergy” AND “pyramid” con cero resultados. Para el resto de bases de datos se siguió la misma estrategia de búsqueda, pero adaptadas a cada una de ellas, y con el mismo resultado. Se amplió a buscadores no científicos, google y yahoo, obteniendo una coincidencia[8]. Sin embargo, esta se basa en el resultado gráfico de una empresa que comercializa un método diagnóstico no validado científicamente[9], cuya ilustración no persigue un fin educativo y de soporte al colectivo en materia de nutrición y/o salud, por lo que se descartó. Se consultaron varias guías clínicas[2,3,11], otras pirámides de los alimentos[4,5,10] y artículos científicos[1,6,7] que recopilan información de cada una de las alergias. Se usaron las Tablas de Composición de CESNID[12], para verificar la composición de alimentos, la sustitución de alimentos con el mismo valor nutricional o similar, teniendo en cuenta una calibración de una semana. Teniendo especial atención a las proteínas totales y al valor biológico de las mismas. Se usaron las recomendaciones de frecuencia de consumo y raciones estándar de distintas guías, teniendo en cuenta las edades a las que dirigimos el presente estudio, para la distribución y frecuencia de consumo[3,4].

Resultados

Se diseñaron ilustraciones de pirámides alimenticias para alérgicos a huevo (fig. 1) y APLV (fig. 2), adaptadas a cada colectivo, así como una pirámide conjunta a ambas alergias (fig. 3). Además se incluyeron recomendaciones generales para la alimentación saludable, así como otras que han ido surgiendo con un notable



Fig. 1.—



Fig. 2.—

grado de importancia, como comer en familia o reducir el sedentarismo (fig. 4). De forma más específica se han incluido ciertas recomendaciones para el colectivo de alérgicos a alimentos: higiene alimentaria, aditivos alimentarios, productos de cosmética, medicamentos, etc. (fig. 5).

Discusión

Para la equiparación nutricional se utilizaron las tablas de composición de CESNID[12]. Tanto en la pirámide de APLV, como en la de huevo y en la conjunta, no se tuvieron en cuenta los posibles aportes de proteinas



Fig. 3.—

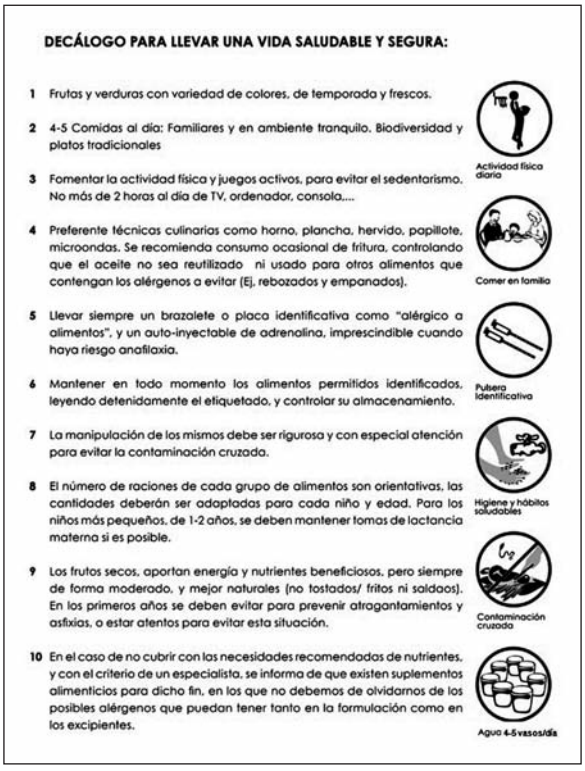


Fig. 4.—

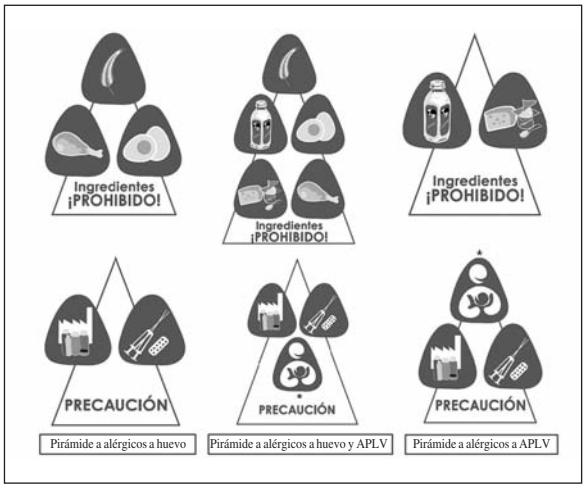


Fig. 5.—

o micronutrientes de los productos restringidos o de consumo ocasional, a parte de los huevos o leche, como son la bollería industrial, chucherias, etc ya que su consumo tanto en personas alérgicas como no alérgicas, se debería reducir al máximo.

La herramienta debe ser: intuitiva, lógica y fácil de entender, sin la necesidad de un manual, y debe ser dirigida a los niños mayores de 6 años de edad y siempre adaptadas[5]. Por lo tanto, nuestra pirámide esta dirigida a los padres, familiares, tutores y profesores de estos niños.

A continuación se describe el porqué se han incluido algunos símbolos y alimentos en estas condiciones concretas, empezando por las bases de las pirámides ("decálogo para llevar una vida saludable y segura"), subiendo en cada peldaño. Para ello se tuvieron en

cuenta las recomendaciones de otras tablas y guías[2,5], como frutas y verduras con variedad de colores; Productos de temporada y frescos; Biodiversidad y platos tradicionales; Comidas familiares, en ambiente tranquilo; Actividad física; Es preferible el uso de técnicas culinarias como horno, plancha, hervido, papillote, microondas, que frito, rebozado, guisos, etc; además se introdujeron elementos nuevos para el colectivo al que se dirige en concreto, como "evitar la contaminación cruzada y mantener buena manipulación e higiene de los alimentos" e "identificación con una pulsera". Sin embargo, en general, se tuvo atención a que los niños y adolescentes tienen necesidades nutricionales específicas y un plan diario de actividades diferentes a los adultos[5]. Aunque algunos estudios relacionan una buena higiene con la salud en general[13], en este colectivo adquiere un papel fundamental y de gran importancia tanto la correcta manipulación de alimentos, como la de evitar la contaminación cruzada. Con respecto a la hidratación, hay pocos datos publicados en la literatura sobre el agua y la ingesta de bebidas en los jóvenes[14]. Se estima apropiado unos 0,9 y 1,2 litros/día en forma de bebida para niños de 1-3 años y de 4-8 años respectivamente[15,16], por lo que se ha recomendado la ingesta de 1 litro de media, correspondiente a 4-5 vasos de agua. Se han incluido una recomendación de 4-5 comidas al día, por la existencia de evidencia científica que apoya este hecho para la salud global del individuo, y que además estas sean en un ambiente relajado y apropiado[5]. El número de raciones de cada grupo de alimentos son orientativas, las cantidades deberán ser adaptadas para cada niño y edad. Para los niños más pequeños, de 1-2 años, se deben mantener tomas de lactancia materna si es posible. Con respecto al ejercicio físico, la mayoría de los expertos están de acuerdo en la reducción de las conductas sedentarias (TV, computadora) a menos de 2 horas por día)[17,18]. Ya que son muchos los estudios que asocian el beneficio de la práctica diaria de actividad física con la salud cardiovascular, menor prevalencia de enfermedades, mejores hábitos de vida en niños, etc, y por ello se ha incluido[19,20].

En cuanto a la estacionalidad de los productos frescos, ha sido un punto importante, recomendando preferencia por los de temporada, frescos y mínimamente alimentos procesados. Estos pueden, en la mayoría de los casos, maximizar el contenido de nutrientes de la dieta. Además de aquellos que respondan a "tradicionales, locales, ecológicos y de biodiversidad" que enriquecerán unas buenas prácticas locales, respetuosas con el medio ambiente y sostenibles a largo plazo[5]. Además, en este decálogo se advierte de que en el caso de no cumplir con las necesidades recomendadas de nutrientes, y con el criterio de un especialista, existen suplementos alimenticios para dicho fin, en los que no deben de olvidar los posibles alérgenos que puedan tener tanto en la formulación como en los excipientes.

Semillas, granos y derivados que nos aportarán hidratos de carbono principalmente y base de todas las pirámides alimentarias. Preferiblemente de grano entero, ya que normalmente se eliminan en el procesado, fibras y algunos valiosos nutrientes (Mg, Fe, vitaminas, etc.)[21]. Su consumo debe ser diario, 3-5 raciones al día. Verduras y hortalizas: dos o más porciones por día. Para asegurarse el correcto aporte de vitaminas y minerales, en esta ingesta diaria, por lo menos una de las porciones, debe consumirse en crudo (una comidas/día)[22]. Las frutas deben suponer al menos 2 raciones al día, para ayudar a la ingesta de vitaminas, minerales y de fibra. Por ello será recomendable su ingesta, después de estar bien lavada, y preferiblemente entera frente a zumo natural, ya que parte de la fibra y de las vitaminas se verían eliminadas por el procesado[2]. Más allá del aporte en nutrientes esenciales, el consumo diario de frutas y verduras está directamente relacionado con una incidencia menor de algunos cánceres, enfermedad cardiovascular, enfermedades inflamatorias e inmunológicas y estreñimiento[23-27]. Se sugiere un consumo de aceite de oliva virgen extra de 3-5 raciones al día, debido a su asociación inversa con algunos tipos de cáncer[28,29], la salud cardiovascular[30,31] y del estrés oxidativo[32,33]. Además de los anteriores, los frutos secos son buena fuente de ácidos grasos insaturados, proteínas, vitaminas, minerales y fibra[34]. Aportan energía y nutrientes beneficiosos, por lo que se recomienda un consumo moderado, y mejor naturales (no tostados/fritos/ni salados). Además en los primeros años se deben evitar para prevenir atragantamientos y asfixias, o estar atentos para evitar esta situación. En cuanto a alimentos protéicos para cubrir la demanda de la privación de cada uno de los grupos de alimentos en cada una de las pirámides, tenemos varias opciones para cubrir este macronutriente de forma conjunta al aporte de las proteinas aportadas por el resto de grupos ya mencionados anteriormente. La combinación de las leguminosas y los cereales es una proteína, puede ser considerada como una alternativa a la carne, puesto que los aminoácidos limitantes en los cereales se complementarán con los de las legumbres. Por lo que será una buena forma de presentar proteína, y su recomendación esta algo incrementada con respeto a lo habitual[2]. Pescados grasos o no grasos, mariscos, carnes blancas y carnes magras, por ser una buena fuente de proteína tanto cuantitatívamente como cualitatívamente, sin altos niveles de grasa saturada como otras fuentes serán recomendados con un reparto semanal algo superior al habitual, que combinando las diferentes posibilidades nos otorga un consumo diario de algunos de ellos. Además, los pescados grasos por su contenido en ácidos grasos insaturados de cadena larga, los hacen idoneos como elección. La carne roja no se limita dramáticamente, suponiendo un encaje con el resto de carnes, y debe ser consumida con más frecuencia en niños y adolescentes, que en adultos[5]. Lo que supone un aumento de la proteína y minerales claves, como el hierro. Se ha descartado el incremento de "carne grasa" como una posibilidad de incremento proteico, una diferencia con respecto a algunos autores que aceptan hasta 2 raciones a la semana de estas carnes grasas o embutidos, etc[4], donde en nuestra recomendación pasarán a una ingesta ocasional o nula.

"Ingredientes prohibidos" y "precaución"

Se han añadido 2 tipos de nomenclaturas e imágenes acompañando a cada pirámide, con los nombres "ingredientes prohibidos" y "precaución" (fig. 5). El primero hace referencia a compuestos presentes en productos manufacturados o como ingredientes en platos de la alimentación de este colectivo. Por su relación directa en la reacción inmunológica en personas alérgicas a leche, huevo o leche y huevo, respectivamente, deben ser evitados en todo momento con la mayor rigurosidad. Es habitual, que algunas personas alérgicas a estos compuestos, tengan cierta adaptación o tolerancia a alguno de los alérgenos en particular o a los que se engloban en reacción-cruzada. En tales casos, siempre bajo el criterio de un profesional, podrá ser introducido dicho alimento propuesto como excluido, aunque la recomendación inicial, como medida de seguridad, será la de retirar estos compuestos de la dieta por completo. Por lo tanto, conjuntamente a estas figuras, se acompañan el siguiente texto:

Prohibido: Pirámide para alergia a huevo

Ni carne, ni huevos de ninguna ave (por la similitud de sus proteínas, puede producir igualmente reacción alérgica). Evite cualquier contacto con el plumaje de aves ponedoras.

Globulina, livetina, albúmina, ovoalbúlmina, ovomucina, ovomucoide, ovoavitelina, vitelina, lecitina (de origen diferente a soja, E-322), lisozima (E-1105), coagulante, emulsificante, conalbúmina, avidina, ovoinhibidor, flavoproteinas, catalasas, apolivetinas, alfa (α)-livetinas, ovomacroglobulina, apriteleninas, fosvitina, E-161b (luteina, pigmento amarillo).

Prohibido: Pirámide para alergia a proteína de leche de vaca

Ningún tipo de lácteo o derivado de vaca, cabra u oveja, ya que por la similitud de sus proteínas, puede producir igualmente reacción alérgica (leche, yogur, cabra, nata, helado ….), Caseinas ((α)alfacaseina, (β)betacaseina, kappacaseina), (α)alfalactoglobulina, (β)betalactoglobulina, seroalbúmina, seroalbúmina bovina, inmunoglobulinas bovinas, lactoferrina, transferrina. Aditivos E-325, E-326, E-327, E-472, E478, E-480, E-481, E482, E-575, E-585, E-966, H-4511,H-4512, H-4513. Ingredientes o aditivos como: láctico, lactato, lactilato, lactona, lactiol.

El segundo tipo de nomenclatura e imagen de acompañamiento a las pirámides, es "Precaución". En este caso, hace referencia a situaciones de evitación, es decir, productos o situaciones especiales que frecuentemente pueden poner en riesgo a personas con alergia alimentaria.

Precaución: Pirámide para alergia a huevo

Lea detenidamente las etiquetas de los productos manufacturados, cosmética, material escolar, medicamentos y vacunas. Productos a granel y sin envase. Caramelos, espesantes, pastas, bollería, salsas, carne, etc, pueden contener estos componentes.

Precaución: Pirámide para alergia a proteína de leche de vaca

En niños lactantes que muestren síntomas al tomar la leche de la madre, esta deberá eliminar las proteínas de leche de vaca de su dieta. Lea detenidamente las etiquetas de los productos manufacturados, cosmética, material escolar, medicamentos y vacunas. Productos a granel y sin envase. Caramelos, espesantes, pastas, bollería, embutidos, salsas, carne, etc, pueden contener estos componentes.

En la pirámide para ambas alergias se ha combinado la nomenclatura y la leyenda de cada una de ellas.

Este apoyo visual y de recomendaciones están sin duda enfocados a la parte de seguridad, suponiendo un aporte innovador con respecto a otras guías y pirámides existentes hasta el momento, ya que no suponía una necesidad a cubrir. Para llegar a él, se tuvieron en cuenta distintas recomendaciones y estudios. Resulta un aspecto importante la vigilancia en productos manufacturados y procesados, vendidos al consumidor como envasados o no. En todos estos productos es crucial que la persona encargada de realizar la compra atienda a los ingredientes sugeridos en cada una de las pirámides[35-37].

En APLV excluir también leche de cabra, búfala oveja, ya que por la similitud de sus proteínas, puede producir igualmente reacción alérgica, así como yogures, quesos, o productos lácteos derivados de ellos. Se informa además de que algunos cosméticos y medicamentos pueden contener alguno de los compuestos que se sugiere eliminar y vigilar, expuestos anteriormente[38]. Aunque no hay evidencia de la supuesta relación entre el consumo de leche por la madre, durante el periodo de lactancia[6], no obstante se requieren más estudios para verificar dicha relación, ya que hay estudios que apuntan a ello[39], además de tener reportes clínicos en esta línea. Por ello se sugiere, como "precaución", que en "*en niños lactantes que muestren síntomas al tomar la leche de la madre, esta deberá eliminar las proteínas de leche de vaca de su dieta"*, siempre supervisado por un profesional.

En alérgicos a huevo, se deben evitar todas las formas de presentación posibles, crudo, yema, clara, cocinado. Además se deben evitar los huevos de otras aves: pavo, pato, gaviota, codorniz; La α-livetina o albúmina sérica está presente en plumas, carne y huevo de aves (gallina, pato, pavo, gaviota, codorniz), explica la aparición del síndrome ave-huevo, en el que el paciente presenta síntomas de alergia al inhalar partículas de plumas o comer huevo y carne de aves. Por ello sugerimos precaución

con el plumaje y con la ingesta de carne de aves, la cual puede ser evaluada y supervisada por un profesional. Algunas vacunas como la triple vírica, la antigripal, la fiebre amarilla y algunas presentaciones de la hepatitis A, que han sido cultivadas en embriones de pollo pueden arrastrar pequeñas cantidades de la proteinas de huevo. Su seguridad ha sido estudiada y publicada, y se concluye con el beneficio frente al riesgo. No obstante, en aquellos pacientes anafilacticos, es recomendable que el médico determine en cada caso la mejor opción, personalizada al historial clínico del paciente. También algunos preparados vitamínicos, medicamentos o inhaladores contienen lisozima de huevo[7]. Y algunos medicamentos por la presencia de lisozima[7].

Con respecto a la parte nutricional en la APLV, al ser la leche el primer alimento no homólogo que se introduce en la dieta de un lactante, es la APLV la primera alergia que debuta. Incluir alimentos que sean fuente de proteínas similares a las eliminadas de la dieta (de alto valor biológico), así como nutrientes esenciales, como el calcio, clave en estas edades, es el objetivo principal de esta pirámide. Para compensar las 2-4 raciones de lácteos/día, se calculó la pérdida en nutrientes que estos aportan, tomando una media de 3 raciones/día. Estos nos aportan 18 g de proteínas aproximadamente/día (media de 2 raciones de leche semidesnatada (400 ml) y una de yogur natural (125 g)). En total suponen unos 126 g de proteina a la semana. Estas proteínas se sustituyeron, ampliando las raciones de productos proteicos. Para compensar estas proteínas se sugiere ampliar, tal y como indicamos en la pirámide, con 1 ración más de pescado/semana (150 g de atún = 32,8 g); 1 ración más de legumbre/semana (70 g de lentejas = 16,9 g); 1 ración más de carne magra/semana (125 g de pechuga de pollo = 27,72 g), 1 ración más de huevos/semana (60 g huevo = 7,62 g), 1 ración más de bebida de vegetales/día (200 ml de bebida de soja = 6,2 g/día). La suma de los gramos de proteinas de estos alimentos supone un total a la semana de 127 g de proteinas. Por lo que cubrimos perfectamente las proteinas excluidas por el grupo de lácteos. Otras posibilidades de bebidas sustitutivas de leche, siempre que cumpliesen con la inexistencia en su lista de ingredientes tipificados en este trabajo como "prohibidos", serían: bebidas vegetales de almendra, arroz, soja, quinoa, etc; fórmulas hidrolizadas y fórmulas elementales, siempre bajo el consejo profesional.

Con respecto a la parte nutricional en la pirámide del huevo, resulta menos complicado cubrir los requerimientos excluidos, sin embargo, al ser la causa mas frecuente de alergia alimentaria en niños, surge una necesidad real. Para compensar las 2-4 raciones de huevos, se calculó la pérdida en nutrientes que estos aportan, tomando una media de 3 huevos/semana. Estos nos aportan 23 g de proteínas aproximádamente (3 huevos tamaño M). Estas proteínas se sustituyeron, ampliando las raciones de productos protéicos. Con los mismos ejemplos propuestos anteriormente para el cálculo, este nutriente se cubriría con 1 ración mas de pescado (32,8 g) y 1 ración más de legumbre (16,9 g) o carne magra de cerdo (22,5 g), para asegurar la misma cantidad de proteína, y el resto de nutrientes de interés: especialmente vitaminas y minerales.

Con respecto a la parte nutricional en la pirámide del huevo y APLV de forma conjunta, se siguió la misma pauta que con las dos anteriores por separado, pero en este caso, eliminando la ración de huevos, y cambiando las carnes de aves por otras carnes magras, cuya variación en proteinas no es significativa. Así, se propone un aumento en 1 ración más de legumbres/semana, 1 más de marisco y subir 1 más las raciones/día de bebidas vegetales, sustitutivas o fórmulas. Además se propone completar con frutos secos, semillas, algas, para asegurar la misma cantidad de proteína, y el resto de nutrientes de interés: especialmente vitaminas (vit. D) y minerales (calcio).

Conclusión

Debido a la importancia que la nutrición adquiere en la infancia y las dificultades subyacentes al colectivo de alérgicos a los alimentos, poder planificar adecuadamente la alimentación es muy importante, pues se puede prevenir accidentes y carencias nutricionales a largo plazo. Por ello, facilitar herramientas gráficas y prácticas para este fin, es de gran importancia comunitaria y medico-científico.

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Original / *Síndrome metabólico*

Women with metabolic syndrome improve antrophometric and biochemical parameters with green banana flour consumption

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Abstract

Background: **Consumption of green banana flour (GBF) may promote health benefits, such as, decreased appetite, weight loss, glycemic control, intestinal function and lipid profile improvement, aging delay, cancer and heart disease prevention. The aim of this study was to evaluate the effects of green banana flour consumption on anthropometric and biochemical parameters in overweight women.**

Methods: **The glycemic index of flour in the study was determined. The effects of consumption of 20 g of green banana flour/day on weight, body mass index (BMI), blood pressure, waist and hip circumference, body composition, hemoglobin, lipid profile, glucose, insulin, insulin resistance, liver function and energy intake were evaluated in 25 overweight women for 45 days.**

Results: **The glycemic index of the flour under study was classified as low. Reduction ($p < 0.05$) in systolic blood pressure, hip circumference and fasting glucose levels were found in women who had metabolic syndrome criteria.**

Conclusions: **Consumption of green banana flour (20 g/day) for 45 days did not promote weight loss or changes in body composition in overweight women. It was noted, however, decreased hip circumference. Significant health parameter improvements were also noted in individuals with metabolic syndrome, which showed a reduction in systolic blood pressure and fasting glucose.**

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Key words: *Musa. Flour. Body composition. Glycemic index. Metabolic syndrome X.*

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LAS MUJERES CON SÍNDROME METABÓLICO MEJORAN LOS PARÁMETROS ANTROPOMÉTRICOS Y BIOQUÍMICOS CON EL CONSUMO DE "GREEN BANANA FLOUR"

Resumen

Introducción: **El consumo de "green banana flour" (GBF) puede contribuir para la salud como, por ejemplo, aumento em las sensaciones de saciedad , pérdida de peso , control de la glucemia y mejora de la función intestinal y el perfil lipídico, retraso del envejecimiento y la prevención de el cáncer y de las enfermedades del corazón. El objetivo del estudio fue evaluar los efectos del consumo de GBF sobre el parámetros antropométricos y bioquímicos de las mujeres con exceso de peso.**

Métodos: **Se determinó el índice glucémico de la harina en el estudio. Los efectos del consumo diario de 20 g de GBF en peso, índice de masa corporal (IMC), presión arterial, circunferencia de la cintura y de la cadera, la composición corporal, los niveles de hemoglobina, glucosa e insulina, resistencia insulínica, en la función del hígado y la ingesta alimentaria se evaluaron en 25 mujeres con exceso de peso durante 45 días.**

Resultados: **El índice glucémico de harina estudiada fue clasificada como bajo. Fue encontrado reducción ($p < 0,05$) en la presión arterial sistólica, en la circunferencia de la cadera y en la glicemia en mujeres que tenían los criterios de síndrome X metabólico.**

Conclusiones: **El consumo de harina de plátano sin madurar durante 45 días no promueven la pérdida de peso o los cambios en la composición corporal en mujeres con sobrepeso. Sin embargo, hubo una reducción de la circunferencia de la cadera. Se observó también una mejoría significativa en importantes factores de salud en mujeres con síndrome X metabólico, tales como una reducción en la presión arterial sistólica y de la glucemia.**

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Palabras clave: *Musa. Harina. Composición corporal. Índice glucémico. Síndrome X metabólico.*

Abbreviations

AC: Abdominal circumference.
AU: Uric acid.
AUC: Area under the curve .
BF%: Body fat percentage.
BMI: Body Mass Index.
BMR: Basal metabolic rate.
BP: Blood pressure.
C3: C3 complement.
CP: Ceruloplasmin.
DBP: Diastolic blood pressure.
DEXA: Dual Energy X-Ray Absorptiometry.
EBI: Electrical bioimpedance.
GBF: Green banana flour.
GI: Glycemic index.
GOT: Glutamic oxaloacetic transaminase.
GPT: Glutamic-pyrovate transaminase .
Hb: Hemoglobin.
HC: Hip circumference.
HDL: High density lipoprotein.
HOMA-IR: Homeostasis Model Assessment of Insulin Resistance Index.
IDF: International Diabetes Federation.
IMI: Initial metabolism index.
IPAQ: International Physical Activity Questionnaire.
kg: Kilograms.
LDLc: Low density lipoprotein-cholesterol.
LM: Lean mass.
m: Meters.
Max: Maximum.
MG: Minas Gerais.
Min: Minimum.
MS: Metabolic Syndrome.
NCEP-ATP III: Third Report of the National Cholesterol Education Program.
QUICKI: Quantitative Sensitivity Check Index.
RS: Resistant starch .
SBP: Systolic blood pressure.
SD: Standard deviation.
T: Time.
TAG: Triacylglycerol.
TC: Total cholesterol.
TFEQ: Three Factor Eating Questionnaire.
TP: Total protein.
UFV: Federal University of Viçosa.
VAS: Visual Analog Scale.
WHR: Waist-hip ratio.

Introduction

Food consumption in the form of bran and powders is widely spread in the media as complementary foods able to promote health benefits, like the green banana flour (GBF). Some of the possible effects are appetite reduction, weight loss, glycemia control, intestinal function and lipid profile improvement, aging delay, cancer and heart disease prevention.

The GBF gained space in the market for being a promising new weight loss treatment. According to studies, the GBF can be used in preparations like cookies[1], juices[2], cakes[3] and cereal bars[4]. When added to preparations, the GBF enhances fiber, protein, potassium, iron, magnesium, calcium, phosphorous and sodium levels, besides increasing product yield[5]. The supposed nutritional benefits attributed to the use of the GBF are associated to elevated total starch level (73.45%), resistant starch (RS) (17.5%) and fiber content (nearly 14.5 %)[6].

RS presents important physiologic effects in the prevention of intestinal constipation, diverticulitis and hemorrhoids, besides helping in the excretion of toxic compounds considered carcinogenic. It has also been associated to the control of some Metabolic Syndrome (MS) parameters, such as glycemia, LDLc (low density lipoprotein-cholesterol) cholesterol and triglycerides. RS is not digested in the small intestine, thus, it can serve as substrate for microorganisms growth, acting as potential prebiotic agent[7]. In healthy individuals, the consumption of RS was directly associated with lower caloric ingestion[8].

Considering the necessity of evidencing the effects of GBF on health and the real impacts of its consumption, the purpose of this study was to investigate the implications of the consumption of GBF on food ingestion, weight loss, body composition and biochemical profile of overweight adult women exhibiting or not MS.

Materials and Methods

Subjects

This is an intervention study, in which 40 overweight women aged 20 to 45 years were recruited by the media (fig. 1). The adopted exclusion criteria were the presence of allergy/intolerance to test foods (reported before or during the study), level of physical activity classified as active or very active according to the International Physical Activity Questionnaire (IPAQ), restrictive food behavior, according to the Three Factor Eating Questionnaire (TFEQ), use of medication (except oral contraceptives), tobaccoism, metabolic-chronic diseases, (diabetes mellitus, systemic arterial hypertension, hypothyroidism). Sample calculation was carried out considering an expected loss of 2.5 kg body weight[9,10] and 90% statistical power, resulting in 23 volunteers.

MS diagnosis was carried out in accordance with criteria of International Diabetes Federation (IDF)[11], which has as compulsory component the waist circumference higher than 80 cm associated to two or more of the following criteria: plasmatic glucose ≥ 100 mg/dL, triglycerides ≥ 150 mg/dL, high density lipoprotein (HDL) < 50 mg/dL, systolic blood pressure ≥ 130 mmHg or diastolic ≥ 85 mmHg.

The study was approved and conducted according to the Ethics Committee in Human Research of the Fede-

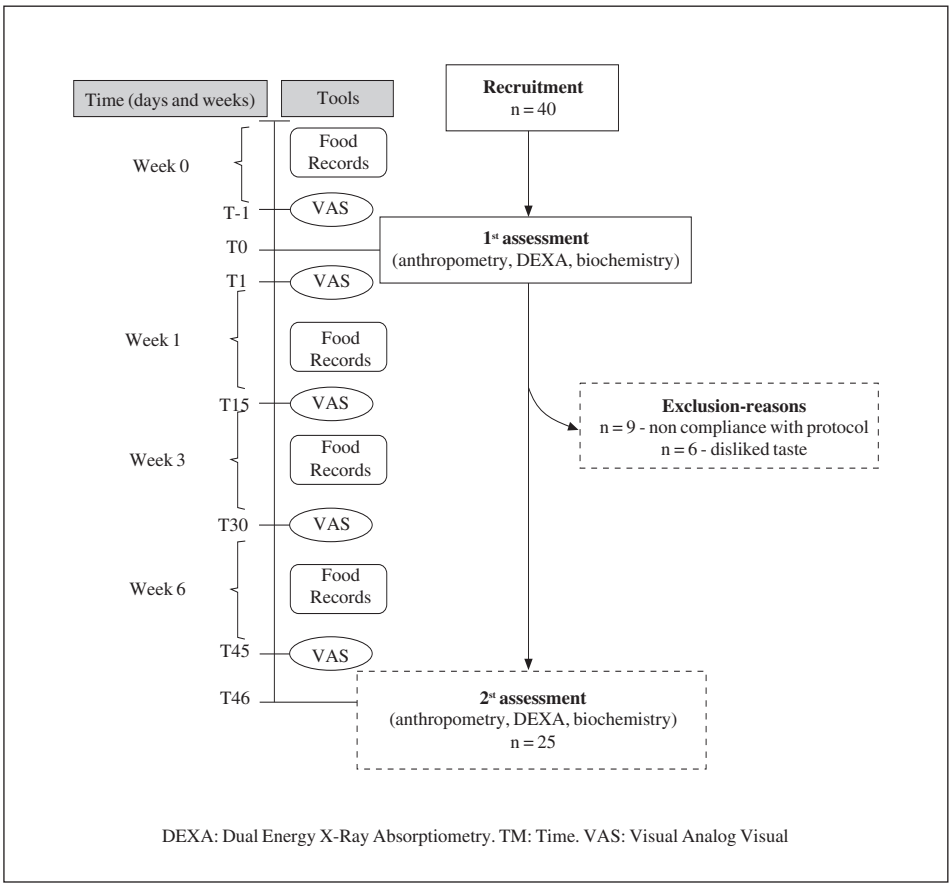


Fig. 1.—Study flow chart. Viçosa (MG, Brazil), 2012.

ral University of Viçosa (process number 147/2011-UFV, MG, Brazil) and participants signed a free and informed consent form.

Consumption of Green Banana Flour

The GBF consumed by participants was obtained in the local market. The portions were distributed weekly in individual plastic bags containing 20 g, identified with the participant name and date for consumption. Participants were instructed to consume the portion of GBF for breakfast, with milk, yogurt, milkshake or fruit juice.

Evaluation of Physical Activity Level

The level of physical activity was quantified by the IPAQ, short version proposed by the World Health Organization, validated for the Brazilian population, according to Matsudo et al.[12]. Volunteers were asked to keep their physical activity habits during the experimental period.

Evaluation of Food Behavior

The food behavior of volunteers was evaluated by application of the TFEQ, before the beginning of the study. This questionnaire analyzed three food behavior aspects: (i) cognitive restriction scale, which verifies food prohibition to influence weight or body shape; (ii) emotional food scale, which measures the tendency to eat exaggeratedly in reply to negative emotional status, like solitude, anxiety and depression; (iii) uncontrolled eating scale, which verifies the tendency to lose control in presence of hunger or external stimuli. For food restriction, level ≤ 14 was adopted as inclusion criterion. This cut point was adopted aiming to exclude volunteers with very restrictive food behavior, which might influence test food consumption[13].

Anthropometry

The anthropometric evaluation was carried out before and after 45 days of intervention with GBF (fig. 1). The body mass in kilograms (kg) was obtained in a digital electronic scale (Tanita®) with 150 kg capacity and 50 g accuracy. Height was registered in meters (m) and obtained using a vertical anthropometer, according to recommendations of Jellife (1968).

The anthropometric evaluation was carried out by Body Mass Index (BMI) calculation. The abdominal circumference was measured at the umbilical level, using a non-extensible tape measure, with the volunteer standing and after complete exhalation. The hip

circumference was measured at its largest circumference. Body composition measurements were obtained by electrical bioimpedance (Biodinamics, Model 310) and by Dual Energy X-Ray Absorptiometry (DEXA) (Lunar Densiometry - GE®) aided by Encore 2010 software (version 13.3) conducted by a specialized technician. Evaluations were carried out in the morning with fasting participants after 15 minutes of rest.

Blood pressure (BP) measurement

Blood pressure measurement was obtained using stethoscope and column sphygmomanometer device, both calibrated in accordance with the standards established by the Brazilian Society of Cardiology[14] and carried out by a trained professional. Three measurements were carried out, with one minute interval, and the average of the last two considered the blood pressure of the individual. If the diastolic pressure presented differences higher than 4 mmHg, new measurement was carried out until difference lower than this value was obtained.

Biochemical evaluation

Blood collection was carried out at the beginning and end of the experiment (after 45 days of GBF consumption) in individuals with 12 hours fasting at the Health Division of the UFV (MG, Brazil). Determination of plasmatic triglycerides, total cholesterol and fractions and uric acid levels was done by the enzymatic colorimetric method. Blood count was carried out by electrical impedance and total proteins by the biuret method. Glutamic oxaloacetic transaminase (GOT) and glutamic-pyrovate transaminase (GPT) were analyzed by the kinetic method and ceruloplasmin by nefelometry. C3 complement and fasting serum insulin were measured by immunoturbidimetric assay and electrochemiluminescence, respectively. Fasting plasma glucose levels were determined by the glucose-oxidase method. Tests were carried out in the biochemical analyzer Cobas Mira Plus (Roche®).

The Homeostasis Model Assessment of Insulin Resistance Index (HOMA-IR) was calculated according to the formula below[15]. Value higher than 2.5[16] was adopted as criterion for presence of insulin resistance.

$$\text{HOMA-IR} = \frac{\text{fasting plasma glucose (mmol/L)} \times \text{fasting serum insulin (µU/mL)}}{22.5}$$

The Quantitative Sensitivity Check Index (QUICKI) was also used, which values inferior or equal to 0.33 suggest insulin resistance[17]. This value was calculated following the formula below.

$$\text{QUICKI} = \frac{1}{\log(\text{fasting serum insulin}) + \log(\text{fasting plasma glucose})}$$

Dietetic evaluation

Food consumption was evaluated by food registers filled out on alternate days, including one day of the weekend, at the following moments: one week prior to beginning of study, first, third and sixth weeks of GBF consumption (fig. 1). The registers were revised in the presence of volunteers to guarantee higher information precision. The domestic measures of ingested foods were then converted into grams and the caloric ingestion of macro and micronutrients were analyzed using the DietProâ (version 5.0) software.

Evaluation of Subjective Appetite Sensation

For evaluation of subjective appetite sensation a bipolar visual analogy scale (Visual Analog Scale-VAS) with a 0 to 100 mm, non-milimetered scale adapted for the study was used, according to recommendations of Blundell et al.[18]. VAS was prepared with questions that evaluated the different subjective components that lead to food ingestion, such as, hunger, gastric plenitude, satiety, craving for food and salty, sweet and greasy foods.

The volunteers were instructed to fill out scales for five different days according to the study protocol: day prior to beginning of consumption (T-1), first day of consumption (T1), at 15 days (T15), at 30 days (T30) and at last day of consumption (T45) (fig. 1). The volunteers filled out the scales at seven different times: immediately before breakfast, every 30 minutes until two hours after breakfast and immediately before lunch and dinner. The volunteers were reminded, by telephone, to fill out of the scale. The quantification was done by the distance between the marked point by the volunteers and the left end of the line[18].

By means of the trapezoidal method[18] it was possible to calculate the area below the curve produced by each question related to one subjective appetite sensation. Calculation of areas was carried out using the SlideWrite Plus (version 7.0 Demo) software.

Determination of GBF Glycemic Index (GI)

Ten adult volunteers of both sex, mean age of 25.3 years and 24.7% (± 3.8) fat percentage were recruited. Absence of past or familiar history of diabetes or insulin resistance and use of medication that could affect glycemia or the energetic metabolism were considered inclusion criteria. Tests were conducted at the Clinical Analyses Laboratory of UFV (MG, Brazil).

The tested load consisted of 46.3g of GBF (containing 25 g of available carbohydrates) diluted in 250 mL water. The test load was ingested at once by the volunteers. Glucose was chosen as reference food, which portion of 25 g was diluted in 250 mL and ingested for three non-consecutive days. After 10 hours of fast the volun-

teers went to the University Laboratory to ingest the GBF load or glucose. The total portion was ingested 15 minutes after fast glycemia determination (baseline).

Glycemic alterations were evaluated by capillary blood glucose concentrations determination, using Accucheck Active® device, at baseline (immediately before ingestion), 15, 30, 45, 60, 90 and 120 minutes (after beginning of ingestion). By the trapezoidal method the positive area formed below the glycemic response curve was calculated, using Slide Write (7.0 version demo) software. GBF Glycemic Indexes were expressed as mean percentages of glycemic responses obtained after glucose ingestion. GI was determined by arithmetical average of values obtained by ten volunteers and classified ad according to international standards[19].

Statistical analysis

The normality of variables was verified by the Shapiro-Wilk test. The effects of intervention on anthropometric, biochemical parameters and on food ingestion were evaluated by paired *t*-test, for variables with normal distribution, by Wilcoxon test, for variables that presented not normal distribution and by Friedman test for evolution evaluations along the study period. Statistical analyses were carried out in the SPSS *Statistics* 17.0 *software*. Significance level of 5% was adopted.

Results

Sample Characterization

Out of 40 volunteers who began the study, 25 completed the study protocol (fig. 1). Participant's mean age was 34 years, with mean BMI of 27.73 kg/m², being 12 participants classified as sedentary and 13 as moderately active, according to the IPAC. Regarding food behavior, mean scores of 11 were noticed for cognitive restriction, 8.6 for desinhibition and 6 for uncontrolled eating, which is classified as high, low and medium scores, respectively. According to criteria of the *International Diabetes Federation*[11], 68% of evaluated women (n = 17) presented Metabolic Syndrome.

Anthropometry, Body Composition and Biochemical Parameters

GBF consumption did not cause weight or body composition alteration in the evaluated women. It was observed, however, reduction of the hip circumference and consequent increase of the waist-hip ratio (table I).

In the MS group, besides hip circumference reduction and ratio waist-hip increase, reduction of systolic blood pressure was observed (table II). In the group without MS, no anthropometric and body composition parameter presented significant alteration after the intervention period (not presented data).

Regarding the biochemical parameters, MS group presented reduction (p = 0.032) in glucose levels when compared with the group composed by volunteers without MS (table II). No significant alteration was noticed in the levels of GOT, GPT, lipid profile and in the evaluated inflammatory markers (uric acid, C3-complement and ceruloplasmin).

There was no statistically significant difference for HOMA-IR and QUICKI indexes before and after GBF consumption. However, according to the HOMA-IR calculation, seven volunteers presented insulin resistance and according to QUICKI, six volunteers. Difference was also not found for HOMA-IR and QUICKI indexes, before and after consumption of GBF in the group of volunteers with MS.

It can be suggested, thus, that women with metabolic disorders present more significant response to GBF consumption when compared with women that although overweight, still do not meet the MS criteria.

Dietetic intake

Increase in mean fiber consumption was observed comparing the period previous to beginning of study (Week 0 = 12.72 g) with the last intervention week (Week 6 = 14.16 g) (p = 0.03). Although GBF consumption increased diet fiber levels, mean ingestion value did not reach the daily recommendation of 25 g for women aged 19 to 50 years[20].

The caloric ingestion averages of each meal were quantified, to verify whether GBF interfered in the caloric consumption of meals after breakfast, along the day. When comparing Week 0 with Week 1, a significant reduction was observed in the caloric consumption of the afternoon snack (329.51 kcal in Week 0 *vs* 227.47 kcal in Week 1; p = 0.019) However, this effect was not supported along the study.

There was no difference in the total caloric ingestion of each volunteer in the different study moments (Week 0, Week 1, Week 3 and Week 6), indicating that GBF was not able to alter the diet caloric ingestion during 45 days of study.

Nutrients (carbohydrates, proteins, lipids, cholesterol, calcium, iron and sodium) presented higher inter-individual variation as for the mean consumed quantity, with no difference between the different times considered in the study. Low calcium consumption was observed, which remained below the daily recommendation for women aged 19 to 50 years, of 1000 mg[21] in all weeks, even with part of the volunteers having consumed the GBF with milk or yogurt.

Mean consumption of full fatty acids, mono and poly-unsaturated was analyzed in order to verify whether volunteers would compensate the consumption of a weight-reducing food, like the GBF, with in-

Table I
Anthropometric, biochemical and body composition parameters before and after consumption of green banana flour of evaluated volunteers (n = 25). Viçosa, 2013

	Baseline (T_0)		*Final (T_{45})*		
Parameters	*Mean ± SD*	*Median (Min-Max)*	*Mean ± SD*	*Median (Min-Max)*	*p*
Weight (kg)	72.86 ± 6.97	71.70 (59.75-87.10)	72.81 ± 6.75	72.00 (59.25-86.80)	0.851[a]
Height (m)	1.61 ± 0.05	1.62 (1.51-1.71)	1.62 ± 0.05	1.62 (1.51-1.71)	0.273[b]
BMI (kg/m²)	27.72 ± 1.78	27.40 (25.15-31.34)	27.67 ± 1.67	27.47 (25.13-31.15)	0.619[b]
AC (cm)	94.00 ± 7.24	96.00 (77.80-105.00)	94.31 ± 6.66	95.50 (78.00-105.00)	0.408[b]
HC (cm)	107.48 ± 6.47	105.50 (96.50-122.50)	106.41 ± 5.33	105.00 (99.00-121.00)	**0.043**[b]
WHR	0.87 ± 0.05	0.88 (0.74-0.97)	0.88 ± 0.06	0.90 (0.75-1.01)	**0.007**[a]
SBP (mmHg)	111.70 ± 12.74	110.00 (89.00-149.00)	107.52 ± 10.66	109.00 (80.00-125.00)	0.101[a]
DBP (mmHg)	78.00 ± 17.41	77.00 (60.00-149.00)	75.60 ± 9.97	76.00 (60.00-99.00)	0.750[b]
BF% (EBI)	33.54 ± 3.49	34.5 (26.30-38.80)	33.38 ± 3.36	32.8 (27.30-38.80)	0.581[b]
LM (EBI)	48.31 ± 3.90	48.40 (39.10-54.80)	48.36 ± 3.69	48.60 (40.20-54.40)	0.851[a]
BMR (kcal)	1469.48 ± 118.72	1471 (1188.0-1666.0)	1470.48 ± 112.46	1479 (1221.00-1655.00)	0.913[a]
BF% DEXA	40.77 ± 4.98	42.00 (30.90-51.60)	40.84 ± 5.05	41.80 (32.00-49.40)	0.819[a]
LM DEXA	40.31 ± 3.35	41.21 (33.21-46.60)	40.26 ± 2.93	40.93 (33.42-45.38)	0.837[a]
Hb (g/dL)	12.68 ± 1.45	13.0 (7.0-15.0)	12.84 ± 1.34	12.8 (8.0-15.0)	0.339[b]
TC (mg/dL)	175.36 ± 31.85	173.0 (103.0-245.0)	179.46 ± 28.06	180 (119.0-242.0)	0.334[a]
HDLc (mg/dL)	45.16 ± 8.96	44.0 (31.0-68.0)	45.79 ± 10.44	45.0 (32.0-77.0)	0.747[b]
LDLc (mg/dL)	106.93 ± 26.51	109.0 (37.0-164.0)	109.82 ± 26.57	109.8 (39.0-156.0)	0.257[a]
TAG (mg/dL)	116.36 ± 63.37	94.0 (53.0-312.0)	119.28 ± 50.82	110.0 (51.0-239.0)	0.597[b]
GOT (U/L)	21.24 ± 8.19	20.0 (9.0-56.0)	21.08 ± 8.15	19.0 (13.0-55.0)	0.687[b]
GPT (U/L)	15.48 ± 6.61	14.0 (6.0-33.0)	16.12 ± 6.52	14.0 (7.0-34.0)	0.367[b]
Glucose (mg/dL)	88.72 ± 7.64	89.0 (76.0 -101.0)	85.74 ± 7.97	87.0 (73.0-112.0)	0.088[b]
TP (g/dL)	6.71 ± 0.46	6.79 (6.0-7.0)	6.81 ± 0.49	6.8 (6.0-8.0)	0.374[b]
UA (mg/dL)	3.1 ± 0.71	2.9 (2.0-5.0)	3.11 ± 1.07	2.9 (2.0-6.0)	0.831[b]
CP (mg/dL)	36.53 ± 9.32	33.8 (25.0-58.0)	37.31 ± 12.5	34.8 (23.0-73.0)	0.989[b]
C3 (mg/dL)	137.98 ± 17.68	134.7 (99.0-193.0)	134.64 ± 26.18	129.9 (90.0-197.0)	0.397[a]
Insulin (UI/mL)	9.7 ± 5.81	8.9 (4.0-27.0)	10.05 ± 4.57	8.6 (4.0-25.0)	0.590[b]
HOMA-IR	2.14 ± 1.39	1.8 (0.8-6.2)	2.12 ± 0.95	2.2 (0.8-5.0)	0.937[a]
QUICKI	0.35 ± 0.03	0.35 (0.29-0.39)	0.34 ± 0.02	0.34 (0.30-0.39)	0.570[a]

SD: standard deviation; Min: minimum; Max: maximum; BMI: Body mass index; AC: abdominal circumference; HC: hip circumference; WHR: waist-hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; BF%: body fat percentage; EBI: electrical bioimpedance; LM: lean mass (kg); BMR: basal metabolic rate; IMI: initial metabolism index; DEXA: Dual-energy X-ray absorptiometry; Hb: hemoglobina; CL: total cholesterol; HDLc: high density lipoprotein-cholesterol; LDLc: low density lipoprotein-cholesterol; TAG: triacylglycerol; GOT: glutamic oxaloacetic transaminase; GPT: glutamic-pyrovate transaminase; TP: total protein; AU: uric acid; CP: ceruloplasmin; C3: C3 complement. [a]parired t-test. [b]Wincoxon test.

gestion of caloric, fat-rich foods. The consumption of these fatty acids was changed in percentage regarding total caloric consumption, before and at the end of study, and compared with recommendations of Third Report of the National Cholesterol Education Program (NCEP-ATPIII): full fatty acids lower than 7%; monounsaturated fatty acids higher than 20%; and polyunsaturated fatty acids higher than 10%[22]. It was noticed that 100% and 96% of volunteers consumed lower quantity than that recommended by the NCEP-ATPIII for mono and poly-unsaturated fatty acids, respectively, at the two evaluated times (Week 0 and Week 6). The percentage of volunteers who consumed quantities above the recommendations for full fatty acids increased from 60%, at Week 0, to 80% at Week 6. The results demonstrated a possible food compensation attitude by volunteers, with addition of fat-rich foods in the diet and consumption of a weight-reducing food.

Evaluation of Appetite Sensation

The paired analyses between T3 and T1 showed increase in subjective satiety sensation (p = 0.035) and gastric plenitude (p = 0.046) as well as reduction in appetite sensation for salty (p = 0.012), sweet (p = 0.025) and greasy (p = 0.044) foods (fig. 2). In analyses between T1 and T45, only reduction of "desire for salty foods" (p = 0.009) maintained.

The analyses of VAS were repeated, subsequently, excluding results before lunch and dinner, as these were not standardized intervals of time among volunteers, which might interfere in the results. However, significant results were not found. The time intervals between breakfast and lunch and from breakfast to dinner also did not show significant difference along the GBF consumption days.

Table II
Anthropometric, biochemical and body composition parameters before and after green banana flour consumption by volunteers with Metabolic Syndrome (n = 17). Viçosa, 2013

	Baseline (T_0)		*Final (T_{45})*		
Parameters	*Mean ± SD*	*Median (Min-Max)*	*Mean ± SD*	*Median (Min-Max)*	*p*
Weight (kg)	74.44 ± 6.28	72.80 (65.70 - 87.10)	74.17 ± 6.12	73.50 (65.15 - 86.80)	0.398[a]
Height (m)	1.62 ± 0.04	1.62 (1.53 - 1.71)	1.63 ± 0.04	1.62 (1.54 - 1.71)	0.068[b]
BMI (kg/m²)	28.05 ± 1.89	27.77 (25.15- 31.35)	27.92 ± 1.84	27.92 (25.13 - 31.15)	0.124[b]
AC (cm)	96.49 ± 4.64	97.00 (87.00 - 105.00)	96.55 ± 4.24	97.50 (88.00 - 105.00)	0.886[a]
HC (cm)	109.11 ± 5.70	109.00 (102.50 - 122.50)	107.72 ± 4.93	106.50 (101.50 - 121.00)	**0.022**[a]
WHR	0.88 ± 0.04	0.88 (0.792 - 0.966)	0.89 ± 0.04	0.90 (0.82 - 0.975)	**0.031**[a]
SBP (mmHg)	111.68 ± 9.11	110.00 (98.00 - 126.00)	107.05 ± 10.89	109.00 (80.00 - 120.00)	**0.033**[a]
DBP (mmHg)	75.31 ± 9.43	75.50 (60.00 - 92.00)	74.35 ± 8.57	71.00 (60.00 - 90.00)	0.423[a]
BF% (EBI)	33.86 ± 3.49	35.20 (27.40 - 38.80)	33.68 ± 3.46	32.80 (27.30 - 38.80)	0.581[b]
LM (EBI)	49.14 ± 3.50	48.60 (42.600- 54.80)	49.07 ± 3.33	49.00 (40.80 - 54.40)	0.850[a]
BMR (kcal)	1495.17 ± 106.37	1478.00 (1294.00 - 1666.00)	1491.64 ± 101.74	1490.00 (1239.00 - 1655.00)	0.775[a]
BF% DEXA	41.34 ± 4.96	42.00 (34.50 - 51.60)	41.40 ± 4.92	42.20 (34.00 - 49.40)	0.889[a]
LM DEXA	40.80 ± 3.24	40.76 (35.57 - 46.60)	40.76 ± 2.56	40.93 (36.94 - 45.38)	0.931[a]
Hb (g/dL)	12.8 ± 1.08	12.9 (10.1-14.7)	13.08 ± 0.95	12.9 (11.1-14.7)	0.135[a]
TC (mg/dL)	171.76 ± 35.01	161.0 (103. - 245.0)	179.0 ± 32.55	174.0 (119.0-242.0)	0.210[a]
HDLc (mg/dL)	40.82 ± 5.65	41.0 (31.0-52.0)	42.41 ± 6.68	42.0 (32.0-53.0)	0.322[a]
LDLc (mg/dL)	105.11 ± 26.55	103.2 (37.0-145.0)	111.36 ± 28.19	110.4 (39.0-156.0)	0.054[a]
TAG (mg/dL)	128.9 ± 72.53	128.9 (59.0-312.0)	120.2 ± 50.45	120.2 (69.0-239.0)	0.642[b]
GOT (U/L)	20.88 ± 9.72	19.0 (9.0-56.0)	21.479.72	19.0 (13.0-55.0)	0.830[b]
GPT (U/L)	15.65 ± 7.44	14.0 (6.0-33.0)	16.65 ± 7.57	16.0 (7.0-34.0)	0.242[b]
Glucose (mg/dL)	91.29 ± 6.89	93.0 (78.0-101.0)	86.7 ± 8.34	87.0 (76.0-112.0)	**0.032**[b]
TP (g/dL)	6.65 ± 0.44	6.56 (6.02-7.28)	6.77 ± 0.47	6.76 (6.1-7.6)	0.413[a]
UA (mg/dL)	3.04 ± 0.48	2.9 (2.5-4.1)	3.02 ± 0.82	2.9 (1.7-4.6)	0.836[b]
CP (mg/dL)	36.11 ± 8.56	33.8 (25.1-58.3)	37.11 ± 12.92	34.8 (22.7-72.5)	0.925[b]
C3 (mg/dL)	140.05 ± 19.29	138.1 (99.2-192.9)	134.18 ± 24.9	133.4 (89.8-195.3)	0.198[a]
Insulin (UI/mL)	9.51 ± 5.24	9.7 (2.5-25.7)	9.78 ± 2.91	8.6 (5.5-15.1)	0.619[b]
HOMA-IR	2.15 ± 1.28	2.2 (0.8-6.2)	2.1 ± 0.69	2.2 (1.0-3.5)	0.979[b]
QUICKI	0.35 ± 0.03	0.34 (0.29-0.39)	0.34 ± 0.02	0.34 (0.32-0.38)	0.537[b]

SD: standard deviation; Min: minimum; Max: maximum; BMI: Body mass index; AC: abdominal circumference; HC: hip circumference; WHR: waist-hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; BF%: body fat percentage; EBI: electrical bioimpedance; LM: lean mass (kg); BMR: basal metabolic rate; DEXA: Dual-energy X-ray absorptiometry; Hb: hemoglobina; TC: total cholesterol; HDLc: high density lipoprotein-cholesterol; LDLc: low density lipoprotein-cholesterol; TAG: triacylglycerol; GOT: glutamic oxaloacetic transaminase; GPT: glutamic-pyrovate transaminase; TP: total protein; AU: uric acid; CP: ceruloplasmin; C3: C3 complement. [a] t-test paired. [b] Wilcoxon's test.

Determination of Glycemic Index (GI)

The mean area below the glycemic response curve was considerably higher with glucose consumption when compared with the area that represents GBF consumption (fig. 3). Using the proportion between these responses it was determined that the GBF GI is 15.3, being classified as a low GI food (< 55)[19].

Discussion

The present study demonstrated that daily consumption of 20 g of GBF contributed for reduction of the hip circumference and consequent waist/hip ratio increase, reduction of systolic blood pressure and plasma glucose only in MS group. These data could be explained by low GI found in the green banana flour.

It has been demonstrated that food fiber provides important health results and contributes to prevention of several diseases. GI of carbohydrates and fiber consumption are relevant dietetic factors that can influence ponderal control and SM components[23].

Sharma et al.[7], Scholz-Ahrens et al.[24] and Nugent[25] report beneficial properties of fiber RS, such as protective effects against diabetes, colorectal cancer, cardiovascular diseases and obesity, including potential physiologic effects, as glycemic control and insulin response, increase of satiety and reduction of caloric ingestion. However, these RS physiologic properties and, consequently, possible beneficial effect, can widely vary depending on the study design and differences in source, type and quantity of consumed RS[25].

The group of volunteers with MS showed significant reduction (p = 0.032) in glucose levels when compared with the group without MS (table II). A study carried out with diabetic animals or animals receiving high dosage of sucrose showed reduction in serum glucose levels, after being supplemented with native banana RS in different concentrations and forms for four weeks[26],

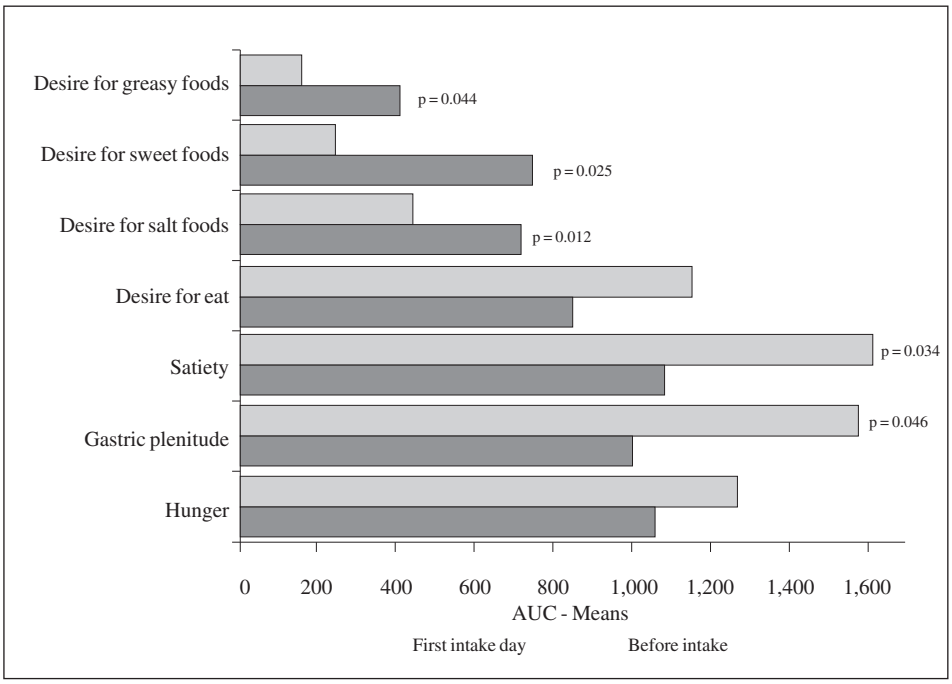


Fig. 2.—Average of area under the curve (AUC) of day before intake and first day of Green Banana Flour intake and sensations evaluated by Visual Analogy Scale (VS), p of pairet t-*test.*

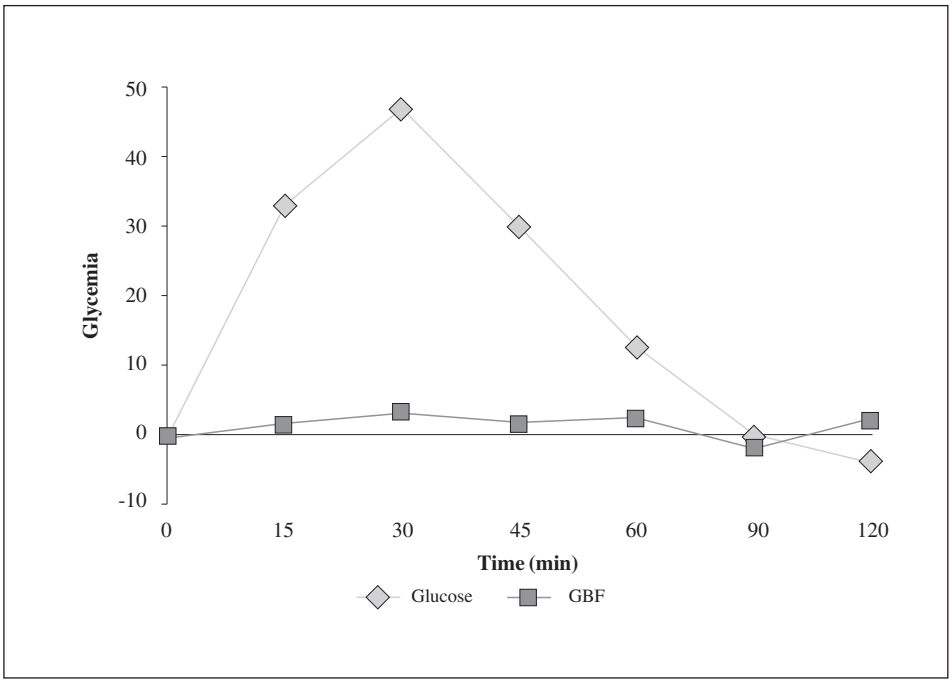


Fig. 3.—Representation of glycemic responses after glucose and green banana flour (GBF) ingestion.

corroborating the results of the present study. Nevertheless, the same group of investigators, using supplementation of 24 g/day of native banana RS for four weeks in obese and type 2 diabetes patients, found significant reduction of body weight and BMI when compared with control groups. However, no significant result was observed fasting glycemia, fat percentage and serum levels of triglycerides, cholesterol, LDL and HDL-cholesterol[27].

Park et al.[28] carried out a study with supplementation of 24g/day RS in healthy individuals with excess weight, observing fast glycemia reduction in individuals when compared with the group control. No alteration was observed in body weight or other anthropometric parameters, serum insulin or C3 complement in the period of 21 days of RS consumption. In our study, GBF addition, which has an important quantity of RS, reduced fast glycemia of volunteers with MS.

RS consumption improved insulin sensitivity of individuals with MS[29]. In our study, HOMA-IR index, which is correlated with invasive insulin sensitivity tests, did not indicate alteration in insulin resistance, or

QUICKI index. Since fast glycemia reduction was observed, it is suggested that the intervention time has been insufficient to demonstrate insulin sensitivity improvement.

Regarding dietetic ingestion of volunteers, significant modifications in food consumption or diet calories reduction were not noticed. Only at the first week of GBF consumption, calories reduction was observed in the afternoon snack. In addition, the evaluation of appetite sensations by VAS showed significant results for appetite reduction only at the first day of GBF consumption. Such results can be explained by the fact that our organism adapts to food habit modifications by physical mechanisms related to energetic compensation[30], minimizing the functional effects of a food consumed for a long time.

The motivation of volunteers with the possibility to lose weight and improve some health parameters may still have influenced the food choices in the initial period. However, as time passed, reduction of adherence to treatment occurred along with the attention to daily dietetic consumption[31,32].

The increase of satiety sensation found in our study can be due to the elevated fiber content and/or GBF RS. According to Ramos et al.[33], GBF can present 10 to 40% of RS, which has the property of promoting satiety[34]. Studies using VAS demonstrated higher satiety verified by RS[35]. However, Bodinham et al.[8] while testing the effects of RS in healthy adults concluded that nutrients promoted lower caloric consumption, although VAS analysis has not shown hunger reduction and satiety increase results. In our study, there were no differences in caloric consumption, which was also not observed in the results of satiety and hunger evaluated by VAS. Although VAS is a subjective mensuration, according to Blundell et al.[18], in appropriate study delineation and analyses, this method is sensitive and reliable to analyze the subjective appetite sensations in free-living conditions. The results obtained by VAS are coherent with the hunger perception mean score found, with absence of food consumption reduction and, consequently, not reduction of weight.

It is worth emphasizing that this study aimed to investigate the isolated effect of the consumption of the GBF in the control of the weight, satiety, physical composition and biochemical profile, considering the food consumption of free life of the volunteers. Nutritional directions were not given during the study and flour consumption was not associated to any food plan and/or caloric restriction.

In these conditions, the results of this study demonstrate that GBF itself was not able to increase satiety, reduce appetite or caloric consumption and, consequently, promote weight loss. It is suggested that diets with caloric restriction are the main factor for continued weight reduction[36] along with professional support[32] and that diet macronutrient composition, alone, is not able to cause such an effect[36]. Rocha et al.[37] in a study with a similar study experimental design failed to certify functional allegations of weight reduction and increased satiety of "Human Ration". This product is a mix of cereals with consumption stimulated as a meal replacement, which should not be encouraged[37]. Meta-analysis that evaluated the magnitude of the effect of green tea or its extracts (caffeine and catechins) on body weight and body composition did not find significant results that would substantiate the recommendation of this food / product[38].

Moreover, the consumption of a food with functional allegations can induce the individual to a "compensation" idea by consuming more caloric and fat-rich foods and simple carbohydrates. In other words, the individual may tend not to follow the principles of healthy eating due to believing that the studied food can minimize dietary excesses and inadequacies.

The GBF low GI[3,12] is of great interest for the control of glycemia, diabetes and other pathologies. In the long run, consumption of foods with high GI can lead to development of insulin resistance and type 2 diabetes mellitus, besides being associated to other non-communicable chronic diseases, such as cardiovascular diseases, obesity and some types of cancer[39]. Studies have demonstrated that low GI carbohydrates play an important role in the improvement of insulin sensibility, contributing to metabolic processes and body weight control[40]. For Pereira[34], RS contributes to a slower digestion, which brings lower glycemic and, consequently, insulin response. This author still highlights the insoluble and soluble fiber role practiced by RS, respectively, carrying molecules of fat and sugar that will be absorbed more slowly, promoting satiety.

Studies have found expressive quantities of RS in the GBF[41], being this, perhaps, the main responsible for low GI. Thakorlal et al.[42], while analyzing the RS content of different green banana species, concluded that the level oscillates greatly between the fruit varieties, ripening time and processing.

Borges et al.[3], while characterizing the GBF showed that this is a rich source of starch, protein, potassium, phosphorous, magnesium, copper, manganese and zinc, able to substitute other foods since they have high caloric value and higher nutritional content than other types of existing flours in the market. When used in partial substitution to the plain flour for cookies production, it did not alter the sensory characteristics of this food and presented good acceptance in different age groups[1-4]. This suggests that the GBF can be used as nutritional enrichment raw material of foods, contributing to reduce GI of meals[1] representing an alternative for patients who need to exclude plain flour from the diet, such as the celiac disease.

Conclusion

The consumption of green banana flour (20 g/day) for 45 days did not promote alteration of weight or

body composition in overweight women. It was observed, however, reduction of the hip circumference and increase of the hip-waist circumference. After classification of volunteers as bearers or not of metabolic syndrome, the group with MS showed reduction of systolic blood pressure and fast glycemia. This last result might be attributed to low glycemic index of the test food.

Thus, women with metabolic syndrome respond better to the product, although it has been observed that the use of GBF alone did not reach the supposed effects on lipid profile improvement, appetite reduction, satiety increase and weight loss. Therefore, the consumption of this food must be associated to directions on healthy eating and a diet plan with caloric restriction, including regular practice of physical activity, so that the health benefits and improvement of other MS parameters are reached.

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Original / *Síndrome metabólico*

Improved metabolic response after 16 weeks of calorie-restricted low-glycaemic index diet and metformin in impaired glucose tolerance subjects

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Abstract

Aim: **This study analyzed the metabolic effects of dietary advice to follow calorie-restricted low-glycaemic index diet with metformin in overweight / obese impaired glucose tolerance subjects.**

Methods: **Sixteen subjects with body mass index between 27-38 kg/m² were followed monthly for 16 weeks and treated with metformin (1 g/day) and dietary prescription for low-glycaemic index diet with energy reduction of 25-30% their total energy expenditure. Glucose metabolism, lipid profile, anthropometric and body composition, and food intake parameters were measured before and after the treatment. Paired t-tests/Wilcoxon tests were used to compare differences from baseline, with a statistical significance criterion of $p \leq 0.05$.**

Results: **There were significant reductions in anthropometric and body composition parameters, decrease in HOMA2-%β and triglycerides concentrations, and increase in Cederholm index. These results show enhanced peripheral insulin sensitivity and preservation of pancreatic beta-cell function.**

Conclusion: **Calorie-restricted low-glycaemic index diet and metformin was benefit to metabolic and anthropometric parameters in overweight/obese subjects with impaired glucose tolerance.**

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Key words: *Glycemic index. Caloric Restriction. Glucose. Metformin. Type 2 diabetes mellitus.*

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MEJORA DE LA RESPUESTA METABÓLICA DESPUÉS DE 16 SEMENAS DE DIETA CON RESTRICCIÓN CALÓRICA Y BAJO ÍNDICE GLUCÉMICO JUNTO CON METFORMINA EN SUJETOS CON INTOLERANCIA A GLUCOSA

Resumen

Objetivo: **Este estudio analizaba los efectos metabólicos del consejo dietético de seguir una dieta con restricción calórica y un índice glucémico bajo junto con Metformina en individuos con sobrepeso / obesidad y tolerancia alterada a la glucosa.**

Métodos: **Se siguió mensualmente durante 16 semanas a 16 individuos con un índice de masa corporal entre 27-38 kg/m² y se les trató con Metformina (1 g/día) y una prescripción dietética con un índice glucémico bajo y una reducción del energía del 25-30 ¡% de su gasto energético total. Se midieron el metabolismo de la glucosa, el perfil lipídico, la composición antropométrica y corporal y los parámetros de consumo de alimentos antes y después del tratamiento. Se emplearon las pruebas t pareadas y de Wilcoxon para comparar las diferencias con respecto al basal, con un criterio de significación estadística de $p \leq 0,05$.**

Resultados: **Hubo reducciones significativas en los parámetros de composición corporal y antropométricos, una disminución en las concentraciones de HOMA2-% y e triglicéridos y un aumento del índice de Cederholm. Estos resultados muestran una mejora de la sensibilidad periférica a la insulina y una conservación de la función de las células beta pancreáticas.**

Conclusión: **la dieta con restricción calórica y un índice glucémico bajo junto con Metformina fueron beneficiosas para los parámetros metabólicos y antropométricos en individuos con sobrepeso/obesidad y una tolerancia a la glucosa alterada.**

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Palabras clave: *Índice glucémico. Restricción calórica. Glucosa. Metformina. Diabetes mellitus tipo 2.*

Introduction

Obese subjects show progressive increases in glucose and insulin post-prandial responses, which lead to impairment glucose tolerance (IGT) and an increased risk of type 2 diabetes mellitus (T2DM)[1]. First-line intervention for the treatment of obesity and T2DM involves lifestyle modification, including weight management, a healthy diet, and, when necessary, medication[2]. Calorie-restricted diets show improvement in anthropometric and glucose tolerance parameters[3], and low-glycaemic index (low-GI) diet contributes to a lower glucose response and is associated with reduced insulin demand, favouring adequate glycaemic control, lipid profiles, and body composition[4]. Metformin is a potent antihyperglycaemic agent recommended as the first-line oral therapy for T2DM[5] and used to decrease the rate of conversion from IGT to T2DM[6].

Research on low-GI diets has been widely performed; however, the combination with metformin has been poorly investigated. Previous investigations testing metformin in combination with low-glycaemic index foods in T2DM subjects[7,8], women with polycystic ovary syndrome[9] or modified diet in women[10] concluded that it may be an effective adjunct to dietary intervention in the treatment of pre-obese/obese with or at risk of T2DM. The study aims to evaluate the effects of a calorie-restricted low-GI diet combined with metformin on metabolic and body composition parameters of overweight/obese type 1 subjects with impaired glucose tolerance. The aim is to contribute to the information on how the combined treatment helps to improve insulin sensitivity.

Methods

Subjects

The sample size was established considering the CI as the main response variable, assuming 80% power and a 5% significance level. A total of 15 subjects were determined as necessary[11].

This study involved the participation of 18 subjects recruited through public advertisements. The inclusion criteria were adults (19-50 y), of both sexes, with IGT (glycaemia ≥ 7.8 - < 11.1 mmol/L and insulin > 277.8 pmol/L) and body mass index (BMI) between 25 and 40 kg/m², non-smokers, not pregnant or lactating, no diagnosis of any metabolic diseases, and not under medication or therapeutic diets, except for oral contraception in the women.

The protocol of this study was approved by the Ethics Committee in Human Research of the Faculty of Health Sciences at the University of Brasília, Brazil (n°035/2004). All of the volunteers signed a written informed consent form.

Study design

On the first visit, the subjects arrived at the laboratory between 0730 and 0800 hours after a 12-hour overnight fast. Height, waist circumference, body weight, and body composition were recorded and a 2-hour oral glucose tolerance test (OGTT) was administered. The subjects were enrolled for 16 weeks with a monthly follow-up visit (total of 5 visits) to verify adherence and to adjust the dietary treatment and to receive the metformin. The metformin was donated by the Medley Laboratory (São Paulo, SP, Brazil). The dose of metformin was 1 g/day divided in two doses (500 mg) taken with breakfast and dinner.

Dietary counselling

The assessments of physical activity were performed using a short version of the International Physical Activity Questionnaire (IPAQ)[12], and was estimated[13] corrected by the appropriate Physical Activity Level (PAL) of each subject[14]. The dietary energy reduction was set between 25 and 30% of the total energy expenditure, and the dietary macronutrient percentages were set according to the acceptable macronutrient distribution ranges[12]. The dietary energy was distributed by food groups according to the portions defined by the Brazilian food pyramid[14]. A food-grouped portion size equivalent table was created with selected plant-based carbohydrate-fiber foods to help the subjects adhere to the diet.

The dietary adherence was computed for the subjects who completed 5 visits, did not eat more than the proposed dietary energy, consumed 4 - 6 meals per day and had fibre intake 60-70% of the dietary reference value[13].

Food intake assessment

Food intake was assessed by two 24-hour recalls (R24h) at baseline period and five R24h at each follow-up interview during the study intervention. To ensure accuracy, subjects were shown a photographed food portion guide and household items to estimate the food portions consumed. Dietary data were analysed using Nutrition Data System for Research software (version 2011, University of Minnesota, Minneapolis, MN) with inclusions of typical Brazilian food preparations based on standardized recipes. Multiple Source Method was used to estimate the usual dietary intake adjusted by within-person variability[16]. The data provided represents the baseline and intervention usual dietary intake.

Anthropometric and body composition assessment

Body weight was assessed using an electronic platform scale (Plenna, São Paulo, Brazil) with range of 0-

150 kg and precision of 0.1 kg. Height was measured using a stadiometer (Alturaexata, Belo Horizonte, Brazil) with a range of 0-210 cm and a precision of 0.1 cm. BMI was computed and classified[17], and body fat percentage was measured by tetrapolar electrical bioimpedance (Quantum II-RJL Systems, Clinton Township, MI, USA)[18]. The waist circumference was measured and classified according to NCEP-ATP III[19].

Physical activity level

The short version of IPAQ was adapted to obtain physical activity description at initial and monthly return visits[12]. A partial activity ratio was calculated by time spent on each activity multiplied by the energy costs of activities, expressed as multiples of basal metabolic rate. The partial results were added and divided by 24 to give the PAL by the FAO/WHO/UNU factorial approach[20].

Biochemical analyses

Capillary blood samples were taken to verify the fasting state for the OGTT using a glucometer (Roche Diagnostics, Mannheim, Germany). At baseline and at 16 weeks, blood samples were collected after a 12-hour overnight fast. The concentrations of serum insulin, triglycerides, total cholesterol (TC), HDL-c, LDL-c, and VLDL-c were determined. Serum insulin was measured by electrochemiluminescence (Elecsys 2010, Roche Diagnostics, Mannheim, Germany) and plasma glucose by the glucose oxidase method (Immulite 2000, DPC, Los Angeles, USA). The TC, HDL-c fraction, and triacylglycerol were measured using enzymatic colorimetric kits (Labtest Diagnostica S.A., Belo Horizonte, Brazil). The fractions of LDL-C and VLDL-c were calculated using the Friedewald equation[21]. Four millilitres of blood were collected in ice-cooled EDTA-plasma vacutainers to determine the value of glycated haemoglobin (HbA1c) by high performance liquid chromatography method[22].

Oral glucose tolerance and insulin sensitivity tests

A 2-hour OGTT was performed after an overnight fast and blood samples were drawn at baseline, 30, 60, 90, and 120 minutes. The incremental area under the curve (AUC) for glucose and insulin was calculated excluding any value below the baseline value using the trapezoidal method[23]. Values for the homeostasis model assessment insulin resistance (HOMA2-IR), HOMA β-cell function (HOMA2-%β), HOMA insulin sensitivity (HOMA2-%S)[24], and the Cederholm index (CI)[25] were calculated to determine insulin resistance, β-cell function, and insulin sensitivity.

Statistical analysis

The Kolmogorov-Smirnov test was applied to verify the normality of the variables and residual data plots were examined to determine the homogeneity of variance. Paired t-tests/Wilcoxon tests were used to compare differences between baseline and 16 weeks intervention. Pearson's correlation coefficient was used to evaluate linear dependence between fat loss against the change (final-initial) in metabolic and anthropometric parameters. All statistical analyses were performed using the SAS software package, version 9.1 (SAS Institute Inc., Cary, NC, USA), with a statistical significance criterion of $p \leq 0.05$, two-tailed.

Results

Subject characteristics

Of the 18 subjects recruited, 16 successfully completed the intervention (9 male, mean age 34.6 ± 7.0 years old, and BMI 31.6 ± 2.9 kg/m^2). The individuals maintained the pattern of physical activity during the intervention (initial PAL 1.36 ± 0.09 and final PAL 1.39 ± 0.06, $p = 0.58$).

Clinical and biochemical parameters

The intervention resulted in significant reductions from baseline values in weight ($p < 0.0001$), BMI ($p < 0.0001$), waist circumference ($p < 0.0001$), body fat ($p < 0.0001$) and increases in fat-free mass ($p < 0.0001$). Significant decreases in HOMA2-%β ($p = 0.04$), TAG and VLDL-c (both $p = 0.03$), and increased CI ($p = 0.04$) values were observed (table I). There was no significant modification in AUC glucose and AUC insulin, but there was a significant ($p = 0.03$) reduction in insulin concentration at 120 minutes (fig. 1).

There were significant correlations between fat loss (kg) and change (**Δ**) in body weight (r = 0.65; p = 0.006), **Δ**BMI (r = 0.66; p = 0.006), and tendency for **Δ** HOMA2-%S (r = 0.46; p = 0.09). Furthermore, a significant negative correlation was observed between fat loss and **Δ** insulin (r = -0.56; p = 0.04) and **Δ** AUC glucose (r = -0.50; p = 0.04) (table II).

Food Intake

There were improvements in the usual nutrient intake during the study intervention compared to baseline period. There were reductions in energy ($p < 0.001$), protein ($p = 0.02$), lipids ($p = 0.004$), carbohydrate ($p < 0.001$), PUFA ($p < 0.001$), and cholesterol ($p = 0.005$) intake, and increase in fibre ($p = 0.002$) intake. Furthermore, glycaemic index and glycaemic load determination of the usual intake confirmed the expected

Table I
Anthropometric, body composition and biochemistry variables analysed at baseline and after 16 weeks of dietary treatment and metformin

	Baseline		*16 weeks*			
Variables	*Mean*	*SD*	*Mean*	*SD*	Δ	*p*
Weight (kg)	86.62	14.00	82.28	12.98	-4.34	<0.0001
BMI (kg/m²)	31.57	2.88	30.03	2.94	-1.54	<0.0001
Waist (cm)	96.59	7.93	91.73	7.18	-4.86	<0.0001
Body fat (%)	33.11	7.04	30.58	7.22	-2.53	<0.0001
FFM (%)	66.89	6.76	69.42	7.14	2.53	<0.0001
HbA1c (%)	6.24	0.68	6.04	1.05	-0.2	0.62
Glucose (mmol/L)	4.68	0.52	4.69	0.46	0.01	0.96
AUC Glucose	7390	2232	6894	2438	-496	0.38
Insulin (pmol/L)	88.55	49.93	77.57	55.00	-10.98	0.45
AUC Insulin	13267	8226	10219	6065	-3048	0.19
CI	0.008167	0.001864	0.009306	0.001765	0.001139	0.04
HOMA2-IR	1.53	0.60	1.23	0.60	-0.30	0.09
HOMA2-%β	158.09	75.44	124.05	42.85	-34.05	0.04
HOMA2-%S	75.17	30.51	96.29	38.33	21.13	0.10
TAG (mmol/L)	1.78	0.80	1.47	0.55	-0.31	0.03
TC (mmol/L)	4.76	1.20	4.50	0.88	-0.26	0.47
LDL-c (mmol/L)	2.64	1.03	2.47	0.77	-0.17	0.56
VLDL-c (mmol/L)	0.82	0.36	0.68	0.25	-0.14	0.03
HDL-c (mmol/L)	1.30	0.31	1.35	0.22	0.05	0.56
TC/HDL-c	3.77	1.24	3.34	0.48	-0.43	0.14

Statistical analysis: Paired t-test/Wilcoxon test was applied to analyse baseline *vs* 16 weeks. FFM, fat-free mass; HbA1c, glycated haemoglobin; AUC Glucose, area under the glycaemic curve; AUC Insulin, area under the insulinaemic curve; CI, cederholm index; HOMA2-%β, homeostasis model assessment β-cell function; HOMA2-IR, homeostasis model assessment insulin resistance; HOMA2-%S, homeostasis model assessment insulin sensitivity; TAG, triglyceride; TC, total cholesterol; TC/HDL-c, total cholesterol / high-density lipoprotein cholesterol ratio.

change in the dietary pattern imposed by the intervention (table III).

Discussion

Hyperglycaemia maintained over a period of years leads to β-cell failure which causes impaired glucose tolerance and type 2 diabetes[26]. Low-glycaemic index diet and metformin improve glucose metabolism parameters and prevent the development of T2DM among IGT subjects[27,28].

In the present study the combined intervention was positive for weight loss and improvement in HOMA2-%β and the CI. The results were highly significant for body composition and significant for the TAG and VLDL concentrations, which indicate a positive progression of the lipid profile. Furthermore, we observed a significant correlation between fat loss and changes in body weight, BMI, and negative correlation between fat loss and changes in insulin and AUC glucose.

Obesity, and especially visceral adiposity, is associated with an increased risk of insulin resistance and type 2 diabetes. Excess adipose tissue releases increased amount of non-esterified fatty acids, glycerol, hormones, pro-inflammatory cytokines and other factors that are involved in the development of insulin resistance. A chronic excess of non-esterified fatty acids results in an increase in fat deposits in muscle and liver and increased metabolites, such as diacylglycerol and ceramide, which activate isoforms of protein kinase C, impairing cellular insulin signalling. Chronically high lipid levels affect the beta cell function and insulin sensitivity leading to hyperglycaemia[29,30]. Fat loss therefore leads to improvement in beta cell function and glucose metabolism.

Lifestyle modification (diet plus physical activity) and metformin were recommended as the first-line therapy for IGT and T2DM. Results from the U. S. Diabetes Prevention Program trial[31], which evaluated over 3000 subjects divided in three treatments, showed that in the metformin group (1.7 g/day), diabetes risk, insulin sensitivity, and beta-cell function at 1 year were intermediate between those in the intensive lifestyle and placebo groups. The combination of dietary intervention (calorie-restricted low-glycaemic index diet) and metformin was able to improve insulin parameters in a shorter treatment period, without the intensive lifestyle modification (diet and physical activity). Dietary changes and exercise are factors known to positively affect improvements in insulin sensitivity[32], but these intense lifestyle changes are difficult to adhere to[32,33]. Also, since the improvement in insulin sensitivity due to exercise rapidly disappears after its cessation[34], a continued treatment scheme is still being sought. The Indian Diabetes Prevention Programme

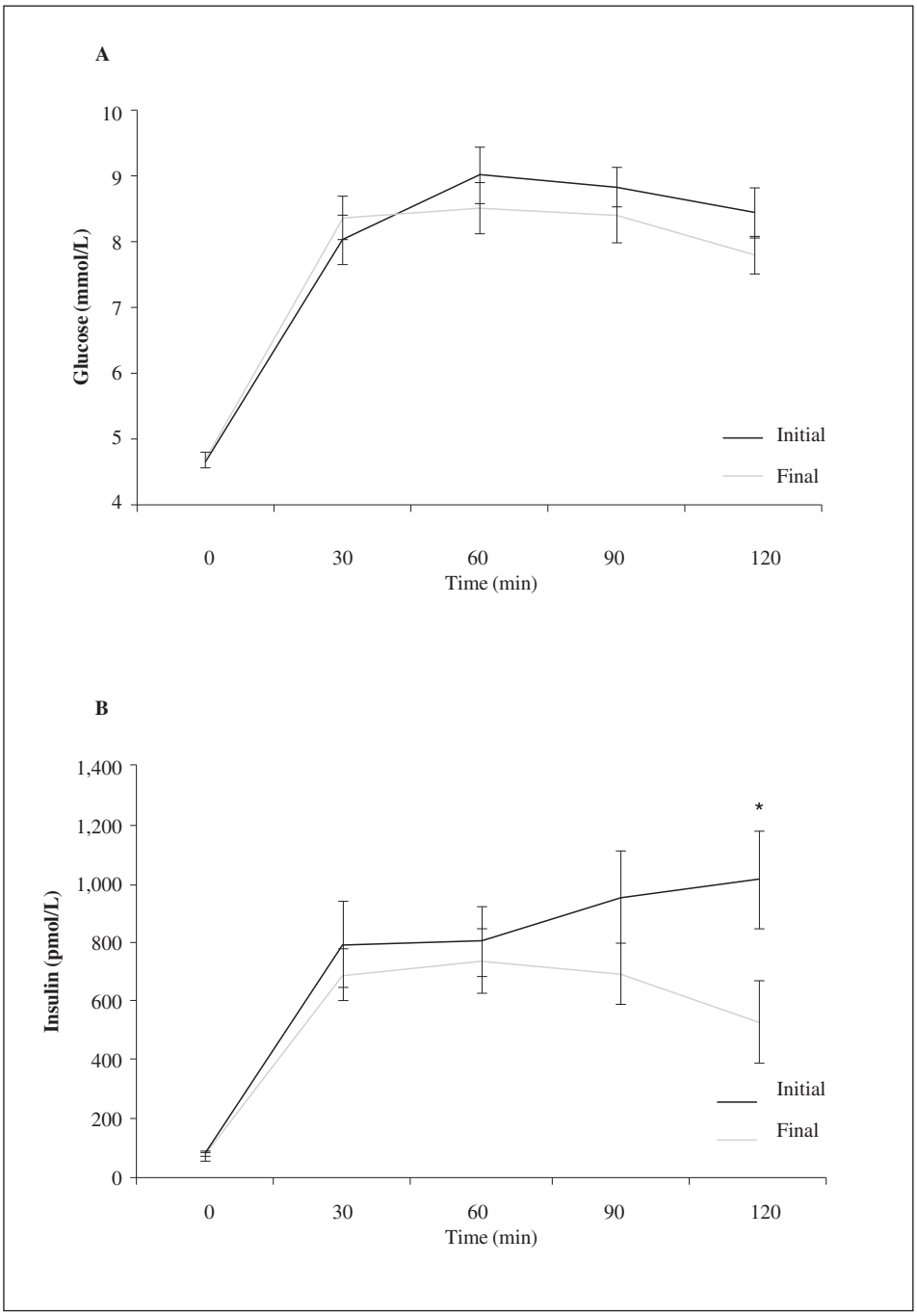


*Fig. 1.—Two hours postprandial glycaemic **(A)** and insulinaemic response **(B)** to a calorie-restricted low-glycemic index diet and metformin (LGI + MET).*
*Data are expressed as the mean ± standard error. * $p \leq 0.05$.*

followed a similar design to the U.S Diabetes Prevention Program, but it also included a combined lifestyle change and metformin group (0.5 g/day)[33]. The addition of metformin to lifestyle modification (diet and exercise) in the Indian study did not enhance the effectiveness. One possible explanation is the low dosage of metformin used in the trial. So the question related to the combined treatment is still debatable.

The mechanisms of action of metformin include a decrease glucose output from the liver and increased glucose uptake from peripheral tissues[35]. It also reduces postprandial glycaemic peaks and improves insulin action, presenting anti-oxidative and anti-inflammatory actions[36]. Several studies showed that the beneficial metabolic effects of metformin involve AMP-activated protein kinase (AMPK)[5,36-39]. Moreover, metformin has an anorexic effect which involves AMPK[37,38], inhibition of the hypothalamic orexigenic peptides, neuropeptide Y and agouti-related protein[40] and incretin[38]. AMPK activation increases glucose uptake by skeletal muscles, increases lipid catabolism and leads to control of the appetite and satiety by the hypothalamus[40]. The AMPK system may be partly responsible for the health benefits of exercise. This enzyme is a key player in the

Table II
Pearson correlation among Δ fat loss (final-initial) (kg) after 16 weeks of dietary treatment and metformin

Δ *Variables (final-initial)*	*r*	*p value*
Weight (kg)	0.65	0.006
BMI (kg/m²)	0.66	0.006
Waist (cm)	0.32	0.23
HbA1c (%)	-0.41	0.15
Glucose (mmol/L)	-0.03	0.92
AUC glucose	-0.50	0.04
Insulin (pmol/L)	-0.56	0.04
AUC insulin	-0.10	0.71
CI	0.34	0.19
HOMA2-%β	-0.26	0.38
HOMA2-IR	-0.37	0.19
HOMA2-%S	0.46	0.09
Triglycerides (mmol/L)	-0.20	0.45
Total cholesterol (mmol/L)	-0.35	0.18
LDL-c (mmol/L)	-0.35	0.18
VLDL-c (mmol/L)	-0.19	0.49
HDL-c (mmol/L)	-0.14	0.61

HbA1c, glycated haemoglobin; AUC glucose, area under the glycemic curve; AUC insulin, area under the insulinemic curve; CI, cederholm index; HOMA2-%β, homeostasis model assessment β-cell function; HOMA2-IR, homeostasis model assessment insulin resistance; HOMA2-%S, homeostasis model assessment insulin sensitivity.

development of new treatments for obesity, T2DM, and the metabolic syndrome[37,39,41].

The measurements of peripheral and central actions of metformin on insulin control of glycaemia are important. Among the various methods to evaluate insulin sensitivity from fasting measurements HOMA is the most commonly used. HOMA is indicative of the balance between hepatic glycogenesis and gluconeogenesis when fasting[42]. On the other hand, the CI is based upon a physiological model and estimates the mean enhancement of glucose effectiveness due to plasma insulin during the OGTT, correcting for the total body glucose space[25]. Generally, HOMA is commonly taken to represent central or hepatic insulin sensitivity, and the CI is indicative of peripheral insulin sensitivity. Under the combined dietary-metformin intervention we showed an increase in the peripheral insulin sensitivity with an increase in CI. There was a significant reduction in HOMA2-%β and a 20% reduction in HOMA2-IR (1.53 ± 0.60 to 1.23 ± 0.60) and 28% increase in HOMA2-%S (75.17 ± 30.51 to 96.29 ± 38.33), which did not reach statistical significance but is physiologically relevant. These responses are compatible with the actions of metformin on muscle mass through the AMPK system described above.

Furthermore, we observed significant correlation between fat loss and changes in body weight and BMI. These results show that higher fat loss is related to improvement in these parameters, which is compatible with the activation of the AMPK by diet and metformin[39]. On the other hand, fat loss was negatively correlated with change in insulin and AUC glucose, which means that a poor body fat loss is correlated to a decrease in these parameters. This result is unexpected and should be investigated using a multiple regression model that permits an evaluation of mechanism controlling glucose uptake under the effects of metformin.

This study has many limitations, as the therapy was tested in a small number of subjects in a pairwise, short follow-up protocol. Furthermore the study design is weak because was not included a true (untreated) control group, so it is not possible to determine the real effects of the metformin in the analyzed variables compared with a group who received no drug. However, these results contribute to the perspective of combined treatment of low-GI benefits associated with a relatively low dose of metformin, as there is a lack of data on the combination of lifestyle intervention and antidiabetic agents in pre-diabetic patients[43].

In conclusion, we showed the benefits of calorie-restricted low-glycaemic index diet with metformin on metabolic and anthropometric parameters in overweight/obese IGT subjects. The increase in Cederholm index is compatible with improvement in peripheral insulin sensitivity, associated with an improved response of the beta cell. However, longer duration follow-up trials are necessary to understanding the metabolic

Table III
Usual nutrient intake analysed at baseline and during the 16 weeks of dietary treatment and metformin

	Baseline		*16 weeks*		
Variables	*Mean*	*SD*	*Mean*	*SD*	*p*
Energy (Kcal)	2138	683	1583	351	< 0.001
Protein (g)	96.7	32.0	78.4	24.1	0.02
Lipids (g)	82.4	32.3	57.7	14.3	0.004
Carbohydrate (g)	254.4	76.2	191.0	34.4	< 0.001
Fibre (g)	14.3	3.8	18.9	3.8	0.002
PUFA (g)	18.2	5.1	12.2	3.5	< 0.001
Cholesterol (mg)	302.9	161.9	196.2	60.5	0.005
Glycemic index	60.7	2.1	55.2	2.7	< 0.001
Glycemic load	146.3	42.5	95.3	21.2	< 0.001

Statistical analysis: Paired t test/Wilcoxon test was applied to analyse baseline *vs* 16 weeks. PUFA, polyunsaturated fatty acid.

effects and effectiveness of low-GI diets and metformin in glycaemic and insulinaemic responses to prevent pre-diabetes from progressing to T2DM.

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Original / *Síndrome metabólico*

Metabolic disorders of liver and iron in diabetic and non-diabetic patients BMI < 35 or > 35 before gastric bypass

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Abstract

Introduction: **The presence of abnormalities in the metabolic pathways of iron and liver functioning can produce insulin resistance or metabolic syndrome. Therefore, it is important to examine those alterations that may lead to the development of diseases. Nutritional status is another important factor that is intimately linked to diabetes and obesity.**

Patients and Methods: **We studied 131 patients (78 non-diabetic patients and 53 diabetic), 37 patients BMI ≤ 35 (3 BMI < 25, 18 BMI 25-29.9, 16 BMI 30-34.9) and 94 patients BMI ≥ 35 (81 BMI 35-49.9 and 13 BMI ≥ 50). Subjects underwent to laboratory studies related to liver functioning and iron metabolism. Nutritional status was also determined in our patients.**

Results: **Iron was altered 14% of patients BMI >35 and diabetics reached 3% to 25%. Vitamin B12 was low 4% of non-diabetics BMI > 35, and high in 6% of diabetics BMI < 35. The 6% of diabetics BMI < 35 had hyperbilirubinemia. Transaminases are elevated in patients BMI >35 but exacerbated on diabetics. GGT is raised 41% to 47% in BMI >35. ALP is elevated in 25% of diabetics. Total protein and serum albumin were altered in diabetics causing mild malnutrition. 90% of patients had normal nutrition and 10% mild malnutrition.**

Conclusions: **The metabolisms Hepatic and iron are closely related to the onset of obesity and diabetes. If there is weight gain, cumulative metabolic risks rise. The presence of diabesity and increased duration of diabetes produce altered metabolism. Nutritional status is altered in obesity but is worse with the addition of diabetes.**

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Key words: *Obesity. Diabetes mellitus. Diabesity. BMI. Metabolism.*

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TRASTORNOS DEL METABOLISMO DEL HÍGADO Y EL HIERRO EN PACIENTES DIABÉTICOS Y NO DIABÉTICOS CON IMC < 35 Ó > 35 ANTES DE BYPASS GÁSTRICO

Resumen

Introducción: **La presencia de anormalidades en las vías metabólicas del hierro y el funcionamiento del hígado pueden producir resistencia a la insulina o síndrome metabólico. Por lo tanto, es importante examinar esas alteraciones que pueden conducir al desarrollo de enfermedades. El estado nutricional es otro factor importante que está íntimamente ligada a la diabetes y la obesidad.**

Pacientes y métodos: **Se estudiaron 131 pacientes (78 pacientes no diabéticos y 53 diabéticos), 37 pacientes IMC ≤ 35 (3 IMC < 25, 18 IMC 25-29,9, 16 IMC 30-34,9) y 94 pacientes IMC ≥ 35 (81 IMC 35-49,9 y 13 de IMC ≥ 50). Los sujetos fueron sometidos a estudios de laboratorio relacionadas con el funcionamiento del hígado y el metabolismo del hierro. Se determinó también el estado nutricional en nuestros pacientes.**

Resultados: **El hierro estuvo alterado en 14% de los pacientes IMC >35 y los diabéticos alcanzaron 3% a 25%. La vitamina B12 fue baja en 4% de los no diabéticos IMC > 35, y alta en el 6% de los diabéticos IMC < 35. El 6% de los diabéticos IMC < 35 tenía hiperbilirrubinemia. Las transaminasas estuvieron elevadas en pacientes IMC > 35, pero exacerbados en los diabéticos. GGT se eleva del 41% al 47% en BMI > 35. ALP estuvo elevada en el 25% de los diabéticos. Las proteínas séricas totales y la albúmina estuvieron alterados en los diabéticos causando desnutrición leve. 90% de los pacientes tenían una nutrición normal y 10% desnutrición leve.**

Conclusiones: **El metabolismo hepático y del hierro están estrechamente relacionadas con el inicio de la obesidad y la diabetes. Si hay un aumento de peso, los riesgos metabólicos acumulados se elevan. La presencia de la diabesidad y el aumento de la duración de la diabetes empeoran el metabolismo. El estado nutricional se altera en la obesidad, pero es peor con la adición de la diabetes.**

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Palabras clave: *Obesidad. Diabetes mellitus. Diabesidad. IMC. Metabolismo.*

Introduction

Alterations of metabolic pathways in the human body can cause several diseases, so it is necessary to explore the relationship between the predisposition, onset, progression and the etiology among alterations of metabolism that can lead to develop diseases[1]. Behind obesity and Type 2 Diabetes Mellitus (T2DM), a complex metabolic disorder causes a strong link between the two diseases[2] on an intricate environment[3]. The increase in body weight predominantly visceral fat accumulation causes alterations as ectopic triglycerides[4] which can cause insulin resistance and metabolic syndrome (MS), factors that favor the onset of T2DM[4,5] in genetically predisposed individuals with impaired beta cell through the long process of the defects in insulin action and secretion[6].

Obesity therefore is an important factor for the development of T2DM considered epidemic by the very high rates worldwide[7]. Today, half of patients with T2DM diagnosis are obese[2], showing altered metabolic states and oxidative stress with inflammatory cytokines released by adipose tissue[8].

Other metabolic pathways linked to the development of diabetes are the iron and hepatic metabolism altered. The increased total levels of stored iron are positively correlated with insulin resistance and metabolic syndrome[8]. The association of impaired liver enzymes with development of diseases has been demonstrated. Raising the glutamyltransferase (GGT) and alanine aminotransferase (ALT) are linked to peripheral and hepatic insulin resistance[9]. Elevation of bilirubin is considered as antioxidant in the prevention of cardiovascular diseases[10]. Higher levels of alkaline phosphatase (ALP) circulating is closely linked to body fat so it can be used as a predictor of obesity[11].

Besides, deficiency of vitamin B12 is linked to the use of metformin in obese and/or patients with T2DM causes diverse clinical manifestations[12].

Both obesity and/or diabetes can cause malnutrition[13], and have a direct impact on the clinical outcome of patients. Diagnosis of obesity is made by Body Mass Index (BMI)[14] which is considered as the main tool for the classification of weight but it is not related to the nutritional status of patients[15]. Ulíbarri et al[16] shows that 30 to 55% of hospitalized patients and 77 to 84% of diabetic patients have malnutrition, which increases morbidity and worsens the prognosis of patients by taking them to complications or death[13].

Therefore, obesity should be prevented from an early age, because of morbidity increases with the time of evolution, and reverse it is a real challenge[17] that could be achieved through bariatric surgery that are considered as definitive treatment of obesity and T2DM[2]. Metabolic surgery causes high rates of remission of T2DM and diseases such as MS[18] by different mechanisms. The reorganization of gastrointestinal transit[19] and visceral fat reduction are the goals of treating obesity[4] and diabetes[19]. Schauer et al[20] evaluated the specific effects of bariatric surgery on BMI > 35, and others authors on BMI < 35[21,22]. However, bariatric surgery treatment is still controversial on BMI < 35[23] despite the results of long-term remission of obesity and diabetes as well as protective against T2DM[24].

Patients and methods

Patients

We studied 131 patients (78 non-diabetic patients and 53 diabetic), 37 patients BMI ≤ 35 (3 BMI < 25, 18 BMI 25-29,9, 16 BMI 30-34,9) and 94 patients BMI ≥ 35 (81 BMI 35-49,9 and 13 BMI ≥ 50). We analyzed BMI, gender, presence of diabetes and its time of evolution. Age was clustered in ranges 15-20, 21-30, 31-40, 41-50, and 51 years of age and older. The duration of T2DM was clustered into 1-5, 6-10, 11-15, 16-20, 21-30 and 31-40 years.

Patients attended medical consultation in order to be undergoing to tailored One Anastomosis Gastric Bypass (BAGUA) for his current state of diabetes, obesity or both conditions.

Preoperative evaluation

In all patients, a preoperative study were conducted following the indications of the Clinical Practice Guideline (CPG) of the European Association for Endoscopic Surgery (EAES)[25].

The total cholesterol, serum iron, vitamin B12, total bilirubin, transaminase AST, transaminase ALT, gamma glutamyltransferase (GGT), alkaline phosphatase (ALP), total protein, serum albumin and total lymphocyte were evaluated after at least 12-hour fasting.

Surgical procedure

Before surgery, all patients eat only liquid diet during 5 (BMI 23-34) to 7 days (BMI 35-50) depending of preoperative BMI, received antibiotic and antithrombotic prophylaxis. Tailored BAGUA[19,26] consisted in the construction of a gastric pouch from the gastroesophageal junction to the end of the minor gas-

Table I
Number of patients by BMI

Group of patients	*Non-diabetic patients*	*Diabetic patients*
BMI < 25	0	3
BMI 25-29.9	1	17
BMI 30-34.9	3	13
BMI 35-49.9	62	1
BMI ≥ 50	12	1
Total	**78**	**53**

Figure represents the number of patients and distribution studied.

tric curvature at the lower level of the cisura angularis. The stapler line of the gastric pouch was fixed approximately 12 cm to the intestinal loop (first layer of the anti-reflux mechanism of BAGUA), and it was anastomosed in a laterolateral position to the mesenteric border of a small bowel loop 100 cm (BMI 23-29), 120 cm (BMI 30-32), 150 cm (BMI 33-34), 200 cm (BMI 35-40), 250 cm (BMI 40-45), and 280 cm distal (BMI 45-50) to the treitz ligament. The anti-reflux mechanism is completed fixing the afferent loop to the gastric remnant and the efferent loop to the antrum.

The size of the gastric pouch depends on the BMI of the patient. In BMI 23-32 we performed a floppy 36 French bougie pouch, while in BMI > 33 a narrow 36 French bougie one's is performed. We left systematically a drainage during the 48 h of hospital stay. After surgery, they eat liquid diet in the 1st week, semifluids in 2nd week, purée in 3-4th weeks and normal diet after one month of surgery. The patient were reviewed at 10 days, 1, 3, 6 and 12 months.

Blood sample processing

Laboratory personnel of the Analysis Unit Clinical Laboratory of University Associated Hospital Parque San Antonio performed the extraction of blood samples from patients with at least 12 hours fasting. The laboratory samples analyzed were total cholesterol, total bilirubin, transaminases AST and ALT, GGT, ALP, serum iron and total protein by ultraviolet-visible spectroscopy. The serum albumin was analyzed by capillary electrophoresis, vitamin B12 by chemiluminescence, and total lymphocyte by count and electronic formula.

Normal levels of our laboratory are total cholesterol 130-220 mg/Dl, total bilirubin < 1,2 mg/Dl, GGT 7-35 U/L, AST < 40 U/L, ALT < 40 U / L, ALP 30-120 U/L, total protein 65-82 g/L, serum albumin 36-54 g/L (3,6-5,4 g/Dl), serum iron 40-150 µg/Dl, vitamin B12 189-883 pg/Ml and total lymphocytes 900-5175/µL.

With the data obtained we made the determination of the nutritional status of patients through screening tool developed by Ulíbarri et al[16] validated in 2002 with 92,3 sensitivity and specificity of 85.

The filter tool uses serum albumin and total cholesterol as biochemical parameters, and uses total lymphocytes as immune parameters. The levels of the three parameters are set according to the degree of malnutrition. Assigned scores are divided into four ranges based on alteration of each laboratory studies (table II).

Statistical analysis

Descriptive statistics was used for comparisons. Differences among groups were analyzed by ANOVA when appropriate, and measures of central tendency according to study variables. Besides, we use percentages on gender, age, BMI, presence or absence of diabetes and its evolution time. For quantitative variables were used mean and standard deviation. We use SPSS (version 20 for Windows, SPSS, Chicago IL) and Excel 2010 programs.

Table II
Percentage of patients by BMI having glucose altered

Group of patients	*Non-diabetic patients*	*Diabetic patients*
BMI < 25		100%
BMI 25-29.9	25%	85%
BMI 30-34.9	33%	100%
BMI 35-49.9	27%	88%
BMI ≥ 50	9%	9%

The data represents the percentage of patients with altered glucose depending of the BMI. It shows how super obese patients have a different behavior from the other groups. There was non-diabetic patients BMI < 25 to compare to diabetics in same group.

Results

The predominant age range was 51 years and older (32% of patients). The mean age was 44 ± 13 years. The mean of BMI was 39 ± 14. The mean of T2DM evolution was 13 ± 8 years. Morbid obesity was predominant (61% of patients).

Non-diabetic patients had total cholesterol 208 ± 45 mg/dl, serum iron 78 ± 32 µg/dL, vitamin B12 414 ± 190 pg/mL, total bilirubin 2 ± 14 mg/dl, AST 25 ± 13 U/L, ALT 37 ± 27 U/L, GGT 42 ± 36 U/L, ALP 89 ± 25 U/L, total proteins 73 ± 3 g/L, serum albumin 4 ± 0 g/L, and total lymphocytes 2,546 ± 773 L.

Diabetic patients had total cholesterol 188 ± 40 mg/dl, serum iron 77 ± 32 µg/dL, vitamin B12 489 ± 419 pg/mL, total bilirubin 3 ± 11 mg/dl, AST 27 ± 15 U/L, ALT 38 ± 29 U/L, GGT 51 ± 50 U/L, ALP 84 ± 29 U/L, total protein 74 ± 4 g/L, serum albumin 4 ± 0 g/L and total lymphocyte 2,504 ± 737 µL.

The iron metabolism was altered in 20% of non-diabetic BMI < 35, but the 13% of patients with BMI > 35 was affected. Diabetic patients reached levels of 7% in BMI < 35, but increases to 26% with gain of weight (BMI > 35). Vitamin B12 is altered in certain groups of patients as you can see in table III.

We found hyperbilirubinemia in 6% of diabetic patients BMI < 35. The transaminases AST and ALT are elevated in high percentage of patients BMI > 35 but exacerbated on diabetics. GGT is raised from 41% to 44% of patients BMI > 35. ALP is elevated up in 35% of diabetic patients. Total protein and serum albumin predominated altered especially in patients with diabetes (18%) (table III).

Nutritional Status

We use the filter tool developed by Ulíbarri et al[16] to perform nutrition status. We found normal nutrition in

Table III
Increment or decrement in the levels of specific profile studies

Levels of studies of laboratory	*kg*			*BMI*			*Age*			*Year of evolution T2DM*		
	↑	↓	*P*	↑	↓	*P*	↑	↓	*P*	↑	↓	*P*
Triglycerides		0.06	**0.017***		0.012	**0.000***	0.16		**0.000***	0.4		**0.000***
Total cholesterol	0.0	0.0	**0.000***	0.008		**0.000***		0.06	**0.000***	0.0	0.0	**0.000***
LDL cholesterol	0.0	0.0	**0.000***	0.21		**0.000***	0.7		**0.000***	0.0	0.0	**0.000***
HDL cholesterol	0.0	0.0	**0.000***	0.0	0.0	**0.006***	0.0	0.0	**0.085**	0.0	0.0	**0.047**
Glucose		0.03	**0.000***		0.24	**0.000***	0.44		**0.000***	0.19		**0.000***
C-peptide	4.0		**0.000***	1.0		**0.000***	0.034		**0.000***	0.0	0.0	**0.000***
HbA1c		5.0	**0.014***		1.0	**0.000***	3.0		**0.000***		0.09	**0.000***

The data show that with increasing weight per kg and BMI in units, age in years, and every year since onset of T2DM, some laboratory studies were altered and may have deleterious effects on the human body. *Statistically significant ($p < 0.05$).

90% of patients and mild malnutrition in 10%. We do not found any moderate and severe malnutrition (table IV).

About mild malnutrition, diabetics have higher percentage than non-diabetic patients (table V).

Discussion

When there are abnormalities in the metabolic pathways can produce different diseases. Therefore, it is important to examine the relationships between alterations of the metabolism that may lead to the development of diseases. The alterations of the metabolic pathways of iron metabolism and liver are associated with the development of insulin resistance and metabolic syndrome. Diseases such as diabetes and obesity are considered difficult to treat because they are intimately linked and could affect the nutritional status.

The purpose of this paper is to know how the iron and the liver metabolism are linked to obesity and diabetes, and how they affect the nutritional status of patients linked to weight gain cumulative type.

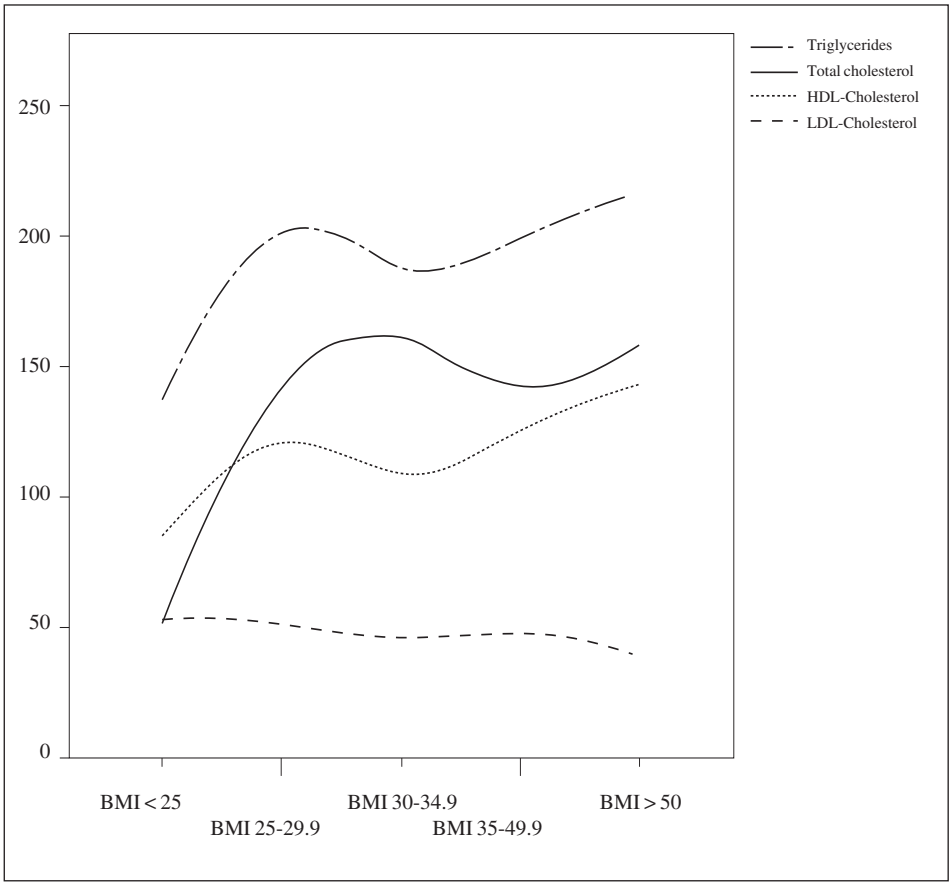


Fig. 1.—Altered metabolism of lipid with increased BMI.

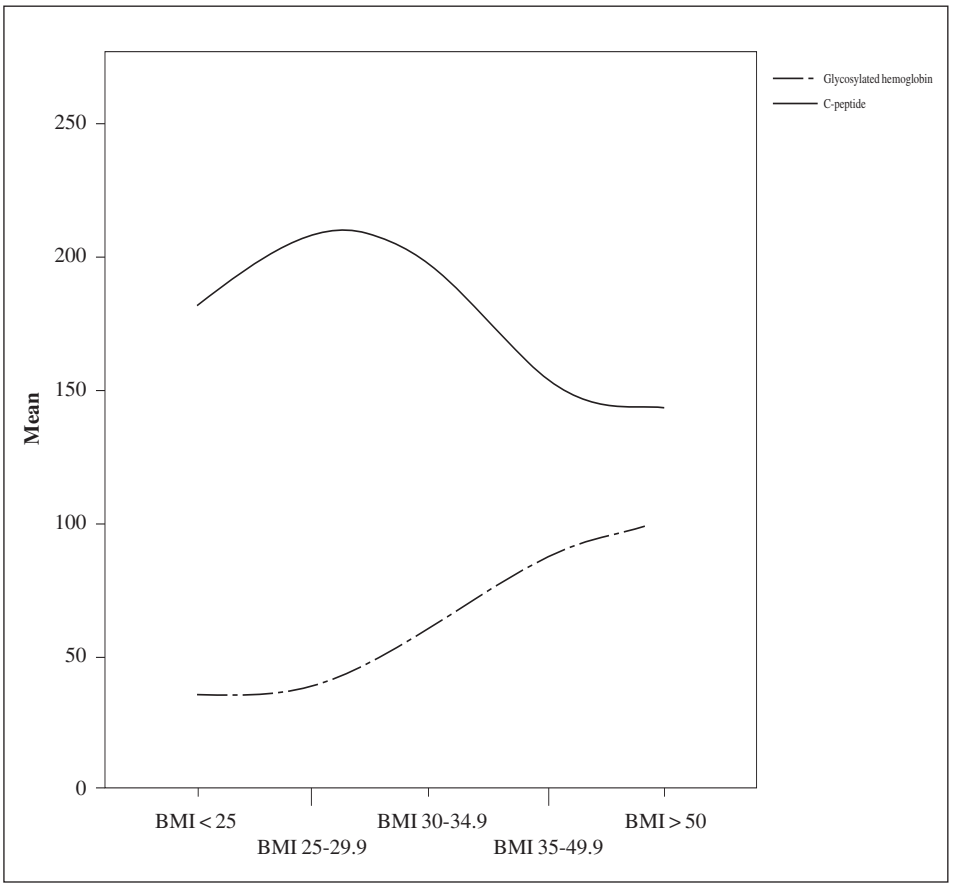


Fig. 2.—Glycated hemoglobin and C-peptide alterations according to BMI.

Table IV
Percentage of patients an their nutritional status determined by the filter tool developed by Ulibarri et al.

BMI	*Nutritional status*				*Total*
	Normal	*Mild malnutrition*	*Moderate malnutrition*	*Severe malnutrition*	
BMI < 25	0%	2%	0	0	2%
BMI 25-29.9	8%	3%	0	0	11%
BMI 30-34.9	2%	2%	0	0	3%
BMI 35-49.9	68%	3%	0	0	72%
BMI > 50	12%	0%	0	0	12%
Total	**90%**	**10%**	**0**	**0**	**100%**

Figure represent the nutritional status of patients by the Ulibarri et al. filter tool where most of patients had normal status followed by mild and moderatate malnutrition.

We evaluated 131 patients attended to the clinic in order to underwent to tailored One Anastomosis Gastric Bypass (BAGUA) because of their status of obesity and/or diabetes mellitus. The presence of obesity and/or diabetes in these patients caused comorbidities such as metabolic syndrome, respiratory diseases, polycystic ovary syndrome, anxiety-depressive disorder or complications of diabetes type micro and macro vascular[19].

The patients were submitted a series of laboratory studies and the results show big abnormalities in patients with diabetes and greater degree of obesity. These data indicate that increased BMI produces alterations in laboratory studies analyzed. Alterations are predominant in patients BMI > 35 where usually are associated comorbidities mentioned by WHO[27].

Abnormal laboratories were most frequently found in the age range of 51 years and older, and predominant in male gender. The patients with diabesity clustered higher percentage of altered laboratory studies.

In non-diabetic patients BMI > 35, 13% showed iron altered, but the percentage increases with the addition of diabetes (26%). We are agree with Fernandez-Real et al[8] because of alterations of iron metabolism are directly related to insulin resistance, the metabolic syn-

Table V
Differences in mild nutritional status between diabetic and non-diabetic patients

BMI	Nutritional status		Total
	Mild malnutrition		
	Non-diabetic patients	Diabetic patients	
BMI < 25	0%	17%	17%
BMI 25-29.9	0%	32%	32%
BMI 30-34.9	0%	17%	17%
BMI 35-49.9	17%	17%	34%
BMI 35-49.9	17%	17%	34%
Total	**17%**	**83%**	**100%**

Diabetic were more affected by slight under-nutrition than non-diabetic patients.

drome and diabetes development in the presence of oxidative stress and release of cytokines inflammatory destabilizing the human body.

Vitamin B12 is low in some patients probably by several mechanisms as Kibirige and Mwebaze[12] describe, where that deficiency of vitamin B12 is associated with intake of metformin in 5,8 to 33% of patients with T2DM. The 6% of our diabetic patients share these characteristics. The mechanisms of altered vitamin B12 are explained by alterations in small bowel motility with bacterial flora impact, competitive inhibition, inactivation of the absorption, abnormal intrinsic factor receptor, the interaction with cubulin or nutritional status by inadequate intake could determine their deficiency[16], and it is closely linked to abnormalities of iron and its consequences.

The components of liver metabolism are proteins that serve as markers for the diagnosis of obesity and liver diseases as fatty liver and others comorbidities, which are important clinical manifestations of metabolic syndrome. Nayeen et al[11] demonstrated that the alkaline phosphatase and transaminases are used as predictors for obesity and they are closely related to the amount of lean tissue.

Hsieh et al[28] shown that the prevalence of diabetes is higher in patients with liver disease. Transaminases and alkaline phosphatase are elevated in patients with diabetes but in a significantly higher in patients with diabesity. Vozaroba et al[29] demonstrated that the presence of high levels of ALT are associated with obesity and insulin resistance with its depletion and the subsequent development of T2DM, therefore suggests using as a predictive marker. The elevated ALT is also associated with increased risk of cardiovascular disease and metabolic syndrome demonstrated by Pirola and Sookoian[30].

On the other hand, elevated levels of bilirubin are associated with low prevalence of peripheral arterial disease that are correlated with amputations in diabetic patients as demonstrated by Chan et al[31]. Have protective effect on the antioxidant properties that prevent cardiovascular disease[10]. In our study we found that 6% of diabetic patients BMI < 35 have elevated bilirubin. Besides, GGT is predominantly elevated in patients BMI > 35 and this could indicate liver damage, cardiovascular risk and metabolic syndrome as demonstrated by Giannini et al[32]. Bonnet et al studied 1309 non-diabetic patients for 3 years, where GGT proved to be better predictor of T2DM than ALT[9]. Our patients with higher BMI had altered GGT and transaminases too.

Hepatic profile has also proteins that reflect the nutritional status[16]. The 2% of non-diabetic patients and 5% of diabetics with BMI < 35 had elevated total protein. The albumin was elevated in our patients that may reflect liver damage of various etiologies including systemic diseases as mentioned by Giannini et al[32].

We determined that certain studies of iron metabolism and liver function have cumulative effects when altered. We realized that with the increase in BMI, there are a greater percentage of patients with altered laboratory studies. However, total bilirubin, iron, albumin and total protein are affected without regard to the gradual increase in BMI.

Huffman et al[33] mentioned that there are associations among micronutrient deficiency, diet low in fiber and high saturated fat intake with the deteriorating health of patients with T2DM. He found deficiencies of iron, vitamin and calcium according to different characteristics of the patients.

We use the filter developed by Ulíbarri et al[16] to determine the degree of nutrition, showing that 10% of total patients have mild malnutrition, but the percentage of diabetic patients with mild malnutrition have almost five times more the than non-diabetic patients.

Patients who achieved higher obesity were shown not to be more affected, possibly because of the adipose tissue expandability described by Lumeng et al[34].

Finally, we agree with Soloirzano-Pineda et al[13] who mentioned that the high incidence of malnutrition in surgical patients should receive advice of nutritional status with a docketed method and prevent complications.

We are aware that further studies with more patients and longer follow-up are needed to find solutions related to the prevention and treatment of disorders of the metabolic pathways linked to the development of obesity, diabetes or metabolic syndrome.

The main limitation of our study is the number of patients. However, there are no studies about the influence of obesity and/or diabetes linked to weight gain cumulative type, and this may be the watershed to study in depth.

All this new knowledge, help us not only to understand the pathophysiological mechanisms of diseases of fashion, but also to improve surgical techniques bariatric or metabolic rate for the treatment of weight control and long-term improvement or cure of diabetes for surgical treatment.

Conclusions

Iron metabolism in 7% of diabetic patients < 35, and 26% of BMI > 35 was altered. The iron alterations

looks like correlated to altered levels of vitamin B12 (lower in 4% of non-diabetics BMI > 35, and higher 6% of diabetics BMI < 35).

In 6% of diabetic patients BMI < 35 had hyperbilirubinemia. The transaminases AST and ALT are elevated in high percentage of patients BMI > 35 but exacerbated on diabetic patients. GGT is raised from 41% (non-diabetics) to 44% (diabetics patients) of BMI > 35. ALP is elevated up in 35% of diabetic compared to non-diabetic patients (10%). Total protein and serum albumin were altered especially in diabetic patients.

The filter tool developed by Ulibarri et al demonstrates that diabetics are more affected with malnutrition than non-diabetic patients.

With these data, we conclude that once the anomalies in different metabolic pathways are present, are closely related to the onset of obesity, metabolic syndrome and diabetes, caused by the cumulative effects of weight gain.

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Original / *Síndrome metabólico*

Glycemic and lipid metabolic disorders in diabetic and non-diabetic patients bmi < 35 or > 35 before gastric bypass

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Abstract

Introduction: **Obesity and diabetes are diseases with high prevalence worldwide. There is currently no effective medical treatment for combat the weight gain. It is precursor of diseases such as diabetes or metabolic syndrome. It is necessary to know if weight gain has cumulative effects on the glycemic and lipid metabolism as precursors of complications or comorbidities.**

Patients and methods: **We studied 131 patients (78 non-diabetic and 53 diabetic), 37 BMI ≤ 35 (3 BMI < 25, 18 BMI 25-29.9, 16 BMI 30-34.9) and 94 BMI ≥ 35 (81 BMI 35-49.9 and 13 BMI ≥ 50).We analyzed BMI, gender, diabetes and the time of evolution. Lipid profile, glucose, HbA1c and C-peptide evaluated after 12-hour fasting.**

Results: **Diabetic and diabese patients showed high triglycerides. Non-diabetics have impaired glucose (58% BMI < 35 and 36% BMI > 35). The 20% of non-diabetics BMI < 35 had high C-peptide, and 19% of BMI > 35 had high levels. The 5% of diabetics BMI < 35 had low C-peptide and 36% of BMI > 35 had high levels. HbA1c was higher in 40% of non-diabetic patients BMI < 35 compared to 13% BMI > 35.**

Conclusions: **Glucose and triglycerides increase with age and years of development of T2DM. Age of 51 and more, and men are more affected. The weight increase has cumulative effect by altering the metabolism favoring the onset of diabetes and comorbidities. Despite having intensive control treatment of diabetes, it continues its deleterious effects on patients through the years.**

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Key words: *Obesity. Diabetes mellitus. Diabesity. BMI. Metabolism.*

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TRASTORNOS DEL METABOLISMO GLICÉMICO Y LIPÍDICO EN PACIENTES DIABÉTICOS Y NO DIABÉTICOS CON IMC < 35 Ó > 35 ANTES DE BYPASS GÁSTRICO

Resumen

Introducción: **La obesidad y la diabetes son enfermedades de alta prevalencia a nivel mundial. Actualmente no existe un tratamiento médico eficaz para combatir el aumento de peso. La obesidad es precursora de enfermedades tales como la diabetes o el síndrome metabólico. Es necesario saber si el aumento de peso tiene efectos acumulativos sobre el metabolismo de la glucemia y los lípidos *como precursores de complicaciones o comorbilidades.***

Pacientes y métodos: **Se estudiaron 131 pacientes (78 no diabéticos y 53 diabéticos), 37 IMC ≤ 35 (3 IMC < 25, 18 IMC 25-29,9, 16 IMC 30-34,9) y 94 IMC ≥ 35 (81 IMC 35-49,9 y 13 de IMC ≥ 50). Se analizó el IMC, el género, la diabetes y su tiempo de evolución. El perfil lipídico, glucosa, HbA1c y el péptido C fueron evaluados después de un ayuno de 12 horas.**

Resultados: **Los pacientes diabéticos y diabesos mostraron niveles altos de triglicéridos. Los pacientes no diabéticos tienen alteración de la glucosa (58% IMC <35 y 36% IMC > 35). El 20% de los no diabéticos IMC <35 tenía péptido C alto, y un 19% de IMC >35 tenían niveles altos. El 5% de los diabéticos IMC < 35 tenía bajos niveles de péptido C y 36% de IMC > 35 tenían niveles altos. HbA1c fue mayor en 40% de pacientes no diabéticos IMC < 35 frente al 13% de IMC > 35.**

Conclusiones: **La glucosa y los triglicéridos aumentan con la edad y los años de evolución de la DMT2. La edad de ≥51 años y los hombres son los más afectados. El aumento de peso tiene efecto acumulativo alterando el metabolismo favoreciendo la aparición de la diabetes y sus comorbilidades. A pesar de tener un tratamiento de control intensivo de la diabetes, esta continúa con sus efectos nocivos sobre los pacientes a través de los años.**

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Palabras clave: *Obesidad. Diabetes mellitus. Diabesidad. IMC. Metabolismo.*

Introduction

There is a growing epidemic of chronic diseases related to dietary changes and lifestyle[1]. Over-weight and obesity are result of excess of energy intake. Fat intake in meals exceeds at least 10% of the daily recommendations[2]. This can lead to abdominal obesity and insulin resistance, factors that increase 5 times the risk of developing diabetes[3].

Obesity is proposed as an inflammatory disease that may develop insulin resistance and type 2 diabetes mellitus (T2DM) as consequence. Obesity has unexpected connections to the risk of develop of cancer, lung diseases, and others diseases. There are a close relationship between excess of nutrients and energy consumption with the alterations in the innate immune response and the cellular and molecular mediators of immunity, where the delicate balance between the immune response and metabolism becomes a pathological relationship[4].

World Health Organization (WHO)[5] mention that T2DM is a condition with permanent hyperglycemia that increase the risk of micro and macro vascular damage, which is associated with lower quality of life and reduced life expectancy. On the other hand, for the American Diabetes Association (ADA)[6], T2DM is a metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion and/or action associated with damage, dysfunction, and long-term failure of several organs.

Worldwide, 4,8 million of deaths per year were attributed to T2DM. The people with diabetes in 2012 was 371 million and will increase to 552 million in 2030, or one adult in ten[7].

In America, the highest prevalence of T2DM is found in the United States of America (USA) and Mexico. The Centers for Disease Control and Prevention (CDC)[8] of USA has estimated that 11.3% to 26.9% of U.S. citizens were diabetic in 2011.

The Mexican Diabetes Federation A.A. and the National Survey of Health and Nutrition 2006 (ENSANUT)[9] in Mexico, determined the prevalence of T2DM by 14%. In the population of the Mexican Institute of Social Security (IMSS), the diabetes prevalence was 10,5% for 2010[10].

In Europe, the prevalence of diabetes by 2010 is diverse. The lowest in Iceland 1.6%, Norway and England 3.6%, Sweden and Ireland 5.2%, Italy 5.9%, France 6.7%, Germany 8.9% and the highest in Cyprus with 9.1%[11]. In Spain the Diabetes Strategy National Health System[12] estimated the prevalence of T2DM in 6,5%.

Obesity is another epidemic disease that could develop T2DM. The increment of 1 kg/m^2 increases 9.5% the risk of fasting hyperglycemia, and 8.4% the risk to develop T2DM. The increment of 1 cm in waist circumference increases 3.2% the risk too[13].

There are several processes involved in the onset of T2DM as autoimmune destruction of cellular function, decrement by β-pancreatic exhaustion, abnormalities of metabolism of carbohydrate, fat or proteins with insulin resistance, etc.[14].

According to the ADA[6] the diagnosis is made with FPG ≥126 mg/dl (7.0 mmol/l) fasting with at least 8 hours, confirmation is needed with test oral glucose tolerance 2 hours with result ≥ 200 mg/dl (11,1 mmol/l). The International Expert Committee[15] recommends glycosylated hemoglobin (HbA1c) too for the diagnosis of diabetes.

The National Institute for Health and Clinical Excellence recommends physical activity; lose weight in order to get healthy BMI, eat diet rich in fiber, fruit and vegetables, and reducing fat of the diet[13]. ADA and the European Association for the Study of Diabetes (EASD)[16] recommend individualize each treatment according to the patient state for which there are several drugs.

Metabolic surgery is now considered as definitive treatment of diabetes, because of the immediate effect that is achieved with the improvement or resolution of T2DM after surgery, where the patient is discharged without antidiabetic treatment. The immediate resolution of T2DM depends on mechanisms due to the change of the gastrointestinal transit[17,18].

The obesity prevalence in USA for 2009 was 35,5% for women, and 32.2% for men. The Behavioral Risk Factor Surveillance System (BRFSS) and the CDC[19] showed progressive increase of 1.1% of national prevalence of obesity in previous years, so some researchers suggest that by the year 2050, where perhaps 100% of U.S. citizens will have over-weight.

The National Institute of Public Health[20] of Mexico for 2012 estimated that over-weight and obesity prevalence is 38,8% and 32,4% respectively.

In Europe, the obesity prevalence is higher in Italy, Portugal, Poland, Czech Republic, Romania and Albania. Eastern Europe and the Mediterranean countries have higher obesity prevalence than Western and Northern Europe[21]. The consensus SEEDO 2007 of Spain estimated the obesity prevalence as 15,5%[22].

The increase in obesity is due to the presence of an obesogenic environment produced by the sedentary lifestyle and dietetic global changes[23]. Besides, the cognitive aspects of reward and emotional factors play important roles in food intake that may override the homeostatic systems[24].

On the other hand, adipose tissue is an active endocrine organ that releases hormones and inflammatory mediators that regulate adipose tissue expansion, control of food intake, energy balance, and others. These effects are involved in the regulation of insulin signaling and lipid metabolism in peripheral tissues that can produce insulin resistance, T2DM or metabolic syndrome[23]. When the adipose tissue becomes dysfunctional, insulin resistant and dysfunctional lipid storage begins as a sentinel event in the progression of obesity metabolic imbalance[4]. Each increase of 5 kg of BMI over 25 kg/m^2 are associated with 29% increased of total mortality, 41% of mortality associated to vas-

cular disease and 21% of mortality associated with T2DM[25].

Treatments for obesity are limited due to the complexity of the disease. Diet and physical activity are effective but adherence is needed[26]. Behavioral therapy, physical activity, stress management, stimulus control, problem solving, cognitive restructuring, contingency management, and social support are effective too. Specific drugs for obesity are limited and have not been approved for use indefinitely, despite the chronic nature of obesity[27].

When treatment fails, weight recovery begins. The safest option for long-term weight loss is through bariatric surgery that provides too resolution of comorbidities[19,20], and could protect against the development of T2DM[28]. Diabetic lean or obese patients, have improvement or remission of their diseases after surgery, secondary to the modification of the gastrointestinal transit[29-31].

Patients and methods

Patients

We evaluated 131 patients (78 non-diabetic patients and 53 diabetic), 37 patients BMI ≤ 35 (3 BMI < 25, 18 BMI 25-29,9, 16 BMI 30-34,9) and 94 patients BMI ≥ 35 (81 BMI 35-49,9 and 13 BMI ≥ 50). We analyzed BMI, gender, presence of diabetes and its time of evolution. The laboratory studies were evaluated after at least 12-hour fasting (lipid profile, blood glucose, HbA1c and C-peptide).

BMI was classified as showed in table I. Age was clustered in ranges 15-20, 21-30, 31-40, 41-50, and 51 years of age and older. The duration of T2DM was clustered into 1-5, 6-10, 11-15, 16-20, 21-30 and 31-40 years.

Patients attended medical consultation in order to be undergoing to tailored One Anastomosis Gastric Bypass (BAGUA) for their current state of diabetes, obesity or both conditions.

Surgical procedure

Before surgery, all patients eat only liquid diet during 5 (BMI 23-34) to 7 days (BMI 35-50) depending of preoperative BMI, received antibiotic and antithrombotic prophylaxis. Tailored BAGUA[18,31] consisted in the construction of a gastric pouch from the gastroesophageal junction to the end of the minor gastric curvature at the lower level of the cisura angularis. The stapler line of the gastric pouch was fixed approximately 12 cm to the intestinal loop (first layer of the anti-reflux mechanism of BAGUA), and it was anastomosed in a laterolateral position to the mesenteric border of a small bowel loop 100 cm (BMI 23-29), 120 cm (BMI 30-32), 150 cm (BMI 33-34), 200 cm (BMI 35-40), 250 cm (BMI 40-45), and 280 cm distal (BMI 45-50) to the treitz ligament. The anti-reflux mechanism is completed fixing the afferent loop to the gastric remnant and the efferent loop to the antrum.

The size of the gastric pouch depends on the BMI of the patient. In BMI 23-32 we performed a floppy 36 French bougie pouch, while in BMI > 33 a narrow 36 French bougie one s is performed. We left systematically a drainage during the 48 h of hospital stay. After surgery, they eat liquid diet in the 1st week, semifluids in 2nd week, purée in 3-4th weeks and normal diet after one month of surgery. The patient were reviewed at 10 days, 1, 3, 6 and 12 months.

Table I
Number of patients by BMI

Group of patients	*Non-diabetic patients*	*Diabetic patients*
BMI < 25	0	3
BMI 25-29.9	1	17
BMI 30-34.9	3	13
BMI 35-49.9	62	1
BMI ≥ 50	12	1
Total	**78**	**53**

Figure represents the number of patients and distribution studied.

Blood sample processing

Laboratory personnel of the Analysis Unit Clinical Laboratory of University Associated Hospital Parque San Antonio performed the extraction of blood samples from patients with at least 8 hours fasting.

The laboratory samples analyzed were total cholesterol, HDL cholesterol, triglycerides and glucose by ultraviolet-visible spectroscopy. LDL-cholesterol was calculated by Friedman formula. C-peptide by chemiluminescent, and glycated hemoglobin by high performance liquid chromatography (HPLC)/UV-visible detector.

Normal levels of our laboratory are total cholesterol 130-220 mg/dL, HDL cholesterol >35 mg/dL, LDL cholesterol <150 mg/dL, triglycerides 40-160 mg/dL and glucose 65-105 mg/dL.

Statistical analysis

Descriptive statistics was used for comparisons. Differences among groups were analyzed by ANOVA when appropriate, and measures of central tendency according to study variables. Besides, we use percentages on gender, age, BMI, presence or absence of diabetes and its evolution time. For quantitative variables were used mean and standard deviation. To determine the association among explanatory and dependents variables was performed linear regression analysis.

We use SPSS (version 20 for Windows, SPSS, Chicago IL) and Excel 2010 programs.

Results

The 60% were non-diabetic and 40% were diabetic patients. By gender, 51% were women and 49% were men. The predominant age group was ≥ 51 years old (32% of patients). The mean age was 44 ± 13 years. The morbid obesity was predominant. The mean of evolution of T2DM was 13 ± 8 years.

Non-diabetic patients presented triglycerides 161 ± 144 mg/dl, total cholesterol 208 ± 45 mg/dl, HDL cholesterol 48 ± 13 mg/dl, LDL cholesterol 134 ± 44 mg/dl, glucose 97 ± 22 mg/dl, C-peptide 3 ± 1 ng/mL and HbA1c 5 ± 0%.

Diabetic patients presented triglycerides 165 ± 99 mg/dl, total cholesterol 188 ± 40 mg/dl, HDL cholesterol 45 ± 14 mg/dl, LDL cholesterol 112 ± 33 mg/dl, glucose 188 ± 68 mg/dl, C-peptide 2 ± 1 ng/mL and HbA1c 8 ± 1%.

Lipid metabolism

Patients with diabesity were most affected in certain laboratory studies as follow: Triglycerides were higher in diabetic patients (35% of BMI < 35, and 63% of BMI > 35) compared to non-diabetic patients (40% of BMI < 35, and 31% of BMI > 35). The 10% and 34% of non-diabetic patients BMI < 35 and > 35 respectively, had higher total cholesterol compared to 20% and 30% of diabetic patients BMI < 35 and > 35 respectively. Patients with the lowest levels of HDL cholesterol were 12% of non-diabetic compared to 42% of BMI > 35. Once again, the presence of diabetes increases the percentage of patients with LDL cholesterol abnormalities. LDL cholesterol is altered without a tendency to weight gain or adding T2DM.

Lipid profile is altered if the weight or BMI increases as show in figure 1.

As shown in the figure 1, there is a tendency to altered laboratory results with the increment of body weight. This upward trend of lipid profile may explain the vascular complications that may cause higher mortality in these patients.

Glycemic metabolism

There are high percentage of non-diabetic patients with altered serum glucose (58% of BMI < 35 compared to 36% of BMI > 35). C-peptide were found higher just in non-diabetic patients (20% of BMI < 35, and 19% of BMI > 35). The 32% of diabetics BMI < 35 had low C-peptide, and 8% had high levels. The 5% of diabetics BMI > 35 had low C-peptide and 36% had high levels.

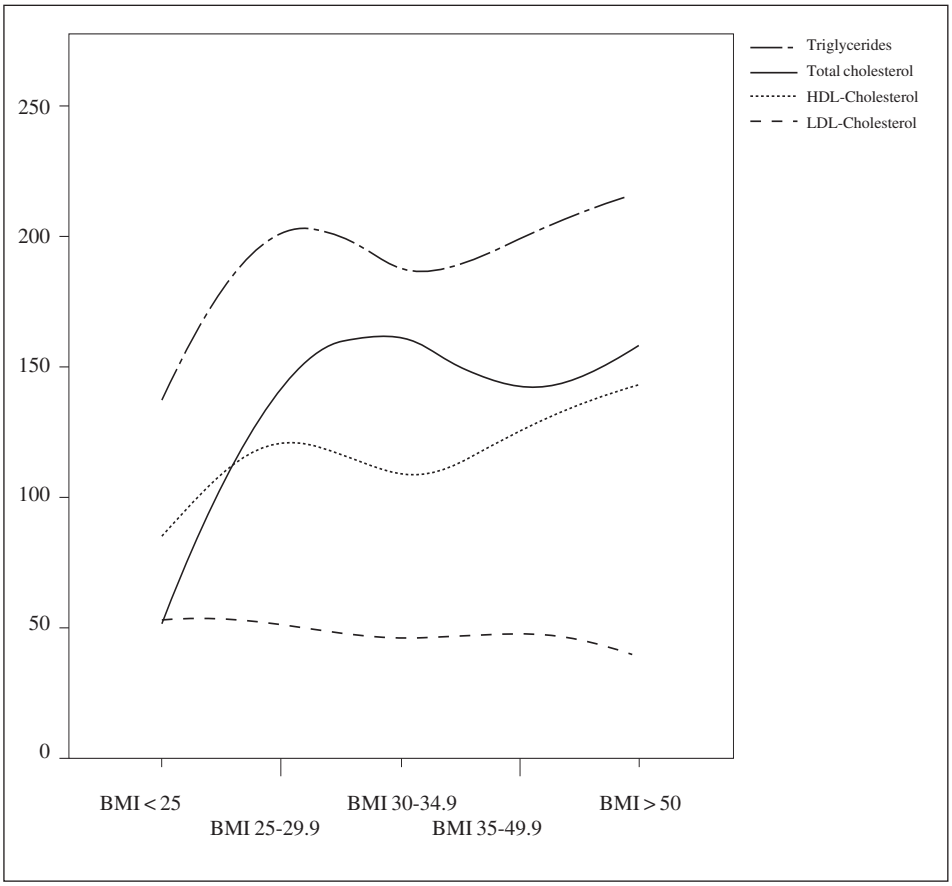


Fig. 1.—Altered metabolism of lipid with increased BMI.

Glycosylated hemoglobin was found higher in non-diabetic patients BMI < 35 (40%) compared to BMI > 35 (13%), but diabetic patients had higher levels (100% of BMI < 35, and 84% of BMI > 35).

The data obtained showed how the weight gain is closely linked to the onset of metabolic diseases like diabetes.

Table II, show in detail the percentage of glucose alteration according to the level of BMI and the presence or absence of diabetes.

We found a high percentage of non-diabetic patients with hyperglycemia and still no diagnosis of diabetes, therefore it is important that all patients considered as non-diabetics performed serum glucose test in order to prevent the onset of diabetes.

We too found a high percentage of patients with poorly controlled diabetes. Figure 2 shows the mean trend of glycosylated hemoglobin and C-peptide as BMI increases.

By linear regression analysis, we obtained the following results (table III).

The increment of weigh increases the C-peptide, BMI increases total cholesterol, LDL cholesterol and C-peptide. Age increases triglycerides, LDL cholesterol, glucose, C-peptide and glycated hemoglobin. The evolution of T2DM increases the triglycerides and glucose. These data strongly suggest that the addition of factors mentioned in the table III may cause worsening of diabetes.

Table II
Percentage of patients by BMI having glucose altered

Group of patients	*Non-diabetic patients*	*Diabetic patients*
BMI < 25		100%
BMI 25-29.9	25%	85%
BMI 30-34.9	33%	100%
BMI 35-49.9	27%	88%
BMI ≥ 50	9%	9%

The data represents the percentage of patients with altered glucose depending of the BMI. It shows how super obese patients have a different behavior from the other groups. There was non-diabetic patients BMI < 25 to compare to diabetics in same group.

Discussion

Diabetes and obesity are diseases with high prevalence worldwide. Diabetes can lead to micro and macro vascular complications with significant impact on the patient and society[6]. The impact of obesity on T2DM,

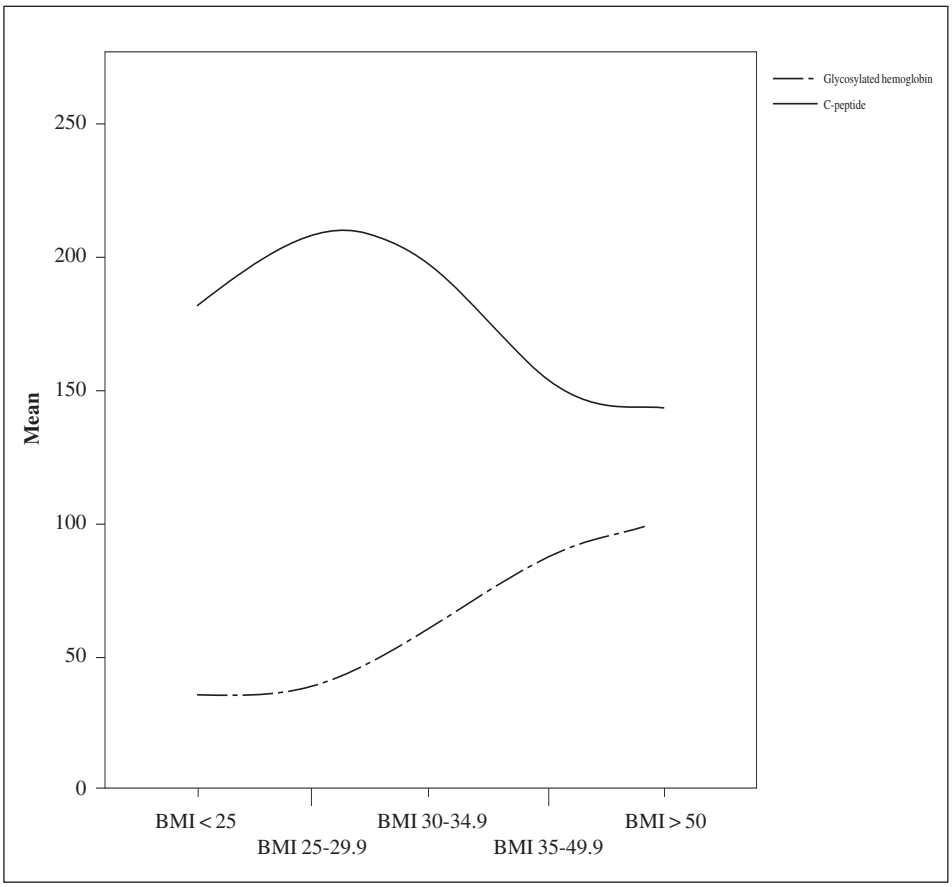


Fig. 2.—Glycated hemoglobin and C-peptide alterations according to BMI.

Table III
Increment or decrement in the levels of specific profile studies

Levels of studies of laboratory	*kg*			*BMI*			*Age*			*Year of evolution T2DM*		
	↑	↓	*P*	↑	↓	*P*	↑	↓	*P*	↑	↓	*P*
Triglycerides		0.06	**0.017***		0.012	**0.000***	0.16		**0.000***	0.4		**0.000***
Total cholesterol	0.0	0.0	**0.000***	0.008		**0.000***		0.06	**0.000***	0.0	0.0	**0.000***
LDL cholesterol	0.0	0.0	**0.000***	0.21		**0.000***	0.7		**0.000***	0.0	0.0	**0.000***
HDL cholesterol	0.0	0.0	**0.000***	0.0	0.0	**0.006***	0.0	0.0	**0.085**	0.0	0.0	**0.047**
Glucose		0.03	**0.000***		0.24	**0.000***	0.44		**0.000***	0.19		**0.000***
C-peptide	4.0		**0.000***	1.0		**0.000***	0.034		**0.000***	0.0	0.0	**0.000***
HbA1c		5.0	**0.014***		1.0	**0.000***	3.0		**0.000***		0.09	**0.000***

The data show that with increasing weight per kg and BMI in units, age in years, and every year since onset of T2DM, some laboratory studies were altered and may have deleterious effects on the human body. *Statistically significant ($p < 0.05$).

metabolic syndrome and several diseases are important, since they have both physical and psychological effect[5,13,27]. Worst of all is that there is no medical treatment to eliminate the progression of these diseases.

Both diseases have different effect on the metabolic state if one adds to the other[13]. It is important to know the functioning of the human body in its different types of metabolism for understanding the health damage, as occur if there is a sustained increase in weight that can impair health[1,2].

There are a variety of treatments for both diseases, but just bariatric surgery offers long-term changes improving both disease and its comorbidities[24,27].

The importance of this study is because there is no information about the cumulative effect of the weight on the metabolism of lipids and glycemic with the addition of diabetes.

We evaluated 131 patients attending medical consultation in order to undergo to tailored One Anastomosis Gastric Bypass (BAGUA) because of their obesity and/or T2DM state. The presence of obesity and/or diabetes in these patients caused comorbidities as previously described[18].

Subjects underwent a series of laboratory studies and were interpreted and analyzed statistically. These data indicate that increased BMI produces alterations in laboratory studies analyzed. The changes are predominant in patients with BMI > 35 where several comorbidities commonly are associated according to WHO[5,7]. Suzuki et al[24] associate obesity with cardiovascular risk factors and T2DM. The Ontario Health Quality Study in 2005[27] mention that obesity is associated with higher mortality independent of factors such as smoking. Patients with BMI < 30 are 50% more likely to die than non-obese people are, and the risk is twice from IMC > 35.

We agree with Diabetes Strategy National Health System of Spain 2012 National[32], because they mention that obesity increases with age, and men are more affected than women are. As they said, our patients have altered laboratory studies especially in the age range of 51 years and predominantly in male patients. Diabesity patients have higher percentage of involvement.

The percentage of diabetic patients with abnormal lipid profile is higher. From 31% to 63% of patients have hypertriglyceridemia, being most frequent in diabetic and obese patients. The 10% to 60% of patients had higher total cholesterol. From 12% to 45% have higher HDL cholesterol (predominantly in diabesity), and 57% to 100% had lower HDL cholesterol. This data shows higher cardiovascular risk with the increment of BMI as described by Savill[13]. These patients usually have insulin resistance due to hyperlipidemia as evidenced by Hu[33]. The CDC (8) mentions that higher BMI produces greater elevation of lipids associated with cardiovascular complications. Bille et al[34] found that central obesity is related to higher levels of insulin and triglycerides circulating due to inflammatory role of adipose tissue that causes insulin resistance, ectopic lipid storage and release of dysfunctional inflammatory mediators affecting pancreatic islets, liver, muscle and hypothalamus, causing metabolic dysfunction as evidenced by other studies[4,23].

The 32% of non-diabetic patients have hyperglycemia, 19% have higher C-peptide and 15% have elevated HbA1c. This shows undiagnosed diabetes as mentioned by Centers for Disease Control and Prevention[8].

In general, the percentage of patients with high levels of C-peptide is higher if BMI increases, probably due to greater body mass that can lead to depletion of insulin production by excessive use of β-pancreatic cell in time, as demonstrated by studies ADA and EASD[16].

Almost all diabetic patients have decreased C-peptide and elevated HbA1c. This highlights the higher risk of micro and macro vascular complications on this type of patients as mentioned by the United Nations[5].

We found that diabetic patients have a greater increase in triglycerides and serum glucose with decreased C-peptide in relation to non-diabetics. These data confirm that dysfunctional adipose tissue causes

hypertriglyceridemia, insulin resistance, hyperglycemia and decrease of β-pancreatic cell function because of depletion (reduced C-peptide)[17]. If all these data come together, the human body deteriorate with the development of the known complications. Diabetic patients despite having hypoglycemic treatment, continue with the progression of diabetes, as mentioned by the ADA and EASD[16].

Previous data confirmed that weight gain leads to increase of lipid metabolism alteration[34].

Patients who achieved morbid obesity were more affected than other kind of obesity, possibly because of the imbalance of adipose tissue expandability as described by Lumeng et al[4] capable of triggering the comorbidities known by several mechanisms[33]. It is impossible to identify obese patients who will have this imbalance, making it better preventing obesity and thereby directly influence the onset of diabetes[12-14].

Although the number of our patients is the main limitation of the study, the findings are very interesting and important, and should encourage further research into metabolic pathways, study larger amounts of patients long-term in order to prevent the development of several metabolic diseases.

Physicians are encouraged to advise bariatric or metabolic surgery in a timely manner to eliminate obesity and improvement or resolution of the whole complex of conditions including T2DM actions that can not only extend life, but also improve the quality of life[17,18,27,30].

Conclusions

The increment of weight produces metabolic disorders. Diabesity is well known that has serious and deleterious effects on the body. Diabesity and an increased duration of T2DM, generate higher percentages of patients with metabolic disorders compared to non-diabetics. The increment of age in years, the increment of weight, presence of diabetes and its time of evolution, produce cumulative alterations in specific metabolisms. There are high percentage of patients without diagnosed diabetes who have hyperglycemia. Although patients have a treatment for diabetes, advancing age and the years of evolution of diabetes, the glucose is rising along with triglycerides, which can influence the deleterious effects of complications on human body. The patients studied, due to its metabolic condition, took the best decision to undergo bariatric surgery for improvement or resolution of their diseases including diabetes mellitus, so it is important to inform the general population the benefits achieved today.

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Original / *Síndrome metabólico*

Hypocaloric diet associated with the consumption of jam enriched with microencapsulated fish oil decreases insulin resistance

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Abstract

Background: **The metabolic syndrome is related to the increase in cardiovascular diseases. Polyunsaturated fatty acids from fish oil help in reducing cardiovascular risk factors and are natural bindings of PPARγ2.**

Objective: **To evaluate the impact of hypocaloric diet associated with microencapsulated fish oil supplementation in women with metabolic syndrome.**

Methods: **We conducted a randomized, single-blind and placebo-controlled clinical trial with adult women who presented metabolic syndrome (n = 30) for 90 days. The volunteers were divided into two groups: placebo group (n = 15) and microencapsulated fish oil group (n = 15) (3 g/day of microencapsulated fish oil containing 0.41 g/day of eicosapentaenoic acid and decosahexaneoic acid). Anthropometric, body composition, clinical and laboratory parameters were assessed before and after the intervention. Paired t-test was used for comparisons within groups and Student's *t*-test for comparison between groups. We considered p < 0.05 as significant values.**

Results: **The comparison between groups revealed a significant reduction of blood glucose, insulinemia and the homeostasis model assessment in the microencapsulated fish oil group after 90 days, as opposed to the placebo group. We also observed reduction of the systolic arterial pressure in the microencapsulated fish oil group.**

Conclusion: **A hypocaloric diet associated with the consumption of microencapsulated fish oil was effective in reducing blood glucose, insulinemia and insulin resistance in women with MS.**

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Key words: *Metabolic syndrome. Fish oil. Insulin resistance. Hypocaloric diet. Microencapsulation.*

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LA DIETA HIPOCALÓRICA JUNTO CON MERMELADA ENRIQUECIDA CON ACEITE DE PESCADO MICROENCAPSULADO DISMINUYE LA RESISTENCIA A LA INSULINA

Resumen

Antecedentes: **El síndrome metabólico se relaciona con un incremento de las enfermedades cardiovasculares. Los ácidos grasos poliinsaturados del aceite de pescado ayudan a reducir los factores de riesgo cardiovascular y son ligandos naturales del PPARγ2.**

Objetivo: **Evaluar el impacto de la dieta hipocalórica asociada con suplementación de aceite de pescado microencapsulado en mujeres con síndrome metabólico.**

Métodos: **Realizamos un ensayo clínico de distribución aleatoria, simple ciego y controlado con placebo en mujeres adultas con síndrome metabólico (n = 30) durante 90 días. Se dividió a las voluntarias en dos grupos: el grupo placebo (n = 15) y el grupo con aceite de pescado microencapsulado (n = 15) (3 g/día de aceite de pescado microencapsulado que contienen 0,41 g/día de ácido eicosapentaenoico y de ácido decosahexaneoico). Se evaluaron parámetros antropométricos, clínicos y de laboratorio y la composición corporal antes y después de la intervención. Se emplearon la prueba t pareada para las comparaciones dentro de los grupos y la prueba t de Student para la comparación entre grupos. Consideramos valores significativos de p < 0,05.**

Resultados: **La comparación entre grupos reveló una reducción significativa de la glucosa sanguínea, la insulinemia y la evaluación del modelo homeostático en el grupo de aceite de pescado microencapsulado tras 90 días, en comparación con el grupo placebo. También observamos una reducción de la presión arterial sistólica en el grupo con aceite de pescado microencapsulado.**

Conclusión: **La dieta hipocalórica asociada con el consumo de aceite de pescado microencapsulado fue eficaz en la reducción de la glucosa sanguínea, la insulinemia y la resistencia a la insulina en mujeres con SM.**

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Palabras clave: *Síndrome metabólico. Aceite de pescado, Resistencia a la insulina. Dieta hipocalórica. Microencapsulación.*

Introduction

Metabolic syndrome (MS) is characterized by a set of cardiovascular risk factors[1] associated with central obesity and insulin resistance (IR) responsible for increased cardiovascular mortality[2]. The frequency of MS has been greater in women in Brazil[3] and in countries like China[4] and Spain[5].

N-3 polyunsaturated fatty acids (PUFA) –derived from fish oil (FO), eicosapentaenoic acid (EPA) and decosahexaneoic acid (DHA) –act by increasing insulin sensitivity[6]. N-3 PUFA in FO is susceptible to lipid oxidation[7]. This characteristic leads to changes in its physical and chemical structure and compromises its sensory characteristics, such as odor and taste[8]. Microencapsulation increases the stability of PUFA,[9] in addition to improving its palatability and avoiding the discontinuity of treatments.

Microencapsulation is a procedure that consists in coating of active materials (core) by an encapsulating matrix (water-soluble agents or insoluble in water) with the production of microcapsules whose size can vary from a few nanometers to several micrometers[10]. It is a procedure that has been successfully used by cosmetics, pharmaceutical and food industries[10]. Microencapsulation can be used in the enrichment of food with FO.

In Brazil, there is no food enriched with microencapsulated fish oil(ME FO). Studies of individuals with MS treated with food fortified with ME FO are nonexistent. Available studies on foods enriched with ME OP are scarce and have been conducted with healthy individuals[11,12]. This fact justifies our study and led to the elaboration of light strawberry jam enriched with ME FO. This study attempted to assess the impact of a hypocaloric diet associated with the consumption of light jam enriched with ME FO on insulin resistance in women with metabolic syndrome.

Patients and Methods

Study group

Adult women (aged 30 to 45 years) diagnosed with MS according to the International Diabetes Federation[13] were recruited through advertisements in newspapers. Exclusion criteria were: allergy to strawberry; pregnancy; lactation; using fatty acid supplements; submission to bariatric surgery; and nutritional or pharmacological treatment for the reduction of body weight during the last three months before the trial.

The volunteers were informed about the research and signed an Informed Consent Form, in accordance with resolution 196/96 of the National Health Council. The study protocol was approved by the Committee of Ethics on Research of the Clementino Fraga Filho University Hospital, Federal University of Rio de Janeiro (181/10 Protocol).

Study design

We conducted a randomized single-blind and placebo-controlled clinical trial. The volunteers (n = 30) were distributed into two groups that received jam enriched with ME FO fortnightly (3 g/day, totaling 0.4 g/day of EPA and DHA) or placebo (jam not enriched) for 90 days. We performed blood collection and assessment of clinical, anthropometric, body composition, biochemical and insulin resistance parameters at the beginning (T0) and the end (T90) of the study.

Nutritional treatment

A hypocaloric diet was prescribed by predicting a body mass reduction of 2 kg/month with an estimated total energy value[15,16]. The macronutrient composition was in accordance with the recommendations of the Ministry of Health that suggests a distribution of 50 to 60% of the total energy value (TEV) of carbohydrates, 15% of TEV od proteins or 0.8% -1g/weight current/day and 25 to 30% in the form of lipids, in which saturated fatty acids correspond to less than 10% of TEV, polyunsaturated fatty acids up to 10% and monoinsaturated fatty acids up to 20%[17]. We assessed the adhesion to the eating plan through food records evaluated with the Food Processor software (version 12)[18]. During the 90 days of testing, fortnightly consultations, delivery of jams and nutritional follow-ups of the volunteers were conducted.

Microencapsulation, elaboration and enrichment of light strawberry jam with ME FO

We used the complex coacervation method for microencapsulation of FO[19], through which we obtained a paste. Microencapsulation was performed at Mikron Microcapsules Laboratory (São Paulo, Brazil). The percentage of ME FO in the paste was 30%. For the preparation of jam, strawberries purchased on the market, sugar (reduced by 30%), sucralose, pectin and citric acid were used. The ME FO paste and the jam were mixed (ratio 2:1) manually and packed in food packaging kept under refrigeration until delivery. The placebo was strawberry jam without FO enrichment.

For the calculation of the amount to be provided to volunteers per consultation, we considered 16 days (one extra day as safety margin). The women were guided to consume the jam enriched (30 g/day, totaling 3 g/day of ME FO) at breakfast and keep it stored under refrigeration. The participants were instructed to not washing the pots and returning them fortnightly in order to assess jam leftovers.

Clinical, anthropometric and body composition assessments

Blood pressure (BP) was measured by auscultatory method with the use of aneroid sphygmomanometer

and stethoscope[20]. Body mass (kg), height (m)[21] and waist circumference[22]were measured and the body mass index (BMI) calculated[14]. Fat and fat-free masses were assessed by the method of electric bioimpedance (BIA 450 bioimpedance analyzer-Biodynamics Corporation, USA). The volunteers were previously guided to the assessment of body composition[23].

Blood collection and biochemical assessment

After a 12-hour night fasting, the volunteers were subjected to blood collection using tubes without anticoagulant (Vacutainer tubes,Becton, Dickinson & Company, USA). Aliquots of serum were obtained by centrifugation (4,000 rpm for 15 minutes) and stored at-20 °C until the analysis.

Serum concentrations of triglycerides, total cholesterol and HDL cholesterol were determined by enzymatic-colorimetric method (commercial kit, Bio-Systems), with the reading performed in an A15Automated Analyzer (BioSystems). Serum concentrations of LDL cholesterol were calculated using Friedwald's formula - [LDL - cholesterol = Total Cholesterol - (HDL-Cholesterol + triglyceridemia/5)], only valid for individuals with triglyceridemia < 400 mg/dL[24].

Insulinemia was assessed by the radioimmunoassay method (commercial ImmuChem™ Coated Tube kit of MP Biomedicals®, Insulin, CT) using the 2470 WIZARD Automatic Gamma Counter (Perkin-Elmer Inc.). Insulin resistance was estimated by Homeostasis Model Assessment: Insulin Resistance (HOMA-IR)[25].

Statistical analysis

The results were expressed as mean ± standard error. We used the Student's *t*-test and the paired *t*-test. We also used the Statistical Package for the Social Sciences (SPSS), version 17 and p value < 0.05 was considered significant.

Table I
General information about the groups studied

	Control group	*ME FO group*
	(n = 15)	(n = 15)
Year (years)	40.4 ± 1.0	39.7 ± 0.9
BMI (kg/m²)	32.4 ± 0.5	32.9 ± 0.4
Income per capita (R$ - BRL)	612.94 ± 319.30	588.92 ± 290.80
Skin color (non white) (%)	84.6	74.2
Marital status (married) (%)	61.5	54.8
Practice physical activity (%)	39	35
Schooling		
< 9 years of schooling (%)	53.8	35.5

Results expressed as mean ± standard deviation and percentage (%).
*statistically significant for $p < 0.05$.

Results

Women with MS selected for the study showed grade 1 obesity (32.6 ± 1.8 kg/m²)[14] and their general characteristics can be observed in table I. Adhesion to jam consumption was assessed by observation of leftovers contained in the packs returned at fortnightly consultations. There were no reports of gastrointestinal discomforts.

The average consumption of macronutrients in the groups revealed to be in accordance with the prescriptions; however, the average energy intake was below the prescription (table I). There were no significant differences within and between groups (ME FO and placebo).

Both groups showed significant reduction of body mass, BMI and waist circumference (table II). Placebo

Table II
Dietary intake of control group and ME FO group during the study

		Control			*ME FO*		
Nutrient	*Prescription*	*1st Month*	*2nd Month*	*3rd Month*	*1st Month*	*2nd Month*	*3rd Month*
TEV (kcal/day)	1.537,5 ± 31,5[a] 1.533,3 ± 37,4[b]	1226.7 ± 30.7	1259.3 ± 31.3	1350.3 ± 36.5	1271.5 ± 42.8	1254.4 ± 46.6	1192.8 ± 21.5
Carbohydrates (% TEV)	50-60[d]	53.0 ± 0.5	50.2 ± 0.6	51.2 ± 1.8	51.2 ± 1.9	55.0 ± 1.6	51.9 ± 14
Proteins (% TEV)	about 15[d]	22.0 ± 0.8	22.1 ± 0.5	20.3 ± 0.3	21.0 ± 0.6	20.3 ± 0.8	21.5 ± 1.1
Lipids (% TEV)	25-30[d]	25.0 ± 0.6	26.2 ± 04	28.6 ± 1.7	27.7 ± 1.7	26.0 ± 1.3	26.6 ± 0.7
SFA (% TEV)	< 10[d]	8.6 ± 0.4	9.8 ± 0.3	10.4 ± 0	9.8 ± 1.0	9.0 ± 0.3	9.5 ± 0.5
MFA (% TEV)	≤ 20[d]	7,9 ± 0.2	8.0 ± 0.3	8.7 ± 0.6	9.4 ± 0.4	8.2 ± 0.6	8.7 ± 0.2
PUFA (% TEV)	≤ 10[d]	4.2 ± 0.3	4.5 ± 0.3	3.8 ± 0.2	4.9 ± 0.2	4.6 ± 0.2	4.3 ± 0.1
TFA (% TEV)	< 1[e]	0.4 ± 0.02	0.5 ± 0.1	1.0 ± 0.5	0.5 ± 0.1	0.6 ± 0.05	0.5 ± 0.05
Cholesterol (mg/day)	< 300[d]	171.1 ± 17.7	189.0 ± 21.0	207.3 ± 18.9	185.3 ± 24.1	163.4 ± 24.0	194.8 ± 25.6
Fiber (g/day)	20-30[d]	16.7 ±0,8	15.3 ± 0.3	16.5 ± 1.1	17.6 ± 1.6	17.3 ± 2.2	16.4 ± 0.6
Na (mg/day)	<2400[d]	1292.7 ± 51.1	1245.6 ± 78.9	1462.1 ± 41.1	1124.4 ± 232.7	1205.3 ± 106.4	1198.8 ± 38.3

TEV: total energetic value; SFA: saturated fatty acids; MFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids; TFA: trans fatty acids; Na: sodium; [a e b] mean ± standard error of TEV prescribed to placebo group and ME FO group, respectively; [d] I Brazilian Guideline for Diagnosis and Treatment of Metabolic Syndrome (2005); [e] World Health Organization (2003).

group showed a significant reduction in body fat. ME FO group found no difference in body composition. The variation of these data did not differ significantly between the groups. ME FO group had a significant reduction in systolic arterial pressure, as opposed to the placebo group (table II).

Blood glucose concentrations, insulinemia and HOMA-IR showed significant reduction in the ME FO group (fig. 1); whereas in the placebo group there was no significant reduction of these parameters (table III).

We did not observe significant differences on the lipid profile between the groups at the end of the study. This shows that the hypocaloric diet was also effective in the improvement of these data (table III).

Discussion

This study found that consumption of jam enriched with 3 g/day of ME FO, containing 0.41 g/day of EPA and DHA, resulted in the reduction of blood glucose, insulinemia and HOMA-IR after a 90-day intervention, as opposed to the hypocaloric diet.

Giacco et al.[26] supplemented 3.6 g/day of FO (2.1 g of EPA and 1.5 g of DHA) for 90 days and did not observe any effect of FO on reducing blood glucose. The same result was observed by Brandy et al.[27] who used 4 g of FO (2.5 g of EPA and DHA). On the other hand, 3 g/day of FO (180 mg of EPA and 120 mg of DHA) were used in a study carried out by Simon et al.[28] and they observed increased blood glucose after 90 days.

These different results in blood glucose can occur due to the profile of subjects studied and the amount of EPA and DHA supplemented. Giacco et al.[26] assessed overweight individuals, whereas the volunteers in our study suffered from grade 1 obesity.

The effect of FO in blood glucose can be attributed to the activation of PPARγ2 by EPA and DHA ligands[29]. PPARγ2 operates in the metabolism of glucose by increasing the expression of genes related to glucose transporter 4 (GLUT4) in the skeletal muscle and has high affinity for insulin, facilitating the absorption of glucose by the cells, thus aiding in reduction in blood glucose[30].

Similar to our research, a study carried out by Ramelet al.[31] with grade 1 obese patients undergoing a hypocaloric diet associated with 3 g of FO (1.3 g of EPA and DHA) supplementation also found insulinemia reduction after eight weeks. The same result was observed in a study carried out by Krebs et al.[32] who supplemented 1 g of FO (1.3 g of EPA and 2.9 g of DHA). On the other hand, Waite et al.[33] did not observe change in insulinemia after 60 days.

A study by Simon et al.[28] resulted in an increase in HOMA-IR after 90 days of treatment with 3g/day of FO (180 mg of EPA and 120 mg of DHA). Such results are contrary to those found in the literature and our study, probably due to the amount of EPA and DHA supplemented. We can observe that the higher the dose (> 3 g dose) of EPA and DHA supplemented the more deleterious effect on glycidicmetabolism[34].

N-3 PUFA can improve IR by several mechanisms, such as reducing the production of pro-inflammatory eicosanoids by inhibiting the phospholipase A2 enzymes[35] and increasing the expression of the gene that encodes the adiponectin[36], which promotes the oxidation of fatty acids and increases insulin sensitivity in muscles and liver[37]. This pathway is mediated by receptors of adiponectin leading to activation of protein kinase activated by adenosine monophosphate (AMPK), which is an important modulator of lipid metabolism and glucose. It increases the oxidation of lipids, reducing the concentration of free fatty acids in the plasma and thus improves the absorption of glucose in muscles by increasing their sensitivity to insulin[38]. In addition, PPARγ directly modulates the signaling pathway of insulin transduction in adipose tissue by increasing the expression of intracellular proteins that stimulate the transport of glucose[39].

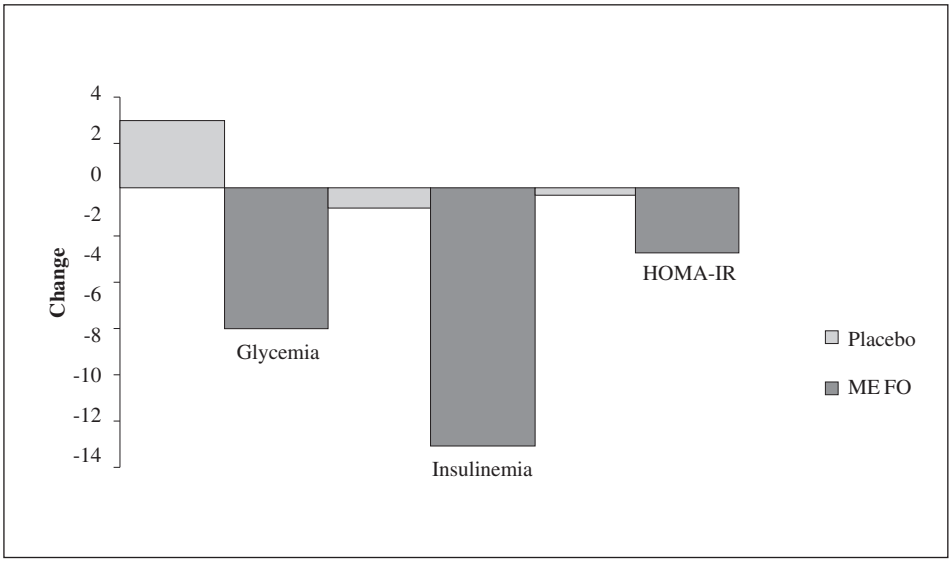


Fig. 1.—Changes in blood glucose, insulin and HOMA-IR and control groups OP ME throughout the study.

Table III
Impact of lifht strawberry jam enriched with ME OF (3 g/day) on the biochemical variables in the groups assessed at the beginning of the study and after 90 days

Variables	*Control group*	*ME OF Group*
Glucose (mg/dL)		
Before	85.3 ± 2.3	93.3 ± 2.8
After	88.2 ± 1.7	87.2 ± 3.2*
Variation	2.9 + 0.4	- 6.1+0.4 ‡
Uric acid (mg/dL)		
Before	4.7 ± 0.3	4.8 ± 0.3
After	4.5 ± 0.3	4.8± 0.3
Variation	- 0.2 ± 0.0	0.0±0.0
Triglycerides (mg/dL)		
Before	171.6 ± 23.4	135.9 ± 11.4
After	144.9 ± 24.2	145.7 ± 14.7
Variation	- 26.7 ± 0.8	9.8 ± 3.3
Total Cholesterol (mg/dL)		
Before	194.5 ± 9.8	198.9 ± 8.4
After	195.9 ± 9.0	195.9 ± 7.5
Variation	1.4 ± 0.8	- 0.3 ± 0.9
HDL-C (mg/dL)		
Before	52.2 ± 4.2	52.2 ± 2.6
After	52.3 ± 3.9	49.7 ± 1.9
Variation	0.1 ± 0.3	- 2.5 ± 0.7
LDL-C (mg/dL)		
Before	106.1 ± 5.8 (n=14)	119.5 ± 7.4
After	114.5 ± 6.2	117.2 ± 6.7
Variation	8.4 ± 0.4	- 2.3 ± 0.6
VLDL-C (mg/dL)		
Before	31.0 ± 3.4 (n=14)	27.2 ± 2.3
After	29.1 ± 4,9	29.0 ± 2.9
Variation	- 1.9 ± 1.5	1.8 ± 0.6
Insulin (μU/mL)		
Before	36.1 ± 4.3	28.9 ± 7.3
After	35.2 ± 4.5	17.6 ± 3.4 (n=14)*
Variation	- 0.9 ± 0.2	- 11.3 ± 3.9 ‡
HOMA-IR		
Before	7.8 ± 1.0	6.6 ± 1.7
After	7,6 ± 1,0	3.6 ± 0.6 (n = 14)*
Variation	- 0.2 ± 0.0	- 3.0 ± 1.2 ‡

Values expressed as average ± standard-deviation (minimum - maximum). HDL: high density lipoprotein; LDL: low-density lipoprotein; VLDL: very low density lipoprotein, *P < 0.05 *vs* before (difference within the group), P < 0.05: ME FO group *vs* control group, #P < 0.05: ME CLA group vs. ME OF group.

PPARγ2 activation by FO has been associated with the reduction of serum concentrations of fatty acids whose increase is related to the IR. This is another mechanism that could explain the reduction of IR by using FO[40].

According to data observed in this study, supplementation with ME FO seems to promote greater SAP and DAP reduction than a hypocaloric diet. These results are in accordance with those observed in the literature[41]. It was demonstrated that adiponectin helps in reducing arterial pressure due to its direct action on the vascular endothelium, promoting endothelium-dependent vasodilatation[41]. We can observe that the activation of PPARγ2 by n-3 PUFA present in the FO has direct effects on the regulation of the vascular structure and protective effect on the endothelium by inhibiting the production of endothelin 1 (ET-1)[42]. ET-1 is an important vasoconstrictor peptide secreted by endothelial cells in response to insulin. This way, high concentrations of ET-1 are observed in individuals with IR[43].

Conclusion

A hypocaloric diet associated with the consumption of jam enriched with ME FO reduced blood glucose, insulinemia and HOMA-IR in women with MS.

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Original / *Alimentos funcionales*

Antioxidant responses of damiana *(Turnera diffusa* Willd) to exposure to artificial ultraviolet (UV) radiation in an *in vitro* model; part I; UV-C radiation

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Abstract

Introduction: **Ultraviolet type C (UV-C) radiation has higher energy than the UV-B radiation and has been less studied because it is completely absorbed by the ozone layer. However, artificial UV-C radiation can generate diverse modifications in the plants. Given that exposure to UV-C for short periods of time increases the antioxidant content, improving the appearance and shelf-life of products, its potential application in postharvest treatments to modify the antioxidant content of medicinal plants, such as damiana *(Turnera diffusa),* is novel and relevant.**

Objective: **To determine the effects of UV-C radiation on enzymatic and non-enzymatic antioxidant defenses, as well as oxidative damage levels, in damiana *(Turnera diffusa)* plants *in vitro.***

Results: **UV-C radiation decreased superoxide dismutase (SOD, EC 1.15.1.1) and total peroxidases (POX, EC 1.11.1) activities, the concentration of chlorophylls *(a* and *b),* carotenes, vitamin C, and total antioxidant capacity. UV-C radiation increased the phenolic compound levels in damiana. Loss of antioxidant defenses was higher in damiana plants exposed to higher UV-C doses and/or for longer periods. This study suggests that UV-C radiation induces oxidative stress, evidenced as increased protein carbonyls and phenolic compound content, in damiana *(T. diffusa).***

Conclusion: **Low dose, short exposure to UV-C stimulates phenolic compound content in damiana. Thus, controlled UV-C treatments could be used as postharvest treatment to increase phenolic compound content in damiana plants.**

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Key words: *Antioxidants. Antioxidant capacity. Phenolic compounds.* Turnera diffusa. *UV-C radiation. Vitamin C.*

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RESPUESTA ANTIOXIDANTE EN DAMIANA *(TURNERA DIFFUSA* WILLD) EXPUESTA A RADIACIÓN ULTRAVIOLETA (UV) ARTIFICIAL EN UN MODELO *IN VITRO;* PARTE I; RADIACIÓN UV-C

Resumen

Introducción: **La radiación ultravioleta tipo C (UV-C) presenta mayor energía y es menos estudiada que la radiación UV-B, debido a que se considera que es totalmente absorbida por la capa de ozono. Sin embargo, la radiación UV-C artificial es capaz de generar diversas modificaciones en las plantas. Dado que la exposición a UV-C por intervalos de tiempo cortos incrementa la concentración de compuestos antioxidantes, mejorando la apariencia y vida de anaquel de los productos, su potencial aplicación en tratamientos poscosecha para modificar el contenido antioxidante de plantas medicinales, como la damiana *(Turnera diffusa),* es novedoso y relevante.**

Objetivo: **Determinar el efecto de la radiación UV-C sobre las defensas antioxidantes enzimáticas y no enzimáticas, así como en los niveles de daño oxidativo de damiana *(Turnera diffusa) in vitro.***

Resultados: **La radiación UV-C disminuyó la actividad de las enzimas superóxido dismutasa (SOD, EC 1.15.1.1) y peroxidasas totales (POX, CE 1.11.1), la concentración de clorofila *(a y b),* carotenos, vitamina C y la capacidad antioxidante total, e incrementó el contenido de compuestos fenólicos en damiana. La disminución de las defensas antioxidantes fue mayor en plantas de damiana expuestas a dosis más altas de UV-C o por períodos más largos. Estos resultados sugieren que la radiación UV-C induce estrés oxidativo, evidenciado por el incremento del contenido de carbonilos proteicos y el contenido de compuestos fenólicos en damiana *(T. diffusa).***

Conclusión: **Dosis bajas y menor exposición a UV-C estimulan la síntesis de compuestos fenólicos en damiana. Por ello, tratamientos controlados con UV-C podrían emplearse como tratamientos poscosecha para incrementar el contenido de compuestos fenólicos en plantas de damiana.**

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Palabras clave: *Antioxidantes. Capacidad antioxidante. Compuestos fenólicos. Radiación UV-C.* Turnera diffusa.

Abbreviations

DPPH: 2,2-diphenyl-2-picrylhidrazyl.
GAE: Gallic acid equivalents.
GAEAC: Gallic acid equivalent antioxidant capacity.
HPLC: High-performance liquid chromatography.
POX: Total peroxidases.
SOD: Superoxide dismutase.
TBARS: Thiobarbituric acid-reactive substances.
UV: Ultraviolet radiation.
UV-C: Ultraviolet radiation type C.

Introduction

Ultraviolet type C (UV-C) radiation produces harmful effects because it is highly energetic and can induce damage to DNA[1-2]; thus, is widely used artificially as germicide and for the conservation of food, mainly in postharvest handling and in minimally processed products, requiring only short-duration treatments[3-4]. UV-C radiation, as compared to UV-A and UV-B radiation, is considered to be totally absorbed by ozone[2,5]. The weakening of the ozone layer over the past years has generated an increase in the ultraviolet (UV) radiation levels that reach the troposphere[6]. Plants respond to increased UV radiation by modifying the antioxidant defense system to minimize oxidative damage[7]. UV-C radiation can induce modification of the antioxidant content in plants[8], mainly due to stimulation of the activity of phenylalanine ammonia-lyase (PAL), which is a precursor in the synthesis of phenolic compounds[9]; essential nutrients and the major contributors of the antioxidant potential in the human diet[10]. Therefore, UV-C radiation could be used to stimulate the production of molecules of biological and/or commercial interest, avoiding the use of genetically modified organisms[11]. The importance of including spices and/or plants products with elevated concentration of phenolic compounds in the diet and their contribution to human health have been recently reported[12].

Damiana (*Turnera diffusa*, Willd) is used in traditional medicine, as treatment of genito-urinary diseases, and as an aphrodisiac[13,14]. Despite the traditional and economic importance of this plant, knowledge of the composition and properties of bioactive molecules in damiana is scarce[15]. The potential application of exposure to UV-C as a postharvest treatment in order to increase the antioxidant content, with the possibility of the additional benefits of improving the appearance and shelf-life of medicinal plants, such as damiana, is novel and relevant. The objective of this study was to determine if exposure to UV-C radiation can be an alternative for increasing phytochemical compounds of interest in damiana (*T. diffusa*) plants in an *in vitro* model. The effect of UV-C radiation was assessed by quantifying the enzymatic and non-enzymatic antioxidant compound content, total antioxidant capacity, and oxidative damage (TBARS and protein carbonyls) levels in damiana leaves.

Materials and methods

Plant material and experimental setup

Damiana plants were introduced in tissue culture following the methodology of Alcaraz-Meléndez *et al.*[16], where Murashigee-Skoog (MS) medium culture was used. Five plantlets were used in triplicate as the experimental unit per treatment and day of irradiance. Bottles were covered with plastic and plantlets were grown for 6 weeks in 24 h photoperiod with white light at 25°C. UV-C radiation treatments were performed within a wooden box fully lined on the inside with aluminum foil. Germicidal lamps (G15T8 of 253.7 nm, The Medical Technology, Neuhäusler. A. G.) with an output of 0.38 mW cm^{-2} were used as a source of artificial UV-C radiation. The UV-C lamp was positioned and fixed at 45 cm above the cup of the plants. Treatments were: 1) control, plants grown with white light for 24 hours each day; 2) 5 min of exposure to UV-C daily; 3) 10 min of exposure to UV-C daily; 4) 20 min of exposure to UV-C daily. The rest of the time, the plantlets were under white light (24 hours). At the onset of the experiment (day zero), recently irradiated (day one), and every third day, samples were collected for up to 10 days of treatment. Samples were fixed by immersion in liquid N_2 and stored at -80°C prior to being analyzed.

Enzymatic and non-enzymatic antioxidants

Analytical methods used to obtain plant extracts and homogenates, and to quantify the antioxidant defenses in damiana plants have been described previously[15,17]. All the leaves from 5 plantlets were pooled and used for analysis; all analyses were run in triplicate. Briefly, chlorophyll *a*, chlorophyll *b*, and total carotenoid content were analyzed by the method of Lichtenthaler and Wellburn[18] and are expressed in μg g^{-1} of fresh weight. The coefficients of variability for chlorophyll *a*, chlorophyll *b*, and total carotenoid content were 5.5, 7.3, and 24.3, respectively. Superoxide dismutase (SOD, EC 1.15.1.1) activity was spectrophotometrically determined at 560 nm (Beckman Coulter DU-800, CA, USA) using the method of Suzuki[19]. One unit of SOD activity is defined as the quantity of enzyme necessary to inhibit the maximal rate of NBT reduction by 50%; the coefficient of variability for this method was 8.8. Total peroxidases (POX, EC 1.11.1) activity was detected spectrophotometrically at 420 nm[20]. One unit of POX activity is considered as the amount of enzyme required to increase absorbance by 0.1. The coefficient of variability for POX activity was 9.0. Antioxidant enzyme activities are expressed in units mg^{-1} protein.

Vitamin C (L-ascorbic acid) and vitamin E (α-tocopherol) content was quantified using high-performance liquid chromatography (HPLC, Waters, Milford, MA, USA). Chromatographic conditions and methods were

as described by Gratzfeld-Hüsgen and Schuster[21] and Soriano-Melgar *et al.*[15,17] Results were obtained by using standard curves of L-ascorbic acid (5-200 ng μL^{-1}) and α-tocopherol (5-200 ng μL^{-1}), respectively. Results are expressed as mg vitamin C g^{-1} fresh weight and mg of vitamin E g^{-1} fresh weight. The coefficients of variability for vitamin C and E were 0.26 and 4.0, respectively.

Total phenolic compound content was quantified by using the method of Singleton and Rossi[22], modified to use on a microplate reader (BioRad™, CA, USA), and using a standard curve of gallic acid (0-350 µg mL^{-1}). Results are expressed as mg gallic acid equivalents (GAE) g^{-1} fresh weight. The coefficient of variability was 3.2 for this method.

Total antioxidant capacity was determined following the method described by Brand-Williams *et al.*,[23] using the commercial free radical 2.2-diphenyl-2-picryl-hidrazyl (DPPH) and a standard curve of gallic acid (50-300 mg mL^{-1}). Total antioxidant capacity is reported as µM gallic acid equivalent antioxidant capacity (GAEAC) g^{-1} fresh weight; the coefficient of variability was 7.0.

Oxidative damage

The concentrations of thiobarbituric acid reactive substances (TBARS), as indicator of lipid peroxidation, and of protein carbonyls were analyzed as proxy for oxidative damage as previously described[15,17]. Briefly, the method of Persky *et al.*[24] was employed to quantify TBARS levels by using a standard curve of 1-bis tetraetoxipropane (TEP, 0-20 nmoles mL^{-1}); results are expressed as nmol of TBARS mg^{-1} protein. The coefficient of variability for TBARS analyses was 8.3. The content of protein carbonyls was analyzed following the method of Levine *et al.*[25], and results are expressed in µM protein carbonyls g^{-1} fresh weight. The coefficient of variability for protein carbonyls was 10.0.

Total protein content

Total protein content was used to standardize results of enzyme activities and TBARS levels, and were analyzed by the method of Bradford[26] modified for use in a microplate reader (BioRad™) as previously described[15,17]; a curve of bovine serum albumin (BSA) was included as standard. Total protein content was expressed in mg g^{-1} fresh weight. The coefficient of variability was 17.9 between days and treatments in this methodology.

Statistical analyses

Data were tested for normality and homoscedasticity of variance. Analysis of variance (ANOVA) and Tukey post-hoc tests were used to determine significant differences between days (0, 1, 4, 7 and 10 days) and treatments (control, 5, 10 and 20 min UV-C treatments). Statistical significance was considered when $p < 0.05$. All statistical analyses were run using the software Statistica 6 (StatSoft, Inc., 2001). Data are shown as mean ± standard error.

Results and Discussion

UV (UV-A, -B and -C) radiation, mainly UV-C, has been used to increase the content of bioactive molecules (flavonoids and phenolic compounds) in medicinal plants[27]. Therefore, in this study, the effect of UV-C on antioxidant compounds in damiana was determined in an *in vitro* model. Figure 1 shows the morphological conditions of plants treated with different UV-C doses for up to 10 days. Damiana plants showed immediate responses to the UV-C radiation; loss of leaves was observed after the initial exposure (day one), and on the following (4, 7 and 10) days of treatment. By the 10th day of treatments, damiana plants showed damage (chlorosis) in leaves; the most extensive damage was observed in the plants exposed to UV-C radiation for 20 min day^{-1} (fig. 1). Exposure to UV-C can generate damage to chloroplasts, produce premature senescence, and growth reduction[1,28-29]. In damiana plants irradiated with UV-C no growth of new leaves and signs of senescence in mature leaves were observed. Chlorophyll *a* content significantly decreased in damiana plants exposed to UV-C radiation for 5 and 20 min day^{-1} relative to control plants ($p = 0.001$, table I). Chlorophyll *b* and carotenoid content significantly decreased in damiana treated with UV-C radiation for 20 min day^{-1} when compared to control plants ($p = 0.001$ and $p = 0.035$, respectively; table I). Similar reduction in chlorophyll *a* and *b* were observed by Najeeb *et al*.[1] in shoots of mat rush (*Juncus effusus* L .) at different exposure times (15, 30 and 45 min) of UV-C radiation. Maharaj *et al.*[4] observed a significant increase in carotenoid content in tomato fruits in postharvest treat-

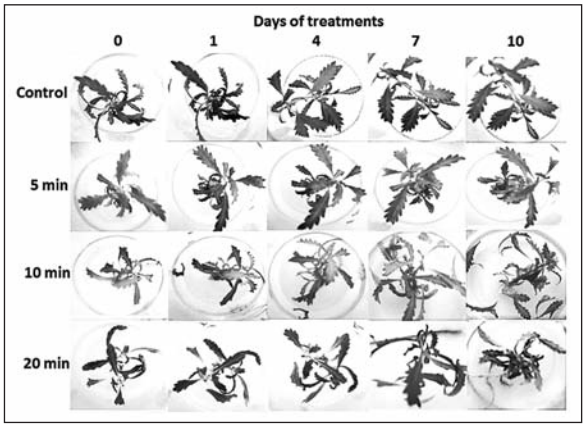


Fig. 1.—Appearance of damiana (Turnera diffusa) *plants irradiated* in vitro *with ultraviolet type-C (UV-C; 5, 10 and 20 min day^{-1}) and control (white light) for 10 days.*

Table I

Content of photosynthetic pigments, chlorophyll a (μg g^{-1} fresh weight), chlorophyll b (μg^{-1} fresh weight), and carotenoids (μg g^{-1} fresh weight) in leaves of damiana (Turnera diffusa) *plants irradiated* in vitro *with ultraviolet type-C (UV-C; 5, 10 and 20 min day^{-1}) for 10 days*

Treatment	*Chlorophyll a (μg g^{-1} FW)*					*Chlorophyll b (μg g^{-1} FW)*					*Carotenoids (μg g^{-1} FW)*				
Day	*0*	*1*	*4*	*7*	*10*	*0*	*1*	*4*	*7*	*10*	*0*	*1*	*4*	*7*	*10*
Control	277.09±7.44a*	277.09±7.44a*	323.42±17.68a*	347.76±7.62a*	331.42±8.22a*	276.16±6.55a*	276.16±6.55a*	332.65±20.60a*	318.54±2.97a*	327.28±10.86a*	36.59±3.02a*	36.59±3.02a*	44.60±8.69a*	51.16±3.06a*	47.04±4.44a*
5 min UV-C	277.09±7.44a*,**	248.14±4.83a*,**	325.30±10.15a*,**	212.47±0.89b*,**	290.31±1.82b*,**	276.16±6.55a*,**	255.28±3.40a*,**	340.970±43.00a*,**	233.52±5.41b*,**	297.15±5.70b*,**	36.59±3.02a*,**	33.71±2.08a*,**	57.80±17.06a*,**	19.88±1.88b*,**	36.20±2.51a*,**
10 min UV-C	277.09±7.44a*,**	239.74±6.70a*,**	318.15±17.83a*,**	254.90±3.97c*,**	366.63±15.28a*,**	276.16±6.55a*	252.84±5.99a*	314.32±20.16a*	314.62±29.10a*	357.91±21.41ab*	36.59±3.02a*,**	30.66±3.64a*,**	45.02±9.49a*,**	22.70±8.55b*,**	48.63±8.36a*,**
20 min UV-C	277.09±7.44a*,**	253.07±12.62a*,**	269.11±7.91a*,**	228.11±12.58bc*,**	103.71±2.61c*,**	276.16±6.55a*,**	264.23±12.01a*,**	277.97±11.65a*,**	262.42±15.49ab*,**	102.84±2.25c*,**	36.59±3.02a*,**	33.09±7.15a*,**	35.91±3.12a*,**	24.17±6.51b*,**	13.23±1.40b*,**
• p value (day)	—	0.06	0.22	<0.001	<0.001	—	0.20	0.39	0.018	<0.001	—	0.82	0.57	0.01	0.003
• p value (treatment)			<0.001					0.001					0.035		

Day one is considered as newly irradiated.
Data are shown as mean ± standard error of a sample of n = 5; all analyses were run in triplicate.
• ANOVA and Tukey's post-hoc tests were applied to probe for differences between treatments.
Different letters indicate significant differences between days within each treatment; * denotes significant differences between treatments; p < 0.05.

ments with UV-C radiation in comparison with non-irradiated fruits. It is possible that different plant tissues have a specific capacity to react to UV-C radiation, and the pigment concentration in each tissue may reflect its potential for protection against UV radiation damage. A decrease or loss of photosynthetic compounds might be due to UV-C radiation being too severe[6].

Protein content in plants decreases in response to UV-C radiation[1]. Thus, the specific activity of antioxidant enzymes was determined in damiana plants exposed *in vitro* to UV-C radiation. No significant differences were found in SOD activity of damiana leaves between UV-C irradiated and control plants ($p = 0.078$, table II). Total POX activity significantly decreased in damiana plants irradiated with UV-C compared to control plants ($p = 0.003$, table II). In contrast, in shoots of mat rush (*Juncus effusus* L.) activity of SOD, POX and ascorbate peroxidase (APX) increased in response to UV-C radiation for 15 and 30 min, and antioxidant enzyme activities decreased at 45 min, at the same time when the protein content decreased[1]. In pepper (*Capsicum annuum* L.) leaves and roots activities of antioxidant enzymes, such as SOD, increased in response to UV-C radiation (5.7 W m^{-2} for 27 min per day during 14 days)[30]. In strawberry fruits irradiated with UV-C (0.25, 0.5 and 0.75 kJ m^{-2}) in postharvest treatments, SOD activity decreased[31]. Tang *et al.*[32] suggest that changes in antioxidant enzyme activities may be involved in the oxidative stress induced by UV-C exposure.

UV-C radiation did not have an effect on vitamin C (ascorbic acid equivalent) content in damiana plants throughout the experimental period ($p = 0.911$, table II). However, vitamin C content had a tendency to decrease (up to 40%) in both irradiated and control plants (table II), but no significant differences ($p = 0.911$) were observed between treatments. Artés *et al*.[33] reported similar results in minimally processed watermelon cubes irradiated with UV-C at different doses (1.6, 2.8, 4.8 and 7.2 kJ m^{-2}), as well as a decline of vitamin C content throughout the storage period[33].

In this study, higher vitamin E (α-tocopherol equivalent) content was observed in leaves of damiana irradiated with UV-C for 20 min day^{-1} than in controls ($p = 0.048$, table II). Given its solubility in lipids and its antioxidant properties, vitamin E contributes to the protection of membranes[34]. The increased vitamin E content in damiana plants exposed to UV-C radiation may provide protection against the oxidative damage potentially induced by UV-C radiation.

The phenolic compounds have beneficial effects in the organism and are present in spices and vegetables[10,12]. Wang *et al.*[8] reported in blueberry (*Vaccinium corymbosum* L.) fruits that UV-C doses significantly increased phenolic content compared to control (non-irradiated) fruits. Phenolic compound content in damiana increased immediately upon exposure to UV-C radiation for 5 min day^{-1} ($p < 0.001$), and in all UV-C treatments by day 7 ($p < 0.001$, table III). However, on

Table II

Enzymatic and non-enzymatic oxidant defenses, activity of superoxide dismutase (SOD, U mg^{-1} protein) and total peroxidase (POX, U mg^{-1} protein); vitamin C content (mg ascorbic acid g^{-1} fresh weight), and vitamin E concentration (mg α-tocopherol g^{-1} fresh weight) in leaves of damiana (Turnera diffusa) *plants irradiated in vitro with ultraviolet type-C (UV-C, 5, 10 and 20 min day^{-1}) for 10 days*

Treatment	*SOD (U mg^{-1} protein)*					*POX (U mg^{-1} protein)*					*Vitamin C (mg ascorbic acid g^{-1} FW)*					*Vitamin E (mg α-tocopherol g^{-1} FW)*				
Day	*0*	*1*	*4*	*7*	*10*	*0*	*1*	*4*	*7*	*10*	*0*	*1*	*4*	*7*	*10*	*0*	*1*	*4*	*7*	*10*
Control	9.49 ±0.26a	9.49 ±0.26b	4.26 ±0.36a	14.81 ±0.35a	7.99 ±0.54a	0.32 ±0.02a*	0.32 ±0.02a*	0.134±0.01b*	0.44 ±0.01a*	0.20 ±0.01b*	1.11 ±0.03a	1.11 ±0.03a	0.76 ±0.02b	0.76 ±0.03a	0.64 ±0.03b	0.83 ±0.09a**	0.83 ±0.09a**	0.08 ±0.02a**	0.83 ±0.21a**	0.04 ±0.01c**
5 min UV-C	9.49 ±0.26a	12.94 ±0.25a	5.234 ±0.14a	8.50 ±0.46b	7.72 ±0.10ab	0.32 ±0.02a*,**	0.26 ±0.07b*,**	0.185±0.07a*,**	0.25 ±0.01b*,**	0.22 ±0.02a*,**	1.11 ±0.04a	1.27 ±0.21a	0.79 ±0.01b	0. 70 ±0.02a	0.78 ±0.03a	0.83 ±0.09a*,**	0.90 ±0.36a*,**	0.92 ±0.43a*,**	1.01 ±0.15a*,**	0.16 ±0.02c*,**
10 min UV-C	9.49 ±0.26a	9.39 ±0.24b	4.689 ±0.28a	8.49 ±0.15b	6.34 ±0.25b	0.32 ±0.02a*,**	0.15 ±0.01c*,**	0.17 ±0.02a*,**	0.24 ±0.01c*,**	0.24 ±0.01a*,**	1.11 ±0.03a	1.21 ±0.01a	0. 77 ±0.01b	0.69 ±0.05a	0.66 ±0.01b	0.83 ±0.09a*,**	0.25 ±0.01b*,**	1.20 ±0.09a*,**	0.87 ±0.34a*,**	1.16 ±0.16a*,**
20 min UV-C	9.49 ±0.26a	6.46 ±0.76c	4.72 ±0.26a	7.78 ±0.35b	6.83 ±0.29ab	0.32 ±0.02a**	0.16 ±0.01c**	0.13 ±0.01b**	0.24 ±0.02c**	0.134 ±0.02c**	1.11 ±0.03a	0.92 ±0.03a	0.99 ±0.02b	0.67 ±0.05a	0.72 ±0.01ab	0.83 ±0.09a*	1.16 ±0.04a*	1.19 ±0.43a*	0.93 ±0.09a*	0.67 ±0.25b*
• p value (day)	—	<0.001	0.17	<0.001	0.02	—	<0.001	<0.001	<0.001	<0.001	—	0.21	<0.001	0.35	<0.001	—	0.04	0.09	0.93	0.001
• p value (treatment)			0.078					0.003					0.911					0.048		

Day one is considered as newly irradiated.
Data are shown as mean ± standard error of a sample of n=5; all samples were analyzed in triplicate.
• ANOVA and Tukey's post-hoc tests were applied to probe for differences between treatments.
Different letters indicate significant differences between days of treatments; *denotes significant differences between treatments; $p < 0.05$.

Table III

Phenollic compound content (mg gallic acid g^{-1} fresch weight), total antioxidant capacity (mM gallic acid g^{-1} fresch weight) and oxidative damage (lipid peroxidation (nM TBARS g^{-1} protein) and protein carbonyls (μM protein g^{-1} fresch weight)) in leaves of damiana (Turnera diffusa) *plants irradited* in vitro *with ultraviolet type-C (UV-C; 5, 10 and 20 min day^{-1}) for 10 days*

Treatment	*Phenolic compounds (mg gallic acid g^{-1} FW)*					*Antioxidant Capacity (mM fg allic acid g^{-1} FW)*					*Lipid Peroxidation (nM TBARS g^{-1} protein)*					*Protein Carbonyls (μM protein g^{-1} FW)*				
Days	*0*	*1*	*4*	*7*	*10*	*0*	*1*	*4*	*7*	*10*	*0*	*1*	*4*	*7*	*10*	*0*	*1*	*4*	*7*	*10*
Control	9.49 ±0.26a	9.49 ±0.26b	4.26 ±0.36a	14.81 ±0.35a	7.99 ±0.54a	0.32 ±0.02a*	0.32 ±0.02a*	0.134±0.01b*	0.44 ±0.01a*	0.20 ±0.01b*	1.11 ±0.03a	1.11 ±0.03a	0.76 ±0.02b	0.76 ±0.03a	0.64 ±0.03b	0.83 ±0.09a**	0.83 ±0.09a**	0.08 ±0.02a**	0.83 ±0.21a**	0.04 ±0.01c**
Control	12.04 ±0.13a**	12.04 ±0.13b**	12.45 ±0.36b**	9.19 ±0.40c**	10.85 ±1.27b**	330.43 ±5.37a*	330.43 ±5.37a*	366.82 ±9.70ab*	448.38 ±7.04a*	440.63 ±5.50b*	213.13 ±10.89a	213.13 ±10.89ab	155.02 ±2.07b	181.95 ±10.12a	169.56 ±8.58a	494.40 ±31.05a	494.40 ±31.05a	281.96 ±2.55b	170.00 ±16.61b	194.57 ±26.24c
5 min UV-C	12.04 ±0.13a*	29.59 ±1.08a*	13.17 ±0.39b*	30.29 ±2.23b*	37.69 ±4.50a*	330.43 ±5.37a**	265.39 ±2.60b**	332.57 ±11.43b**	295.80 ±10.52c**	349.70 ±12.91c**	213.13 ±10.89a	245.77 ±3.71a	74.75 ±5.27c	198.33 ±10.65a	174.90 ±13.29a	494.40 ±31.05a	241.33 ±17.88b	315.57 ±20.09b	236.31 ±13.98a	337.99 ±16.84ab
10 min UV-C	12.04 ±0.13a*	14.82 ±1.47b*	10.83 ±1.35b*	33.11 ±1.12b*	41.07 ±1.76a*	330.43±5.37a*,**	227.81 ±1.76c*,**	352.20 ±6.45ab*,**	393.01 ±9.79b*,**	432.09 ±5.27b*,**	213.13 ±10.89a	145.36 ±8.61c	218.08 ±11.53a	165.56 ±7.93a	172.42 ±8.11a	494.40 ±31.05a	206.19 ±31.06b	374.63 ±10.53ab	275.17 ±8.01a	271.03 ±9.47bc
20 min UV-C	12.04 ±0.13a*	12.70 ±1.38b*	36.01 ±1.96a*	41.24 ±0.42a*	17.04 ±1.01b*	330.43 ±5.37a*	345.12±5.85a*	384.42 ±9.67a*	383.54 ±13.25b*	501.72 ±21.14a*	213.13 ±10.89a	194.20 ±8.71b	206.33 ±3.30a	183.09 ±1.83a	173.82 ±3.90a	494.40 ±31.05a	266.92 ±26.38b	425.58 ±40.77a	222.30 ±5.84ab	355.66 ±10.11a
• p value (day)	—	<0.001	<0.001	<0.001	<0.001	—	<0.001	0.014	<0.001	<0.001	—	<0.001	<0.001	0.129	0.977	—	<0.001	0.0107	0.0017	<0.001
• p value (treatment)			<0.001					0.0001					0.763					0.743		

Day one is considered as newly irradiated.
Data are shown as mean ± standard error of a sample of n=5; all samples were analyzed in triplicate.
•ANOVA and Tukey's post-hoc tests were applied to probe for differences between treatments.
Different letters indicate significant differences between days of treatments; * denotes significant differences between treatments; $p < 0,05$.

the 10th day of exposure to UV-C radiation for 20 min day^{-1} phenolic compound content decreased significantly ($p < 0.001$, table III). These results suggest that while low, short exposure doses stimulate, excessive UV-C radiation reduces phenolic compound content in damiana. Therefore, it is important to assess the appropriate UV-C dosage in order to maximize the content of phenolic compounds in plants; it has been suggested that obtaining compounds such as carotenoids, vitamin C and vitamin E in the human diet is preferred to intake of supplements[10].

The DPPH radical is usually employed to analyze the total antioxidant capacity of vegetables[12]. In damiana, total antioxidant capacity decreased significantly ($p < 0.001$) on day one in plants treated for 5 and 10 min day^{-1} with UV-C radiation (table III). By the 7th day of treatment, plants irradiated with UV-C (for 5, 10 and 20 min day^{-1}) had lower antioxidant capacity than control plants ($p < 0.001$, table III). This may be the product of the combined decreases in non-enzymatic (photosynthetic pigments and carotenoids, table I) and enzymatic antioxidants (SOD and POX activities, table II) observed in UV-C irradiated damiana.

No significant differences in TBARS levels were found in damiana between treatments and control ($p = 0.763$) throughout the exposure period (table III). This could be due to the simultaneous increase in vitamin E levels in UV-C irradiated plants (table II). However, higher protein carbonyl content was observed on the 7th and 10th days in UV-C treated damiana plants in comparison with control plants ($p = 0.0017$ and $p < 0.001$, respectively; table III). Protein carbonyl levels are an indicator of damage to proteins due to oxidative stress[35]. These results suggest that antioxidant defenses in damiana plants are sufficient to curtail oxidative damage to lipids but not to proteins.

UV-C radiation increased total phenolic compound and vitamin E content in damiana plants. The time course of the observed effects of UV-C radiation in damiana plants suggests that the strongest responses occur immediately upon exposure, and that the effects may lessen with time. Similar results were reported by Wang *et al.*[8] in blueberry fruits exposed to UV-C radiation, and Ribeiro *et al.*[35] mentioned that the UV-C effects depend on the dosage. Therefore, exposure to controlled, mild levels of UV-C radiation may be an alternative to increase the content of antioxidants and other phytochemicals in damiana plants, as suggested by Jacobo-Velázquez and Cisneros-Zevallos[11] and Ribeiro *et al.*[35].

Conclusion

UV-C radiation had differential effects on the antioxidant defenses of damiana (*T. diffusa*) plants *in vitro,* depending on the time of the exposure. Short-term exposure increased vitamin E and phenolic compound content in damiana. Results suggest that UV-C treatment, when appropriately controlled, can be used as an alternative mechanism to increase the content of antioxidants and other phytochemicals in damiana plants.

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Original / *Alimentos funcionales*

Antioxidant responses of damiana *(Turnera diffusa* Willd) to exposure to artificial ultraviolet (UV) radiation in an *in vitro* model; part II; UV-B radiation

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Abstract

Introduction: **Ultraviolet type B (UV-B) radiation effects on medicinal plants have been recently investigated in the context of climate change, but the modifications generated by UV-B radiation might be used to increase the content of antioxidants, including phenolic compounds.**

Objective: **To generate information on the effect of exposure to artificial UV-B radiation at different high-doses in the antioxidant content of damiana plants in an *in vitro* model.**

Methods: **Damiana plantlets (tissue cultures in Murashige-Skoog medium) were irradiated with artificial UV-B at 3 different doses (1) 0.5 ± 0.1 mW cm^{-2} (high) for 2 h daily, (2) 1 ± 0,1 mW cm^{-2} (severe) for 2 h daily, or (3) 1 ± 0.1 mW cm^{-2} for 4 h daily during 3 weeks. The concentration of photosynthetic pigments (chlorophylls *a* and *b*, carotenoids), vitamins (C and E) and total phenolic compounds, the enzymatic activity of superoxide dismutase (SOD, EC 1.15.1.1) and total peroxidases (POX, EC 1.11.1), as well as total antioxidant capacity and lipid peroxidation levels were quantified to assess the effect of high artificial UV-B radiation in the antioxidant content of *in vitro* damiana plants.**

Results: **Severe and high doses of artificial UV-B radiation modified the antioxidant content by increasing the content of vitamin C and decreased the phenolic compound content, as well as modified the oxidative damage of damiana plants in an *in vitro* model.**

Conclusion: **UV-B radiation modified the antioxidant content in damiana plants in an *in vitro* model, depending on the intensity and duration of the exposure.**

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Key words: *Antioxidants. Antioxidant capacity. Phenolic compounds.* Turnera diffusa. *UV-B radiation. Vitamin C.*

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RESPUESTA ANTIOXIDANTE EN DAMIANA *(TURNERA DIFFUSA* WILLD) EXPUESTA A RADIACIÓN ULTRAVIOLETA (UV) ARTIFICIAL EN UN MODELO *IN VITRO;* PARTE II; RADIACIÓN UV-B

Resumen

Introducción: **Los efectos de la radiación ultravioleta tipo B (UV-B) sobre las plantas medicinales se han investigado recientemente en el contexto del cambio climático, pero las modificaciones que genera la radiación UV-B podrían emplearse para modificar el contenido de compuestos antioxidantes, incluyendo los compuestos fenólicos.**

Objetivo: **Generar información sobre el efecto de una alta exposición a UV-B artificial en el contenido antioxidante de damiana *(Turnera diffusa,* Willd) en un modelo *in vitro.***

Método: **Plántulas de damiana en cultivo de tejidos (medio Murashige-Skoog) fueron irradiadas con UV-B artificial en 3 diferentes dosis: (1) 0,5 ± 0,1 mW cm^{-2} (alto) por 2 h diarias, (2) 1 ± 0,1 mW cm^{-2} (severa) por 2 h diarias, o (3) 1 ± 0,1 mW cm^{-2} durante 4 horas diarias por 3 semanas. Se cuantificó la concentración de pigmentos fotosintéticos (clorofilas *a* y *b,* carotenoides), vitaminas (C y E) y compuestos fenólicos totales, la actividad enzimática de la superóxido dismutasa (SOD, EC 1.15.1.1) y las peroxidasas totales (POX, EC 1.11.1), así como la capacidad antioxidante total y la peroxidación de lípidos para evaluar el efecto de la alta radiación UV-B artificial en el contenido antioxidante de damiana *in vitro.***

Resultados: **Dosis altas y severas de radiación UV-B artificial modificaron el contenido antioxidante incrementando el contenido de vitamina C y disminuyendo el contenido de compuestos fenólicos totales, además de modificar el daño oxidativo de plantas de damiana en un modelo *in vitro.***

Conclusión: **La radiación UV-B modifica el contenido antioxidante en damiana en un modelo *in vitro,* dependiendo de la intensidad y el tiempo de exposición.**

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Palabras clave: *Antioxidantes. Capacidad antioxidante. Compuestos fenólicos. Radiación UV-B.* Turnera diffusa. *Vitamina C.*

Abbreviations

DPPH: 2,2-diphenyl-2-picrylhidrazyl.
BCS: Baja California Sur.
GAEAC: Gallic acid equivalent antioxidant capacity.
HPLC: High-performance liquid chromatography.
ROS: Reactive oxygen species.
SOD: Superoxide dismutase.
TBARS: Thiobarbituric acid-reactive substances.
UV: Ultraviolet radiation.
UV-B: Ultraviolet type B.

Introduction

Plants are naturally exposed to all components of sunlight, including ultraviolet (UV) radiation. UV radiation is divided, based on wavelength range, in UV-A (315-400 nm), UV-B (280-315 nm) and UV-C (100-280 nm). Climate changes due to natural and anthropogenic causes increase UV-B radiation levels on Earth's surface[1]. UV-B radiation possesses high energy levels and induces a wide variety of physiological and morphological responses, most of which are only occasionally beneficial, in terrestrial organisms[2,3]. In plants, UV-B radiation has different effects on growth and development, metabolic processes such as photosynthesis, morphology and biochemistry (concentrations of secondary metabolites and other compounds)[2-6]. In addition, UV radiation generates an increase in the production of reactive oxygen species (ROS) potentially causing oxidative stress[7] and, likely, decreasing the yield and quality of plants[8]. As a mechanism to prevent oxidative damage due to increased ROS production induced by UV-B radiation the plant's antioxidant defenses change; depending on the species, exposure to a small to moderate UV-B dose may increase, while larger UV-B doses may overwhelm the antioxidant defenses[9,10]. This is an especially interesting alternative for medicinal plants because they constitute an important source of molecules with pharmaceutical and economic value[1,11-12], as reflected in the growing number of studies addressing UV-B radiation effects in the production of secondary compounds in wild medicinal plants and herbs[10-11,13-15]. Phenolic compounds, such as flavonoids, are expected to increase in response to UV-B radiation given their effectiveness in absorbing UV-B radiation and antioxidant properties[6]. Recently, Kumari and Prassad[1] suggested the importance of UV-B treatment on medicinal plants to increase natural compounds as an alternative to pharmacological manufacture.

Damiana (*Turnera diffusa*, Willd) plants are used for medicinal purposes and in the elaboration of diverse dietary products[16]. These shrubs grow wild in arid and semiarid climates, such as those prevalent in Baja California Sur (BCS), Mexico [16], where plants are subject to elevated intensity of solar radiation (maximum 7 kWh m^{-2} day^{-1} in Summer)[17]. Therefore, damiana is exposed naturally to high UV radiation levels; elevated antioxidant compound content was observed recently in damiana plants from BCS[18,19], and previous results suggest differences in antioxidant content between damiana plants grown in different regions with similar environmental conditions but different natural solar radiation levels[19]. This medicinal plant has a large antioxidant potential, perhaps due to the environmental conditions and exposure to naturally elevated UV-B radiation[19]. Studies on the effect of UV-B radiation suggest that exposing plants to artificial UV radiation can be an alternative to increase phytochemicals of interest. Therefore, the objective of this study was to analyze the effect of exposure to artificial UV-B radiation at different high-doses in the antioxidant content of damiana plants in an *in vitro* model.

Materials and methods

Plant material and experimental setup

Damiana (*T. diffusa*) plantlets were grown aseptically in tissue culture in Murashige-Skoog (MS) medium following the method described by Alcaraz-Melendez *et al.*[20]. Damiana plants were grown for 4 weeks (to reach 7.5 cm of size) prior to being irradiated with artificial UV-B (UV-B Lamp F875, 315 nm, BioRad, Hercules. CA, USA). Lamps were placed 25 cm above the top of the plants maintaining this distance constant throughout the experiment. Aluminum strips were placed on top of the lamps and plants were placed inside a box, fully covered with aluminum foil, to increase UV-B reflection. Treatments were as follows; 1) control, plants grown in white light (fluorescent light to 100 µE m^{-2} sec^{-1}) at 25 ± 2°C without exposure to UV-B; 2) plants exposed to 0.5 ± 0.1 mW UV-B cm^{-2} for 2 h per day and 22 h of white light at 25 ± 2°C; 3) plants exposed to 1 ± 0,1 mW UV-B cm^{-2} for 2 h per day and 22 h of white light at 25 ± 2°C; 4) plants exposed to 1 ± 0,1 mW UV-B cm^{-2} for 4 h per day and 20 h of white light at 25 ± 2°C. A radiometer (ultraviolet intensity meter, General Tools and Instruments, NY, USA) was used to quantify UV-B radiation below and above the tops of the experimental damiana plants within each container. Samples were collected after the first irradiation treatment and subsequently every week, during 3 weeks. Plants collected at the onset of the experiment were labeled as day zero and newly irradiated as day one. Leaves were separated from stems, samples were immersed in liquid nitrogen, and stored at -80°C until analyzed.

Chlorophylls a and b, and total carotenoids

Prior to pigment quantification using the method of Lichtenthaler and Wellburn[21], damiana leaves (250 mg) were extracted with water:methanol:acetone (2:3:5) at 4°C in the dark. Pigment content in each sample was

determined at 666, 653 and 470 nm by using a microplate reader (BioRad™ 550, Japan) as previously described[18-19]. Chlorophyll *a*, chlorophyll *b*, and total carotenoid content are expressed in μg g^{-1} of fresh weight. The variability coefficients calculated for the methodologies employed to quantify chlorophyll a, chlorophyll *b*, and total carotenoid content were 4.8, 5.8, and 21.8, respectively.

Superoxide dismutase activity

Damiana leaves were homogenized in phosphate buffer ($KHPO_4$, 0.1 M, pH 6.8) with polyvinylpyrrolidone (PVP), and centrifuged at 3,000 × g for 20 min at 4°C. Supernatant was used immediately to assess total superoxide dismutase (SOD, EC 1.15.1.1) activity following the method of Suzuki[22] at 560 nm (Beckman Coulter DU-800, CA, USA) as previously described[18-19] Results are expressed in units of SOD activity mg^{-1} protein. One unit of SOD activity is defined as the amount of enzyme necessary to cause 50% inhibition of the maximum rate of NBT reduction at 560 nm. The variability coefficient for this method was 14.2.

Peroxidase activity

Leaf samples (250 mg) were homogenized in phosphate buffer ($KHPO_4$, 0.1 M, pH 6.8) with PVP, centrifuged at 3,000 × g for 20 min at 4°C. Reaction mixture containing hydrogen peroxide (H_2O_2, 50 μM), pyrogallol (50 μM), and plant extract was incubated for 1 min at 25°C. Reaction was stopped by adding 0.5 mL of H_2SO_4 (5%, v/v), following the method described by Kar and Mishra[23] as previously described[18-19]. Total peroxidases (POX, EC 1.11.1) activity was detected spectrophotometrically at 420 nm in a Beckman Coulter DU 800 (USA) spectrophotometer. Results are expressed in units of POX activity mg^{-1} protein. One unit of POX activity is defined as the amount of POX enzyme required to increase the absorbance by 0.1. The coefficient of variability was 11.7 for this methodology.

Vitamin C

Vitamin C (L-ascorbic acid) content was quantified using high-performance liquid chromatography (HPLC, Waters, Milford, MA, USA). Conditions and methods used to assess vitamin C content in damiana leaves were previously described[18]. Leaves (0.2 g), metaphosphoric acid (3% w/v), acetic acid (8% w/v), and EDTA (0.01 M) were mixed and incubated for 40 min at 4°C in the dark. The homogenate was centrifuged at 23,895 × g for 15 min, and filtered with cellulose acetate filters. Samples (10 μL) were injected into an HPLC and two mobile phases were employed, acidified deionized water (pH 2.4 with H_2SO_4) and acetonitrile (HPLC grade 100%) in a BDS hypersyl C8 column as previously described[18-19]. The internal standard method and a calibration curve of L-ascorbic acid (5-200 ng μL^{-1}) at 245 nm were used to calculate vitamin C content in damiana leaves. Results are expressed as mg vitamin C g^{-1} fresh weight; the variability coefficient was 0.3.

Total phenolic compound content and antioxidant capacity

Leaf extracts were obtained using acetone-methanol-water (5:3:2 respectively, v/v) and were used for determinations of total phenolic compound content and total antioxidant capacity. Total phenolic compound content in leaf samples was determined following the method of Singleton and Rossi[24] in a microplate reader (BioRad™ 180 550, CA, USA) at 750 nm and was calculated from a standard curve of gallic acid (0-350 μg mL^{-1}) as previously described[18-19]. Briefly, samples (10 μL) were mixed with Folin-Ciocalteu reagent (1:1, v/v diluted with water) and incubated for 1 min with sodium carbonate (2% v/v); then sodium hydroxide (0.4% w/v) was added and the mixture was allowed to incubate for another 20 min at room temperature in the dark. Results are expressed as mg gallic acid equivalents (GAE) g^{-1} fresh weight. The coefficient of variability was calculated to be 9.9.

Total antioxidant capacity of damiana leaves was quantified in a microplate reader (BioRad™ 550, CA, USA) at 515 nm by using the method of Brand-Williams *et al.*[25] and using the commercial free radical 2,2-diphenyl-2-picrylhidrazyl (DPPH) as previously described[18,19]. A standard curve of gallic acid (50-300 μg mL^{-1}) was employed to calculate total antioxidant capacity in damiana leaves. Results are expressed as μM gallic acid equivalent antioxidant capacity (GAEAC) g^{-1} fresh weight. The coefficient of variability for this method was 7.5.

Lipid peroxidation

The concentration of thiobarbituric acid-reactive substances (TBARS) was quantified as an indicator of lipid peroxidation, at 535 nm with correction at 600 nm (Beckman Coulter DU 800), following the method of Persky *et al.*[26]. Samples were homogenized with phosphate buffer (K_2HPO_4, 50 mM, pH 6.8) and centrifuged at 2,200 × g 20 min at 4°C. The homogenate was incubated with trichloroacetic acid (20% w/v in HCl 1 M), and thiobarbituric acid (TBA, 1 % w/v) at 90°C for 30 min. The reaction was stopped on an ice-bath and centrifuged at 3,000 × g for 15 min at 4°C as previously described[18-19]. Samples and standard curve (1-bis tetraetoxipropane TEP, 0-20 nmoles mL^{-1}) were quantified spectrophotometrically. TBARS levels are expressed as nmol of TBARS mg^{-1} protein; the variability coefficient for this method was 10.5.

Total protein content

To standardize the results for antioxidant enzyme activities and lipid peroxidation levels, total soluble protein content was determined following the method of Bradford[27], modified for use with a microplate reader (BioRad™), and using a standard curve of bovine serum albumin (BSA, 5-400 µg mL^{-1}) as previously described[18-19]. Results are expressed as mg protein g^{-1} fresh weight.

Statistical analyses

All samples (the pool of all leaves from 5 plantlets in each treatment, n = 5) were analyzed in triplicate, and data are expressed as mean ± standard error. Data were tested for normality and homoscedasticity of variance. Analysis of variance (ANOVA) and post-hoc tests (Tukey) were used to determine significant differences between treatments. Statistical significance was considered when $p < 0.05$. All statistical analyses were run with Statistica 6 software (StatSoft, Inc., 2001).

Results and discussion

Chlorophyll *a* and *b* content in damiana (*T. diffusa*) leaves increased significantly during the first day of treatment with high and severe UV-B doses compared to control plants ($p = 0.001$, table I). Chlorophyll *a* and *b* levels remained constant in control plants throughout the experimental period (table I). In contrast, from experimental day 7, chlorophyll *a* and *b* levels decreased in damiana plants irradiated with UV-B in comparison with control plants ($p < 0.001$, $p = 0.022$, respectively, table I). Carotenoid content was not affected by UV-B treatment ($p = 0.322$, table I). The amount of UV radiation used may be too severe and may produce loss of photosynthetic pigments in damiana (*T. diffusa*) plants in a dose-dependent manner (table I). Similar decrease in the chlorophyll content was reported by Mohammed and Tarpley[28] in rice leaves as a result of high UV-B levels, which generate chlorophyll degradation. Katerova *et al.*[29] suggest that exposure to UV-B and UV-C radiation damages photosynthetic pigments due to the fact that UV radiation has enough energy to destroy chemical bonding of biomolecules. Hideg[9] proposed that exposure to UV-B increases light sensor pigments, but excessive radiation can generate photoinhibition as well as structural and functional damage to photosystems and photosynthetic pigments since they are sensitive to UV-B radiation[30,31]. UV-B radiation can modify chlorophyll content directly or indirectly by binding proteins to chlorophylls or affecting the chlorophyll biosynthesis pathways[2]. Therefore, it is possible that UV-B radiation affects damiana plants either via photoinhibition or the synthesis of photosynthetic pigments.

In the present study, damiana SOD (EC 1.15.1.1) activity increased following exposure to UV-B radiation, mainly at severe dose treatments (UV-B severe 2 h and UV-B severe 4 h) ($p < 0.05$, table I). The response appears to be immediate, since plants showed a significant increase in SOD activity when compared to non-irradiated controls after the first exposure to severe UV-B doses for 2 h or 4 h ($p < 0.05$, table I). No significant differences were observed in POX (EC 1.11.1) activity between control damiana plants and those exposed to UV-B radiation ($p = 0.547$, table I). A similar increase in SOD activity after exposure to supplementary UV-B doses was observed in sweeflag, *Acorus calamus* L.[32]; Ravindran[13] observed increased SOD and POX activity in true indigo (*Indigofera tinctoria*, L.) seedlings, and Hassan *et al.*[6] in bean (*Vicia faba* L.) plants exposed to supplementary UV-B radiation. Rybus-Zajac and Kubis[33] reported that UV-B radiation induces increased SOD, guaiacol peroxidase and syringaldazine peroxidase activities in cucumber seedlings. Hagh *et al.*[34] described an increase in guaiacol peroxidase and ascorbate peroxidase activities in roots and shoots of sunflowers plants. Recently, Ramya and Balakrishnan[15] observed increased POX activity (84%) in sola pith (*Aeschynomene aspera*) plants irradiated with different doses of UV-B radiation for 9 days, this increase along with the other antioxidant enzymes generate protection to the plant during the oxidative stress produced by increased UV-B radiation. The increase in SOD activity in damiana (*T. diffusa*) plants after exposure to UV-B radiation may be due to increased ROS production. UV-B radiation increases ROS production, which activates both enzymatic and non-enzymatic antioxidant responses in plants[9].

Vitamin C content was 0.8 ± 0.18 mg ascorbic acid g^{-1} FW in control damiana (*T. diffusa*) plants (table I). UV-B radiation increased vitamin C levels in damiana leaves to 1.4 ± 0.04 mg ascorbic acid g^{-1} FW at 0.5 mW cm^{-2} 2 h of UV-B radiation treatment for 21 days (table I). The content of vitamin C, translated to the same units as those reported in the present study, is in the range of 25 to 46.76 mg ascorbic acid g^{-1} in acerola (*Malpighia glabra*) fruits, 0.506 mg ascorbic acid g^{-1} in orange pulp[35], and 0.135 to 0.149 mg ascorbic acid g^{-1} in tomato fruits[36]. Therefore, the content of vitamin C in damiana (*T. diffusa*) is within the range reported for fruits and vegetables considered rich in vitamin C. Furhter, exposure to UV-B radiation increased the vitamin C content in damiana. Nasibi and Kalantari[37] reported increased vitamin C content in plants of *Brassica napus* in response to UV-B radiation (5.8 Wm^{-2}). However, Kumari *et al.*[32] reported the lack of an effect of supplementary UV-B radiation (1.8 kJ m^{-2} d^{-1} and 3.6 kJ m^{-2} d^{-1}) on vitamin C levels in *A. calamus* plants. It is possible that increasing levels of ascorbic acid, perhaps via the glutathione-ascorbate cycle, aids damiana plants to counteract the increased ROS production presumably induced by UV-B radiation.

Table I

Enzymatic and non-enzymatic antioxidant content in damiana (Turnera diffusa Willd) plantlets exposed to UV-B radiation (0 mW cm^{-2} (control), 0.5 mW cm^{-2} 2 h, 1 mW cm^{-2} 2 h, and 1 mW cm^{-2} 4 h)

Treatment	*Clorophyll a (µg g^{-1} FW)*					*Chlorophyll b (µg g^{-1} FW)*					*Total carotenoids (µg g^{-1} FW)*					*POX (U mg^{-1} protein)*					*SOD (U mg^{-1} Protein)*					*Vitamin C (mg ascorbic acid g^{-1} FW)*				
Days	*0*	*1*	*7*	*14*	*21*	*0*	*1*	*7*	*14*	*21*	*0*	*1*	*7*	*14*	*21*	*0*	*1*	*7*	*14*	*21*	*0*	*1*	*7*	*14*	*21*	*0*	*1*	*7*	*14*	*21*
Control	432.6 ±6.9a*	432.6±6.9b*	403.8±3.7a*	379.1 ±2.4a*	414.1±10.3a*	395.2±10.7a*	395.2 ±10.7a*	435.9 ±47.4a*	335.2±3.1a*	356.8±7.3a*	11.5 ±1.0a	11.5±1.0a	2.1 ±0.8b	11.7 ±1.2a	7.4±0.8b	0.279±0.01a	0.279±0.01b	0.106±0.01a	0.051±0.001b	0.048±0.002a	4.1±0.05a**	4.1±0.05b**	3.4±0.27c**	1.8±0.16b**	4.3±0.51a**	0.8±0.18a**	0.8±0.18b**	0.93±0.06a**	0.62 ±0.2c**	0.8±0.04b**
0.5 mWcm^{-2} 2 h	432.6 ±6.9a**	493.3±4.9a**	307.4 ±5.4b**	227.2 ±1.3c**	268.8±4.5b**	395.2±10.7a**	423.3 ±7.8a**	305.7±9.8b**	238.0±1.1c**	262.9 ±1.8b**	11.5 ±1.0a	14.7±1.6a	2.5 ±0.2b	2.9 ±0.2b	5.8±0.3b	0.279±0.01a	0.252±0.02b	0.057 ±0.003bc	0.022±0.001c	0.037±0.002b	4.1±0.05a***	1.6±0.23c***	3.6±0.11c***	1.5±0.4b***	1.4±0.22b***	0.8±0.18a*,**	0.8±0.05ab*,**	0.8±0.03a*,**	1.07±0.05b*,**	1.4±0.04a*,**
1 mWcm^{-2} 2 h	432.6 ±6.9a**	433.3±7.4b**	267.9±4.9c**	251.1 ±8.5b**	151.4±2.9c**	395.2±10.7a**	401.5 ±8.0a**	260.1±3.4b**	297.0±9.3b**	196.9±3.7c**	11.5 ±1.0a	6.2±0.8b	9.9±0.05a	3.3 ±0.3b	22.7 ±0.7a	0.279±0.01a	0.486±0.04a	0.072±0.005b	0.052±0.003b	0.050±0.002a	4.124±0.05a*	5.7±0.09a*	6.6±0.09a*	4.0±0.36a*	4.4±0.41a*	0.8±0.18a*,**	0.9±0.08ab*,**	0.9±0.08a*,**	1.15±0.01ab*,**	0.77±0.04b*,**
1 mWcm^{-2} 4 h	432.6 ±6.9a**	485.8±7.8a**	275.2±0.9c**	209.8 ±3.8c**	ND	395.2±10.7a**	425.8 ±11.5a**	284.4±1.4b**	235.4±6.6c**	ND	11.5 ±1.0a	2.4±0.4b	11.6±0.4a	6.5 ±0.8b	ND	0.279±0.01a	0.205±0.005b	0.033±0.003c	0.067±0.005a	ND	4.1±0.05a*	6.0±0.44a*	4.7±0.13b*	3.5±0.10a*	ND	0.8±0.18a*	1.1±0.03a*	1.0±0.09a*	1.27±0.05a*	ND
• p (day)	—	<0.01	<0.01	<0.01	<0.01	—	0.13	0.003	<0.01	<0.01	—	<0.01	<0.01	<0.01	<0.01	—	<0.001	<0.001	<0.001	0.006	—	<0.01	<0.01	<0.01	0.002	—	0.028	0.165	<0.01	<0.01
• p (treatment)			0.015					0.022					0.321					0.547					<0.001						0.007		

POX = peroxidases; SOD = superoxide dismutase.
Data are shown as mean ± standard error of a sample of n = 5; all analyses were run in triplicate.
• ANOVA and Tukey's post-hoc tests, were applied to probe for differences between treatments.
Different letters denote significant differences between days within each treatment; *denotes significant differences between treatments; p < 0.05. ND = Not detected.

Table II

Phenolic compound content, total antioxidant capacity and oxidative damage (lipid peroxidation) in damiana (Turnera diffusa Willd) plantlets exposed to UV-B radiation (0 mW cm^{-2} (control), 0.5 mW cm^{-2} 2 h, 1 mW cm^{-2} 2 h, and 1 mW cm^{-2} 4 h)

Treatment	*Phenolic compound contents (mg gallic acid g^{-1} FW)*					*Total antioxidant capacity (mM gallic acid g^{-1} FW)*					*Lipid peroxidation (nM TBARS g^{-1} protein)*				
Day	*0*	*1*	*4*	*7*	*10*	*0*	*1*	*4*	*7*	*10*	*0*	*1*	*4*	*7*	*10*
Control	25.497 ±0.953a*	25.497 ±0.953ab*	26.141 ±0.564a*	23.519±0.462a*	29.681 ±0.630a*	901.03±22.85a*,**	901.03 ±22.85b*,**	928.63 ±53.66b*,**	1243.8 ±30.84a*,**	984.45 ±24.91a*,**	19.66±0.17a**	19.66±0.17b**	24.31±2.11c**	20.91±1.74a**	7.53±0.26c**
0.5 mWcm^{-2} 2 h	25.497 ±0.953a**	22.147 ±0.449c**	25.051 ±0.549ab**	22.967 ±0.541a**	22.233 ±0.261b**	901.03 ±22.85a*	1567.4 ±17.47a*	1348.2 ±42.12a*	918.57 ±55.60b*	776.78 ±28.67b*	19.66±0.17a**	19.15 ±2.798b**	30.59±0.38b**	12.96±1.84b**	14.12±0.04b**
1 mWcm^{-2} 2 h	25.497 ±0.953a**	26.257 ±0.469a**	25.002 ±1.062ab**	23.137 ±0.400a**	22.242 ±0.604b**	901.03 ±22.85a**	292.06 ±13.49c**	946.79 ±39.51b**	909.96 ±52.75b**	769.71 ±26.81b**	19.66±0.17a*	35.49±3.81a*	38.61±0.32a*	20.82 ±0.497a*	41.57±1.69a*
1 mWcm^{-2} 4 h	25.497 ±0.953a**	22.948 ±0.496bc**	22.365 ±0.280b**	22.904 ±0.464a**	ND	901.03 ±22.85a**	881.32 ±22.56b**	769.67 ±36.49b**	798.16 ±12.85b**	ND	19.66±0.17a**	13.52±0.44b**	32.58±0.56b**	15.02±0.25ab**	ND
• p (day)	—	0.001	0.01	0.79	<0.001	—	<0.001	<0.001	<0.001	<0.001	—	0.001	<0.001	0.004	<0.001
• p (treatment)			<0.001					<0.001					0.005		

TBARS = thiobarbituric acid reactive substances, determined as indicator of lipid peroxidation.
Data are shown as mean ± standard error of a sample of n = 5; all analyses were run in triplicate.
• ANOVA and Tukey's post-hoc tests were applied to probe for differences between treatments.
Different letters denote significant differences between days within treatments; * denotes significant differences between treatments; p < 0.05. ND = Not detected.

Kumari and Prasad[1] suggested the relevance of studying the effects of UV-B radiation as an alternative to increase the content of molecules that are important to the plant s metabolism, or have nutraceutical properties and, thus, commercial value, such as phenolic compounds. Levels of phenolic compounds, including flavonoids, increase in response to UV-B radiation[38]. In this study, the phenolic compound content in damiana plants decreased significantly following exposure to UV-B radiation in all treatments in comparison to control plants ($p < 0.05$, table II); such decrease could be due to reduction in photo-assimilation at high UV-B radiation doses. Similar decrease in phenolic compound content was reported by Mohammed and Tarpley[8] in rice leaves exposed to 10 kJ UV-B radiation. Thus, exposure to moderate or severe UV-B radiation could be an alternative mechanism to increase the content of phytochemical compounds of interest in damiana.

In *T. diffusa*, carotenoid and phenolic compound content decreased in response to high UV-B doses, suggesting that either this plant is sensitive to UV-B radiation or that the amount of UV-B radiation supplied was beyond the tolerance limit of damiana plants. The treatments used in this study only considered UV-B radiation without photosynthetically active radiation. Exposure of plants directly to UV-B radiation without visible-light may not provide the energy needed for the plant to synthesize the response-elements to protect itself. Caldwell[39] mentioned that the photoreactivation mechanism is initiated by UV-A radiation and visible-light (blue spectrum), but plants irradiated with monochromatic radiation (UV-B radiation only) cannot induce repair mechanisms.

At high UV-B doses (UV-B high 2 h), total antioxidant capacity of damiana (*T. diffusa*) plants increased significantly compared to non-irradiated control plants ($p < 0.05$, table II) during the first 7 days of treatment; at severe UV-B doses (UV-B severe 2 h and 4 h) total antioxidant capacity of damiana plants decreased (table II) during 7 days of irradiation. Oxidative damage, quantified as lipid peroxidation levels (TBARS), increased in damiana plants irradiated with UV-B as compared to non-irradiated plants ($p < 0.05$, table II). Hassan *et al.*[6] reported an increase of 40% in bean (*Vicia faba* L.) plants in response to UV-B radiation. UV-B radiation increases ROS production, which can cause oxidative damage to lipids, proteins and DNA[10,40]. Plants vary in their ability to withstand UV radiation based on the increase in ROS production[30] and their capacity to synthesize compounds that prevent or reduce oxidative damage[37].

Damiana plants irradiated with UV-B showed dose-dependent changes in both enzymatic and non-enzymatic antioxidants. The loss of phenolic compounds (table II) and photosynthetic pigments (table I) in response to UV-B exposure suggest that either antioxidant defenses in damiana plants are not sufficient to provide protection against artificial UV-B irradiation, that damiana in BCS may be near its maximal capacity to induce antioxidant defenses, or that the UV-B dosage used in this study exceeds the tolerance capacity of this plant. Ramya and Balakrishnan[15] mentioned that plants have different sensibility to UV-B radiation, depending on treatments and intensity of radiation. In a previous study[18], the antioxidant content in wild and cultivated damiana plants from BCS, naturally exposed to high solar radiation, was reported. In wild and cultivated damiana plants the phenolic compound levels are lower than in *in vitro* damiana irradiated with UV-B in this study. Yet, wild and cultivated damiana had lower lipid peroxidation levels than damiana irradiated *in vitro* with UV-B. The results from this study suggest that artificial UV-B radiation decreases the defense capacity, decreases the antioxidant content, and increases oxidative damage in leaves of damiana plants. Even so, photosynthetic pigments and vitamin C content increased in damiana irradiated *in vitro* with UV-B.

Conclusion

Antioxidant defense mechanisms, such as SOD activity and vitamin C, are activated by artificial UV-B radiation to protect damiana plants *in vitro*. At high UV-B doses (UV-B high 2 h), total antioxidant capacity of damiana plants increased while at severe UV-B doses (UV-B severe 2 h and 4 h) total antioxidant capacity of damiana plants decreased significantly compared to non-irradiated control plants. At severe doses, UV-B exposure increased SOD activity, photosynthetic pigments (chlorophylls), vitamin C content and lipid peroxidation. Phenolic compound content in damiana plants decreased significantly following exposure to UV-B radiation in all treatments.

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Nutrición Parenteral Domiciliaria; satisfacción de los pacientes y sus cuidadores con la Unidad de Nutrición Clínica y el Servicio de Farmacia

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Resumen

Introducción: **La Nutrición Parenteral Domiciliaria (NPD) es una práctica en continuo crecimiento por las importantes ventajas que presenta para el paciente y el sistema sanitario. En la investigación de los resultados en salud resulta hoy en día fundamental evaluar el punto de vista del paciente. Dentro de las medidas centradas en el paciente con NPD se han realizado varios estudios sobre la calidad de vida, pero no se ha evaluado el grado de satisfacción con esta modalidad de tratamiento.**

Objetivos: **Evaluar el grado de satisfacción de los pacientes que reciben NPD y sus cuidadores con los médicos, farmacéuticos y enfermeros de hospital.**

Métodos: **Se repartió una encuesta anónima y que constaba de 48 preguntas cerradas a los pacientes que recibían NPD y a sus cuidadores, los cuales contestaron de forma voluntaria. Con las respuestas recogidas se creó una base de datos en el programa SPSS con las siguientes variables: datos personales, socioculturales, clínicos y relacionados con la NPD y valoración del personal sanitario implicado (área de nutrición del Servicio de Farmacia y Unidades Médica y de Enfermería de Nutrición) y de las instalaciones del hospital relacionadas con la NPD. También se incluyó un apartado de sugerencias con respuesta abierta.**

Resultados: **Se repartieron 24 encuestas, 12 a pacientes y 12 a cuidadores. La tasa de respuesta fue un 91,7% en el caso de los pacientes y un 58,3% en los cuidadores. El 63,6% de los pacientes y el 42,9% de los cuidadores eran mujeres. La media de edad fue, respectivamente, 46,1 años (DE: 13,7) y 47,0 años (DE: 3,6). La mayoría de los pacientes (54,5%) y de los cuidadores (42,9%) tenían estudios secundarios y eran pensionistas (72,7% y 71,4%, respectivamente). Las enfermedades de base de los pacientes fueron: enteritis rádica (27,3%), obstrucción intestinal (18,2%), carcinomatosis intestinal (45,5%) y enfermedad de Crohn (9,1%). Con respecto a los ítems que evaluaban la satisfacción con médicos, enfermeros y farmacéuticos, en general tanto pacientes como cuidadores estuvieron satisfechos. Las sugerencias recogidas fueron: mayor amplitud del horario de entrega de la NPD e inclusión de información audiovisual.**

Conclusiones: **El grado de satisfacción de los pacientes que reciben NPD y sus cuidadores con el servicio dado por médicos, enfermeros y farmacéuticos es adecuado, aunque se pueden introducir mejoras para optimizar la calidad de todo el proceso.**

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Palabras clave:*Nutrición Parenteral Domiciliaria. Satisfacción del paciente. Encuesta. Atención domiciliaria.*

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HOME PARENTERALNUTRITION; SATISFACTION OF PATIENTS AND THEIR CAREGIVERS WITH NUTRITION UNIT AND PHARMACY SERVICE

Abstract

Introduction: **Home Parenteral Nutrition (HPN) is a practice in continually growing by the significant advantages involved for the patient and the healthcare system. Today, in the investigation of health outcomes is essential to assess the patient s opinion. Among the measures focused on patients with HPN, several studies about quality of life have been done, but the degree of satisfaction with this treatment modality has not been evaluated.**

Objective: **To evaluate the degree of satisfacion of patients and their caregivers receiving HPN with doctors, pharmacists and nurses in a hospital.**

Material and methods: **An anonymous survey was distributed, which consisted of 48 closed questions to patients and their caregivers receiving HPN who voluntarily answered. With survey responses a database in SPSS with the following variables was created: personal, sociocultural, clinical and related to HPN data and valoration of health personnel involved (nutrition area of the Pharmacy Service and Nursing and Medical Nutrition Units) and hospital facilities related to HPN. Also a section of open response suggestions was included.**

Results: **24 surveys were distributed, 12 to patients and 12 to caregivers. Response rate was 91.7% in the case of patients and 58.3% in the caregivers. 63.6% of patients and 42.9% of caregivers were women. Mean age was, respectively, 46.1 years (SD: 13.7) and 47.0 years (SD: 3.6). Most of patients (55.6%) and caregivers (60.0%) had secondary studies and were pensoniers (72.7% and 71.4%, respectively). Underlying diseases of patients were: radiation enteritis (27.3%), intestinal obstruction (18.2%), intestinal carcinomatosis (45.5%) and Chron s disease (9.1%). With respect to items assessing satisfaction with physicians, nurses and pharmacists, in general both patients and caregivers were satisfied. Suggestions made were: greater amplitude of delivery schedule of HPN and inclusion of audiovisual information.**

Conclusions: **The degree of satisfaction of patients receiving HPN and their caregivers with the care given by doctors, pharmacists and nurses is appropriate, but it s possible to make improvements to optimize the quality of the whole process.**

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Key words: *Home-based Parenteral Nutrition. Patient's satisfaction. Survey. Home assistance.*

Introducción

La Nutrición Parenteral Domiciliaria (NPD) consiste en la infusión de nutrientes por una vía central en el domicilio del paciente, utilizando generalmente un catéter permanente (tunelizado o reservorio subcutáneo). Puede indicarse de forma transitoria o indefinida según los casos[1]. El progreso en los sistemas sanitarios, con equipos especializados en el soporte nutricional y una mayor capacidad de seguimiento de los pacientes en el domicilio, ha dispuesto los medios necesarios para que estos pacientes puedan recibir la nutrición parenteral sin necesidad de aislarlos de su ambiente social, evitando hospitalizaciones innecesarias y disminuyendo las posibles complicaciones nosocomiales, con el consiguiente ahorro para el Sistema Nacional de Salud[2,3]. Aunque la NPD es uno de los tratamientos domiciliarios más costosos, supone un ahorro del 65-80% frente a la administración de la nutrición en el hospital[4].

Las indicaciones más frecuentes de la NPD son el síndrome de intestino corto y la obstrucción intestinal. En la actualidad, la patología maligna (cáncer avanzado) constituye la principal enfermedad de base en los pacientes subsidiarios de NPD en nuestro país, seguida de patologías benignas, entre las que se incluye la enteritis rádica, pseudoobstrucción crónica intestinal, isquemia mesentérica o la enfermedad inflamatoria intestinal, entre otras[5,6].

En España, los primeros datos sobre pacientes con NPD son de 1980, siendo su prevalencia en el 2010 de 3,15 pacientes/millón de habitantes[7]. El número total de pacientes registrados en el 2010 por el Grupo de Trabajo de Nutrición Artificial Domiciliaria y Ambulatoria (NADYA) fue de 148 pacientes (41,89% varones y 58,11% mujeres); el 93,67% fueron adultos y el 6,22%, niños. El 70% de los casos eran de Madrid (41%) y Cataluña (29%), lo que se traduce en una prevalencia de 9,5 pacientes/millón de habitantes en Madrid y de 6,2 pacientes/millón de habitantes en Barcelona[3]. En Europa la tasa de prevalencia oscila entre 0,3 y 12 pacientes/millón de habitantes, siendo más frecuente en el grupo de edad entre 41 y 60 años (44%). Existe un cierto predominio de mujeres y alrededor del 10% de los pacientes con NPD son niños[5].

La atención al paciente con NPD en su domicilio requiere de un equipo multidisciplinar formado por médicos, farmacéuticos, enfermeros, dietistas y psicólogos de hospital[8]. Es necesario conocer el grado de satisfacción de estos pacientes en relación con las distintas disciplinas implicadas en su seguimiento nutricional para evaluar los puntos fuertes y débiles y conseguir la máxima calidad asistencial en todo el proceso. El diseño de los procesos asistenciales ha cambiado sustancialmente cuando los clínicos han empezado a preocuparse por satisfacer no solo las necesidades de sus pacientes, sino también las expectativas de los mismos. Uno de los canales por los que el paciente participa en la actualidad en el Sistema Sanitario es aportando su opinión sobre el funcionamiento del mismo (su organización y prestaciones) y participando en la evaluación de los resultados que se alcanzan manifestando su grado de satisfacción con los mismos, tanto desde el punto de vista asistencial como desde otros[9]. Actualmente, la literatura sobre la opinión del paciente es extensa, pero se centra en valoraciones de carácter general de la asistencia prestada, siendo menos frecuente la evaluación de la satisfacción relacionada con los resultados de salud alcanzados, o sobre cómo se ha desarrollado un proceso asistencial específico[9]. Por tanto, es necesario entender que significa "calidad del cuidado" para los pacientes con NPD[10]. Ya en 1986, Feletti y cols. llegaron a la conclusión de que las dimensiones más importantes de la satisfacción del paciente son: comunicación (explicaciones claras, intimidad en la conversación, que se escuche con interés); actitudes profesionales (no adoptar un rol dominante); competencia técnica (los conocimientos propios de su especialidad); clima de confianza (paciente capaz de discutir con el profesional problemas personales) y percepción del paciente de su individualidad (respeto mutuo)[11]. Además, se ha observado que la satisfacción del paciente varía en función de ciertas condiciones de la interacción con el personal sanitario, como por ejemplo: duración de la consulta, habilidades de comunicación, grado de ayuda, comprensión y accesibilidad de los profesionales, informaciones incongruentes, respeto de la intimidad del paciente, cortesía o trato recibido[9]. Se ha analizado si la edad o el nivel educativo del paciente condiciona su nivel de satisfacción y se han obtenido resultados contradictorios en varios estudios[9,12].

Uno de los métodos para recoger estas opiniones es a través de la encuesta de satisfacción anónima, como medida de resultado de la actividad asistencial. La mayoría de las encuestas se basan en una estructura de respuesta tipo Likert, que permite ordenar los sujetos en base a sus respuestas a lo largo del continuo "favorable/desfavorable". Estas encuestas presentan normalmente un formato multidimensional que incluye información sobre: empatía, tipo y cantidad de información prestada al paciente y familiares, competencia técnica del personal sanitario, facilidades de acceso, continuidad de los cuidados y otras cuestiones sobre el confort de las instalaciones[9].

Objetivos

El objetivo de nuestro estudio es evaluar el grado de satisfacción de los pacientes que reciben NPD y sus cuidadores con los médicos, farmacéuticos y enfermeros del hospital relacionados con el proceso de la NPD y de las instalaciones relacionadas con la misma.

Métodos

En nuestro hospital, el servicio prestado a los pacientes con NPD incluye las siguientes prestaciones: cuatro médicos especialistas en Endocrinología y Nutrición

de la Unidad de Nutrición y Dietética responsables de proporcionar al paciente información sobre todo el proceso, de la prescripción de la NPD, de la decisión de la vía de acceso, del seguimiento del paciente y del tratamiento de las complicaciones asociadas al tratamiento; una enfermera responsable de la educación del paciente sobre la técnica de administración de la NPD y los cuidados del catéter y una farmacéutica especialista y un residente del Servicio de Farmacia, encargados de la información al alta del paciente y de la dispensación de la NPD y del material fungible.

Se realizó un estudio observacional descriptivo transversal desde junio de 2012 a diciembre de 2013. La población de estudio fueron los pacientes que recibían NPD en nuestro hospital y sus correspondientes cuidadores y que llevaban como mínimo 3 meses en tratamiento.

Se elaboró una encuesta anónima que constaba de 48 preguntas cerradas (Anexo I). La encuesta evaluaba datos personales (fecha de nacimiento, sexo, localidad del domicilio), socioculturales (nivel de estudios, situación laboral), clínicos (enfermedad de base) y relacionados con la NPD (personal elaborador –Servicio de Farmacia o catering– y número de bolsas de nutrición por semana). Las preguntas que evaluaban el grado de satisfacción se dividieron en los siguientes bloques: evaluación de la Unidad Médica y de Enfermería de Nutrición, del área de nutrición del Servicio de Farmacia y de las instalaciones del hospital relacionadas con la NPD. Al final se incluía un apartado de sugerencias con respuesta abierta. La encuesta se entregaba en el Servicio de Farmacia por duplicado (una para el paciente y otra para su correspondiente cuidador) y se informó sobre la voluntariedad de la participación y el anonimato. Posteriormente eran depositadas en sobre cerrado en el buzón de sugerencias de dicho Servicio.

El soporte informático empleado para el análisis estadístico fue IBM SPSS Statistics 19®. Las variables continuas se han descrito con la media y desviación estándar (DE) o con la mediana y rango intercuartílico (IQ) según siguieran criterios de normalidad. Las variables categóricas se expresaron como frecuencias y porcentajes.

Resultados

Se entregó la encuesta a 12 pacientes y a sus correspondientes cuidadores. La tasa de respuesta fue de un 91,7% en el caso de los pacientes (hubo uno que no contestó por éxitus, por lo que fue excluido del estudio) y de un 58,3% en el caso de los cuidadores.

La edad media de los pacientes fue de 46,1 años (DE 13,7 años) y la mediana fue de 51,1 años (IQ 39,6-53,7 años). La distribución por sexo fue: 4 (36,4%) hombres y 7 (63,6%) mujeres. La edad media de los cuidadores fue de 47,0 años (DE 3,57 años) y la mediana fue de 46,9 años (IQ 43,9-50,1 años), de los cuales 4 (57,1%) eran hombres y 3 (42,9%) mujeres.

En cuanto a la localidad del domicilio, 7 (63,6%) pacientes y 4 (57,1%) cuidadores eran de Madrid capital, 3 (27,3%) pacientes y 1 (14,3%) cuidador eran de la Comunidad de Madrid y 1 (9,1%) paciente y 2 (28,6%) cuidadores eran de otra provincia.

Cuando se analizó la distribución por nivel de estudios, se obtuvo que 1 (9,1%) paciente y 1 (14,3%) cuidador tenían estudios primarios, 6 (54,5%) pacientes y 3 (42,9%) cuidadores tenían estudios secundarios y 4 (36,4%) pacientes y 3 (42,9%) cuidador tenían estudios universitarios. En cuanto a la situación laboral, 1 (9,1%) paciente y 1 (14,3%) cuidador estaba en activo, 8 (72,7%) pacientes y 5 (71,4%) cuidadores eran pensionistas, 1 (9,1%) paciente y 1 (14,3%) cuidador eran estudiantes y 1 (9,1%) paciente estaba de baja laboral.

Las enfermedades de base de los pacientes fueron: 1 (9,1%) paciente con enfermedad de Crohn, 3 (27,3%) pacientes con enteritis rádica, 2 (18,2%) pacientes con obstrucción intestinal y 5 (45,5%) pacientes con carcinomatosis intestinal.

6 (54,5%) pacientes recibían NPD elaborada por la empresa de catering y 4 (36,4%) pacientes por el Servicio de Farmacia. Hubo 1 (9,1%) paciente que no contestó. La distribución según el número de NPD por semana se recoge en la figura 1.

La relación entre el cuidador y paciente fue: pareja en 4 (36,4%) pacientes y en 4 (57,1%) cuidadores y padre/madre-hijo en 3 (27,3%) pacientes y 2 (28,6%) cuidadores. 4 (36,4%) pacientes y 1 (14,3%) cuidador no contestaron a esta pregunta. 6 (54,5%) pacientes y 6 (85,7%) cuidadores vivían en el mismo domicilio y 1 (9,1%) paciente vivía en distinto domicilio. 4 (36,4%) pacientes no contestaron.

En la pregunta a los cuidadores de si se había tenido experiencia previa como cuidador, 6 (85,7%) contestaron que no y 1 (14,3%) no contestó, y a la pregunta de si se sentía capacitado para realizar los cuidados, 6 (85,7%) contestaron que sí y 1 (14,3%) no contestó.

En cuanto al grado de satisfacción con los médicos de la Unidad de Nutrición, con las enfermeras de la Unidad de Nutrición y con los farmacéuticos del área de Nutrición del Servicio de Farmacia, los resultados obtenidos se presentan en las tablas I, II y III, respectivamente.

El tipo de información proporcionada por parte de las enfermeras de la Unidad de Nutrición fue oral en el caso de 3 (27,3%) pacientes y 2 (28,6%) cuidadores, escrita en 1(9,1%) paciente y 1 (14,3%) cuidador, oral y escrita en 4 (36,4%) pacientes y 2 (28,6%) cuidadores y oral, escrita y audiovisual en 3 (27,3%) pacientes y en 2 (28,6%) cuidadores. Cuando se preguntaba si existen informaciones incongruentes por parte de varios enfermermeros/as, 10 (90,9%) pacientes y 7 (100%) cuidadores contestaron que no.

Los resultados obtenidos en la evaluación del grado de satisfacción con las instalaciones del hospital relacionadas con la NPD se recogen en la tabla IV.

Los resultados obtenidos cuando se preguntaba por el grado de satisfacción general con los servicios prestados por los médicos, enfermeros y farmacéuticos fueron: 10 (90,9%) pacientes y 7 (100%) cuidadores estaban satisfechos y 1 (9,1%) paciente estaba insatisfecho.

Anexo I

Encuesta de satisfaccion de pacientes que reciben nutrición parenteral domiciliaria y sus cuidadores

PRESENTACIÓN:

Gracias por realizar esta encuesta de satisfacción sobre los médicos, enfermeras y farmacéuticos que manejan su Nutrición Parenteral Domiciliaria (NPD). No tardará más de diez minutos en completarla y nos será de gran ayuda para mejorar nuestros servicios. Los datos que en ella se consignen se tratarán de forma anónima. A poder ser, se deben rellenar las dos encuestas que se encuentran dentro de este sobre: una es para recoger la opinión del paciente que recibe la nutrición y, la otra, es para la opinión de su cuidador (en caso de existir). Una vez cumplimentadas, puede depositar el sobre (cerrado) en el buzón de sugerencias situado en la primera planta del Servicio de Farmacia. Si usted tiene alguna duda para rellenar la encuesta, puede ponerse en contacto con nosotros.

ENCUESTA

Recuerde: tenga en cuenta únicamente lo relacionado con la Nutrición Parenteral.
Persona que cumplimenta la encuesta (seleccione una):

- Paciente.
- Cuidador.

DATOS GENERALES DEL PACIENTE:

- Fecha de nacimiento del paciente: __/__/_____.
- Sexo:
  - Hombre.
  - Mujer.
- Localidad en la que vive: _____.
- Nivel de estudios:
  - Primarios.
  - Secundarios.
  - Universitarios.
  - Sin estudios.
  - Otros (especificar): _____.
- Situación laboral:
  - Activo.
  - Parado.
  - Jubilado.
  - Estudiante.
  - Otros (especificar): _____.

- Enfermedad diagnosticada:
  - Enteritis rádica.
  - Síndrome de intestino corto.
  - Pseudoobstrucción intestinal.
  - Enfermedad de Crohn.
  - Enfermedad de Hirchsprung.
  - Carcinomatosis intestinal.
  - Otra (indicar): _____.
- ¿Quién le prepara la nutrición parenteral?:
  - Servicio de Farmacia.
  - Catering.
- Nº de bolsas de nutrición a la semana: ____ bolsas.

DATOS GENERALES DEL CUIDADOR: (en caso de que el paciente y el cuidador coincidan rellenar solamente las dos últimas preguntas de este apartado:

- Fecha de nacimiento del cuidador: __/__/____.
- Sexo del cuidador:
  - Mujer.
  - Hombre.
- Localidad en la que vive el cuidador: _____.
- Nivel de estudios del cuidador:
  - Primarios.
  - Secundarios.
  - Universitarios.
  - Sin estudios.
  - Otros (especificar): _____.
- Situación laboral del cuidador:
  - Activo.
  - Parado.
  - Jubilado.
  - Estudiante.
  - Otros (especificar): _____.

Anexo I *(cont.)*
Encuesta de satisfaccion de pacientes que reciben nutrición parenteral domiciliaria y sus cuidadores

- Relación entre la persona que realiza los cuidados y el paciente (marido, mujer, hijo, hermano, uno mismo…): _____.
- ¿Vive en el mismo domicilio que la persona a la que cuida?
  - Sí.
  - No.
- ¿Ha tenido experiencia previa como cuidador?
  - Sí.
  - No.
- ¿Se siente capacitado para realizar los cuidados?:
  - Sí.
  - No.
  - Regular.

ASPECTOS RELACIONADOS CON LA UNIDAD DE NUTRICIÓN:
Por favor, puntúe su grado de satisfacción con las siguientes afirmaciones en relación con el médico que le atiende normalmente:

	Satisfecho	No satisfecho
Amabilidad y cortesía con que se le trató		
Preparación y profesionalidad del médico		
Eficacia y resolución de su problema de salud		
Atención con la que el médico escuchó sus preguntas		
Confianza y seguridad que le inspiró el médico que le atendió		
Claridad de la información que el médico le dio sobre su enfermedad		
Tiempo de consulta		
Tiempo de espera para la consulta		
Capacidad de resolución del médico frente a la presencia de efectos adversos		
Accesibilidad del médico		

ASPECTOS RELACIONADOS CON LAS ENFERMERAS DE LA UNIDAD DE NUTRICIÓN:
- Por favor, puntúe su grado de satisfacción con las siguientes afirmaciones en relación con la enfermera que le ha explicado el manejo del catéter de la nutrición parenteral domiciliaria previamente al alta:

	Satisfecho	No satisfecho
Amabilidad y cortesía con que se le trató		
Eficacia y resolución de los problemas con la nutrición		
Atención con que escuchó sus preguntas		
Preparación y profesionalidad de las enfermeras		
Confianza y seguridad que le inspiró quien le atendió		
Claridad de la información que le dio		
Duración del entrenamiento		
Accesibilidad de las enfermeras		

ASPECTOS RELACIONADOS CON EL ÁREA DE NUTRICIÓN DEL SERVICIO DE FARMACIA:

	Satisfecho	No satisfecho
Amabilidad y cortesía con que se le trató		
Eficacia y resolución de los problemas con la nutrición		
Atención con que el farmacéutico escuchó sus preguntas		
Preparación y profesionalidad del farmacéutico		
Confianza y seguridad que le inspiró el farmacéutico que le atendió		
Claridad de la información que el farmacéutico le dio		
Horario y días de entrega de la NPD		
Modo en el que se le entrega la NPD		
Cantidad del material que recibe en el Servicio de Farmacia		

ASPECTOS RELACIONADOS CON LAS INSTALACIONES DEL HOSPITAL RELACIONADAS CON LA NPD:

	Satisfecho	No satisfecho
Confortabilidad y limpieza		
Accesibilidad y señalización		
Grado de intimidad		

GRADO DE SATISFACCIÓN GENERAL CON LOS MÉDICOS, ENFERMERAS Y FARMACÉUTICOS:
- Satisfecho.
- Insatisfecho.

SUGERENCIAS:

Muchas gracias por su colaboración.

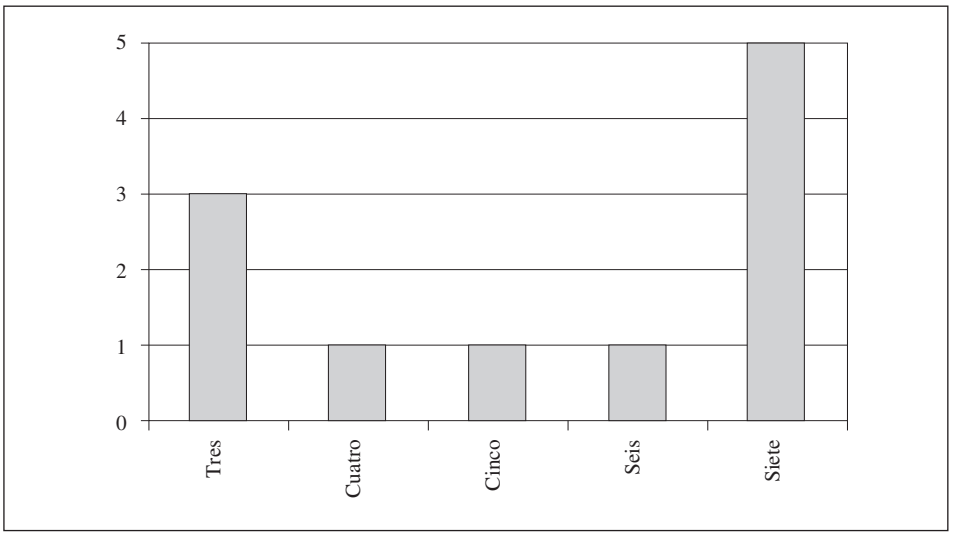


Fig. 1.—Distribución de la frecuencia de administración de la nutrición parenteral domiciliaria.

Tabla I
Distribución de frecuencias según ítem evaluado y según la respuesta dada en la evaluación del grado de satisfacción con los médicos de la unidad de nutrición

	Número de pacientes/cuidadores y porcentaje por respuesta dada					
	Satisfecho		*Insatisfecho*		*No contesta*	
Ítem evaluado	*Pacientes*	*Cuidadores*	*Pacientes*	*Cuidadores*	*Pacientes*	*Cuidadores*
Amabilidad y cortesía con que se le trató	9 (81,8%)	6 (85,7%)	1 (9,1%)	0	1 (9,1%)	1 (14,3%)
Preparación y profesionalidad del médico	9 (81,8%)	6 (85,7%)	1 (9,1%)	0	1 (9,1%)	1 (14,3%)
Eficacia y resolución de su problema de salud	7 (63,6%)	5 (71,4%)	3 (27,3%)	1 (14,3%)	1 (9,1%)	1 (14,3%)
Atención con la que el médico escuchó sus preguntas	9 (81,8%)	6 (85,7%)	1 (9,1%)	0	1 (9,1%)	1 (14,3%)
Confianza y seguridad que le inspiró el médico que le atendió	9 (81,8%)	6 (85,7%)	1 (9,1%)	0	1 (9,1%)	1 (14,3%)
Claridad de la información que el médico le dio sobre su enfermedad	9 (81,8%)	6 (85,7%)	1 (9,1%)	0	1 (9,1%)	1 (14,3%)
Tiempo de la consulta	10 (90,9%)	6 (85,7%)	0	0	1 (9,1%)	1 (14,3%)
Tiempo de espera para la consulta	6 (54,5%)	5 (71,4%)	4 (36,4%)	1 (14,3%)	1 (9,1%)	1 (14,3%)
Capacidad de resolución del médico frente a la presencia de efectos adversos	10(90,9%)	6 (85,7%)	0	0	1 (9,1%)	1 (14,3%)
Accesibilidad del médico	9 (81,8%)	5 (71,4%)	0	1 (14,3%)	2 (18,2%)	1 (14,3%)

Por último, en el apartado de sugerencias contestaron dos cuidadores: uno proponía tener acceso al servicio de catering, ya que tiene que ir a recoger la NPD al hospital dos días en semana y el otro, la organización de charlas educativas.

Discusión

El número de pacientes y cuidadores que participan en la encuesta podría parecer muy reducido si se considera de forma aislada, pero no lo es cuando se tiene en cuenta la prevalencia en Madrid de pacientes con NPD, ya que suponen un 18,0% de los casos registrados por el grupo de trabajo NADYA en 2010[3]. Todos los participantes tienen estudios primarios, por lo que el analfabetismo no es un limitante a la hora de leer y completar las encuestas.

Las enfermedades de base tienen una distribución variada entre los pacientes y la frecuencia de administración de la NPD es diaria en la mayor parte de los pacientes.

Respecto a la valoración de los médicos de la Unidad de Nutrición, en aspectos como la amabilidad, la profe-

Tabla II
Distribución de frecuencias según ítem evaluado y según la respuesta dada en la evaluación del grado de satisfacción con la unidad de enfermería

	Número de pacientes/cuidadores y porcentaje por respuesta dada					
	Satisfecho		*Insatisfecho*		*No contesta*	
Ítem evaluado	*Pacientes*	*Cuidadores*	*Pacientes*	*Cuidadores*	*Pacientes*	*Cuidadores*
Amabilidad y cortesía con que se le trató	9 (81,8%)	7 (100%)	1 (9,1%)	0	1 (9,1%)	0
Eficacia y resolución de los problemas con la nutrición	9 (81,8%)	7 (100%)	1 (9,1%)	0	1 (9,1%)	0
Atención con que se escuchó sus preguntas	9 (81,8%)	7 (100%)	1 (9,1%)	0	1 (9,1%)	0
Preparación y profesionalidad de las enfermeras	9 (81,8%)	7 (100%)	1 (9,1%)	0	1 (9,1%)	0
Confianza y seguridad que le inspiró quien le atendió	8 (72,7%)	7 (100%)	1 (9,1%)	0	2 (18,2%)	0
Claridad de la información que se le dio	9 (81,8%)	7 (100%)	1 (9,1%)	0	1 (9,1%)	0
Duración del entrenamiento	10 (90,1%)	6 (85,7%)	1 (9,1%)	0	0	1 (14,3%)
Accesibilidad de las enfermeras	10 (90,1%)	6 (85,7%)	0	1 (14,3%)	1 (9,1%)	0

Tabla III
Distribución de frecuencias según ítem evaluado y según la respuesta dada en la evaluación del grado de satisfacción con el servicio de farmacia

	Número de pacientes/cuidadores y porcentaje por respuesta dada					
	Satisfecho		*Insatisfecho*		*No contesta*	
Ítem evaluado	*Pacientes*	*Cuidadores*	*Pacientes*	*Cuidadores*	*Pacientes*	*Cuidadores*
Amabilidad y cortesía con que se le trató	10 (90,9%)	7 (100%)	1 (9,1%)	0	0	0
Eficacia y resolución de los problemas con la nutrición	10 (90,9%)	7 (100%)	1 (9,1%)	0	0	0
Atención con que el farmacéutico escuchó sus preguntas	9 (81,8%)	7 (100%)	1 (9,1%)	0	1 (9,1%)	0
Preparación y profesionalidad del farmacéutico	9 (81,8%)	7 (100%)	1 (9,1%)	0	1 (9,1%)	0
Confianza y seguridad que le inspiró el farmacéutico que le atendió	9 (81,8%)	7 (100%)	1 (9,1%)	0	1 (9,1%)	0
Claridad de la información que se le dio	9 (81,8%)	7 (100%)	1 (9,1%)	0	1 (9,1%)	0
Horario y días de entrega de la NPD	10 (90,9%)	7 (100%)	1 (9,1%)	0	0	0
Modo en el que se le entrega la NPD	10 (90,9%)	7 (100%)	1 (9,1%)	0	0	0
Cantidad del material que recibe en el Servicio de Farmacia	11 (199%)	7 (100%)	0	0	0	0

sionalidad, la atención, la confianza inspirada, la claridad de la información y la accesibilidad la gran mayoría opinan que están satisfechos y solo hay un paciente que está insatisfecho. El 100% de los cuidadores y de los pacientes están satisfechos con el tiempo de duración de la consulta médica y con la capacidad de resolución del médico frente a la presencia de efectos adversos. Los aspectos peor valorados son la eficacia y resolución del problema de salud, pero hay que tener en cuenta que la cronicidad de las enfermedades que padecen estos pacientes hace que su percepción de su estado de salud tras el tratamiento afecte más a su nivel de satisfacción que la mejoría que hayan logrado con el mismo[9], y el tiempo de espera para la consulta, que no depende de los médicos, sino que es debido a la escasez de recursos sanitarios.

La mayoría de los pacientes y cuidadores están satisfechos con la amabilidad, la eficacia en la resolución de

Tabla IV
Distribución de frecuencias según ítem evaluado y según la respuesta dada en la evaluación del grado de satisfacción con las instalaciones del hospital relacionadas con la NPD

	Número de pacientes/cuidadores y porcentaje por respuesta dada					
	Satisfecho		*Insatisfecho*		*No contesta*	
Ítem evaluado	*Pacientes*	*Cuidadores*	*Pacientes*	*Cuidadores*	*Pacientes*	*Cuidadores*
Amabilidad y cortesía con que se le trató	9 (81,8%)	7 (100%)	1 (9,1%)	0	1 (9,1%)	0
Confortabilidad y limpieza	8 (72,7%)	5 (71,4%)	3 (27,3%)	2 (28,6%)	0	0
Accesibilidad y señalización	9 (81,8%)	7 (100%)	2 (18,2%)	0	0	0
Grado de intimidad	7 (63,6%)	6 (85,7%)	4 (36,43%)	1 (14,3%)	0	0

los problemas, la atención prestada, la profesionalidad, la confianza inspirada, la claridad de la información, la duración del entrenamiento y la accesibilidad del personal de enfermería de la Unidad de Nutrición. Además, ninguno opina que haya incongruencias en la información dada por éstos. Cabe destacar que uno de los cuidadores está insatisfecho con su accesibilidad. Un objetivo clave es dar información oral y escrita al 100% de los pacientes y de los cuidadores, ya que ha habido casos en los que solo se ha dado información oral, lo que puede propiciar que se olvide explicar algunos aspectos, y otros casos en los que solo se ha dado información escrita, lo cual puede dar lugar a problemas de comprensión. Además, un posible avance en esta materia sería entregar a los pacientes información audiovisual en soporte informático, ya que ayuda a entender mejor las explicaciones. En este sentido, el grupo NADYA de la Sociedad Española de Nutrición Enteral y Parenteral (SENPE) ha realizado unos videos educativos sobre el cuidado de los diferentes tipos de catéteres empleados en los pacientes con NPD (tunelizados, reservorios subcutáneos y catéteres centrales de inserción periférica o PICC)[13]. También se podrían organizar charlas educativas periódicamente para el reciclaje de pacientes y cuidadores, según una de las propuestas sugeridas.

En la valoración de los farmacéuticos del área de nutrición del Servicio de Farmacia, la mayoría de pacientes están satisfechos con la amabilidad, la eficacia en la resolución de los problemas con la nutrición, la atención prestada, la claridad de la información, el horario, los días y el modo de entrega de la NPD. Ninguno está insatisfecho con el material fungible que recibe en dicho Servicio, lo que puede deberse a que se les entrega lo que cada paciente solicita.

Los resultados menos favorables fueron los que conciernen a las instalaciones del hospital, lo cual no depende directamente del equipo multidisciplinar relacionado con la NPD. Además, cabe la posibilidad de que alguno de ellos no haya entendido que la pregunta se refería solo a las instalaciones concernientes a la NPD, y no al hospital en general.

De acuerdo con los resultados, en general los pacientes y cuidadores están satisfechos con el servicio recibido, al igual que en el estudio de pacientes con Nutrición Enteral Domiciliaria realizado por M. Planas y cols. en 2007, en el cual el 50% de los pacientes domiciliarios valoraron la atención recibida como muy buena[14].

Una limitación de este estudio es que el cuestionario no está validado, por lo que podría ocurrir que las medidas de la satisfacción del paciente carezcan de la sensibilidad, validez y fiabilidad óptimas. No obstante, el principal inconveniente metodológico es que la encuesta está realizada por los profesionales sanitarios implicados, lo que puede introducir importantes sesgos ya que éstos no siempre son conscientes de cómo valoran y en qué se fijan los pacientes a la hora de valorar la asistencia sanitaria que reciben[9].

Otra de las limitaciones es que se centra solamente en la evaluación de la satisfacción del paciente, mientras que el estudio de Martínez Olmos[2] es más amplio, ya que además incluye otras dimensiones (indicación, eficacia, efectividad, seguridad, continuidad, temporalidad y disponibilidad), que conforman los factores que influyen directamente sobre la calidad del cuidado asistencial. Sin embargo, el hecho de que nuestro estudio se centre sobre una única dimensión, nos permite profundizar más sobre la misma, creando un posible formato de encuesta que valore a los médicos, farmacéuticos y enfermeros por parte de los pacientes con NPD.

Conclusiones

El equipo multidisciplinar de soporte nutricional constituye un pilar fundamental para conseguir la máxima calidad asistencial posible para los pacientes con NPD, la cual se puede reforzar conociendo el grado de satisfacción de los mismos a través de encuestas anónimas.

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Original / *Vitaminas*

The role of prenatal nutrition assistance on the prevalence of night blindness in pregnant adults

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Abstract

Introduction: **In developing countries, night blindness is a very common public health problem among pregnant women.**

Objective: **Evaluate the effect of the changes occurred on prenatal care concerning prenatal nutritional care on the occurrence of night blindness (XN) in adult pregnant women in public maternity hospital in Rio de Janeiro between 1999-2001 and between 2007-2008.**

Methods: **Two cross-sectional studies were conducted, been the first one conducted between 1999-2001 and the second one between 2007-2008. Were studied 402 puerperal women, 225 between 1999-2001 (GI) and 177 between 2007-2008 (GII). The gestational XN was investigated during the immediate puerperium (GI) and during the prenatal/puerperium (GII), diagnosed by the World Health Organization. The study collected sociodemographic, clinical, obstetric, anthropometric and prenatal care information.**

Results: **It verified significant reduce of prevalence of gestational XN (GI = 18.7% e GII = 0.6%, p < 0.001). The occurrence of gestational XN was associated to sanitary conditions, education level, more than six prenatal consultations, miscarriage at last pregnancy, higher average number of deliveries, average number of prenatal care consultations and prenatal nutritional (p < 0.05). There was no association between gestational XN and marital status, skin color, pre-gestational nutritional status, adequacy of gain of total gestational weight, gestational anaemia and average number of pregnancies (p > 0.05).**

Conclusion: **The inclusion of nutritional care in routine prenatal care may have contributed to the reduction of gestational XN. Studies to assess the nutritional intervention in the prevention and treatment of gestational XN at regions at greatest risk are suggested.**

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Key words: *Night blindness. Vitamin A deficiency. Prenatal nutrition. Pregnancy.*

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EL PAPEL DE LA ASISTENCIA NUTRICIONAL PRENATAL SOBRE LA PREVALENCIA DE LA CEGUERA NOCTURNA EN ADULTAS EMBARAZADAS

Resumen

Introducción: **En los países en desarrollo, la ceguera nocturna (CN) es un problema muy común de la salud pública entre las mujeres embarazadas.**

Objetivo: **Evaluar el efecto de los cambios ocurridos en la atención prenatal sobre el cuidado nutricional prenatal sobre la aparición de CN en mujeres adultas embarazadas en una maternidad pública en Rio de Janeiro entre 1999-2001 y entre 2007-2008.**

Métodos: **Se realizaron dos estudios transversales, el primero entre 1999-2001 y el segundo entre 2007-2008. Se estudiaron 402 mujeres puérperas, 225 entre 1999-2001 (GI) y 177 entre 2007-2008 (GII). La CN gestacional fue investigada durante el puerperio inmediato (GI) y durante el prenatal/puerperio (GII), diagnosticada por la Organización Mundial de La Salud. El estudio incluió informaciones sociodemográficas, clínicas, obstétricas, antropométricas y del cuidado prenatal.**

Resultados: **Se verificó reducción significativa de la prevalencia de CN gestacional (GI = 18,7% e GII = 0,6%, p < 0,001). La ocurrencia de CN gestacional se asoció con las condiciones sanitarias, el nivel de educación, más de seis consultas prenatales, abortos espontáneos en el último embarazo, mayor número promedio de partos, el número promedio de consultas de atención prenatal y de nutrición prenatal (p < 0,05). No hubo asociación entre CN gestacional y el estado civil, color de piel, estado nutricional pregestacional, adecuación de la ganancia de peso durante la gestación, incluyendo anemia gestacional y el número medio de embarazos (p > 0,05).**

Conclusión: **La inclusión de la atención nutricional en el cuidado prenatal de rutina puede haber contribuido para la reducción de CN gestacional. Se sugiere más estudios para evaluar la intervención nutricional en la prevención y el tratamiento de CN gestacional en las regiones de mayor riesgo.**

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Palabras clave: *Ceguera nocturna. Deficiencia de vitamina A. Nutrición prenatal. Embarazo.*

Abbreviation list

CN: Ceguera nocturna.
VA: Vitamin A.
VAD: Vitamin A deficiency.
XN: Night blindness.
PNA: Prenatal nutritional assistance.
GA: Gestational age.
GI: Group I.
GII: Group II.
NB: Newborn.
LBW: Low birth weight.
SGA: Small gestational age.
AGA: Appropriate gestational age.
LGA: Large gestational age.

Introduction

Most pregnancies proceed without complications that pose a health risk to either the mother or child. Most complications that do occur during pregnancy and childbirth are preventable, but they require an appropriate health intervention[1].

Specific deficiencies of micronutrients such as vitamin A (VA) can aggravate and increase the chance of obstetric problems[2,3]. VA has important functions in the body, particularly in the ocular system. It plays a key role in maintaining the integrity of the eye and visual processes, including adaptation to low light environments[4,5].

Pregnant women with vitamin A deficiency (VAD) are more likely to have obstetric complications such as anemia, malnutrition, urinary tract and reproductive system infections, diarrhea, pre-eclampsia/eclampsia, and gastrointestinal symptom (vomiting, nausea, and loss of appetite). These can increase the chance of maternal and fetal death[3,6].

VAD may progress to advanced stages in which functional changes occur, such as ocular changes[7]. Night blindness (XN) is the first manifestation of xerophthalmia and can occur during pregnancy, most commonly in the 2nd and 3rd trimesters. This is characterized by night vision impairment but normal vision during the day[8,9].

VAD is considered a public health problem, especially in developing countries, and its severity is assessed by the prevalence of XN in both pregnant women and pre-school[10].

XN is considered an indicator of high risk pregnancy, identifying women who need special nutrient requirements and greater attention to prenatal care[11,12]. The occurrence of gestational XN can have profound impacts on the fetus, and mortality rates in children of women who had gestational XN is 90 deaths per 1,000 live births, whereas the rate among children of women without gestational XN is 63 deaths per 1,000 live births[13].

Strategies to combat VAD in pregnant women have been suggested. Many emphasize prenatal nutritional assistance (PNA), which has been shown to reduce the prevalence of VAD among pregnant women who received this intervention along with their prenatal care[14].

Based on these concepts, the objective of this study was to analyze the effect of changes in prenatal care (with respect to PNA) on the occurrence of XN in adult pregnant women treated at the maternity public hospital in Rio de Janeiro during 1999-2001 and 2007-2008.

Methods

Study design

Two cross-sectional studies were performed in pregnant and postpartum women treated in a public maternity hospital in Rio de Janeiro during 1999-2001 and 2007-2008. This maternity hospital serves women with similar characteristics to other pregnant and postpartum women treated at other healthcare facilities in Rio de Janeiro[15,16], and it has a multidisciplinary team in prenatal care. On average, 220-230 deliveries are conducted monthly[16]. Data collection in both studies was performed by trained and qualified researchers.

Changes in prenatal care between 1999-2001 and 2007-2008

Prenatal care was altered for the study in the selected period by modifying PNA. During 1999-2001, PNA was limited. Consultation with a nutritionist only occurred upon referral of pregnant women by obstetricians in cases of weight deviation or pregnancy complications at any gestational age (GA). In these cases, the woman received individualized nutritional care according to events or specific anthropometric characteristics.

In 2006, the process was changed, and PNA was expanded to all pregnant women in the unit, and they received either group or individual sessions. Each woman received at least one group consultation with a nutritionist during pregnancy. These group sessions aimed to optimize maternity human resources (number of nutritionists) and allow the exchange of experiences between the participants and the multidisciplinary team.

All pregnant women in the study received specific guidelines regarding gastrointestinal symptoms, pregnancy complications (including specific nutritional deficiencies, particularly VAD, and consumption of foods fortified with VA and supplementation regimens were encouraged and prescribed by the physician), and breastfeeding.

Patients with risk factors had individual nutrition sessions throughout pregnancy. For these, the nutrition care included a nutrition assessment and detailed dietary planning. After estimating the recommended weight gain, an appropriate energy value of the diet was calculated and a suitable diet plan was developed

considering the dietary habits, sociodemographic status and lifestyle of the pregnant woman.

As part of prenatal care, the obstetrician prescribed supplementation with a multivitamin containing VA. The main focus of supplementation was to correct gestational iron deficiency anemia. The amount of VA contained in the supplement were of 3,000 IU, with a combination of β-carotene and retinol.

Study population and inclusion criteria

The study population consisted of pregnant and postpartum women admitted to the hospital during pregnancy and/or childbirth/puerperium. Data were analyzed from a representative sample during the periods of 1999-2001 and 2007-2008. The women were divided into two groups: group I (GI during 1999-2001) and group II (GII during 2007-2008).

Inclusion criteria were as follows: age ≥ 20 years, women currently receiving prenatal care, single fetus pregnancy, no previous medical history before pregnancy, and receipt of information on the diagnosis of gestational XN.

In GI, information about the puerperal period up to 6 hours postpartum and their newborns (NB) was obtained. This group received routine interventions (historical control), and limited PNA was taken into account in this period. In this group, some women only delivered at the healthcare facility under study and underwent prenatal care at other facilities in the municipality.

In GII, data were collected from postpartum women who received prenatal care and delivered at the hospital under study. This group was composed of women that were followed one year after the implementation of new PNA procedures, which were reviewed and updated due to new scientific evidence.

The following information was collected: sociodemographic characteristics (age [20-24, 25-34 or > 35 years], basic sanitation [adequate or inadequate], skin color [white or non-white], marital status [married/living with a partner or living without a partner], education [incomplete primary, complete primary/incomplete high school or complete high school]), clinics and obstetrics (number of pregnancies, interval between pregnancies, parity, history of abortion, frequency of anemia and gestational XN), and prenatal care (length of commute to prenatal care, number of visits to prenatal care [< 6 or ≥ 6 visits] and PNA). The data were collected through interviews and consultation of team records of prenatal care in the medical records.

Anthropometric assessment

The following data were collected: declared pre-pregnancy weight or weight measured up to 13 weeks of gestation and height and weight before delivery or in the last visit before delivery. The following data were collected from the NB: birth weight, birth length and GA at birth.

The taking of anthropometric measurements was performed by nurses, as a routine prenatal care in the unit. In both instances, the procedures were standardized to the purposes of the research, according to international recommendations[17].

For the anthropometric measurements, body mass index was used according to criteria established by the World Health Organization[17]. The total gestational weight gain was calculated by the difference between pre-pregnancy weight and the weight before delivery or registered at the last prenatal visit.

The adequacy of gestational weight gain was ranked as follows: insufficient weight gain (below recommended minimum), suitable (weight gain within recommended range) and excessive weight gain (above recommended maximum)[18]. The analysis of birth weight for GA age was performed according to Pedreira et al. 2011[19].

Gestational and neonatal intercurrences

The following complications were considered: gestational diabetes, hypertensive syndromes during pregnancy, anemia, and urinary tract infection[1,20]. These were identified by asking the obstetrician or interpreting results.

VAD was assessed by functional indicators (gestational XN) based on a standardized interview[7,21] validated for postpartum women[8]. The interview consists of three questions that assess the ability to see the individual in specific situations. They are: 1) "Do you have difficulty seeing during the day?", 2) "Do you have difficulty seeing with decreasing light or at night?", and 3) "Do you have night blindness?"[7]. Cases were defined when there was a NO answer to question 1 and YES to at least one of questions 2 and 3. The interview was conducted using simple language and examples of places with low light common in the city[11].

In GI, this interview was conducted during the postpartum period (up to 6 hours postpartum), but in reference to vision symptoms experienced during pregnancy. In GII, the interview occurred during prenatal care, specifically at the nutrition visits.

In regards to the conditions at birth and neonatal complications, low birth weight (LBW) was considered a birth weight of < 2,500 g and macrosomia was considered a birth weight > 4,000 g[17]. The NB was classified according to GA at birth as preterm (> 21 and < 37 weeks gestation), term (≥ 37 and < 42 weeks gestation), or post-term (≥ 42 weeks of gestation)[20]. Abortions were defined as death or expulsion of the fetus occurring before 22 gestational weeks[22]. The fetuses were classified according to their birth weight for GA as small for gestational age (SGA; <10th percentile),

appropriate for gestational age (AGA; between 10th and 90th percentiles), or large for gestational age (LGA; > 90th percentile)[19].

Statistical analysis

A test of homogeneity between GI and GII was conducted, comparing sociodemographic, obstetric, assistance and anthropometric variables. Measures of central tendency (mean and standard deviation) and *Student's t test* were calculated. For categorical variables, we used the chi-square test (χ^2). The significance level used was $p < 0.05$. The statistical package SPSS for Windows version 17.0 was used for analysis.

Ethical questions

The study was designed respecting the ethical guidelines in Resolution 196/96 of the National Health Council (signer of the Declaration of Helsinki)[23]. The research projects that generated databases were approved by the Ethics in Research of the Maternity School, Federal University of Rio de Janeiro and the National School of Public Health, Oswaldo Cruz Foundation (Registrations nº 75/02 and 35/04).

Results

The final sample consisted of 402 pregnant and postpartum women, 225 in GI (56.0%) and 177 in GII (44.0%). In GI, 96% (n = 216) of the members received prenatal care in the maternity hospital studied. A significant reduction in the prevalence of XN was found, where 18.7% of GI (n = 42) and only 0.6% in GII (n = 1) had ocular manifestations of VAD.

Table I shows the comparison between the groups in regards to sociodemographic characteristics and history of miscarriage. There was a decrease in the proportion of women living in households with unsatisfactory sanitation (p = 0.018). The proportion of non-white (p < 0.001) and married/stable (p = 0.009)

Table I
Maternal sociodemographic and obstetrics characteristics of the groups GI (1999-2001) e GII (2007-2008). Rio de Janeiro, RJ, Brazil (n = 402)

	Study groups					
	GI (n = 225)		*GII (n = 177)*			
Variables	*n*	*%*	*n*	*%*	*Total*	*p*
AGE GROUP						
20-24 y	84.0	37.3	60.0	34.1	144.0	0.726
25-34 y	115.0	51.1	97.0	55.1	212.0	
>35 y	26.0	11.6	19.0	10.8	45.0	
CONDITIONS OF SANITATION						
Satisfactory	211.0	93.8	145.0	98.6	356.0	0.018
Inadequate	14.0	6.2	2.0	1.4	16.0	
SKIN COLOR						
White	100.0	44.5	19.0	18.8	119.0	<0.001
Nonwhite	125.0	55.5	82.0	81.2	207.0	
MARITAL STATUS						
Married/Living with partner	152.0	67.5	119.0	79.8	271.0	0.009
Living without partner	73.0	32.5	30.0	20.2	103.0	
EDUCATION						
Incomplete elementary	83.0	36.9	35.0	20.3	118.0	<0.001
Complete primary and incomplete secondary	78.0	34.7	43.0	25.0	121.0	
High school graduate	64.0	28.4	94.0	54.7	158.0	
HISTORY OF ABORTION						
Yes	33.0	14.7	38.0	21.7	71.0	0.045
No	192.0	85.3	137.0	78.3	329.0	

P: significance level ($p < 0.05$).

women increased. There was also an increase in women who had completed secondary school ($p < 0.001$). History of abortion in the previous pregnancy ($p = 0.045$) decreased between the periods analyzed. There was similarity between the groups with respect to age of the subjects ($p = 0.726$) (table I).

Between GI and GII, we observed an increase in the proportion of women who were overweight pre-pregnancy ($p < 0.001$), which reduced the inadequacy of total gestational weight gain ($p = 0.001$). There was an increased number of women who had more than six visits for prenatal care ($p < 0.001$), and the percentage of participants with access to PNA increased, from 20.4% in GI to 92.6% in GII ($p < 0.001$) (table II). There was similarity between the groups in regards to the frequency of gestational anemia ($p = 0.511$), adequacy of birth weight ($p = 0.133$), and GA at birth ($p = 0.285$). However, there was an increase in pregnancy complications ($p = 0.016$) and a decrease in the number of cases of infants with SGA ($p = 0.001$) between the periods analyzed (table III).

Table IV shows the factors associated with the occurrence of gestational XN. There was no association between XN with marital status ($p = 0.504$), ethnicity ($p = 0.694$), pre-pregnancy nutritional status ($p = 0.348$), adequacy of total gestational weight gain ($p = 0.592$), gestational anemia ($p = 0.411$), or mean number of pregnancies ($p = 0.053$). Among women who developed gestational XN, there were three times more who had inadequate sanitation than those without XN ($p = 0.012$). The level of education was also associated with the outcome ($p = 0.018$). Women who received less than six prenatal visits more frequently developed gestational XN ($p < 0.001$). Among women with XN, the history of miscarriage in previous pregnancy was proportionally higher than those without XN ($p = 0.019$). The prevalence of XN in GII was significantly lower than in GI ($p < 0.001$). Among those without XN, there was a lower average number of births ($p = 0.002$) and prenatal visits ($p = 0.005$). Women who developed gestational XN went to one third of the number of PNA visits than women without XN ($p < 0.001$).

Due to the low prevalence of XN in GII, it was not possible to perform multivariate logistic regression to evaluate the possible factors that could have influenced the associations that were found.

Discussion

The evaluation of PNA importance in reducing specific nutritional issues is not much studied in Brazil. However, these studies show important evidences which support the assumption that the nutritional care during prenatal is effective in reducing obstetric adversities concerning maternal nutritional state[14,24,25].

Based on that, it is important to consider that the results of this study collaborate with these evidences and also notes that this is the first study conducted in Brazil that aimed an evaluation of the changes of the care routines in a public maternity hospital, under an

Table II
Maternal anthropometric and prenatal assitance characteristics of groups GI (1999-2001) e GII (2007-2008). Rio de Janeiro, RJ, Brazil (n = 402)

	Study groups					
	GI (n = 225)		*GII (n = 177)*			
Variables	*n*	*%*	*n*	*%*	*Total*	*p*
NUTRITIONAL STATUS PRE-GESTATIONAL						
Underweight	41.0	19.3	8.0	4.7	49.0	< 0.001
Eutrophic	130.0	61.3	88.0	51.8	218.0	
Overweight	22.0	10.4	55.0	32.3	77.0	
Obesity	19.0	9.0	19.0	11.2	38.0	
ADEQUACY OF WEIGHT GAIN						
Insufficient	72.0	35.0	35.0	20.2	107.0	0.001
Appropriate	71.0	34.4	57.0	33.0	128.0	
Excessive	63.0	30.6	81.0	46.8	144.0	
NÚMBER OF CONSULTATIONS OF PRENATAL ASSISTANCE						
< 6	49.0	21.8	14.0	8.0	63.0	< 0.001
≥ 6	176.0	78.2	163.0	92.0	339.0	
PNA CONSULTATION						
Yes	46.0	20.4	164.0	92.6	210.0	< 0.001
No	179.0	79.6	13.0	7.4	192.0	

PNA: Prenatal nutritional assistance. *P*: significance level ($p < 0.05$).

Table III
Maternal clinical and conditions at birth characteristics of groups GI (1999-2001) e GII (2007-2008). Rio de Janeiro, RJ, Brazil (n = 402)

	Study groups					
	GI (n = 225)		GII (n = 177)			
Variables	*n*	*%*	*n*	*%*	*Total*	*p*
PREGNANCY COMPLICATIONS						
Yes	98.0	43.6	97.0	54.8	195.0	0.016
No	127.0	56.4	80.0	45.2	207.0	
GESTATIONAL ANAEMIA						
Yes	64.0	28.4	51.0	28.8	115.0	0.511
No	161.0	71.6	126.0	71.2	287.0	
ADEQUCY OF BIRTH WEIGHT						
Low birth weight	13.0	5.8	6.0	4.0	19.0	0.133
Appropriate	203.0	91.0	130.0	88.5	333.0	
Macrossomia	7.0	3.1	11.0	7.5	18.0	
GESTATIONAL AGE AT BIRTH						
Preterm	14.0	6.3	12.0	8.4	26.0	0.285
At term and post-term	209.0	93.7	131.0	91.6	340.0	
CORRELATION BW/GA TO CHILDBIRTH (PERCENTILE)						
Small for gestational age	16.0	7.1	3.0	1.7	19.0	0.001
Appropriate for gestational age and large for gestational age	209.0	92.9	174.0	98.3	383.0	

BW/GA: Birth weight to gestational age. *P*: significance level ($p < 0.05$).

important nutritional deficiency that occurs in developing countries: VAD.

The difference in prevalence of XN in GI and GII shows that VAD was a serious problem and that the significant decrease in prevalence may be associated to the changes in prenatal routines. Since 1999, World Health Organization[3] recognizes the importance of nutrition for woman's health for her to have adequate pregnancy and delivery, considering this as one of the actions aiming a maternity without risk. Once PNA was very restricted and XN was a serious problem at the first period of the study, the results have great importance.

The reduction of gestational complications such as VAD by PNA has a lot of implications, once informal assessments suggest that the cost-benefit of this strategy can be compared to or even higher than the standard practices of traditional prenatal routines in developing countries[26].

Even though this study presents some limitations such as the small sample size, the inability to run the multivariate regression (due to the low prevalence of XN in GII), and the use of a historical control group (instead a control group that not received the PNA, simultaneously with the intervention group), which could have some implications regarding baseline characteristics of the study participants, the methodological strategy was adopted to meet the ethics of research, once the positive impact of nutritional intervention during pregnancy is evident, and none of the pregnant women in the study would be without the intervention's benefit[23].

As seen, the groups were different regarding some sociodemographic characteristics and regarding the pre-gestational nutritional state, as the increase of overweighed women in GII. However, this is not an exclusive characteristic of this sample, but it concerns to all Brazilian population, according to Demographic Census 2010 (Censo Demográfico 2010)[27] and Family Budget Research (Pesquisa de Orçamentos Familiares)[28]. The women using the maternity hospital studied have similar characteristics to those pregnant women and puerperal women who use the public health service in Rio de Janeiro. Because of that, the chances of change in the population studied were minimized, reducing a possible selection bias[14-16].

Despite the distinction in the pre-gestational state among the groups, such difference brings no basis to believe that the reduction of low pre-gestational weight with an increase of pre-gestational overweight may affect the results of the study. It is reinforced if we consider some points, such as the existence of studies conducted in Brazil which indicate that the VA status has no association with a pre-gestational nutritional state[15,29]. The National Research for Demography and Health of Children and Women 2006 (Pesquisa

Table IV
Variables associated with the occurrence of night blindness in pregnant adults at maternity public hospital (1999-2001 and 2007-2008). Rio de Janeiro, RJ, Brazil

Variables	*Gestational night blindness*			*p*
	Yes (n = 43) n (%)	*No (n = 359) n (%)*	*Total*	
Categorical variables				
CONDITIONS OF SANITATION				
Adequate	38.0 (88.4)	318.0 (96.7)	356.0	0.012
Inadequate	5.0 (11.6)	11.0 (3.3)	16.0	
MARITAL STATUS				
Married/Living with partner	33.0 (12.2)	238.0 (87.8)	271.0	0.504
Living without partner	10.0 (9.7)	93.0 (90.3)	103.0	
SKIN COLOR				
White	17.0 (15.75)	91 (84.25)	108.0	0.694
Nonwhite	25.0 (14.05)	153 (85.95)	178.0	
EDUCATION				
Incomplete elementary	11.0 (9.3)	107.0 (90.7)	118.0	0.018
Complete primary and incomplete secondary	21.0 (17.3)	100.0 (82.7)	121.0	
High school graduate	11.0 (6.7)	147.0 (93.3)	158.0	
NUTRITIONAL STATUS PREGESTATIONAL				
Underweight	5.0 (10.2)	44.0 (89.8)	49.0	0.348
Eutrophic	29.0 (13.3)	189.0 (86.7)	218.0	
Overweight	6.0 (7.8)	71.0 (92.2)	77.0	
Obesity	2.0 (5.3)	36.0 (94.7)	38.0	
NUMBER OF CONSULTATIONS OF PA				
< 6	15.0 (34.9)	48.0 (13.4)	63.0	0.001
≥ 6	28.0 (65.1)	311.0 (86.6)	339.0	
HISTORY OF ABORTION				
Yes	12.0 (27.9)	22.0 (12.0)	34.0	0.019
No	31.0 (72.1)	161.0 (78.0)	192.0	
STUDY GROUPS				
GI (1999-2001)	42.0 (18.7)	183.0 (81.3)	225.0	<0.001
GII (2007-2008)	1.0 (0.6)	176.0 (99.4)	177.0	
ADEQUACY OF TOTAL GESTATIONAL WEIGHT GAIN				
Insufficient	14.0 (13.1)	93.0 (86.9)	107.0	0.592
Appropriate	14.0 (11.0)	114.0 (11.0)	128.0	
Excessive	13.0 (9.0)	131.0 (9.0)	144.0	
GESTATIONAL ANAEMIA				
Yes	10.0 (23.3)	105.0 (29.2)	115.0	0.411
No	33.0 (76.7)	254.0 (70.8)	287.0	
Numerical variables				
	μ	*SD*	*μ*	*SD*	*P*
AVERAGE OF BIRTHS	1.36	0.53	1.06	0.83	0.002
AVERAGE OF PREGNANCIES	2.56	1.69	2.22	1.36	0.053
AVERAGE OF PA CONSULTATIONS	6.95	2.77	8.15	2.60	0.005
AVERAGE OF PNA CONSULTATIONS	0.42	0.91	1.48	1.79	0.001

PA: prenatal assistance. PNA: prenatal nutritional assistance. μ: mean. SD: standard deviation. *P*: significance level ($p < 0.05$).

Nacional de Demografia e Saúde da Criança e da Mulher 2006) also reveals a very worrying scenario concerning VA's biochemical status[30]. This research showed that the women at reproductive age (15 to 49 years old) living in Southeast (where Rio de Janeiro is located) present the higher inadequacies of serum retinol in Brazil[30]. It might reflect a continuous deficiency during the pregnancy with possibility to present clinical and functional manifestations of VAD such as XN, even when health and socioeconomic scenarios is being improved in the country, but without any specific intervention to eradicate gestational VAD, as recommended by the Ministry of Health. Other important issue is that transition of the pre-gestational nutritional state may not mean the occurrence of a increase of nutritionally adequate food has happen, with micronutrients being more consumed, for example. It is a common situation of the nutritional transition process, which is normally followed by a low quality feeding[31].

Despite some limitations of the report presented by the study in order to allocate the significant reduction of XN gestational occurred mainly by changes in routine prenatal unit is possible to suggest that the implementation of nutritional care occurred during the prenatal extended to all pregnant women in the unit, may have contributed significantly to the reduction of XN pregnancy.

Corroborating such information, recent studies show that in the absence of PNA, the number of gestational issues is higher when compared to women who received this assistance, among them XN[14,15,32], which reinforces the results. Another issue that reinforces the results concerns the reduction of pregnant women which present insufficient gestational weight gain. It is another sign that restructuring the prenatal in the maternity resulted in an improvement of the health of the pregnant women at that moment.

In the context of PNA, regardless the individual education level, it is important to highlight the role that instruction in nutrition plays when fighting VAD[10]. It may bring changes in dietary patterns and reduce the number of cases in which this deficiency is found and its consequences. The higher knowledge about causes and treatment/prevention of XN plays a significant role on reducing the prevalence of this ocular symptomatology[33]. In this study, it is directly related to PNA, once the instruction in nutrition is part of the actions of the nutritionist to obtain a better nutritional state, individual or collective.

The functional indicator, gestational XN, is effective in identifying the pregnant women in nutritional risk related to VAD and it is easy to be applied, cheap and there is no need to have specific ophthalmological knowledge for its application. It is also recommended by World Health Organization[10]. The incorporation of the evaluation of gestational XN during prenatal may contribute in preventing and controlling VAD, bringing more health for the mother-child binomial and for the fact that it can be easily incorporated in health routines[4,14]. The use of the functional indicator was validated for puerperal women by Saunders et al.[8], where the authors suggest the use of standardized interview for evaluation of the nutritional state of gestational VA, identifying women with low serum levels of retinol, which interfere in maternal and fetal health.

It is important to highlight the relation between VAD and iron-deficiency anemia. The study found that 28,8% of GII developed anemia during pregnancy and that this complication was not associated to XN. The occurrence of VAD is considered a factor related to anemia[14]. A decrease was expected in the prevalence of gestational anemia with PNA, once it was founded by other authors[14]. One possible explanation may be related to the amount of VA intake to meet the nutritional needs during pregnancy be more easily achieved[34] to the recommendations of iron[35] compared to the same time biological. The inadequate use of iron supplements during pregnancy may also have influenced this result. However, this problem could be occurring in GI, not only in GII. So, the relation between VA and anemia in this study seems to be without an explanation.

Conclusion

Before the results, the study concludes that the changes in prenatal care routine, counting with the nutritional care for every pregnant woman, may have contributed for the reduction of gestational XN. We suggest the elaboration of studies testing the impact of the nutritional intervention on preventing and treating gestational XN, especially in Brazilian regions with high risk.

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Effects of quercetin on polychlorinated biphenyls-induced liver injury in rats

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Abstract

Introduction: **Polychlorinated biphenyls (PCBs), used as pesticides in agriculture, can lead to irreversible injuries in living organisms, particularly in liver. Oxidative stress has been implicated in the liver pathogenesis induced by different molecules, including PCBs. It has been demonstrated that quercetin, an antioxidant flavonoid found in the diet, exhibits a potent antioxidant effect in different liver pathologies.**

Objective: **To evaluate oxidative stress caused by PCBs in liver and the antioxidant activity of quercetin.**

Methodology: **We used male Wistar rats (n = 36), divided in 4 groups: control, quercetin (50 mg/kg/day), PCBs (0.4 ml/kg/day), and rats treated with both PCBs and quercetin. On day 25 blood was collected to assess liver integrity (enzymes AST, ALT and ALP), and liver samples to measure oxidative stress (TBARS), activity of antioxidant enzymes (SOD, CAT, GPx) and DNA damage (micronucleus assay), and histological damage.**

Results: **TBARS concentration and SOD activity were significantly higher in PCBs animals as compared to the PCB group receiving quercetin. CAT and GPx decreased in PCBs and increased when quercetin was added. The histological analysis showed damage to hepatocytes in PCBs, but quercetin was able to afford protection against such damage. The micronucleus test showed there was an increase in the production of microclenucleus compared to control, and quercetin was able to reduce this effect.**

Conclusion: **Contamination with PCBs led to increased lipid peroxidation and DNA damage, and the use of antioxidant quercetin was effective in reducing PCBs-induced liver injury.**

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EFECTO DE LA QUERCETINA SOBRE LA LESIÓN HEPÁTICA INDUCIDA POR BIFENILOS POLICLORADOS EN RATAS

Resumen

Introducción: **los bifenilospoliclonados (PCBs) son pesticidas ampliamente usados en agricultura que pueden inducir daños irreversibles particularmente en el hígado. El estrés oxidativo ha sido implicado en diversas patogénesis hepáticas, incluidas las relacionadas conPCBs. La quercetina, un flavonoide de la dieta, ha demostrado tener un potente efecto antioxidante en diversos modelos de patología hepática.**

Objetivo: **Evaluar el estrés oxidativo hepático inducido por PCBs y la actividad antioxidante de la quercetina.**

Metodología: **Se usaron ratas macho de raza Wistar (n = 36), divididas en cuatro grupos: control, quercetina (50 mg/kg/día), PCBs (0,4 ml/kg/día) y ratas tratadas tanto con PCBs como con quercetina. Transcurridos 25 días de tratamiento se recogieron muestras de sangre, para evaluar la integridad hepática (AST, ALT y ALP), y de tejido para cuantificar el estrés oxidativo (TBARS), actividad antioxidante (SOD, CAT, GPx), daño al DNA (ensayo de micronúcleos) y daño histológico.**

Resultados: **la concentración de TBARS y la actividad SOD fueron significativamente mayores en los animales que recibieron PCBs que en los que recibían quercetina. La actividad de CAT y GPx se redujo con los PCBs y se incrementó al administrar quercetina. Los análisis histológicos y de micronúcleos mostraron daño hepático y al DNA respectivamente inducido por PCBs que eran revertidos con el tratamiento con quercetina.**

Conclusion: **La contaminación con PCBs induce un incremento en la peroxidación lipídica, modificación en la actividad de enzimas antioxidantes, daño histológico y al DNA en el hígado, siendo el antioxidante quercetina es capaz de reducir dichos cambios.**

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Palabras clave: *Toxicidad hepática. Pesticidas. Antioxidantes.*

Abbreviations

PCBs: Polichlorinated Biphenyls.
OS: Oxidative Stress.
DNA: Deoryribonucleic acid.
SOD: Superoxide dismutase.
CAT: Catalase.
GPx: Gluthathione peroxidase.
GSH: Gluthathione.
Q: Quercetin.
CO: Controle.
AST: Aspartateaminotransferase.
ALT: Alanineaminotransferase.
ALP:Alkaline phosphatase.
TBARS: Thiobarbituric acid-reactive substances.
NADPH: Nicotinamide adenine dinucleotide phosphate.
HE: hematoxylin-eosin.
ROS: reactive oxygen species.
CCL_4: carbon tetrachloride.
TAA: thioacetamid.
DMN: dimetylnitrosamine.

Introduction

Exposure of living organisms to xenobiotic agents, such as polychlorinated biphenyls (PCBs), can facilitate the formation of free radicals. Environmental and nutritional factors interfere with the production of free radicals and thus may lead to a situation of oxidative stress. This has increased environmentalists and researchers' interest in controlling and/or decreasing factors that may interfere with the environment. Polychlorinated biphenyls are a class of synthetic organochlorine compounds that have been used in industry since 1930. Because of their physical properties –resistance to high temperatures and electrical currents– PCBs are used as dielectric fluids in capacitors and transformers[1]. Environmental contamination with PCBs occurs through handling accidents, vapors inhalation, inadequate storage, and leakage of residues reaching sewers, rivers, lakes and oceans[2]. Animals feeding on contaminated grass and water end up accumulating PCBs residues. These have high affinity for lipids, and because of toxicity and great persistence of these compounds in the human body, they are passed on over generations, i.e., from mother to children during gestation. PBCs and other organochlorine pesticides have cumulative effects in the organisms, particularly in humans[3].

Oxidative stress (OS) occurs in living organisms when the production of free radicals surpasses the ability of antioxidant defense systems to remove them[4]. OS is thus characterized by an increase in free radicals or a decrease in antioxidant defenses[5] eventually leading to damage to cell structures, such as lipoperoxidation and oxidation of proteins, enzymes, carbohydrates and deoxyribonucleic acid (DNA), resulting in functional changes and damage to vital functions in several tissues and organs[6].

Free radicals in the organism are quenched by the antioxidant system, which can be endogenous (enzymatic or non-enzymatic) and exogenous[7]. Enzymatic antioxidants include superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), and non-enzymatic antioxidants are glutathione (GSH), histidine peptides, iron-binding proteins (transferrin and ferritin) and $CoQH_2$. The exogenous antioxidants are, those obtained from the diet, with the organism using different substances such as tocopherol (vitamin E), β-carotene (provitamin A), ascorbic acid (vitamin C) and the phenolic compounds, such as flavonoids[6]. Quercetin (Q) is a major flavonoid whose chemical composition allows it to sequester free radicals and chelate metal ions, reported to have an excellent antioxidant response against OS[8].

This work was designed to evaluate liver injury caused by PCBs in rats by assessing lipoperoxidation, antioxidant enzyme levels and DNA damage, as well as the potential of antioxidant quercetin to protect against these deleterious PCB-induced changes.

Materials and methods

Animals

Thirty-six male Wistar rats weighing 170g were used. They were divided in four groups: control (CO), quercetin (Q), polychlorinated biphenyls (PCBs), and polychlorinated biphenyls plus quercetin (PCBs+Q). The animals were kept in the vivarium of the Lutheran University of Brazil (ULBRA) on a 12 hours light/dark cycle and room temperature at 20-25°C. Water and food were given *ad libitum*. Animals received PCBs by gavage and quercetinintraperitoneal *(i.p)*. After treatment with PCBs and Q, animals were anesthetized with xylazine hydrochloride 50 mg/kg and ketamine hydrochloride 100 mg/kg body weight *i.p* to remove the liver, spleen, and femur. Through a heparinized capillary, a blood sample was taken from the retro-orbital plexus. This was followed by euthanasia with exsanguination under anesthesia.

For oxidative stress assessment, organs and blood were collected and assayed in the Laboratory of Oxidative Stress and Antioxidants of the UniversidadeLuteranado Brasil (ULBRA), Canoas, Brazil. For toxicological analyses, collected organs were stored in appropriate glass flasks and transferred to their laboratories and frozen at -20°C until assayed. Experiments followed a protocol approved by the Animal Ethics Committee of the Lutheran University of Brazil (ULBRA) with the recommendations of the European Union regarding animal experimentation.

PCBs doses were determined by the Laboratory of Persistent Pesticides Analysis (LAPP) of the Universidade Federal de Santa Maria (UFSM) (with approval

by the Ethics Committee of UFSM). From these individual solutions we performed contamination of rats of 10 mg L^{-1} of each PCB type, as described in the Normative Instruction # 24 of August 2011 of the Brazilian Ministry of Agriculture[9], Livestock and Food Supply, Agriculture Defense Department, reference range of PCBs summation of item (i). The dose was calculated by the LAPP as 0.4 mL of the above-mentioned solution per kg/animal weight.

AST, ALT and ALP determination

A enzymatic commercial kit (Boehringer Mannheim, Germany) was used for AST and ALT determination in plasma through kinetic measurement at 567 nm. An automated enzymatic method was used to determine plasma ALP activity. We used the para-nitro-phenyl-phosphate substrate plus water, which forms para-nitrophenol, a highly intense yellow compound with maximum absorbance of 400 nm.

Histological analysis

For histological examination, liver portions were placed in buffered formalin. Later they were included in paraffin blocks, and subsequently cut into 3-µm slices using a microtome. Tissue slices were then stained with hematoxylin-eosin (HE) for standard histological examination. A Labophot Nikon binocular microscope at a magnification of 200x was used.

Liver homogenates

Livers were weighed and homogenized for 30 seconds in an Ultra-Turrax (Ika-Werk) for 40 seconds at 4°C in the presence of 1.15% KCl (9 mL per gram of tissue) and methyl phenyl sulfonyl fluoride (PMSF) at a concentration of 100 mM in isopropanol (10 µL per mL of KCl added). Then the homogenates were centrifuged for 10 minutes at 3000 rpm in a refrigerated centrifuge (Sorvall Super T21, Condensed Operating Kendro Laboratory Products, USA). The supernatant was pipetted into Eppendorf flasks, and the precipitate was discarded. The samples were stored again at - 80°C for posterior analyses[10].

Protein

We used the Bradford method to quantify protein, with bovine albumin as the standard (Sigma®). The samples were measured spectrophotometrically at 595 nm, and values expressed in mg/mL were used to calculate TBARS (thiobarbituric acid-reactive substances) values and antioxidant enzymes[11].

Lipid peroxidation

The amount of aldehydes generated by lipid peroxidation is measured by the TBARS method, which measures the amount of substances reacting with thiobarbituric acid. The samples were incubated at 100°C for 30 minutes after addition of 500 µL of 0.37% thiobarbituric acid in 15% trichloroacetic acid and centrifuged at 3,000 rpm (1612.8 × *g*) for 10 minutes at 4°C. Absorbance was determined spectrophotometrically at 535 nm[12].

Antioxidants enzyme analyses

The analysis of superoxide dismutase (SOD) in liver is based on the inhibition of the reaction of the superoxide radical with adrenaline, values expressed in U/mgprot[13]. Glutathione peroxidase (GPx) activity is based on the consumption of NADPH in the reduction of oxidized glutathione and values were expressed in nmol/mgprot. The analysis of catalase (CAT) activity is based on measuring the decrease in hydrogen peroxide, values expressed in pmol/mg prot[14].

Micronucleus assay

The micronucleus assay was performed according to the US Environmental Protection Agency Gene-Tox Program[15]. The bone marrow was extracted from the two femurs. Smears were prepared directly on slides with bone marrow and blood, two per animal and per tissue. Bone marrow smear was prepared with a drop of fetal calf serum. The slides were stained with 5% Giemsa, air dried and coded for blind analysis. To avoid false negative results and as a measure of toxicity in bone marrow, the ratio of polychromatic erythrocytes to normochromatic erythrocytes (PCE/NCE) was scored in 1,000 cells. The incidence of micronuclei (MN) was observed in 2,000 PCE for each animal (i.e. 1,000 from each of the two slides prepared from the duplicate), using bright-field optical microscopy under 200-1000× magnification. All sides were coded for blind analysis. The test groups were compared to the respective negative controls for gender, separately and in combination.

Results

Liver integrity was assessed by determining activity of aminotransferases: aspartate aminotransferase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP). The analysis of liver enzymes (table I) in plasma showed a significant increase in all enzymes in the PCBs group as compared to the other groups. AST was increased by 1,042% in PCBs as compared to CO, and was decreased by 88% in PCBS+Q as

Table I
Activity of liver enzymes aspartate aminotransferase (AST), alanine aminostrasferase (ALT) and alkaline phosphatase (ALP) in serum in the different experimental groups

Groups	*AST (U/L)*	*ALT (U/L)*	*ALP (U/L)*
CO	18.31 ± 1.8	11.55 ± 0.8	12.44 ± 1.24
Q	20.09 ± 7.4	13.03 ± 1.3	12.85 ± 1.18
PCBs	209.07 ± 9.6*	46.43 ± 3.7*	39.71 ± 2.9*
PCBs+Q	25.59 ± 4.7	31.50 ± 2.1**	14.68 ± 1.1

The results appear as means ± standard error. CO: Control. Q: Quercetin. PCBs: polychlorinated biphenyls. PXBs+Q: polychlorinated biphenyls quercetin (n = 36). *Significant difference as compared to CO, Q and PCBs+Q. $p < 0.001$. **Significant difference as compared to CO e Q. $p < 0.001$.

compared to PCBs, thus showing a potentially beneficial effect of quercetin in different tissues. ALT had a 302% increase as compared to CO and in PCBs+Q it was decreased by 32% as compared to PCBs. ALP had a 220% increase in the PCBs as compared to CO and a 63% decrease in PCBs+Q as compared to PCBs.

Figure 1 shows the results of lipoperoxidation analysis. TBARS concentration was significantly increased by 65% in PCBs as compared to CO, and significantly decreased by 35% in PCBs+Q as compared to PCBs. No significant difference was found in TBARS levels in Q as compared to CO and PCBs+Q (fig. 1A).

SOD was increased by 23% in PCBs as compared to CO, and was decreased by 18% in PCBs+Q as compared to PCBs. Groups CO, Q and PCBs+Q did not show significant differences between each other, which demonstrates antioxidant action of quercetin in PCBs+Q (fig. 1B). Evaluation of CAT and GPx showed a 30% decrease of CAT in Q as compared to CO, and a decrease of 40% in PCBs, while GPx activity decreased by 54% in PCBs in relation to its controls. However, PCBs+Q showed a significant increase of both enzymes ($p < 0.05$. Figures 1C and 1 D).

Through hematoxylin-eosin (HE) staining, we found that CO and Q (fig. 2-A and B), had normal hepatocytes, with well-preserved cytoplasm and nucleus. In PCBs (fig. 2-C), there was evidence of disorganization of hepatocyte cords, inflammatory infiltrate (arrow 1) and necrosis (arrow 2). In PCBs+Q (fig. 2-D), note the reorganization of hepatocyte cords and normal aspect of the tissue.

The micronucleusassay (MN) showed (fig. 3) that PCBs had a 300% increase in the formation of micronuclei as compared to CO, with $p < 0.001$.

Discussion

Exposure of organisms to xenobiotics can cause cumulative, often irreversible, injuries in human beings. Polychlorinated biphenyls are used as pesticides for growth of grains and pastures in the animal feeding chain, and accidental exposure to these chemicals may lead to serious, often irreversible, damage to tissues[3]. Morhet al.[1] found that the toxic effect of PCBs is related to their having great affinity for fat, thus accumulating in adipose tissue in humans and animals. The main form of contamination in humans is, therefore, ingestion of contaminated food, especially those of animal origin.

Although all cell components are susceptible to the action of reactive oxygen species (ROS), which arise from toxic agents, the plasmatic membrane is one of the most affected sites because of lipid peroxidation, which leads to changes in the structure and permeability of cell membranes. As a result, there is a loss of selectivity in ion exchange, release of the content of organelles, such as hydrolytic enzymes of lysosomes, formation of cytotoxic products, such as malondialdehyde, culminating in cell death. Lipoperoxidation can be associated with mechanisms of toxicity exacerbation by xenobiotics, with the aging process and with oncogenesis[16].

Liver enzymes (ALT, AST and ALP) are markers of hepatic injury, and an increase in their levels suggest liver dysfunction, which may be related to damage to hepatic tissue or even alterations in cell permeability. An increased level of AST, however, is the result of enzymatic degradation not only of hepatic but also of other tissues, such as musculoskeletal tissue damage resulting from heavy physical exercise, myopathy, and hypo/hyperthyroidism. On the other hand, enzyme ALT is specific to hepatic injuries, like those from steatosis and chronic viral and autoimmune hepatitis. ALP signals to cholestasis present in hepatobiliary disorders arising from intra- or extra-hepatic biliary obstruction, drug-induced cholestasis, biliary cirrhosis, primary sclerosing cholangitis and infiltrative disorders[17].

In this study, animals that received PCBs showed increased ALT, AST and ALP levels s compared to the other groups, suggesting serious injury caused by PCBs at the dose authorized by the Ministry of Agriculture of Brazil, which considers acceptable a level of 10 mg L^{-1} of each PCB type, as described in Normative Instruction # 24 of Aug 2011, determined by the Brazilian Ministry of Agriculture, Livestock and Food Supply, Agriculture Defense Department[9], reference range of PCBs summation of item (i). The dose was calculated in LAPP, with administration of 0.4 mL of the above-mentioned solution per day per kg of animal weight. Concomitant treatment with quercetin for 25 days reduced the hepatic injury caused by PCBs, as demonstrated by the reduced levels of liver enzymes ALT, AST e ALP, evidencing a protective effective by scavenging free radicals, confirmed by reduced lipoperoxidation.

In a trial with rats receiving xenobiotic TAA (liver damage inducer), De David et al.[18] observed an increase in ALT and AST, and upon treatment with

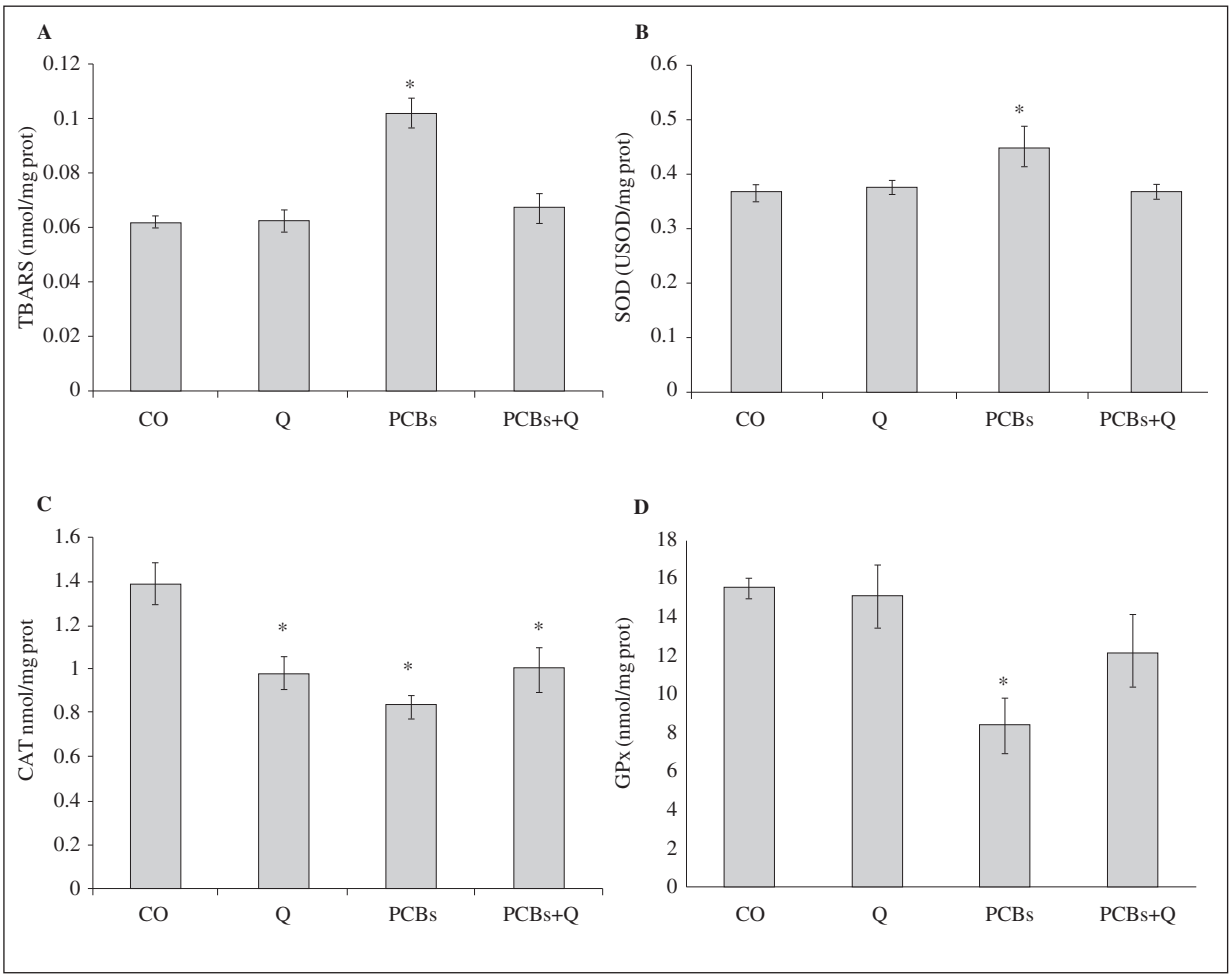


*Fig. 1.—**A:** Lipoperoxidation evaluation through the technique of thiobarbituric acid reactive substances (TBARS) (nmol/mg prot) (*Significant increase in lipoperoxidation in PCBs in relation to CO ($p < 0.001$), Q ($p < 0.001$) and PCBs+Q ($p < 0.05$). **B:** Activity of antioxidant enzyme superoxide dismutase (SOD) (USOD/mg prot), (*Significant difference of PCBs from CO, Q and PCBs+Q ($p < 0.05$). **C:** Activity of catalase (CAT), (nmol/mg prot), (*Significant difference of CO from Q, PCBs and PCBs+Q ($p < 0.05$). **D:** Activity of glutathione peroxidase (GPx) (nmol/min/mg prot), (*Significant difference of PCBs from C, Q and PCBs+Q. ($p < 0.001$). (CO = Control, Q = Quercetin, PCBs = polychlorinated biphenyls; PCBs+Q polychlorinated biphenyls plus quercetin). Data appear as means ± standard error of mean. ($n = 36$).*

antioxidant quercetin for 4 days the animals presented a decrease in the levels of these enzymes, corroborating the data presented here. In a study by Bona et al.[19], liver cirrhosis was induced with carbon tetrachloride (CCl_4), and there was a significant increase in enzymes ALT, AST and ALP and a significant reduction following quercetin treatment. These results corroborate our findings and show the protective effect of quercetin in liver tissue. Using dimetylnitrosamine (DMN), Lee et al.[20], showed that quercetin has a hepatoprotective and anti-fibrinogen action. In their study, daily oral administration of quercetin (10 mg/kg) for 4 weeks prevented loss of body and liver weight and preserved ALT and AST levels. This study is in agreement with our results, in which quercetin significantly reduced ALT and AST levels in the PCBs+Q group as compared with PCBs.

The increase in TBARS values suggests that PCBs are able to change membrane lipids, leading to impairment of normal functioning of the cell. This was also reported in other studies with rats by Kang et al.[21], in which oxidative overload increased lipoperoxidation in the toxicity induced by thioacetamide (TAA) and in many other studies in which a xenobiotic led to increased lipoperoxidation (De David et al.[18], Bona et al.[19], In this study, animals receiving antioxidant quercetin concomitantly with PCBs showed decreased lipoperoxidation as evidenced by TBARS, which confirms the findings of other authors.

Because it has several hydroxyls, quercetin is considered a polyphenol, reacting with free radicals formed in the lipid peroxidation processes to become a non-injurious radical. Besides disrupting lipid propagation, it increases GSH levels, which can convert hydrogen peroxide and organics to water and oxygen, preventing formation of hydroxyl radicals, the most injurious free radicals. Quercetin "sweeps" free radicals off and thereby reduces the oxidative and cyto-

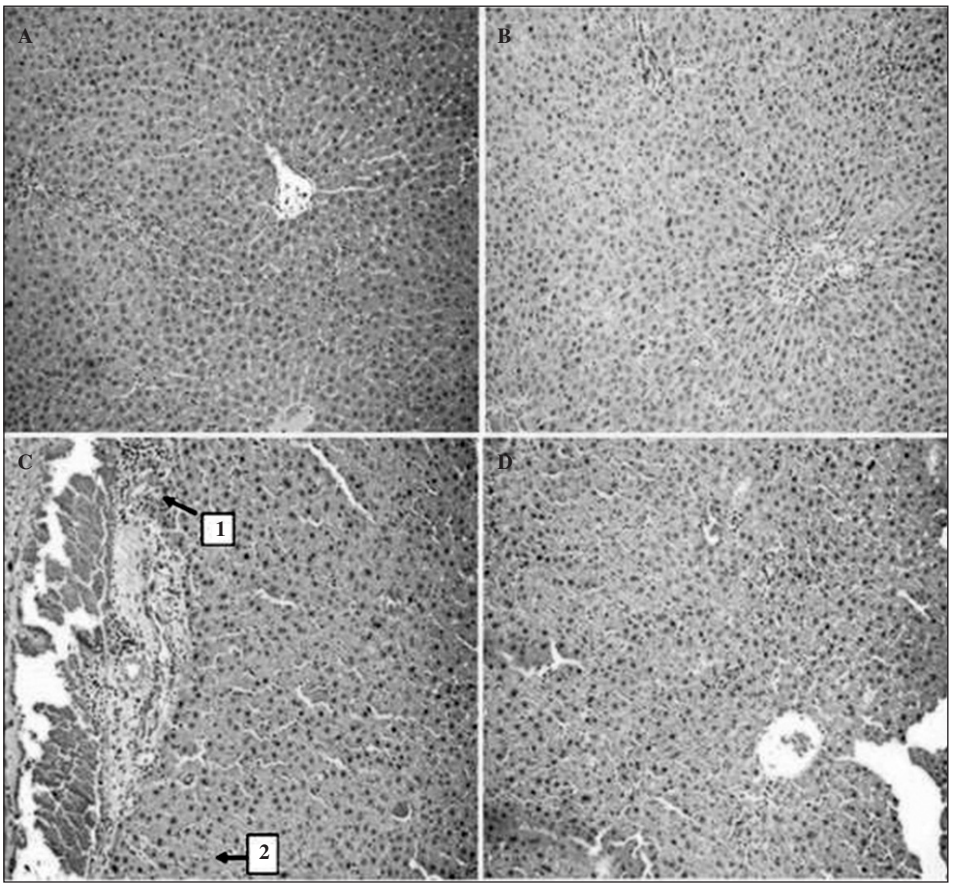


Fig. 2.—Histology of liver tissue through hematoxylin-eosin (HE) at a magnification of 200x, in the different experimental groups (A = CO (control), B = Q (Quercetin), C = PCBs and D = PCBs+Q).

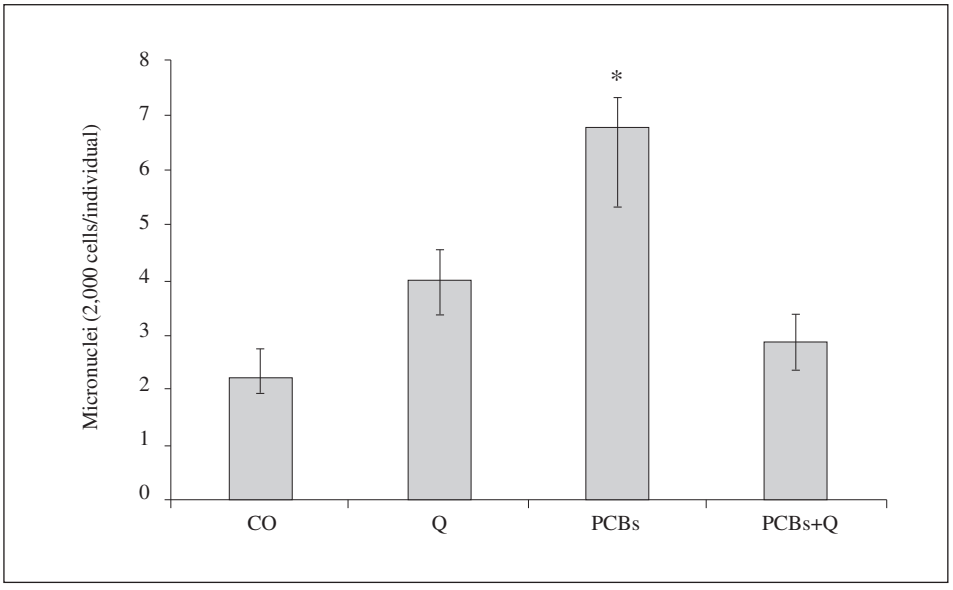


Fig.31.—Micronuclei by non-parametric Kruskal-Wallis test and Dunn Pos t- test, with $p < 0.05$. ($n = 36$). (QCT = Quercetin, PCB = polychlorinated biphenyls; PCB+Q polychlorinated biphenyls plus quercetin). Significant difference of PCBs as compared to CO, $p < 0.001$.*

toxic effect of low density proteins. So, quercetin can inhibit the process of formation of free radicals in three different stages: initiation (by interacting with superoxide anions), formation of hydroxyl radicals (by chelating iron ions) and lipoperoxidation (by reacting with peroxide radicals of lipids)[22]. SOD increase may be a result from dismutation of superoxide anion due to OS increase[23,24]. Here we found a significant increase in SOD activity in the PCBs group, which demonstrates activation of a compensatory mechanism through the xenobiotic on cells, in an attempt to decrease the effects induced by the increase in superoxide anion caused by the stress-inducing xenobiotic. The extent of this effect depends on the "aggressiveness" and dose of

the stressor[25]. Similar results were reported in another study in which hepatic toxicity was induced by organophosphorateClorpirifós, an insecticide used in agricultural crops[26]. Quercetin appears to be protective, for SOD was decreased in the PCBs+Q, as reported by De David et al.[18] using TAA and quercetin.

CAT and GPX were reduced in the PCBs groups as compared to the control group, while treatment with quercetin increased both enzymatic activities ($p < 0.05$). Glutathione peroxidase is mainly responsible for degrading organic peroxides resulting from lipoperoxidation[27]. The use of quercetin was able to significantly increase the activity of this enzyme, suggesting protection through glutathione, thus affording potential protection to the liver in these animals (PCBs+Q).

In the histological analysis of the hepatic tissue using HE, the CO and Q groups showed liver cells organized in hepatocyte chords with normal aspect, clear nuclei and no inflammatory infiltrates. In PCB-exposed animals, however, significant changes were observed: disarrayed hepatocyte chords, presence of inflammatory infiltrates and hepatic necrosis. These findings are consistent with several studies performed by different authors, such as[28,29], using other xenobiotics. Quercetin seems to prevent significantly the toxicity of PCBs, preserving the hepatic tissue, with a reorganization of the hepatic parenchyma, accompanied by the return of antioxidant enzyme activity to those of the control group, and a reduction of TBARS levels. Similar results were obtained by Tieppo[30], in a animal model with common biliary duct ligation to induce secondary biliary cirrhosis, regenerative nodules, fibrosis and necrotic foci and subsequently treat with antioxidant quercetin, which promoted reduction of hepatic alterations. Other authors also corroborate our results, as well as that quercetin and other antioxidants such as N-acetylcysteine and rutin promoted reduction of hepatic fibrosis[4,31]. Caffeine and catechins contained in green tea may have a thermogenic effect favoring weight and body fat loss. The use of green tea (catechins and caffeine) showed contradictory results in a meta-analysis for loss and weight maintenance and reduction of fat mass[32].

Damage to DNA can result from endogenous processes such as errors in DNA duplication, chemical instability in certain DNA bases, or from interactions with exogenous agents such as ionizing and ultraviolet radiation, chemical and biological agents, such as viruses[33]. In our study, the evaluation of micronucleus suggests a genotoxic effect of polychlorinated biphenyls. In evaluating damage to DNA through the micronucleus assay, we found an increase in the formation of MN in the group receiving PCBs, and a decrease in the group treated with quercetin (PCBs+Q), suggesting protection of flavonoid quercetin. Administered PCBs led to the formation of chromosomal fragments which may be due to a clastogenic effect (acentric fragments) or to a aneugenic effect (whole chromosomes), which determines that these chromosomes will not complete the anaphasic migration of cell division, which characterizes the genotoxic potential of PCBs. It is recognized that 35% of malignant tumors are associated with dietary factors, and would be preventable through proper diet and nutrition. Some authors highlight the important role of dietary patterns (meats, fats) in the etiology of several cancers[34].

Quercetin administration caused a 58% decrease of micronuclei as compared to the PCBs group, which demonstrates greater stability to DNA molecules, preventing the formation of micronuclei, even upon exposure to PCBs, acting as a significant antioxidant in this experimental model. PCBs seem to pose risks to both the environment and humans through contaminated food. Studies by Larramendyet al.[35]on pesticide effects using vertebrate cells in vitroand in vivoalso showed induced DNA damage through micronucleus assay, suggesting a genotoxic and/or cytotoxic effect due to their formulation with active ingredients of agrochemicals.

The flavonoid quercetin is able to react with reactive oxygen species, decreasing oxidative damage to DNA, with less DNA oxidation, leading to prevention of tumorogenic processes[36]. In recent studies with Caco-2 cells (colorectal adenocarcinoma), low doses of quercetinled to reduction of DNA breaks. These authors also observed that low concentrations of quercetin induced expression of 8-Oxoguanine DNA glycosylase (hOGG1). HOGG1 is an enzyme involved in DNA repair, and low concentrations of the flavonoid prevent damage and increases DNA repair[37].

Upon these considerations, we suggest that damage to animal liver induced by PBCs is associated with OS by increasing free radicals or reducing endogenous antioxidant defenses. Use of quercetin at the dose here tested can be effective in minimizing oxidative damage and protecting DNA.

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Original / *Valoración nutricional*

Introducción de un método mixto de cribado nutricional (CIPA) en un hospital de tercer nivel

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Resumen

Introducción: **La desnutrición en el paciente hospitalizado es muy prevalente, por lo que es importante incorporar métodos de depistaje. Se ha desarrollado en nuestro centro un método mixto de cribado nutricional (CIPA), que incluye cuatro parámetros: a) control de ingestas 72 h; b) IMC; c) proteínas; y d) albúmina.**

Objetivos: **1) conocer la prevalencia de desnutrición en pacientes hospitalizados en el servicio de Medicina Interna de nuestro centro; 2) analizar variables asociadas a mayor prevalencia de desnutrición; 3) evaluar su efecto pronóstico clínico.**

Material y métodos: **Se revisaron retrospectivamente los resultados de los test de cribado nutricional efectuados a 305 pacientes ingresados en el servicio de Medicina Interna en el periodo noviembre/2012-octubre/2013. Se analizó la prevalencia de desnutrición hospitalaria y la asociación del resultado positivo en el cribado (al menos un ítem positivo) con las siguientes variables: IMC, edad, sexo, patología subyacente, estancia, reingreso precoz (< de 1 mes) y mortalidad.**

Resultados: **El test fue positivo en un 23% de los pacientes. Los pacientes con cribado positivo presentaban un IMC inferior (24,9 ± 7,2 vs 27,8 ± 6,4 kg/m; p = 0,002). La patología neoplásica e infecciosa se asociaron a mayor positividad (35,3 y 28,9%, respectivamente; p=0,006). El sexo y la edad no se asociaron con el resultado del test de cribado. Los pacientes con cribado positivo presentaban mayor estancia media (26,7 ± 25 *vs* 19,4 ± 16,5; p = 0,005), tasa de reingresos precoces (18,6 *vs* 6,8%; p = 0,003) y mortalidad (30 *vs* 10,3%; p < 0,001).**

Conclusiones: **El test de cribado CIPA es capaz de detectar al paciente malnutrido y predecirle un peor pronóstico clínico (mortalidad, estancia media y reingreso precoz).**

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Palabras clave: *Valoración nutricional. Desnutrición. Hospitalización. Soporte nutricional. Pronóstico.*

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INTRODUCING A MIXED NUTRITIONAL SCREENING TOOL (CIPA) IN A TERTIARY HOSPITAL

Abstract

Introduction: **Malnourishment in hospitalized patients is very prevalent and therefore it is important to implement screening methods. A mixed nutritional screening method (CIPA) has been developed at our center; this method includes four parameters: a) control of intakes for 72 h; b) BMI; c) proteins; and d) albumin.**

Objectives: **1) To know the prevalence of malnourishment at the Internal Medicine Department of our Center; 2) To analyze the variables associated to higher prevalence of malnourishment. Materials and method: The results of the nutritional screening tests carried out in 305 patients admitted to the Internal Medicine Department in the period of November of 2012-October of 2013 were retrospectively reviewed. The prevalence of hospital malnourishment was analyzed, as well as the association of a positive screening test (at least one positive item) with the following variables: BMI, age, gender, underlying disease, hospital staying, early re-admittance (< 1 month) and hospital mortality.**

Results: **The test yielded a positive result in 23% of the patients. Patients with a positive screening test had lower BMI (24.9 ± 7.2 *vs.* 27.8 ± 6.4 kg/m; p = 0.002). Neoplastic and infectious pathologies were associated with greater positivity (35.3 and 28.9%, respectively; p = 0.006). Gender and age were not associated with a positive screening test. Patients with a positive screening test had longer mean hospital staying (26.7 ± 25 *vs.* 19.4 ± 16.5; p = 0.005), higher early re-admittance rates (18.6 *vs.* 6.8%; p = 0.003) and higher mortality (30 *vs.* 10.3%; p < 0.001).**

Conclusions: **The CIPA screening test can detect malnourished patients and predict worse clinical prognosis (mortality, mean hospital staying and early re-admittance).**

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Key words: *Nutritional assessment. Malnourishment. Hospitalization. Nutritional support. Prognosis.*

Introducción

La desnutrición hospitalaria (DH) es un problema frecuente en los pacientes que ingresan en un hospital, de forma que oscila entre el 10% y el 85% en función del tipo de pacientes analizados (ancianos, niños, pacientes médicos, quirúrgicos, oncológicos, etc.), de la categoría de hospital donde son admitidos y de los marcadores de valoración nutricional empleados para su evaluación[1-7].

Clínicamente, puede contribuir a incrementar el número y la gravedad de las complicaciones de la propia enfermedad, a debilitar la capacidad de respuesta al tratamiento, a disminuir el grado de respuesta inmune y a incrementar la morbi-mortalidad[8]. Desde el punto de vista económico, aumenta el coste asociado a la prolongación de la estancia hospitalaria y al tratamiento adicional de las complicaciones[9-12]. A pesar de las enormes dificultades metodológicas que suponen los estudios de intervención nutricional, hoy en día tenemos evidencia científica de que la intervención nutricional puede mejorar la evolución clínica del paciente desnutrido y disminuir los gastos asociados a la enfermedad[13-16]. Por ello, resulta de vital importancia el diagnóstico precoz de la misma, no sólo con la finalidad de evitar un aumento en la morbi/mortalidad del paciente ingresado, sino también para poder afrontar un gasto sanitario óptimo y sostenible.

Los métodos de cribado deben ser válidos, fiables, reproducibles, prácticos (fáciles de aplicar, bien aceptados y económicos) y conectados con protocolos específicos de actuación[17]. Existen métodos de cribado nutricional clínicos, automatizados y mixtos. Los métodos de cribado clínicos suelen incluir datos subjetivos y objetivos (peso, talla, cambios en el peso, cambios en la ingesta, comorbilidades,…), mientras que los métodos automatizados se basan fundamentalmente en datos analíticos.

Son muchos los métodos de cribado validados en población hospitalizada, siendo los más ampliamente extendidos el Malnutrition Universal Screening Tool (MUST) [18], el Nutrition Risk Screening (NRS 2002)[19], el Mini-Nutritional Assessment Short Form (MNA SF)[20] o la Valoración Global Subjetiva (VGS)[21,22]. Sin embargo, ninguno de estos métodos es del todo óptimo, por lo que no existe un "gold standard". Desgraciadamente, su utilización en la práctica clínica diaria es baja.

El MUST es el test de cribado que recomienda la ESPEN (European Society for Clinical Nutrition and Metabolism) para pacientes de la comunidad. Tiene escasa variación interobservador y no es complicado de realizar, pero a nivel hospitalario sólo predice positivamente la estancia media, mortalidad en ancianos, el destino al alta en los pacientes ortopédicos y el gasto por malnutrición, por lo que no es ideal para aplicar en un hospital de tercer nivel con pacientes de diversa índole[23].

El NRS 2002, que es el que recomienda la ESPEN para el paciente hospitalizado, es el que mejor valor predictivo aporta, teniendo además buen soporte científico. Tiene mayor variabilidad interobservador que el MUST, respondiendo a que contiene algunos ítems con mayor componente subjetivo tanto para el paciente como para la persona ejecutora del cribado, y como inconveniente, precisa de colaboración por parte del paciente y/o cuidador[19,23].

El MNA está diseñado para pacientes ancianos, por lo que no sirve para realizar un cribado universal, y la VGS precisa de personal cualificado para poder realizar el examen físico, complicando su utilización en hospitales de muchas camas. Además, todos estos cribados incorporan un parámetro de peso perdido (en forma de kg o porcentaje de peso perdido), que siendo un dato interesante de obtener, no deja de ser subjetivo en la mayoría de las veces por parte del paciente, como observamos en la práctica clínica, y también se ha publicado en algún estudio[24].

Como parte de un proyecto de mejora continuada de calidad de la Unidad de Nutrición y Dietética del Hospital Universitario Nuestra Señora de Candelaria (HUNSC), se diseñó inicialmente un impreso de solicitud de suplemementos orales para el paciente hospitalizado que incluía parámetros nutricionales, y que posteriormente han sido destinados a la confección de un test de cribado nutricional mixto denominado CIPA (incluye Control de ingestas, IMC, Proteínas y Albúmina).

Con la intención de estudiar la validez del mismo, se ha empleado la planta de Medicina Interna como "planta piloto" al ser la especialidad que acapara una mayor diversidad de patologías y características basales de los pacientes, a fin de realizar diferentes trabajos, y si se confirma la eficacia del método de cribado CIPA, extenderlo al resto del complejo hospitalario.

En este artículo presentamos el primero de ellos, en los que estudiamos la prevalencia o riesgo de malnutrición mediante el CIPA y su relación con características basales de los pacientes. Así mismo, se estudia la relación de la positividad del cribado con variables clínicas como la mortalidad, estancia media y tasa de reingreso precoz.

Material y métodos

Se ha efectuado un estudio retrospectivo de los pacientes ingresados en el servicio de Medicina Interna del HUNSC en el periodo noviembre/2012-octubre/2013, a los que se efectúo el test de cribado nutricional CIPA. Se incluyó en el estudio a todo paciente que fuera ingresado en la planta primera del HUNSC, en el área de Medicina Interna, en dicho periodo. A su llegada, eran pesados y tallados con la finalidad de conocer dichos datos antropométricos, previamente a la ejecución del test de cribado. El único criterio de exclusión fue que el paciente ingresado tuviese mal pronóstico vital a corto plazo.

El personal de enfermería y auxiliar de la planta de Medicina Interna se encarga de rellenar una plantilla con el control de ingestas e informatizarlo junto con los valo-

res analíticos (albúmina y proteínas totales). Estos datos son enviados a través de la intranet del HUNSC a la Unidad de Nutrición y Dietética. Se consideró que el resultado del CIPA era positivo cuando se cumplía al menos uno de los siguientes requisitos: disminución de la ingesta < 50%; IMC < 18,5 kg/m^2; proteínas totales < 5 g/dl; albúmina sérica < 3 g/dl. En caso de ser positivo, se aportaba soporte nutricional específico y adecuado para el paciente. Aunque el CIPA se realiza cíclicamente cada 10 días, en este trabajo sólo se muestran los resultados del screening en el momento del ingreso, debido al escaso número de datos obtenidos en la reevaluación posterior.

Se recogieron las siguientes variables: edad, sexo, diagnóstico principal, fecha de ingreso, peso, IMC, estancia, reingreso precoz (1 < mes) y mortalidad, así como los resultados de las cuatro variables dicotómicas incluidas en el CIPA y el resultado final del mismo (positivo/negativo). La edad se consideró como variable continua y como variable categórica de 2 categorías (< 70 y > 70 años) y de 4 categorías (< 60, 60-70, 70-80 y > 80 años). A los pacientes se les dividió según la patología principal que justificara el ingreso en cuatro grupos: infecciosa, neoplásica, cardiovascular y otras.

Se efectúo un análisis descriptivo de las variables anteriores. Los resultados para las variables de escala se expresan como media ± desviación estándar, y para las categóricas como las frecuencias absolutas y relativas (%). Posteriormente, se estudió la asociación del resultado positivo en el test de cribado con las siguientes variables: IMC, edad, sexo, patología subyacente, estancia, reingreso precoz (< 1 mes) y mortalidad (se utilizó el test T-Student para muestras independientes para las variables cuantitativas y el chi-cuadrado para las variables cualitativas). El análisis estadístico se efectúo utilizando el programa SPSS 19.0 (versión en español).

Tabla I
Características basales de la muestra y resultados del test de cribado

	Media	*DE*
Edad	64	15,87
Peso (kg)	73,20	18,96
Talla	1,63	0,13
IMC	27,12	6,71
	n	*%*
Sexo		
– Masculino	152	49,8
– Femenino	153	50,2
Patología		
– Infecciosa	135	44,3
– Cardiovascular	43	14,1
– Neoplásica	34	11,1
– Otras	93	30,5
Test de cribado		
– Positivo	70	23
– Negativo	235	77
Albúmina		
– < 3 g/dl	5	26,3
– > 3 g/dl	281	92,1
Proteínas		
– < 5 g/dl	23	7,5
– > 5 g/dl	281	92,1
Disminución de ingesta		
– Si	40	13,1
– No	265	86,9
IMC < 18,5 kg/m^2		
– Si	11	3,60
– No	294	96,39

Resultados

Se recogieron los datos de tests de cribado a su llegada al Servicio de Medicina Interna de 305 pacientes. En la tabla I se recogen las características basales de la muestra y los resultados del test de cribado. La edad media era de 64 ± 15,86 años y el IMC de 27,12 ± 6,71 kg/m^2. La distribución por sexos fue similar, teniendo en cuenta que 152 pacientes (49,8%) eran varones y 153 (50,2%), mujeres. Las patologías más prevalentes que justificaron el ingreso fueron las enfermedades infecciosas (44,3%), seguidas de las de etiología cardiovascular (14,1%) y de las neoplasias (11,1%).

El cribado fue positivo en el 23% (70 pacientes), en tanto que fue negativo en el 77% (235 pacientes). En cuanto a los resultados por sexo, el test resultó positivo en el 24,34% de los varones y en el 20,91% de las mujeres incluidas en el estudio. El sexo y la edad no se asociaron con el resultado del test de cribado. Dentro de los diferentes ítems del cribado, el que fue positivo con mayor frecuencia fue la hipoalbuminemia (26,3%), seguido de la disminución de ingestas (13,1%), de la hipoproteinemia (7,5%) y del IMC (3,6%). Es importante señalar que sólo se efectúo la determinación de albúmina en el 6,22% de los pacientes, en tanto que las proteínas totales se determinaron en el 99,6% y el control de ingestas y el IMC se analizó en todos los pacientes (con peso estimado en los pacientes que no toleraban la bipedestación).

Los pacientes con cribado positivo presentaban un IMC inferior (24,9 ± 7,2 *vs* 27,8 ± 6,4 kg/m^2; p = 0,002). La patología neoplásica e infecciosa se asociaron a mayor positividad en el cribado (35,3% y 28,9% respectivamente; p = 0,006).

En cuanto a las variables clínicas, los pacientes con cribado positivo presentaron mayor estancia media (26,7 ± 25 *vs* 19,4 ± 16,5; p = 0,005), una tasa de reingreso precoz más elevada (18,6 *vs* 6,8%, p = 0,003) y mayor mortalidad (30 *vs* 10,3%, p < 0,001) (fig. 1).

Discusión

En el diseño del método de cribado nutricional CIPA, la principal premisa fue la practicidad y fácil apli-

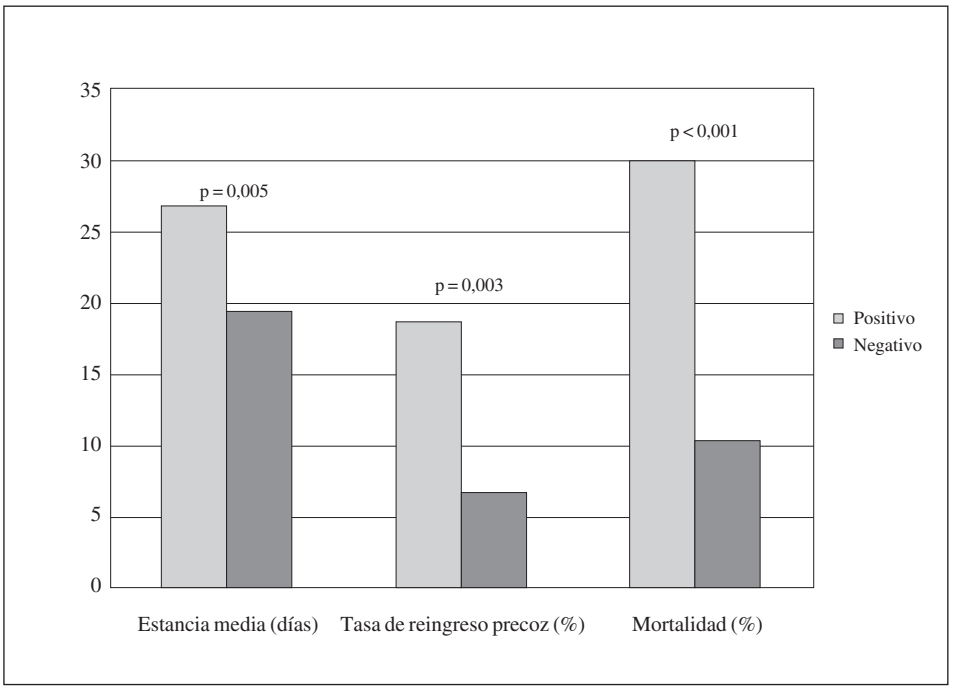


Fig. 1.—Evolución de variables clínicas en función de la positividad de CIPA.

cación del método con el fin de garantizar que todo paciente hospitalizado en nuestro centro se cribara nutricionalmente. Para ello se han incluido parámetros ya utilizados en el día a día por el personal del HUNSC, por lo que no supone una excesiva carga de trabajo para su ejecución, no precisa del entrenamiento de personal específico, ni tampoco colaboración por parte del paciente. No incluye parámetros subjetivos, y se han cubierto los parámetros que consideramos esenciales, como son los proteicos, calóricos, y las ingestas.

Los datos observados mediante el test de cribado CIPA en una planta de Medicina Interna, confirman la elevada prevalencia de DH o riesgo de la misma en estos pacientes (23%), siendo el resultado igual al encontrado en el estudio multicéntrico nacional PREDyCES[7], que ha sido el principal trabajo de DH efectuado hasta la fecha en nuestro país, con más de 1.700 pacientes. Este dato orienta a priori la buena capacidad discriminativa de nuestro test para detectar desnutrición o riesgo de padecerla en los pacientes ingresados.

Aunque todavía no se ha comparado con otros métodos de cribado nutricional de forma prospectiva, el objetivo principal de un cribado nutricional es detectar al paciente malnutrido y predecir si dicho paciente va a tener una peor evolución clínica debido a factores nutricionales, motivo por el cual analizamos la asociación del CIPA con tres variables que consideramos claves: mortalidad, estancia media y tasa de reingreso precoz (éstas dos últimas además con importante impacto económico).

En nuestra muestra de 305 pacientes no quirúrgicos ni críticos, de patologías y características basales de diferente índole, los que dieron positivo al test tuvieron tres veces más de riesgo de mortalidad y de reingreso precoz, y una semana más de estancia hospitalaria. Muchos estudios están centrados en pacientes ancianos, o en poblaciones muy concretas, y salvo con el NRS 2002, es dificil encontrar trabajos que utilicen métodos de cribado nutricional en pacientes hospitalarios de estas características y que obtengan unos resultados de similar impacto[19,25,26].

Dos publicaciones recientes avalan a otras previas que establecían que el uso de suplementos nutricionales orales podía mejorar la evolución clínica de los pacientes hospitalarios, así como el coste sanitario. El primero de ellos es un estudio retrospectivo de gran dimensión con un número muestral mayor de un millón de pacientes, de casos apareados con pacientes de similares características que consumen o no suplementos orales durante su estancia hospitalaria. En él se observó un beneficio en el paciente que usaba los suplementos orales, obteniendo menos estancia media, riesgo de reingreso precoz y menor coste hospitalario[16]. El segundo realiza una revisión sistemática sobre el impacto del uso de suplementos orales sobre el reingreso hospitalario, observándose una reducción significativa de la misma, sobre todo en pacientes ancianos, con importantes implicaciones en el plano económico[27].

Por tanto, a la vista estos resultados, es oportuno considerar que ya que todos nuestros pacientes con cribado positivo fueron tratados nutricionalmente mediante ajuste de dieta y suplementos orales, las diferencias encontradas en nuestro trabajo en cuanto a las variables clínicas a estudio habrían sido más amplias todavía que las ya mostradas de no haber recibido dicho tratamiento.

Al igual que en el estudio PREDYCES en el que se utilizó el NRS 2002, en nuestro trabajo la patología neoplásica es la que más se asocia a DH, e igualmente, un

IMC más bajo se relaciona con mayor prevalencia de malnutrición. A diferencia del mismo, en nuestra muestra no se observó relación entre la positividad del CIPA respecto a la edad o sexo del paciente.

La albúmina fue el parámetro con más sensibilidad para detectar positividad del CIPA (26,3% de las solicitadas), pero fue recogida en menos de un 10% de los pacientes debido a que tienen que pedirla de manera específica en petición no urgente por sus médicos responsables (no así las proteínas totales), y éstos no fueron supervisados estrechamente para solicitar su determinación. Al ser el parámetro más sensible, si se hubiera analizado en la totalidad de los pacientes, el resultado global de la malnutrición o riesgo de la misma mediante el CIPA probablemente hubiera sido mayor. Por el contrario, sólo un 3,6% de los pacientes analizados presentaban un IMC < 18,5 kg/m^2, por lo que fue el parámetro que menos influyó en los resultados.

Consideramos que la principal fortaleza de nuestro método estriba en incluir una variable clínica (control de ingestas de tres días), dado que es sencilla de recoger, está ya implantada en nuestro hospital, y su valor no sólo radica en ser un marcador de riesgo nutricional, sino que es una herramienta eficaz para poder efectuar modificaciones dietéticas y establecer un plan de soporte nutricional adecuado a los paciente en que se objetive DH. De hecho, el método CIPA detecta mayor riesgo de DH que el CONUT, principalmente debido a que éste último no recoge datos sobre las ingestas del paciente, aunque también en parte, a que no contempla parámetros antropométricos[28].

En conclusión, nuestros resultados confirman la elevada prevalencia de DH o riesgo de padecerla, y muestran que el CIPA predice en función de parámetros nutricionales al paciente que ingresa con tres veces más de riesgo de mortalidad y tasas de reingreso precoz, y una estancia media de una semana más. Esto permite actuar sobre los pacientes de riesgo para mejorar su estado nutricional, y sobre todo, el pronóstico clínico del paciente.

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Nutritional status, lipid profile and HOMA-IR in post-liver transplant patients

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Abstract

Introduction: **A high prevalence of overweight, obesity, diabetes and dyslipidemia has been reported following liver transplantation (LT). Although these conditions are known to induce an increased risk for cardiovascular events, which are among the major causes of death in post-LT patients, much debate remains in the literature regarding the applicability of different nutritional assessments methods to this population.**

Objective: **To assess the nutritional status, lipid profile, homeostatic model assessment of insulin resistance (HOMA-IR) and dietary intake adequacy in the post-LT period.**

Methods: **Cross-sectional study of patients after a maximum of 2 years post-LT, involving the assessment of body mass index (BMI), percent weight loss, arm (AC) and arm muscle circumference (AMC), triceps skinfold (TSF), neck (NC) and waist (WC) circumference, lipid profile, HOMA-IR and percent adequacy of dietary intake.**

Results: **In the group of 36 patients, 61.1% were male, mean age 53.2 years (± 10.6). Severe weight loss was noted in 66.7% of patients. Most individuals were eutrophic according to BMI, AC and AMC, while TSF showed malnutrition, NC demonstrated overweight and WC showed metabolic risk. Dyslipidemia was diagnosed in 87.5% of patients, and insulin resistance in 57% of the patients. Most patients had adequate dietary intake, although the time since transplant was positively correlated with AC (r = 0.353; p = 0.035) and negatively correlated with vitamin A intake (r = - 0.382; p = 0.022), with the caloric adequacy (r = -0.338; p = 0.044) and vitamin A adequacy (r = -0.382; p = 0.021).**

Conclusion: **Although anthropometry provided somewhat variable nutritional diagnoses, when combined with biochemical tests, findings showed the prevalence of cardiovascular risk. As such, patients should be provided with transdisciplinary assistance, and strategies should be developed so as to reduce the risk factors recorded in this population.**

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Key words: *Liver transplantation. Nutritional status. Dyslipemia.*

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ESTADO NUTRICIONAL, PERFIL LIPÍDICO Y HOMA-IR EN EL POSTRANSPLANTE HEPÁTICO

Resumen

Introducción: **En el postransplante hepático (TH) hay un aumento de prevalencia de sobrepeso, obesidad, diabetes y dislipidemia. Esos factores están asociados al riesgo de enfermedades cardiovasculares, una de las principales causas de mortalidad en el post-TH. Sin embargo, no se han establecidos cuáles son los mejores métodos de evaluación nutricional de esta población.**

Objetivo: **Evaluar el estado nutricional, perfil lipídico, homeostatic model assessment of insulin resistance (HOMA-IR) y adecuación de ingestión dietética en el post-TH.**

Métodos: **Estudio transversal, incluidos pacientes hasta con 2 años de TH evaluándose por el índice de masa corporal (IMC), porcentaje de pérdida de peso, circunferencia del brazo (CB) y muscular del brazo (CMB), pliegue tricipital (PT), circunferencia del cuello (CP) y de la cintura (CC), perfil lipídico, HOMA-IR y porcentaje de adecuación de ingestión dietética.**

Resultados: **De los 36 pacientes, 61,1% eran de sexo masculino, con un promedio de edad de 53,2 años (± 10,6). En 66,7% de los evaluados, hubo pérdida severa de peso. Hubo predominio de eutrofia por el IMC, CB y CMB, desnutrición por el PT, sobrepeso por la CP y CC muy alta. Se constató dislipidemia en el 87,5% de los pacientes y resistencia a la insulina en el 57%. La mayoría presentó adecuación de la ingestión dietética, pero el tiempo de TH se correlacionó positivamente a la CB (r = 0,353; p = 0,035) y negativamente a la ingestión de vitamina A (r = -0,382; p = 0,022), adecuación calórica (r = -0,338; p = 0,044) y de vitamina A (r = -0,382; p = 0,021).**

Conclusión: **Aunque la antropometría indicó variabilidad en el diagnóstico nutricional, cuando se combina con la evaluación bioquímica, los resultados mostraron la prevalencia de riesgo cardiovascular. Los pacientes deben recibir acompañamiento transdisciplinario, y se deben desarrollar estrategias para reducir los factores de riesgo de la población.**

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Palabras clave: *Trasplante hepático. Estado nutricional. Dislipidemia.*

Abbreviations

AC: Arm circumference.
AMC: Arm muscle circumference.
BMI: Body mass index.
DM: Diabetes mellitus.
EAR: Estimated average requirements for groups.
HDL:High-density lipoprotein.
HOMA-IR: Homeostatic model assessment of insulin resistance.
LDL: Low-density lipoprotein.
LT: Liver transplantation.
MELD-Na: MELD-sodium.
NC: Neck circumference.
TSF: Tricipital skinfold thickness.
WC: Waist circumference.

Introduction

Metabolic complications have been increasingly reported following liver transplantation (LT).[1] LT is the preferred treatment for patients with uncompensated cirrhosis, hepatocarcinoma and acute hepatic insufficiency.[2] Malnutrition is a common finding among patients scheduled for LT, as it is a frequent consequence of cirrhosis, and has been shown to be associated with higher morbidity and mortality rates in these individuals. Some studies also suggest that malnutrition may persist following LT.[3] On the other hand, recent years have also seen an increase in the prevalence of overweight and obesity in post-LT patients, which is often mistakenly interpreted to be a sign of nutritional recovery.[4,5]

Although survival rates among LT patients have increased[6], studies have also found the occurrence of insulin resistance[7] and an increase in the prevalence of dyslipidemia, hypertension, and diabetes mellitus (DM) among these individuals. Together with excess weight, these conditions contribute to the occurrence of metabolic syndrome and to the risk of cardiovascular diseases,[8] which is one of the main causes of death following LT[2].

Although there are a number of ways to assess patients' nutritional status, several methodological difficulties have been found with regard to these processes.[9] Furthermore, despite the high frequency of metabolic complications observed in adult LT recipients, few studies have involved the nutritional assessment of these patients.[10] Therefore, the aim of the present study was to investigate the nutritional status of post-LT patients through anthropometric assessment, lipid profile, homeostatic model assessment of insulin resistance (HOMA-IR) and dietary adequacy.

Methods

Sample

A cross-sectional study was conducted using the following inclusion criteria: age equal to or greater than 19 years, having undergone a LT within 1 to 24 months prior to study enrollment, being in adequate conditions for assessment, and agreeing to participate by providing written informed consent. Retransplant patients, pregnant women, and individuals with physical conditions which interfered with anthropometric measurements were excluded from the study. The sample was divided according to time since each patient's LT (l|- 12 months and 12|- 24 months). Data were collected at the Gastroenterology Outpatient Clinic of the Hospital de Clinicas de Porto Alegre between November 2012 and March 2013. The present study was approved by the research ethics committee of the institution in which it was conducted (protocol number 120373) and all patients signed a written informed consent form.

The following demographic and clinical variables were collected from patient records: sex, age, time since LT, etiology of liver disease and reason for LT (as confirmed by biochemical, clinical and anatomopathological tests), MELD-sodium score (MELD-Na), time on the waiting list, duration of hospitalization, medication use and comorbidities.

Anthropometric assessment

All anthropometric assessments were conducted by the same examiner, and involved the measurement of the following variables: weight, height, body mass index (BMI), percentage of weight loss, arm circumference (AC), triceps skinfold thickness (TSF), arm muscle circumference (AMC), waist circumference (WC) and neck circumference (NC). Weight was measured using a digital scale (Filizola®, São Paulo, Brazil). While being weighed, all patients wore light clothing, were barefoot, and had no objects in their pockets. When edema was present, weight was corrected for the estimated weight of the edema fluid (ankle edema: 1 kg).[11] Height was assessed using a vertical stadiometer (Balmak®, São Paulo, Brazil). During height measurements, patients were barefoot, wore no accessories on their heads, and had their heads positioned in the Frankfurt plane. Patients were classified into adult (malnutrition: < 18.49 kg/m^2; eutrophy 18.5 to 24.9 kg/m^2; overweight: 25 to 29.9 kg/m^2; obesity: > 30 kg/m^2)[12] or elderly (malnutrition: < 22 kg/m^2; eutrophy: 22 to 27 kg/m^2; overweight: > 27 kg/m^2)[13] BMI categories, as applicable. The percentage of weight loss was calculated based on each patient's usual weight, and classified according to the Blackburn model (significant weight loss: 1 to 2% in 1 week, 5% in 1 month, 7.5% in 3 months or 10% in 6 months; severe weight loss: > 2% in 1 week, > 5% in 1 month, > 7.5% in 3 months or > 10% in 6 months)[14].

Circumferences were measured using a non-stretchable measuring tape (Sanny®, São Paulo, Brazil), with the patient in a standing position, and in triplicate (so as to reduce intraobserver variability). WC was measured

and classified according to World Health Organization criteria (increased risk of metabolic complications: > 94 cm in men and > 80 cm in women; greatly increased risk of metabolic complications: > 102 cm in men and > 88 cm in women).[15] NC was measured with the patient standing face to face with the examiner, and the measuring tape placed between mid-cervical spine and mid-anterior neck. In men with a laryngeal prominence, the NC was measured by placing the tape just below this point. NC measurements were classified according to the system proposed by Ben-Noun, Sohar and Laor (overweight: > 37 cm in men and > 34 cm in women; obese: > 39.5 cm in men and > 36.5 cm in women).[16]

The TSF was measured in triplicate using a Lange Skinfold Caliper *(Beta Technology Incorporated* Cambridge, Maryland, USA) with a constant pressure of 10 g/mm^2. The adequacy percentage of AC and TSF measurements (% adequacy = measurement obtained ÷ 50th percentile measurement x 100) was calculated and classified (malnutrition: < 90%; eutrophy: ≥ 90 and < 110%; overweight: ≥ 110 and ≥ 120%; obesity: ≥ 120%), as were AMC values (malnutrition: ≥ 90%; eutrophy: > 90%).[17]

Dietary Intake Assessment

A 24-hour dietary recall was conducted on the same day the anthropometric assessments were conducted, and a photographic record of the portions of food consumed by patients was used so as to improve the quality of the data collected. Dietary intake was calculated using the Nutwin®-Nutrition Support Software (Universidade Federal de São Paulo, São Paulo, Brazil), version 1.6, 2010. The type and amount of dietary supplements consumed was also assessed.

Energy requirements were calculated using the Harris and Benedict equation (for men: 66.5 + 13.8 x weight in kg + 5 x stature in centimeter - 6.8 x age in years; for women: 655 + 9.6 x weight in kg + 1.8 x stature in centimeter - 4.7 x age in years),[18] using activity (1.25 for bedridden patients and 1.3 for active ones) and injury (1 for patients without complications) factors to assess total energy expenditure. Intake recommendations were used to assess protein,[19] cholesterol, and dietary fiber intake;[20] the recommended intake for iron, zinc, and vitamins A and C was drawn from Estimated Average Requirements for Groups (EAR), and calcium was assessed according to Adequate Intake, since EAR for calcium were unavailable.[21] The percent adequacy was calculated for each of these nutrients (% adequacy = amount ingested ÷ amount recommended x 100).

Biochemical assessment

Blood samples were drawn after a 12 h fast, and used to assess serum concentrations of total cholesterol, triglycerides and high-density lipoprotein (HDL) cholesterol through colorimetry (Advia 1800, Siemens®, NY, USA), and of low-density lipoprotein (LDL) through the Friedewald equation.[22] Results were then classified according to the recommended.[20] Insulin levels were determined by chemiluminescence (Advia Centaur XP, Siemens®, NY, USA), and glucose levels were measured using an enzyme hexokinase method (Advia 1800, Siemens®, NY, USA). The coefficients of variation for cholesterol, triglycerides, HDL, glucose and insulin were 3.35%, 2.69%, 5.03%, 3.45% and 7.55%, respectively. The HOMA-IR was classified using a cut-off value of 2.71 for insulin resistance.[23]

Statistical analysis

Quantitative variables were descriptively analyzed using means and standard deviations or medians and interquartile ranges, while categorical variables were expressed as frequencies and percentages. Person and Spearman correlation coefficients (for parametric and nonparametric variables, respectively) were used to assess the correlation between time since the LT and anthropometric, biochemical and dietary variables. The kappa test was used to assess the concordance between BMI < 25 kg/m^2 and AC, TSF and AMC values, as well as between BMI > 25 kg/m^2 and AC, TSF and NC measurements. Results were considered significant at $p < 0.05$. Data were analyzed using the Statistical Package for Social Sciences software, version 19.0.

Results

A total of 37 patients met inclusion criteria during the study period. However, one patient refused to participate, so that only 36 patients were included in the final sample. All individuals underwent orthotopic LT.

Table I contains the demographic and clinical characteristics of the study sample.

Table II contains patients' nutritional status as determined by anthropometry. The TSF measurements of four patients (11%) and the AC and AMC of two patients (5.60%) indicated severe malnutrition. WC measurements could not be obtained from the five patients (13.90%) who had incisional hernia. Weight loss was detected in 12 patients (33.30%).

A positive Pearson's correlation was found between the percent adequacy AC and time since LT ($r = 0.353$; $p = 0.035$). There were no significant correlations among the remaining anthropometric variables, and no concordance between BMI classifications and those of the other anthropometric indicators assessed.

Twenty-eight patients (87.50%) were diagnosed with dyslipidemia according to biochemical assessment. Table III contains patients' nutritional status according to the results of these tests. Six (50%) of the

Table I
Demographic and clinical characteristics of post-liver transplant patients

Characteristics	*Results*
Sex	
Male	22 (61.10)
Age (years)	53.25 ± 10.62
Time on the waiting list (days)	187 (114.25-282.25)
Time since LT (months)	10.50 (3.50-16.75)
1l-12	19 (52.78)
12l-24	17 (47.22)
Etiology of liver disease	
HCV	12 (33.30)
Alcohol	2 (5.60)
HCV+Alcohol	4 (11)
HBV	1 (2.80)
HBV+Alcohol	1 (2.80)
NAFLD	2 (5.60)
Hemochromatosis + HCV	5 (13.90)
Hemochromatosis + HCV + Alcohol	1 (2.80)
Biliary cirrhosis	3 (8.30)
Other	5 (13.90)
Reason for transplant	
Uncompensated cirrhosis	11 (30.60)
HCC	25 (69.40)
MELD-Na	23 ± 10.15
Duration of hospitalization (days)	17 (13-25.50)
Comorbidities	
DM2	19 (52.80)
Hypertension	14 (38.90)
DM2 and hypertension	9 (25)
Immunosuppresants	
Cyclosporine	1 (2.80)
Tacrolimus	33 (91.70)
Prednisone	23 (63.90)
Mycophenolate mofetil	36 (100)
Sirolimus	3 (8.30)

LT: Liver transplant. HCV: Hepatitis C virus. HBV: Hepatitis B virus. NAFLD: Non-alcoholic fatty liver disease. HCC: hepatocellular carcinoma. DM2: Type 2 diabetes mellitus. MELD-Na: MELD-sodium score.
Normally distributed data were expressed as mean ± standard deviation or n (%), while asymmetrically distributed data were described as median (interquartile range).

12 patients without DM who underwent biochemical tests were found to be insulin resistant. Of the 16 patients with type II DM whose test results were available, six (37.50%) were not diagnosed as insulin resistant. No correlations were found among biochemical test results and time since LT.

Analyses of nutritional supplement use revealed that ten (27.80%) patients took calcium carbonate supplements, nine (25%) took vitamin D and one (2.80%) made use of vitamin A supplements. Only two of these patients (5.60%) had calcium adequacy. The patient who took vitamin A supplements did not have adequacy. Data regarding dietary intake and adequacy are displayed in table IV.

Spearman correlation coefficients revealed negative correlations between the time since LT and the caloric adequacy ($r = -0.338$; $p = 0.044$) and vitamin A intake ($r = -0.382$; $p = 0.022$), and the adequacy of vitamin A ($r = -0.382$; $p = 0.021$). No correlations were observed among the time since LT and the remaining dietary variables.

Discussion

The present study characterized the nutritional profile of patients up to 2 years post-LT. The sample demonstrated the prevalence of the following: 1) malnutrition, according to TSF, 2) eutrophy according to BMI, AC and AMC, 3) overweight according to NC, 4) risk of metabolic complications as indicated by WC and 5) dyslipidemia and insulin resistance. The time since LT was also found to be positively correlated with AC, and negatively correlated with vitamin A intake, and with calorie and Vitamin A adequacy. These data illustrate the nutritional alterations as well as the cardiovascular risk of patients in the post-LT period.

The present study confirms the findings of other studies in the literature regarding the predominance of male patients and the prevalence of hepatitis C and of hepatocellular carcinoma among LT patients.[24] In the present study, mean MELD-Na scores were found to be higher than those obtained by the other analyses conducted, and MELD-Na values have also been found to be superior to MELD values in predicting the survival of patients with more severe conditions.[25] Therefore, MELD-Na scores were selected for use in the present study. The high prevalence of type 2 DM and hypertension found in the present study may be explained by the fact that these conditions are frequently reported after LT.[26] However, the present study did not investigate whether the patients who presented with these conditions were diagnosed before or after their transplants.

A high prevalence of eutrophy was also identified based on the following anthropometric parameters: AC (a measure of muscle and adipose tissue), AMC (a measure of muscle tissue), and BMI, which does not distinguish between these two types of tissue. The present findings regarding the prevalence of eutrophy were similar to those obtained in a previous cross-sectional study of patients who were, on average, 4 years post-LT.[9] Although a lower frequency of eutrophy has been observed in LT patients in other studies in the literature, these investigations were conducted on patients who were at least 2 years post-LT, and used lower cutoff scores for eutrophy.[4] The high prevalence of obesity demonstrated by TSF in the present study is in agreement with a previous study on cirrhotic patients, which found that TSF values may increase significantly in the first year post- LT. Such findings underscore the importance of using multiple anthropometric methods since, at the time of writing, there is no gold standard for this type of evaluation,[27] and the combination of several assessment methods, like bioelectrical impedance, could be used to yield more reliable results.

Table II
Anthropometric assessment of post-liver transplant patients

Anthropometric variables	*Time since LT (months)*		
	1|-12 (n = 19)	*12|-24 (n = 17)*	*Total (n = 36)*
Weight (kg)	70.95 ± 15.26	74.18 ± 15.76	72.47 ± 15.36
BMI (kg/m²)	24.63 ± 5.14	26 ± 5.86	25.58 ± 5.56
Malnutrition	1 (56.26)	2 (11.76)	3 (8.30)
Eutrophy	9 (47.37)	6 (35.30)	15 (41.70)
Overweight	7 (36.84)	6 (35.50)	13 (36.10)
Obesity	2 (10.53)	3 (17.65)	5 (13.90)
% Weight Loss*	11 (6-21)	9 (2-9)	9 (4.5-13.25)
Significant	–	1 (20)	1 (8.30)
Severe	6 (85.71)	2 (40)	8 (66.70)
Non-significant	1 (14.29)	2 (40)	3 (25)
% AC adequacy	93.42 ± 17.28	100.59 ± 16.14	96.80 ± 16.90
Malnutrition	8 (42.11)	4 (23.53)	12 (33.30)
Eutrophy	4 (21.05)	7 (41.18)	14 (38.90)
Overweight	7 (36.84)	4 (23.53)	8 (22.20)
Obesity	–	2 (11.76)	2 (5.60)
% TSF adequacy	96.37 ± 42.29	109.94 ± 38.61	102.78 ± 40.60
Malnutrition	10 (52.63)	4 (23.53)	14 (38.90)
Eutrophy	3 (15.79)	5 (29.41)	8 (22.20)
Overweight	2 (10.53)	3 (17.65)	5 (13.90)
Obesity	4 (21.05)	5 (29.41)	9 (25)
% AMC adequacy	95.21 ± 17.44	100.82 ± 16.60	97.86 ± 17.05
Malnutrition	7 (36.84)	4 (23.53)	11 (30.60)
Eutrophy	12 (63.16)	13 (76.47)	25 (69.40)
WC (cm) †	94.29 ± 12.88	95.93 ± 15	95.03 ± 13.66
Adequate	6 (35.30)	4 (28.57)	10 (32.30)
Increased	5 (29.40)	4 (28.57)	9 (29)
Very high	6 (35.50)	6 (42.86)	12 (38.70)
NC (cm)	26.05 ± 3.82	36.12 ± 3.08	36.08 ± 3.44
Eutrophy	7 (36.84)	8 (47.06)	15 (41.70)
Overweight	9 (47.37)	7 (41.18)	16 (44.40)
Obesity	3 (15.79)	2 (11.76)	5 (13.90)

LT: Liver transplant.BMI: Body mass index. AC: arm circumference. TSF: triceps skinfold. AMC: arma muscle circumference. WC: waist circumference. NC: neck circumference.
*Data corresponding to 12 participants (1|-12 = 7; 12|-24 = 5). †Data corresponding to 31 participants (1|-12 = 17, 12|-24 = 14).
Normally distributed data were expressed as mean ± standard deviation or n (%), while asymmetrically distributed data were described as median (interquartile range).

WC measurements suggested that a significant proportion of patients had a greatly increased risk of metabolic complications due to excess visceral fat. These results are similar to those obtained by other studies in the literature, although these investigations used different assessment methods.[24,28] Given the high incidence of incisional hernia following LT, especially in women and in patients with a BMI over[29] 25 kg/m², some post-LT patients are unable to undergo WC measurements. However, NC results did indicate a high prevalence of overweight and provided a measure of upper body fat distribution. Given the limitations of WC measurements, the assessment of NC may be a more adequate method of assessing body fat distribution in this population. An extensive literature search revealed no studies of post-LT patients involving NC measurements. These results underscore the high prevalence of overweight and risk of metabolic complications following LT.

A number of patients in the present study were also found to be malnourished, especially according to TSF, which provide an assessment of adipose tissue. Similar to the present study, some investigations have found poor TSF adequacy in early and late post-LT patients; however, unlike the present investigation, these studies have also reported a low AMC adequacy in these individuals[30]. The prevalence of severe weight loss was also found to be high, especially in recently transplanted patients, which may reflect the resolution of the edema and ascites developed as a consequence of hepatic disease.[10] Interestingly, BMI indicated a low prevalence of malnutrition, confirming that this method should be used in combination with other assessments[31] so as to provide a better evaluation of nutritional status after LT.

The present results indicated that both malnutrition and overweight may occur during the first two years post-LT. The anthropometric methods used allowed

Table III
Biochemical assessment of post-liver transplant patients

	Time since LT (months)		
Biochemical tests	*1|-12 (n = 19)*	*12|-24 (n = 17)*	*Total (n = 36)*
Cholesterol (mg/dL)*	167.06 ± 50.20	155.60 ± 30.01	161.85 ± 42.03
Adequate	13 (72.22)	13 (86.67)	26 (78.80)
High	5 (27.78)	2 (13.33)	7 (21.20)
LDL (mg/dL)†	95.59 ± 36.89	90.47 ± 25.68	93.19 ± 31.73
Adequate	16 (94.112)	15 (100)	31 (96.90)
High	1 (5.88)	–	1 (3.10)
HDL (mg/dL)†	43.53 ± 19.65	38.67 ± 8.38	41.25 ± 15.40
Adequate	5 (29.41)	4 (26.67)	9 (28.10)
Low	12 (70.59)	11 (73.33)	23 (71.90)
Triglycerides (mg/dL)†	172.76 ± 78.36	130.33 ± 48.81	152.88 ± 68.61
Adequate	8 (47.06)	10 (66.67)	18 (56.30)
High	9 (52.94)	5 (33.33)	14 (43.80)
HOMA-IR‡	250 (1.25-5)	2.50 (1-7)	2.50 (1-5)
Resistance	10 (62.50)	6 (50)	16 (57.10)
No resistance	6 (37.50)	6 (50)	12 (42.90)

LT: Liver transplant. LDL: low-density lipoprotein. HDL:High-density lipoprotein. HOMA-IR: Homeostatic model assessment of insulin resistance.
*Data corresponding to 33 participants (1|-12 = 18; 12|-24 = 15). †Data corresponding to 32 participants (1|-12 = 17, 12|-24 = 15). ‡Data corresponding to 28 patients (1|-12 months = 16; 12|-24 = 12).
Normally distributed data were expressed as mean ± standard deviation or n (%), while asymmetrically distributed data were described as median (interquartile range).

Table IV
Dietary intake and adequacy of post-liver transplant patients

	Time of LT (months)		
Nutrients	*1|-12 (n = 19)*	*12|-24 (n = 17)*	*Total (n = 36)*
Energy (kcal)	1601 (1419-2283)	1606 (1341-2172)	1603.50 (1424.50-2174)
% Adeq.	95 (71-110)	85 (66-100.50)	85.50 (67.25-107.75)
Carbohydrates (g)	226 (178-301)	242 (177-266.50)	228.50 (180.50-284)
Lipids (g)	53 (40-64)	52 (39.50-65.50)	52.50 (40-64.75)
Protein (g/kg of CW)	0.99 (0.78-1.49)	1.04 (0.67-1.43)	1 (0.70-1.43)
% Adeq.	99 (78-149)	104 (67.50-143)	100 (70.25-143.50)
Calcium mg	788 (644-1371)	713 (421-901.50)	748.50 (502.75-992.25)
% Adeq.	78 (53-114)	62 (45-79.50)	67 (51-84)
Iron (mg)	10 (8-15)	11 (9.50-14)	10.50 (8.25-14)
% Adeq.	175 (149-254)	211 (166.50-242)	201 (155.75-249.75)
Zinc (mg)	9 (7-11)	10 (6-13.50)	9 (7-11.75)
% Adeq.	110 (90-148)	123 (87-161.50)	119 (90.75-154)
Vit. A (RE)	658 (243-1920)	351 (215.50-706.50)	466.50 (240-1097)
% Adeq.	105 (39-260)	58 (34-113.50)	87 (38.25-140.50)
Vit. C (mg)	121 (28-177)	74 (20-194.50)	91 (27.25-175)
% Adeq.	175 (37-263)	115 (29.50-287)	126 (36.25-276.50)
Dietary fiber (g)	15 (10-32)	18 (12-29)	17 (10.25-29)
% Adeq.	75 (53-162)	94 (62.50-147.50)	87.50 (54.50-148)
Cholesterol (mg)	148 (115-197)	147 (114-220)	147.50 (116-211.75)
% Adeq.	60 (53-98)	61 (48-96.50)	60.50 (49.50-97.50)

LT: Liver transplant. Adeq: Adequacy. CW: Current weight. Vit. A: Vitamin A. Vit. C: Vitamin C.
Data expressed as median (interquartile range).

for an assessment of muscle and adipose reserves, while BMI do not differentiate between these two types of tissue. This distinction may have been responsible for the variability and discordance between the different methods of assessing patient nutritional status.

On the other hand, it was still possible to conclude that the patients for whom a longer time had elapsed since their LT had more adequate AC measurements than those who had been recently transplanted. Over time, renal transplanted female patients presented higher AC values in a previously study.[32] In the initial post-LT period, the surgical trauma has been found to lead to an increased catabolic rate,[33] while in the late post-LT period, weight gain appears to be more common.[4] The data in the present study were in accordance with other studies in the literature, and suggested that AC is more adequate over time.

The prevalence of dyslipidemia in the present study was elevated, and significantly higher than that reported in other studies which assessed patients with a longer time post-LT.[34,35] Studies suggest that dyslipidemia is associated with the development of non-alcoholic fatty liver disease in the year following the transplant,[36] and that it may be the greatest risk factor for cardiovascular diseases and mortality in these individuals.[26] A high prevalence of insulin resistance has also been reported in patients who were 7 to 17 years post-LT.[24] However, a separate study also observed a prevalence of insulin resistance of 38% in hepatitis C patients who were approximately[37] 4 years post-LT, using a HOMA-IR cutoff score of 2.5. Some authors also suggest that insulin resistance may be more common in hepatitis C as compared to other etiologies, and is associated with progressive fibrosis and a smaller antiviral response.[7,38] Corticosteroids, tacrolimus, cyclosporin and sirolimus have been shown to be associated with the development of dyslipidemia and insulin resistance.[39] Therefore, it is possible that the use of multiple immunosuppressants may have contributed to the prevalence of dyslipidemia and insulin resistance in the present sample.

The dietary assessment indicated that most patients had adequate nutrient levels. A cross-sectional study using 3-day records and dietary history to assess dietary intake found that post-LT patients had low levels of calories, dietary fiber, vitamin A and calcium, as well as adequacy for cholesterol, all of which is in agreement with the present findings; however, the present results regarding the adequacy of protein, vitamin C, zinc and iron differed from those obtained by other studies.[28] A cohort study involving 7-day dietary records also demonstrated that, although post-LT patients reported inadequate calorie and protein intake, these values were still higher than those reported in the pre-transplant period.[27] However, a distinct cross-sectional study involving dietary history has also found some reports of excessive calorie intake among these individuals.[5] The variability in the methods used to assess dietary intake limits comparisons between the results of different studies.

Our results demonstrated that a longer time post-transplant was correlated with lower vitamin A intake, lower vitamin A adequacy as well as a lower caloric adequacy compared to those with shorter time post-LT. It is important to note that vitamin A regulates immune functioning,[40] so that, given the increased immune vulnerability of post-LT patients caused by the use of immunosuppressants,[41] the maintenance of adequate vitamin A is especially important following LT. Studies of patients at 6 months post-LT have reported the occurrence of low vitamin A intake and an increased oxidative stress and inflammation.[42] Furthermore, vitamin A deficiency is endemic in Brazil.[43] These may have contributed to the results obtained in the present study.

Although the 24-hour dietary recall may not be representative of usual dietary intake due to intra-individual variability, it allows for an investigation of the average intake of groups.[44] Furthermore, studies suggest that a higher BMI, female gender, socioeconomic and education levels, smoking, diet, psychological factors and dietary habits are associated with misreporting, without significant difference between the methods of weighed food record and estimated food record.[45] The correlation between lower caloric intake observed and a longer time post-transplant may therefore counterbalance the relationship between the latter variable and the higher adequacy of AC measurements and a higher prevalence of overweight. Nevertheless, the limitations associated with the 24-hour dietary recall may have influenced the present results.

The small sample size, the cross-sectional design and the fact that not all participants underwent biochemical testing are the main limitations of the present study. The use of the time since the transplant as a selection criterion may have also restricted the sample size. Patients were only assessed at a minimum of 1 month post-transplant since, during this period, many of the patients still have drains in place, are not back on their normal diet, or are still hospitalized. However, it is important to assess patients within the first 2 years post-transplant so as to allow for the early detection of changes in nutritional status and cardiovascular risk. In spite of these limitations, it was possible to detect a high prevalence of dyslipidemia and insulin resistance in post-LT patients, which indicate the presence of significant cardiovascular risk factors in these individuals. These results should be confirmed in larger samples, so as to confirm their generalization to the population.

Conclusion

There is significant variability in the nutritional diagnosis of post-LT patients depending of the anthropometric measurements used. WC assessments indi-

cate that these patients have a high risk of metabolic complications, and biochemical tests show that they also have dyslipidemia and insulin resistance. The prevalence of cardiovascular risk factors underscores the need for transdisciplinary assessments of these populations, and for the development of strategies to improve nutritional status and, therefore, reduce patient risk factors. However, further studies involving higher samples are still required to confirm the present results.

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Conflicts of interest

The authors declare no conflicts of interest.

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Original / *Otros*

Fluid intake in Spanish children and adolescents; a cross-sectional study

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Abstract

Introduction: **Some studies demonstrated that dehydration process is prevalent among young populations and subsequently, a cause of concern. However, the evaluation of the fluid consumption pattern of children and adolescent populations has not been widely assessed.**

Objective: **To evaluate the total fluid intake from different types of beverages in Spanish children and adolescents.**

Methods: **A total of 238 children and adolescents aged 3-17 years were randomly recruited from all Spanish regions. The information about the quantity and quality of daily fluid intake from different types of beverages was collected using a 24 h fluid-specific diary over 7 consecutive days.**

Results: **Fluid intake was < 80% of the EFSA recommendations in 87% of the study population. In our sample, water was the main contributor to fluid intake, followed by milk and derivates and sweet regular beverages. No differences in consumption patterns were found according to gender. Consumption of hot beverages as well as sweet regular and sweet light beverages increased with age, while milk and milk derivates consumption decreased.**

Conclusion: **The large majority of our young population did not meet the EFSA recommendations for total water intake. Therefore, an increase in plain water consumption in children and adolescents should be promoted in order to fulfill the fluid needs without increasing calorie intake.**

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Key words: *Fluid intake. Spain. Beverages. Water. Children. Adolescents.*

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INGESTA DE LÍQUIDOS A PARTIR DE BEBIDAS EN NIÑOS Y ADOLESCENTES ESPAÑOLES; ESTUDIO TRANSVERSAL

Resumen

Introducción: **Diversos estudios han mostrado que el proceso de deshidratación tiene lugar en población infantil y adolescente, y por ello, son causa de preocupación. Sin embargo, los patrones de consumo de líquidos en poblaciones infantil y adolescente no han sido estudiados en profundidad.**

Objetivos: **Evaluar la ingesta de líquidos total a partir de distintos tipos de bebidas en niños y adolescentes españoles.**

Métodos: **Un total de 238 niños y adolescentes de entre 3 y 17 años de edad fueron reclutados aleatoriamente en las distintas regiones españolas. La información sobre la cantidad y calidad de la ingesta diaria de líquidos se recogió mediante un registro de 24 horas específico para la evaluación de fluidos durante 7 días consecutivos.**

Results: **La ingesta de líquidos estuvo por debajo del 80% de las recomendaciones de la EFSA en el 87% de la población de estudio. En el presente estudio el agua fue la principal fuente de líquidos, seguida de la leche y derivados y de las bebidas azucaradas. No se encontraron diferencias significativas en los patrones de consumo entre géneros. El consumo de bebidas calientes, bebidas azucaradas y edulcoradas incrementó con la edad, mientras que el consumo de leche y derivados disminuyó.**

Conclusion: **La gran mayoría de nuestra población no cumplió con las recomendaciones de la EFSA sobre la ingesta total de agua. Por ello, se debería promover un aumento en el consumo de agua en niños y adolescentes, para poder satisfacer las necesidades de líquidos sin aumentar la ingesta calórica.**

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Palabras clave: *Ingesta de líquidos. España. Bebidas. Agua. Niños. Adolescentes.*

Introduction

Ensuring a good hydration status is essential for adequate body functions. Dehydration is associated with some symptoms linked to mental and physical performance[1]. Fluid needs vary in humans according to several factors. Age, body size and perspiration (affected among other factors by air temperature and intensity of physical exercise) are the main determinants of fluid needs[1].

Childhood and adolescence are crucial periods of life from a nutritional point of view due to the growth and development[2]. Some studies demonstrated that dehydration process is prevalent among young populations and subsequently, a cause of concern[3,4]. During childhood and adolescence, an appropriate level of hydration can be achieved with a wide range of total water intakes because of homeostatic control mechanisms[1]. This large variability of the population needs complicates the establishment of fluid intake recommendations for the general public.

There are well established dietary requirements intakes for most essential nutrients[5]. In Europe, EFSA established recommendations on total water intake (water coming from food and fluids) based on water balance, i.e. water intake calculated in surveys through dietary recalls, minus the average water losses obtained from urine collection during the next 24 hours[1]. However, the basis to establish the recommendations is often different between organisms. For instance, in US, the method to recommend total water intake is based on the median of a defined population group[6]. The methods used in surveys to estimate total water intake and fluid intake (drinking water and all other beverages) in European children are not comparable and underreporting seems to be frequent[1]. International bodies have set guidelines for total water intake in young populations[1]. In Europe, the EFSA (European Food Safety Agency) panel established the reference values of total water intake for adolescents 14 years and older based in the adults needs. For children and adolescents younger than 14 years, 2,100 ml in boys 9 to 13 years old and 1,900 ml in girls 9 to 13 years old, should be apply, respectively. In children, boys and girls 4 to 8 years old, in boys 9 to 13 years old and in girls 9 to 13 years old, 1,300 mL/day, 1,700 mL/day and 1,520 mL/day, are the reference values established by this panel respectively[1].

The sources of water are drinking water, other beverages, food moisture and water from substrate oxidation[1]. Fluids represent approximately 80% of total water intake in European diets, and 20% of the water comes from foods[1]. Based on 3 days food diary, in the Dortmund Nutritional and Anthropometric Longitudinally Designed study, the main sources of water intake for boys and girls 4 to 8 years-old were natural mineral water (13.1%), as much as milk (13.0%). For boys 9- to 13-year old, whose total water intake represented a mean of 1801ml/day, milk (9-17%) and natural mineral water (12-15%) were the most important sources of total water intake. In all these groups, tap water was the least important source of water intake (2.6%, 3.3%, and 3.3%, respectively)[7]. In the Healthy Lifestyle in Europe by Nutrition in Adolescence Cross Sectional Study (HELENACSS), adolescents consumed an average of 1455 ml/day of fluids. Most of the adolescents consumed water (87.9%), representing as well the largest amount of fluid consumed per capita followed by sweet beverages.

Since three decades, the energy intake coming from sweetened beverages increased 135% in children and adolescents**,** along with the obesity rates (50%)[8]. The association between both observations does not imply a causal relationship. However, it seems to be relevant to evaluate if current levels of fluid consumption other than water, can lead to an excess of energy intake and may have further consequences in long-term health outcomes[9]. In fact, results based on the 2003-2004 National Health and Nutrition Examination Survey data in 3098 children and adolescents 2 to 19 years of age, suggested that replacing all SSBs with water would therefore result in an average net reduction of 235 kcal/d[8]. In this sense, plain water would be the healthiest option for hydration, as increasing water consumption is also proposed as strategy to reduce energy intake[10].

There is an agreement about the relevance of an appropriate level of fluid intake in terms of health maintenance. However, the actual fluid or total water intake is not often reported in food or nutrient intake studies, whereas fluids should also be considered in dietary intake assessment.

Information on the fluid consumption patterns and their characteristics in young populations is very scarce. The aim of this paper was to investigate the quantity, the quality and the consumption span of the beverages ingested by individuals within the pediatric age range (from 3 to 17 years of age) according to sociodemographic characteristics.

Methods

Design and study population

The present paper is based on a Spanish cross-sectional study on fluid intake designed to assess all the sources of fluid consumption, from water to different types of beverages, and their association with lifestyle and health. The cross-sectional study took place between March and May 2012, and 1,922 participants were recruited by random selection from an existing Spanish database established for population surveys (all regions were included except Ceuta, Melilla and Canary Islands). This database is considered comparable to the Spanish population in terms of gender, age, region, socioeconomic level and habitat (urban *vs* rural). For the present study, only children and adoles-

cents 3 to 17 years old were taken into account (n = 420). Participants reporting a mean fluid intake less than 0.4 L/day or more than 6 L/day, and those participants with missing data in the fluid intake questionnaire were excluded from the analyses (n = 182). Therefore, the effective sample size for the current study was 238 participants (fig. 1).

Assessment of fluid intake

Fluid intake was assessed using a 24-hours recall during 7 consecutive days. For children and adolescents ≤ 14 years old, parents proxy-reported the usual fluid intake. The questionnaire was delivered and explained during a first interview at the participant's home. After seven days, the filled questionnaire was collected and the interviewer checked for completeness. The participants recorded the moment of the fluid intake throughout the day, type, and volume of beverage using standard portion sizes (one standard serving, cup, glass, can, bottle, etc). The addition of sugar in each beverage was also evaluated (number of added tablespoons). There were eleven response categories to the question "moment of the beverage consumption": Just when you wake up, at breakfast, during the morning, just before lunch, at lunch, during the afternoon, just before dinner, at dinner, after dinner, just before going to bed, during the night. The intake of beverages *outside of the meals* was considered in whenever occasion different than breakfast, lunch and dinner.

The questionnaire items on fluids included: water (tap water, filtered tap water, natural mineral water, sparkling natural mineral water, flavoured water, fountain water); hot beverages (coffee, coffee with milk, espresso with a drop of milk, cappuccino, tea, cereals made beverages, and others infusions and hot beverages); milk and milk products (milk, milkshakes, milkshakes with juice, liquid yogurt, other milk drinks); juices (organic juice, bottled juice, nectar, nectar without added sugar, other fruit drinks); sweet beverages regular (carbonated soft drinks (cola, orange, lemon, bitter, tonic water, other flavours), non-carbonated soft drinks (orange, lemon, sports drinks, energy drinks, ice tea regular, other flavours), other sugared soft drinks); sweet beverages light (diet carbonated soft drinks, (cola, orange, lemon, other flavours), diet non-carbonated soft drinks (orange, lemon, diet iced tea) other diet soft drinks); and alcoholic drinks (beer, alcohol-free beer, lemon beer, wine, wine with soda, alcoholic mixed drinks, other alcohol beverages). Fluid intake was defined as the sum of all these categories. The adequacy of fluid intake was based on the EFSA age and gender specific recommendations for total water intake after extracting 20% of the recommendation accounting for water in foods.

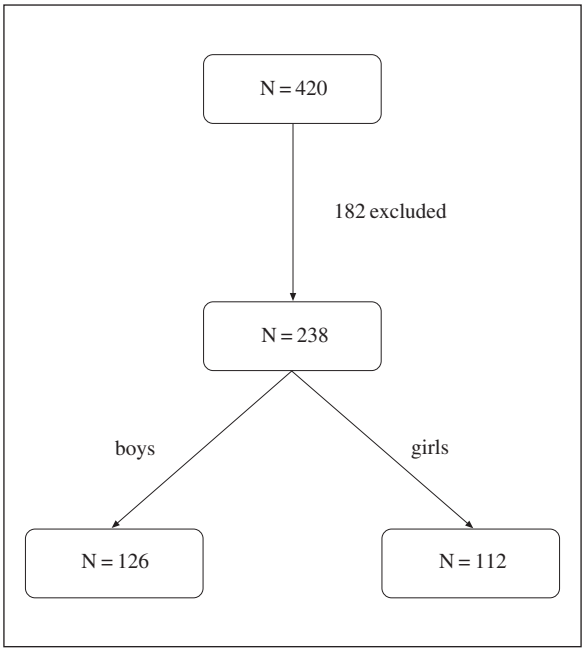


Fig. 1.—Flowchart of the study sample size.

Assessment of other variables and lifestyle factors

Leisure-time physical activity practice for more than thirty minutes was evaluated with a questionnaire, with four possible responses: five times a week or more, between three and four times a week, between one and two times a week and one time every two weeks or less. In addition, variables such as socioeconomic characteristics, region, habitat (urban or rural classification) and parental education level were also evaluated.

Assessment of body composition

Height in metres (m) and weight in kilograms (kg) were evaluated with a self-reported questionnaire. Body Mass Index (BMI) was calculated (in kg/m^2) and categorized following cut-off points according to the criteria of the International Obesity Task Force[11].

Statistical analysis

All the data are presented either as the mean and standard deviation (SD) for continuous variables or numbers and percentages for dichotomous variables. We compared the distribution of the selected characteristics between groups using χ^2 tests for categorical variables or student's t-tests or analysis of variance (ANOVA) as appropriate for the continuous variables. The Bonferroni post-hoc test was used to correct for multiple comparisons. Analyses were performed using the SPSS software version 20.0 (SPSS Inc, Chicago, IL). All statistical tests were two-tailed and the significance level was set at $P < 0.05$.

Results

The baseline characteristics of participants are summarized in table I. A total of 238 participants (126 boys and 112 girls) with a mean age of 9.2 years and recruited from 8 Spanish regions were included. No significant differences were observed in the proportion of individuals for different age categories, region, type of habitat and educational level between the study sample and the total Spanish general population. No gender differences were observed in the prevalence of age categories, region, habitat or socioeconomic level. 24.4% and 11.3% of the total sample was categorized as overweight and obese respectively. No gender differences were found for BMI classification. Most of the study population presented a middle socioeconomic status. The majority of the study population (60.5%) reported at least 3-4 times a week of leisure-time physical activities, being girls more sedentary than boys.

The mean total fluid volume consumed was 1,669 ml per day for whole population, 1,599 ml for girls and 1732 ml for boys (table II). Mean water consumed was 823 ml/day for whole population, 819 ml for girls and 827 ml for boys. Figure 2 shows the percentage of the population according to gender, consuming at least 100% or less of the EFSA recommendations for total water intake (age and gender specific values). 86.6% of the total study population, 87.5% of girls and 85.7% of the boys consumed < 100% of the EFSA recommendations for total water intake.

Table II shows the total daily fluid intake and the amount of each type of consumed beverage according to gender. Girls consumed significantly less sweet regular beverages than boys. No significant differences were observed for total fluid volume, water intake, hot beverages, milk and milk products, juices or sweet light beverages between genders.

Table I
General characteristics of study population

Baseline variables	*All population (n = 238)*	*Girls (n = 112)*	*Boys (n = 126)*	*P value**
Age, years (mean, SD)	9.17 (4.6)	9.0 (4.5)	9.3 (4.6)	0.57
Age categories,% (n)				0.94
3 to 6 years	36.2 (86)	37.5 (42)	34.9 (44)	
7 to 11 years	29.8 (71)	30.4 (34)	29.4 (37)	
12 to 15 years	23.1 (55)	21.4 (24)	24.6 (31)	
16 to 17 years	10.9 (26)	10.7 (12)	11.1 (14)	
BMI, kg/m^2 (mean, SD)	18.8 (3.9)	18.9 (3.7)	18.7 (4.0)	0.79
BMI classification,% (n)[b]				0.17
Under and normal weight	64.3 (153)	63.4 (71)	65.1 (82)	
Overweight	24.4 (58)	28.6 (32)	20.6 (26)	
Obesity	11.3 (27)	8.0 (9)	14.3 (18)	
Region,% (n)				0.96
Region 1 (Catalonia/Aragon)	9.2 (22)	10.7 (12)	7.9 (10)	
Region 2 (east)	13.9 (33)	14.3 (16)	13.5 (17)	
Region 3 (south)	20.6 (49)	18.8 (21)	22.2 (28)	
Region 4 (centre)	8.8 (21)	8.0 (9)	9.5 (12)	
Region 5 (north-centre)	7.1 (17)	8.0 (9)	6.3 (8)	
Region 6 (northwest)	12.2 (29)	10.7 (12)	13.5 (17)	
Barcelona and Madrid	28.1 (67)	29.5 (33)	27.0 (34)	
Habitat,% (n)				0.96
5.000 to 30.000 inhabitants	30.7 (73)	30.4 (34)	31.0 (39)	
30.000 a 200.000 inhabitants	35.7 (85)	36.6 (41)	34.9 (44)	
More than 200.000 inhabitants	33.6 (80)	33.0 (37)	34.1 (43)	
Socioeconomic level,% (n)				0.51
Lower and middle-low	33.6 (80)	34.9 (39)	33.6 (41)	
Middle	43.3 (103)	45.4 (51)	41.3 (52)	
Upper-middle and high	23.1 (55)	19.7 (22)	26.1 (33)	
Leisure-time physical activity,% (n)				0.04
1 time every 2 weeks or less	8.4 (20)	8.0 (9)	8.4 (11)	
1-2 times a week	31.1 (74)	39.3 (44)	23.8 (30)	
3-4 times a week	28.6 (68)	29.5 (33)	27.8 (35)	
5 times a week or more	31.9 (76)	23.2 (26)	39.7 (50)	

Data expressed as mean (SD) or percentage (n). Abbreviations: BMI, body mass index. [a]P values for comparisons between groups were tested by student's t-test or χ^2 as appropriate.
[b]BMI (kg/m^2) was divided in the following categories: underweight and normal weight, overweight and obesity following age and gender specific cut-off points by Cole et al (2000).

Table II
*Total daily consumption of different types of beverages (ml/day) in all population and stratified by gender**

Variables	*All population (n = 238)*	*Girls (n = 112)*	*Boys (n = 126)*	*P value**
Water	823 (556)	819 (576)	827 (541)	0.91
Hot beverages	38 (103)	40 (98)	36 (108)	0.75
Milk and milk products	442 (268)	421 (274)	461 (263)	0.25
Juices	201 (253)	202 (206)	201 (290)	0.97
Sweet regular beverages	120 (250)	89 (160)	148 (306)	0.07
Sweet light beverages	14 (60)	16 (69)	13 (52)	0.67
Alcoholic beverages	-	-	-	-
Total daily liquid volume	1669 (679)	1599 (665)	1732 (688)	0.13

*Data expressed as mean (SD). [a]P values for comparisons between gender were tested by student's t-test.

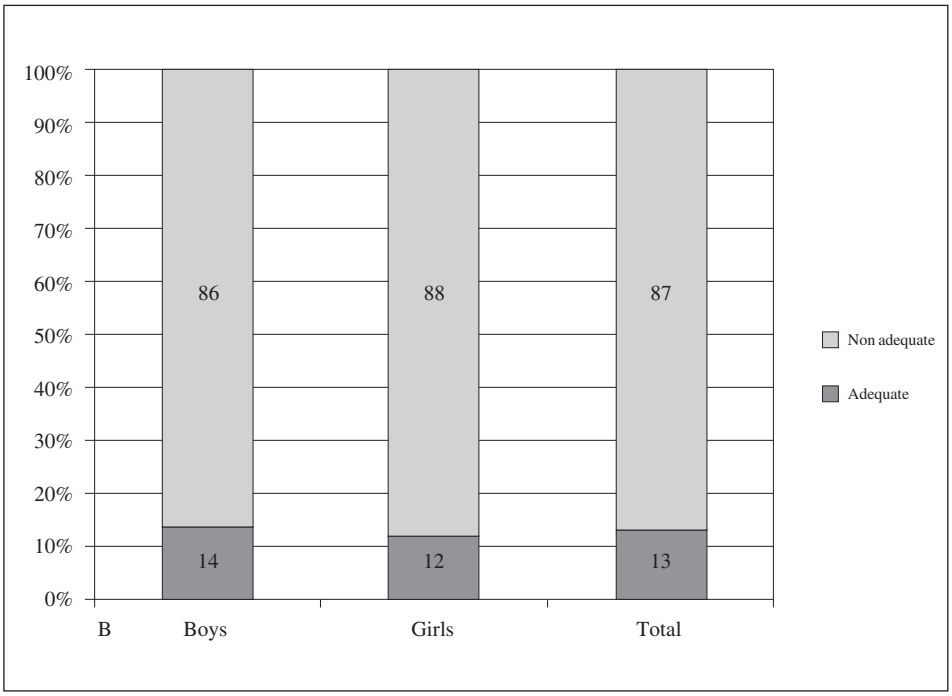


Fig. 2.—Percentage of adequacy to EFSA recommendations for water intake according to gender.

Total daily fluid intake and beverage consumption according to age ranges are shown in table III. Older participants (16-17 years) consumed more hot beverages compared to all other categories ($p = 0.028$). Children corresponding to the younger age groups (3-6 and 7-11 years) consumed more milk and milk products ($p < 0.001$) and less sweet regular ($p < 0.001$) and light beverages ($p = 0.023$) compared to the older categories. No significant differences were found for water and juices intake between age categories.

The total daily intake of different types of beverages and its consumption moment (during the main meals/outside the main meals) are described in table IV. For both genders, fluid intake was significantly higher during the main meals. The consumption of water and sweet regular beverages was significantly higher during the main meals compared with outside the main meals. Juices consumption was significantly higher outside the main meals for both genders. In relation to milk and milk products and sweet light beverages intake, no significant differences between the moments of consumption were observed.

When stratified by BMI, no differences in total fluid consumption or main beverage groups were found between normal weight, overweight and obese participants (data not shown).

Discussion

The results of this cross-sectional study provide important information about the fluid intake in a sample of Spanish children and adolescents. Following the European Food Safety Authority reference values

Table III
*Total daily consumption of different types of beverages (ml/day) stratified by age range**

Variables	*3-6 years (n = 86)*	*7-11 years (n = 71)*	*12-15 years (n = 55)*	*16-19 years (n = 26)*	*P value[a]*
Water	737 (508)[a]	800 (557)[a]	905 (570)[a]	999 (643)[a]	0.113
Hot beverages	30 (95)[a]	26 (70)[a]	41 (115)[a]	93 (156)[b]	0.028
Milk and milk products	538 (267)[a]	452 (243)[a]	376 (266)[b]	246 (214)[c]	<0.001
Juices	212 (296)[a]	194 (188)[a]	225 (293)[a]	136 (152)[a]	0.499
Sweet regular beverages	39 (107)[a]	103 (155)[a]	212 (380)[b]	248 (340)[b]	<0.001
Sweet light beverages	5 (36)[a]	5 (22)[a]	30 (89)[b]	38 (103)[c]	0.010
Alcoholic beverages	–	–	–	26 (75)	–
Total daily liquid volume	1571 (681)[a]	1602 (589)[a]	1828 (726)[a]	1844 (748)[a]	0.066

*Data expressed as mean (SD).
[a]P values for comparisons between groups were tested by bivariate analysis of variance (ANOVA) followed by post hoc tests with the Bonferroni correction.
P < 0.05 for differences between letters ([a] versus [b] and [b] versus [c]).

Table IV
*Total daily intake of different types of beverages (ml/day) by moment of consumption**

	All population (n = 238)			*Girls (n = 112)*			*Boys (n = 126)*		
	During the meal	*Outside the meal*	*P value[a]*	*During the meal*	*Outside the meal*	*P value[a]*	*During the meal*	*Outside the meal*	*P value[a]*
Water	470 (328)	353 (393)	<0.001	473 (322)	345 (386)	0.002	467 (335)	359 (400)	0.017
Hot beverages	23 (66)	14 (59)	<0.001	26 (67)	14 (50)	0.067	21 (64)	14 (66)	0.323
Milk and milk products	230 (167)	212 (214)	0.306	213 (169)	208 (220)	0.861	246 (165)	215 (209)	0.208
Juices	66 (146)	135 (190)	<0.001	60 (149)	141 (137)	<0.001	71 (144)	129 (227)	0.010
Sweet regular beverages	85 (179)	35 (122)	<0.001	65 (151)	23 (56)	0.007	102 (200)	46 (159)	0.002
Sweet light beverages	7 (40)	7 (37)	0.996	8 (53)	7 (44)	0.858	6 (25)	7 (30)	0.578
Alcoholic beverages	–	–	–	–	–	–	–	–	–
Total daily liquid volume	894 (343)	775 (500)	<0.001	849 (334)	749 (451)	0.017	934 (347)	798 (541)	0.011

*Data expressed as mean (SD). [a]P values for comparisons between during and outside the meal were tested by student's t-test.

for total water intake for these age categories, around 87% of the total study population did not meet water intake EFSA recommendations, which suggests the need of a careful monitoring of total water intake of these populations in the coming years.

No large differences in fluid consumption according to gender were found. Gender differences in sweet regular beverages were close to being significant (being girls those who consumed less), in agreement with previous studies[10,12]. One possible explanation for this could be the fact that female adolescents are often more worried by their energy intake than boys[13].

The first observation regarding age in our study was that total daily fluid intake increased with age, as also observed in a French survey[14]. A plausible explanation for this finding are the physiological variables (body size[15], less effective thermoregulators, underdeveloped sweating and skin blood flow mechanisms, and other factors)[16]. The youngest children consumed also more milk and milk products compared to other age categories and less sweet regular beverages. It might be explained by the high influence of their families[17], still present in these periods of life, which considerably decrease during adolescence. 12 to 15 years old adolescents consumed significantly less hot beverages than 16 to 17 years old adolescents did. Plain water represented around 50% of all the consumed fluids in all the study groups. These trends were also observed in the mentioned French survey[14].

The prevalence of overweight and obesity in our population group was 23.5% and 10.3% respectively, slightly lower in comparison to the reported prevalence in a very recent Spanish study (26% and 12.6%)[18]. However, BMI was not related to total fluid consumption or to main beverage group distribution, in line with results obtained in other studies[19,20]. Nevertheless there is mounting evidence about a significant negative association between water consumption and energy intake[21]. As our population group is within the most affected by the obesity pandemic, increasing plain calorie-free water consumption should be a recommendation.

EFSA recommendations for total water intake (including water from all beverages and moisture content of foods) are higher than the current mean values obtained in this study for both boys and girls[1]. In this study, data on water coming from foods was not available. For this reason, we extracted 20% of the current recommendations to calculate the percentage of children and adolescents who did not meet the

recommendations, as this is the amount of water which is accepted to correspond to the water coming from foods[1]. The percentage of population who did not meet EFSA recommendations, was higher compared to the HELENA study[22] (85.7% of males and 87.5% of the females against 69.4% of males and 64.4% of females).

Considering our sample, the main contributor to the total fluid intake was plain water, followed by milk and milk products, juices, sweet regular beverages, hot beverages, sweet light beverages and alcohol. Splitting the analyses by gender, the results were similar for girls and for boys, only differing in the order of the two last types of beverages. This order of contributors is equal for 3-6 and 7-11 year old children and 12-15 years old adolescents. For 16-17 years old adolescents, sweet regular beverages represented the second group instead of milk and milk products, being juices the fourth group. In the French survey[14], the list and the order of the contributors was almost the same (although regular and light sweet beverages were assessed together due to the low proportion of children consuming light sweet beverages). Water represented about one-half of daily fluid intakes for boys and girls, according to what was already described for these population groups in a similar French study[14]. Percentages were also similar in the case of milk and milk products and sweet regular beverages between the two studies. However, in a Brazilian study[23] performed in the same population groups, total daily fluid volume was higher on average, representing plain water a third of the total volume.

In our study, most beverages were ingested during main meals, and this was also observed in a previous Brazilian study[23]. Plain water was the main fluid consumed during main meals. However, American children of all ages were reported to more likely consume other beverages rather than plain water during main meals[24].

The present study is subject to some limitations. They are mainly related with intrinsic aspects of sampling. As the participants were recruited as being part of a database, only individuals having telephone number were included. Therefore, very low socioeconomic groups could be underrepresented. The most important strength is that this quota-based sample method is recognized as the best method to evaluate intakes in a representative sample[25]. Moreover, using 7 days-records to register the fluid consumption could be considered as an important strength (collecting data from both weekend and weekdays).

Conclusions

This study shows valuable data on fluid intake in Spanish children and adolescents. From a public health point of view, the most important obtained data is the very high percentage of this young population who did not meet the EFSA recommendations for total water intake. In our sample, water was the main contributor to total fluid intake, followed by milk and derivates and sweet regular beverages. No differences in consumption patterns were found according to gender. Consumption of hot beverages as well as sweet regular and sweet light beverages increased with age, while milk and milk derivates consumption decreased.

The recommendation generated from these results should be the increase in plain water consumption in these populations, as a number of studies have demonstrated that drinking water can improve cognitive functions, and consuming water instead of sugar-sweetened beverages with added sugar, can also prevent dental caries and may avoid the excess of weight gain[26].

Future research should observe longitudinal changes in different characterized populations (by socioeconomic status, level of physical activity, general diet quality index...) to determine whether the long-term contribution of beverages and the consumption time could impact health from the early stages of life.

Aknowledgements

The data about beverage intake were collected by TNS.

Conflict of interests

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Original / *Otros*

Fluid intake from beverages in Spanish adults; cross-sectional study

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Abstract

Introduction: **Dietary questionnaires usually only assess the intake of drinks that provide calories, but do not accurately evaluate total fluid or water intake. The evaluation of the fluid consumption pattern of a population has been the main objective of only a very few studies.**

Objective: **To evaluate the total fluid intake from different types of beverages in Spanish adults.**

Methods: **A total of 1,262 adults aged 18-70 years were randomly recruited from all Spanish regions. The information about the quantity and quality of daily fluid intake from different types of beverages was collected using a 24h fluid-specific diary over 7 consecutive days.**

Results: **50.4% of the study population had a fluid intake < 80% of the EFSA recommendations for total water intake. The odds of meeting the recommendations of total fluid intake were higher in women [OR: 2.48; 95%CI: 1.81-3.40], and in those with higher leisure-time physical activity (3-4 times/week [OR: 1.57; 95%CI: 1.01-2.46]; 5 times/week or more [OR: 1.97; 95%CI: 1.37-2.83]). Women consumed significantly more hot and sweet light beverages. However, men consumed significantly more sweet regular and alcoholic drinks. A significant higher percentage of young and normal/underweight subjects exceed the WHO recommendations for free sugars (> 10% total energy intake) from beverages alone.**

Conclusion: **Half of the adults studied do not meet the EFSA fluid intake recommendations. Water is the main fluid consumed. Differences in the pattern of fluid consumption were observed between ages and genders. A quarter of the population studied consumes from beverages alone already more sugar than recommended from the total diet.**

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Key words: *Fluid intake. Spain. Beverages. Water. Adult.*

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INGESTA DE LÍQUIDOS A PARTIR DE BEBIDAS EN ADULTOS ESPAÑOLES; ESTUDIO TRANSVERSAL

Resumen

Introducción: **Los cuestionarios dietéticos, solamente evalúan la ingesta de bebidas calóricas. Sin embargo, no evalúan adecuadamente la ingesta total de líquidos o de agua.**

Objetivo: **Evaluar la ingesta total de líquidos procedente de diferentes tipos de bebidas, en adultos españoles.**

Métodos: **1.262 adultos (18-70 años) fueron seleccionados al azar en regiones españolas. La información sobre la cantidad y calidad de la ingesta diaria de líquidos se recogió mediante un registro de 24 horas específico para la evaluación de fluidos durante 7 días consecutivos.**

Resultados: **La ingesta de agua a partir de diferentes bebidas estaba por debajo de las recomendaciones de la EFSA en el 50,4% de la población. La probabilidad de cumplir las recomendaciones de la EFSA para la ingesta de agua fue mayor en mujeres [OR: 2.48, IC95%: 1.81-3.40], y participantes con mayor practica de actividad física (3-4 veces/semana [OR: 1,5, IC95%: 1.01-2.46]; 5 o más veces/semana [OR: 1.97, IC95%: 1.37-2.83]). Las mujeres consumían más bebidas calientes y refrescos light. El consumo de refrescos regulares y de bebidas alcohólicas fue mayor en los hombres. Un mayor porcentaje de hombres, jóvenes y participantes con IMC < 30 kg/m² consumían azúcar procedente de bebidas, por encima de las recomendaciones de la OMS.**

Discusión: **La mitad de la población estudiada no cumple las recomendaciones de la EFSA para la ingesta de fluidos. El agua embotellada o del grifo es la principal bebida consumida. Existen diferencias en el consumo de bebidas en relación a la edad y género. Una cuarta parte de la población estudiada consume un exceso de azúcar procedente de las bebidas.**

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Palabras clave: *Ingesta de líquidos. España. Bebidas. Agua. Adultos.*

Introduction

Water is a natural resource that is essential for life and for human daily nutrition[1]. Total body water represents between 50% and 70% of total body weight[2,3], and is therefore the greatest component of the human body[4]. Body water is essential for the physiological processes of digestion, absorption, metabolism and elimination of non-digestible metabolic wastes, and also for the structure and function of the circulatory system. It also transports nutrients and other body substances, and directly helps to maintain body temperature[5].

It is assumed that the contribution of food to total water intake is approximately 20%, whereas fluids, including tap and bottled water and other types of beverages, provide 80%[6]. Fluids provide not only water but also minerals and other nutrients. For example, water, especially natural mineral water, may provide calcium, magnesium and sodium; tea provides flavonoids, antioxidants and a few micronutrients, and milk provides proteins, calcium and vitamins. In fact, some fluids can provide micronutrient levels comparable with those of some natural foods[7]. The excess or deficiency of these compounds provided by different types of beverages can determine the state of health or disease. For example, a meta-analysis in 2010 demonstrated that a high consumption of sugar-sweetened beverages is associated with the presence of type II diabetes and metabolic syndrome, in part because of their contribution to weight gain[8].

Estimating the total fluid intake and real beverage pattern of a population is a real challenge to nutritional epidemiology. Dietary questionnaires are given to assess food intake but not to assess fluid consumption as a whole, because they usually focus only on the intake of solid foods and drinks providing calories. For this reason and because fluids are often consumed outside mealtimes, and are not perceived as a food, fluid intake tends to be underestimated[9-12]. This may explain the important intra and inter-individual differences observed in the amount and pattern of fluid intake in different populations[4,13-16]. For example, data collected by the same method showed that the main sources of fluid intake are water, sugar-sweetened beverages and hot drinks in Canadian[16], Mexican[17,18] and United Kingdom populations[19], respectively. The main aim of the present study is to evaluate the total fluid and sugar intake provided by different types of beverages in Spain, to assess the percentage of individuals complying with the EFSA recommendations for total fluid intake and the WHO recommendations for sugars coming from total diet, and to assess the associated determinants of the total fluid intake in adult individuals.

Methods

Design and study population

The present study is a cross-sectional analysis of Spanish data, designed to assess the sources of fluid consumption, from water to different types of beverages, and the association of this consumption with lifestyle and health. The study took place between march and may 2012, and 1,502 participants were randomly recruited from a database of voluntary individuals for population surveys after they had been stratified by age, gender, region (except Ceuta, Melilla and Canary Islands), habitat (rural or urban), educational and socioeconomic level.

Participants working in advertising, marketing, market research, media or manufacture, distribution and sale of different types of beverages, participants reporting a mean fluid intake below 0.4 L or higher than 6 L daily, and those participants that did not complete the fluid intake record were excluded (n = 240). So, the effective sample size for these analyses was 1,262 participants, all of whom provided informed consent.

Assessment of fluid intake

A fluid-specific record was provided to all participants so that they could collect information on their usual intake of fluids over 7 consecutive days. The data were collected at two different times: a first interview at home, when the record was delivered and explained, and a second visit after 7 days, when the completed questionnaire was collected after the interviewer had checked it with the participants. The record asked participants when they consumed fluids during the day, what beverages they consumed and in what volumes using standard portion sizes (one standard serving, cup, glass, can, bottle, etc). Sugar from beverages was calculated using updated Spanish food composition tables[20]. The addition (by hand) of sugar to each beverage was also evaluated and participants were asked to state the number of teaspoons used. The total sugar provided by beverages was calculated as the sum of the amount contained in the beverage and added by the participant.

There were eleven possible responses to the question "moment of fluid consumption": Just after you wake up, at breakfast, during the morning, just before the lunch, at lunch, during the afternoon, just before dinner, at dinner, after dinner, just before going to bed, during the night. The intake of fluid *outside the main meals* at whatever time was regarded as being different from breakfast, lunch and dinner.

The questionnaire items on beverages included: water (tap water, filtered tap water, natural mineral water, sparkling natural mineral water, flavoured water, water from a fountain); hot beverages (coffee, white coffee, espresso with a drop of milk, cappuccino, tea, beverages made from cereals, other infusions and hot beverages); milk and milk derivates (milk, milkshakes, milkshakes with juice, liquid yogurt, other milk drinks); juices (home-made juice, bottled juice, nectars, nectar without added sugar, other fruit drinks); sweet regular beverages: carbonated soft drinks (cola, orange, lemon, bitter, tonic water, other flavours) non-

carbonated soft-drinks (orange, lemon, sports drinks, energy drinks, regular iced tea, other flavours), other sugared soft drinks; sweet light beverages: diet carbonated soft drinks (cola, orange, lemon, other flavours), diet non-carbonated soft drinks (orange, lemon, diet iced tea), other diet soft drinks; and alcoholic drinks (beer, alcohol-free beer, lemon beer, wine, wine with soda, alcoholic mixed drinks, other alcoholic drinks).

The percentage of individuals who did not follow the recommendations of the European Food Safety Agency (EFSA) for total water intake was calculated. The EFSA recommends that men should have a total water intake of 2.5 L every day and women 2 L. This water can come from food but also from different types of beverage. As foods usually contribute about 20% of water intake, the EFSA recommendations for total fluid intake in men is 2 L/day and women 1.6 L/day of beverages, of which preferably water[21], since water is the preferred beverage to fulfil daily water needs according to a guidance system in the United States[7].

Assessment of other variables and lifestyle factors

Leisure-time physical activity of more than thirty minutes a day was evaluated with a self-reported questionnaire. There were four possible responses: five times a week or more, between three and four times a week, between once and twice a week, and once every two weeks or less. In addition, variables such as marital status, socioeconomic characteristics, region, habitat (urban or rural) and education level were also assessed. The Institute of Medicine (IOM) equations were used to estimate the total energy expenditure of each individual[22], so that the percentage of individuals consuming more than 10% of energy requirements as free sugar, as recommended by WHO, could also be calculated[23].

Assessment of body composition

Height in metres (m) and weight in kilograms (kg) were evaluated with a self-reported questionnaire. With these values, body mass index (BMI) was calculated in kg/m^2.

Statistical analysis

All the data are presented either as means and 95% confidence intervals (CI) for continuous variables or numbers and percentages for dichotomous variables. We compared the distribution of the selected characteristics between groups using 2 tests for categorical variables or Student's t-tests or analysis of variance (ANOVA), as appropriate, for continuous variables. The Bonferroni post-hoc test was used to correct for multiple comparisons. The odds ratio for meeting the EFSA recommendations or not for water intake (dependent variable) was assessed for several variables by logistic regression models adjusted for gender, age (years), body mass index (kg/m^2), socioeconomic characteristics (lower and middle-low, middle, upper-middle and high), habitat (5,000-30,000 inhabitants, 30,000-200,000 inhabitants, more than 200,000 inhabitants), educational level (primary education, secondary education, high education) and leisure-time physical activity (once every 2 weeks or less, once or twice per week, 3-4 times/week and ≥ 5 times/week). All statistical tests were two-tailed and the significance level was set at $P < 0.05$. All analyses were performed using the SPSS software version 19.0 (SPSS Inc, Chicago, IL).

Results

A total of 1,262 participants (630 men and 632 women) took part with a mean age of 43 years and recruited from all over Spain (except Ceuta, Melilla and the Canary Islands). There were no significant differences in the proportion of individuals in different age categories, region, type of habitat and educational level between the study sample and the Spanish population as a whole. No gender differences were observed in the prevalence of age categories, type of habitat or education level. The baseline characteristics of participants are summarized in table I. The body-mass-index and the proportion of individuals with overweight or obesity was higher in men than in women. Most of the study population were of middle socioeconomic status and secondary educational level, and reported low leisure-time physical activity. Women were more sedentary than men.

The mean volume consumed of water (tap water, filtered tap water, natural mineral water, sparkling mineral water, flavoured water and fountain water) was 1,011 ml/day for the whole population (1,050 ml for women and 973 ml for men). Water intake from different types of beverages was below the EFSA recommendations (1,600 ml/d for women and 2,000 ml/d for men) in 50.4% of the whole population (41.6% of women and 59.2% of men). In total, 40.3% of the study population (31% of the women and 49.5% of the men) consumed < 90% of EFSA recommended for total fluid intake. 20.1% of the whole population (20.9% of the women and 19.4% of the men) consumed between 90 and 110% of the total EFSA recommendations, and 39.6% of whole population (48.1% of the women and 31.1% of the men) consumed > 110% of the EFSA recommendations ($P < 0.001$) (data not shown).

The odds of meeting the EFSA recommendations for water intake (table II) was higher in women [OR: 2.48; 95% CI: 1.81-3.40], and in participants with higher leisure-time physical activity (3-4 times a week [OR: 1.57; 95% CI: 1.01-2.46]; 5 times a week or more [OR: 1.97; 95% CI: 1.37-2.83].

Table III shows the total daily fluid intake and the amount of each type of beverage consumed according

Table I
General characteristics of the study population

Baseline variables	*All population (n = 1,262)*	*Women (n = 632)*	*Men (n = 630)*	*P value*[a]
Age, years	43 (41.9, 43.5)	43 (41.5, 43.7)	43 (41.8, 43.7)	0.74
Age categories,% (n)				0.76
18 to 35 years	34 (431)	33 (212)	35 (219)	
36 to 50 years	35 (447)	37 (233)	34 (214)	
51 to 65 years	24 (305)	24 (149)	25 (156)	
66 to 70 years	6 (79)	6 (38)	6 (41)	
BMI, kg/m²	25.6 (25.4, 25.8)	25.1 (24.7, 25.4)	26.1 (25.8, 26.4)	< 0.001
BMI classification, % (n)[b]				< 0.001
Under and normal weight	51 (638)	58 (367)	43 (271)	
Overweight	36 (453)	28 (177)	44 (276)	
Obesity	13 (171)	14 (88)	13 (83)	
Region, % (n)				0.99
Region 1 (Catalonia/Aragon)	12 (156)	12 (76)	13 (80)	
Region 2 (east)	18 (226)	18 (116)	17 (110)	
Region 3 (south)	20 (251)	19 (122)	20 (129)	
Region 4 (centre)	7 (87)	7 (45)	7 (42)	
Region 5 (north-centre)	8 (98)	8 (48)	8 (50)	
Region 6 (northwest)	9 (115)	10 (60)	9 (55)	
Barcelona and Madrid	26 (329)	26 (165)	26 (164)	
Habitat, % (n)				0.27
5,000 to 30,000 inhabitants	31 (389)	31 (197)	30 (192)	
30,000 a 200,000 inhabitants	36 (450)	37 (236)	34 (214)	
More than 200,000 inhabitants	33 (423)	32 (199)	36 (224)	
Socioeconomic level, % (n)				0.004
Lower and middle-low	31 (391)	34 (215)	28 (176)	
Middle	44 (552)	45 (281)	43 (271)	
Upper-middle and high	25 (319)	22 (136)	29 (183)	
Educational level, % (n)				0.06
Primary education	17 (217)	17 (104)	18 (113)	
Secondary education	64 (803)	67 (421)	61 (382)	
Higher education	19 (242)	17 (107)	21 (135)	
Leisure-time physical activity, % (n)				< 0.001
1 time every 2 weeks or less	41 (521)	48 (301)	35 (220)	
1-2 times a week	20 (246)	16 (100)	23 (146)	
3-4 times a week	15 (191)	12 (78)	18 (113)	
5 times a week or more	24 (304)	24 (153)	24 (151)	

Data expressed as means (95% CI) or percentages (n). Abbreviations: BMI, body mass index. [a]P values for comparisons between groups were tested by Student's t-test or χ^2 as appropriate.
[b]BMI (kg/m²) was divided into the following categories: underweight and normal weight (BMI < 24.9 kg/m²), overweight (BMI between 25-30 kg/m²), and obesity (BMI > 30.0 kg/m²).

to gender. Women consumed significantly more hot and sweet light beverages than men. Consumption of sweet regular beverages and alcoholic drinks was significantly higher in men than in women. No significant differences were observed for total fluid intake or water intake between genders.

Total fluid intake and beverage consumption according to age ranges are shown in table IV. Younger participants (18-35 years) consumed fewer hot beverages, more fruit juices and more sweet regular beverages than others age categories ($P < 0.05$). Participants aged between 51-65 years consumed significantly more alcoholic drinks than younger participants. There were no significant differences in total fluid intake or water intake between age categories.

The total daily intake of different types of beverage and when they were consumed (during the main meals/outside the main meals) are described in table V. No significant differences were observed in the times at which water and juices were consumed throughout the study population for either women or men.

The consumption of hot beverages, sweet regular beverages, and alcoholic drinks was significantly higher during the main meals than at other times of the day. During the main meals –for the whole population and women, but not for men–, the intake of sweet light beverages, and milk and derivates was significantly greater than at other times. In both genders, total fluid intake was significantly higher during the main meals.

Table II
Association (Odds ratio) between compliance with EFSA recommendations for total daily fluid intake and several socio-demographic variables

Variables	*All population (n = 1,262)*	*Women (n = 632)*	*Men (n = 630)*
Gender [a]	2.48 (1.81-3.40)	-	-
Age	0.99 (0.98-1.00)	0.99 (0.98, 1.01)	0.99 (0.97-1.01)
BMI	0.99 (0.96-1.03)	1.00 (0.96-1.05)	1.05 (0.98-1.12)
Habitat			
5,000 to 30,000 inhabitants	1 (ref)	1 (ref)	1 (ref)
30,000 to 200,000 inhabitants	1.30 (0.91-1.85)	1.31 (0.84-2.04)	1.35 (0.73-2.49)
More than 200,000 inhabitants	0.71 (0.48-1.05)	0.63 (0.38-1.05)	0.83 (0.43-1.60)
Socioeconomic level			
Lower and middle-low	1 (ref)	1 (ref)	1 (ref)
Middle	1.12 (0.76-1.64)	1.04 (0.65-1.67)	1.16 (0.59-2.29)
Upper-middle and high	1.22 (0.75-1.99)	1.33 (0.73-2.44)	1.01 (0.43-2.40)
Educational level			
Primary education	1 (ref)	1 (ref)	1 (ref)
Secondary education	0.92 (0.57-1.15)	0.97 (0.53-1.78)	0.90 (0.41-1.98)
Higher education	1.06 (0.56-1.99)	1.38 (0.62-3.09)	0.81 (0.28-2.34)
Leisure-time physical activity			
1 time every 2 weeks or less	1 (ref)	1 (ref)	1 (ref)
1-2 times a week	0.91 (0.57-1.43)	0.98 (0.55-1.74)	0.85 (0.39-1.86)
3-4 times a week	1.58 (1.01-2.46)	1.24 (0.68-2.25)	2.13 (1.05-4.32)
5 times a week	1.97 (1.37-2.86)	1.85 (1.18-2.89)	2.28 (1.19-4.36)

Data expressed as ORs (95% CI). [a]Gender was coded as 0 for men and 1 for women.

Table III
Total daily consumption of different types of beverage (ml/day) in all population and stratified by gender

Variables	*All population (n = 1,262)*	*Women (n = 632)*	*Men (n = 630)*	*P value*[a]
Water	1011 (973, 1049)	1050 (997, 1103)	973 (918, 1027)	0.05
Hot beverages	305 (290, 320)	349 (327, 371)	261 (242, 279)	<0.001
Milk and derivates	103 (92, 114)	94 (83, 106)	111 (93, 129)	0.14
Juices	94 (84, 104)	88 (77, 99)	101 (85, 117)	0.20
Sweet regular beverages	152 (136, 167)	128 (111, 145)	176 (150, 201)	0.003
Sweet light beverages	38 (28, 48)	50 (35, 64)	26 (12, 40)	0.02
Alcoholic drinks	195 (176, 215)	103 (86, 121)	288 (255, 320)	<0.001
Beer and wine	179 (161, 197)	93 (76, 109)	265 (234,297)	<0.001
Spirit drinks	16 (13, 19)	10 (6, 14)	22 (17, 27)	<0.001
Total daily fluid volume	1901 (1856, 1946)	1865 (1804, 1927)	1937 (1872, 2003)	0.12

Data expressed as means (95% CI). [a]P values for comparisons between gender were tested by Student's t-test.

When stratified by BMI, obese participants consumed more hot beverages and less milk and milk derivates than participants from the other BMI categories ($P < 0.05$). Overweight individuals consumed more alcoholic drinks than those with obesity or normal weight ($P < 0.05$) (data not shown).

The whole population consumed a total of 46.7 g/d (187 kcal/d) of sugar added by hand and contained in beverages, men consumed 52 g/d (208 kcal) and women 41.2 g/d (165 kcal) ($P < 0.001$).

The consumption of calories from sweet regular beverages (48.5 kcal in women; 67.4 kcal in men) and alcoholic drinks (13.4 kcal in women; 32.9 kcal in men) was significantly higher in males than females. No significant differences between genders were found for the other beverages (data not shown).

Table VI shows the percentage of participants who consumed more sugar than is recommended by WHO[24] only from beverages (less than 10% of the estimated energy requirements). Younger participants and people with normal or underweight more frequently consume sugar over the recommendations ($P < 0.001$) than old individuals or people with overweight. Compared to men, a higher percentage of women consumed sugar above the recommendations ($P = 0.08$).

Discussion

The main objective of the present pioneering study is to estimate the total fluid intake and the real fluid pattern of a large sample of Spanish individuals. We re-

Table IV
Total daily consumption of different types of beverages (ml/day) stratified by age range

Variables	*18-35 years (n = 431)*	*36-50 years (n = 447)*	*51-65 years (n = 305)*	*66-70 years (n = 79)*	*P value*[a]
Water	1037 (972, 1102)	1019 (953, 1084)	958 (884, 1032)	1036 (867, 1204)	0.46
Hot beverages	224 (202, 247)[b]	330 (305, 356)[c]	370 (340, 399)[c]	352 (297, 407)[c]	< 0.001
Milk and derivates	141 (117, 165)[b]	89 (73, 104)[c]	76 (60, 93)[c]	76 (42, 110)[c]	< 0.001
Juices	117 (101, 134)[b]	96 (76, 115)	64 (50, 79)[c]	76 (45, 107)	0.001
Sweet regular beverages	233 (199, 266)[b]	144 (121, 168)[c, d]	71 (49, 92)[c, e]	79 (30, 104)[c]	< 0.001
Sweet light beverages	53 (35, 71)	38 (25, 52)	23 (0, 49)	8 (0, 17)	0.07
Alcoholic drinks	140 (116, 164)[b]	200 (168, 231)	271 (220, 322)[c]	181 (120, 242)	< 0.001
Beer and wine	113 (92, 135)[b]	189 (159, 220)[c]	257 (207, 306)[c]	179 (118, 197)	< 0.001
Spirit drinks	26 (19, 33)[b]	10 (6, 14)[c]	14 (8, 20)[c]	2 (0, 5)[c]	< 0.001
Total daily fluid volume	1948 (1867, 2028)	1919 (1843, 1994)	1836 (1749, 1923)	1798 (1626, 1970)	0.18

Data expressed as means (95% CI). [a]P values for comparisons between groups were tested by bivariate analysis of variance (ANOVA) followed by post hoc tests with the Bonferroni correction.
P < 0.05 for differences between letters ([b] versus [c] and [d] versus [e]).

Table V
Total daily intake of different types of beverages (ml/day) by moment of consumption

	All population (n = 1,262)			*Women (n = 632)*			*Men (n = 630)*		
Variables	*During the main meal*	*Outside the main meal*	*P value*[a]	*During the main meal*	*Outside the main meal*	*P value*[a]	*During the main meal*	*Outside the main meal*	*P value*[a]
Water	503 (481, 525)	508 (479, 536)	0.78	513 (484, 543)	536 (495, 577)	0.37	492 (460, 525)	480 (440, 520)	0.60
Hot beverages	173 (164, 182)	131 (121, 141)	< 0.001	186 (174, 198)	163 (147, 179)	0.01	160 (147, 173)	100 (88, 111)	< 0.001
Milk and derivates	59 (52, 65)	44 (36, 52)	0.003	55 (46, 63)	39 (32, 47)	0.005	62 (52, 72)	48 (34, 62)	0.09
Juices	48 (42, 55)	45 (39, 51)	0.44	43 (35, 51)	45 (37, 52)	0.71	54 (43, 66)	46 (37, 55)	0.18
Sweet regular beverages	103 (91, 114)	49 (42, 56)	< 0.001	90 (75 105)	38 (31, 45)	< 0.001	116 (97, 134)	60 (47, 72)	< 0.001
Sweet light beverages	25 (18, 31)	12 (7, 18)	< 0.001	34 (23, 45)	15 (9, 20)	< 0.001	15 (9, 21)	10 (1, 20)	0.24
Alcoholic drinks	108 (96, 120)	87 (76, 98)	0.001	60 (49, 72)	43 (34, 52)	0.002	156 (136, 177)	131 (112, 150)	0.03
Beer and wine	106 (95, 118)	72 (62, 82)	< 0.001	59 (47, 70)	33 (25, 41)	< 0.001	154 (134, 175)	111 (93, 128)	< 0.001
Spirit drinks	1 (1, 2)	14 (11, 17)	< 0.001	1 (0, 2)	9 (5, 12)	< 0.001	2 (0, 3)	20 (15, 24)	< 0.001
Total daily fluid volume	1022 (1000, 1044)	879 (844, 914)	< 0.001	984 (955, 1013)	881 (832, 929)	< 0.001	1059 (1027, 1092)	877 (826, 928)	< 0.001

Data expressed as mean (95% CI). [a]P values for comparisons between during and outside meals were tested by Student's t-test.

Tabla VI
Participants exceeding the WHO recommendation of < 10% energy from free sugar, from beverages consumption

	n	*%*	*P value*[a]
Gender			
Women (n = 632)	185	29.3	0.08
Men (n = 630)	156	24.9	
Age, categories			
18-35 years old (n = 431)	164	38.1	<0.001
36-50 years old (n = 447)	122	27.3	
51-65 years old (n = 305)	47	15.4	
66-70 years old (n = 79)	9	11.4	
BMI, categories			
Under and normal weight (n = 638)	204	32	<0.001
Overweight (n = 453)	101	22.3	
Obesity (n = 171)	37	21.6	

[a]P values for comparisons between groups were tested by Student's t-test or χ^2 as appropriate. * Sugar recommendations: < 10% of the daily energy intake[23].

port for the first time that approximately half of the adult population do not cover the total water intake recommended by the EFSA[21].

Our results are in agreement with the data collected by the EFSA[9] evaluating fluid consumption in 13 European countries and which show that only Denmark and Germany consumed a mean of at least two liters of water per individual from all types of beverages. Our findings also add new knowledge to the current scientific literature made by other research[9,13,24], showing that a considerable proportion of Spanish adults do not have a healthy fluid consumption pattern.

Interestingly, in our study compliance with recommendations for total fluid intake was mainly associated with physical activity and with being a woman, but not with education, socioeconomic status or type of habitat (rural or urban). The higher compliance with recommendations for total fluid intake by people who practice physical activity is partly due to the fact that they tend to drink more as they have increased fluid demands[25,26]. The social determinants of the consumption

of water and other types of beverage may explain why women tend to comply more with recommendations for total fluid intake. In fact, women tend to have a better lifestyle pattern[27] and, in general, adults with a healthier dietary pattern usually have a healthier fluid pattern,[28] which leads to greater water consumption[28].

In the present study, fluid consumption was assessed with a 24 h fluid-specific diary over 7 consecutive days. Not only did it assess the type and amount of fluid ingested, but also the times at which beverages were consumed and the amount of sugar added by hand to drinks. The same methodology was used in a French study, and both studies found that water consumption represented more than 50% of the total daily fluid intake in all age groups and in both genders[29]. This is important because plain water is regarded as the healthiest option for hydration, and increasing water consumption is a recommended strategy for reducing energy intake[30].

Total fluid intake in our study was non-significantly higher in men than in women. This is in agreement with other studies evaluating fluid intake in other populations[4,14,16]. However, in our study, the percentage of women who met the EFSA recommendations was higher than the percentage of men (58.4% of women, but only 40.8% of men).

Several of our findings about the pattern of fluid consumption in our population deserve comment. Men generally consumed more of all type of beverages with some exceptions: for example, total water (tap water or mineral water), hot beverages and sweet light beverages, all without or few calories. These finding have also been observed in other populations[28], which suggests that women are more aware of the need to consume fewer calories in the form of drinks to avoid overweight or obesity[31,32]. Age is also an important determinant of the general fluid pattern. As in other studies[13,29,33], the mean total fluid intake in our study progressively decreased as age increased. This can probably be explained by a decrease in the perception of thirst with age[26,34], but social determinants cannot be discounted. The type of fluid consumed also changed with age. The intake of milk, juices, and sweet beverages (regular or light) decreased with age, whereas the intake of hot beverages increased. The decrease in the mean milk intake observed in our population may be partly due to the fact that the percentage of individuals with lactase deficiency is higher in elderly people[35,36].

As reported in other studies in adults and seniors[29,37], more beverages were consumed during the main meals than at other times of the day. For example, Bellisle[29] reported that fluids were consumed more at breakfast, dinner and lunch than at other secondary meals. In our study only spirits were consumed more outside the main meals, and water was consumed in similar amounts.

Beverages can account for a substantial share of daily calories. Most of these calories come from sweet regular beverages, alcohol drinks, milk and milk derivates, and juices[16]. Approximately 27% of our study population consumed more sugar than recommended by the WHO (> 10% of the total daily calories) only from the sugar in beverages (intrinsic or added)[23]. These results are alarming if it is taken into account that other studies show that an excessive consumption of calories from sugar has unhealthy effects[8,38,39].

Several potential limitations of our study deserve comment. The main limitation is that our population is probably not representative of the general Spanish population because individuals were randomly recruited from a database of volunteers for population surveys. Despite this, the final distribution of the individuals studied among age groups, gender, region of Spain and educational categories is very similar to the real distribution of the population in Spain. The second limitation has to do with the cross-sectional design of the study, which means that no conclusions about cause/effect relationships can be drawn. Third, the fact that anthropometric measures were self-reported and not measured may produce some systematic bias. Finally, the 24 h fluid-specific diary over 7 consecutive days must be validated in the future with gold standard methods, so that total fluid intake can be reliably assessed.

One of the strengths of this study is that it uses a 24 h fluid-specific diary over 7 consecutive days that allows to assess the total fluid intake and real fluid pattern. Also, the population was randomly recruited using the quota-based sample method from a database of volunteers for population surveys, which led to a large representative sample of Spanish adults in relation to the stratum considered[40]. Moreover, this report is the first specific description of total fluid intake in Spanish adults.

Total beverage consumption and types of beverage consumed showed some differences between genders and age groups. Approximately half of the Spanish population does not meet the EFSA recommendations for total fluid intake. Water is the main beverage consumed, but a significant amount of dietary calories are provided by other beverages. A quarter of the studied population consume more sugar from beverages than is recommended by the WHO (> 10% of total daily calories)[23]. There is enough evidence to prove that replacing sweet drinks by water has beneficial effects on health[30,41] so it is imperative to promote the consumption of water, especially in children, parents and educators, and also elderly people, and limit the intake of sugar from beverages in Spain. Longitudinal studies should be carried out in various populations to determine the chronic contribution of fluid consumption to health.

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The data about beverage intake were collected by TNS.

Conflict of interests

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Original / *Otros*

Fluid intake in Mexican adults; a cross-sectional study

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Abstract

Introduction: **An adequate hydration is critical for a series of body functions, including proper regulation of core body temperature, elimination of waste metabolites by the kidney and maintenance of normal physical and cognitive functions. Some institutions have set recommendations for adequate intake of water, but these recommendations vary widely.**

Objective: **To estimate the usual daily consumption of fluids (water and all other beverages) by a selective sample of Mexican population.**

Methods: Cross-sectional sample of 1,492 male and female adults between 18-65 years of age, drawn from 16 cities throughout Mexico. Self-reported fluid intake data collected over a 7-day consecutive period, recording intake of water, milk and derivatives, hot beverages, sugar sweetened beverages (SSB), alcoholic beverages and others.

Results: **We found that 87.5% of adult males and 65.4% of adult females reported drinking below their recommended daily fluid intake (3 L for males and 2 L for females), and in 80% of the population SSB, not including hot beverages or milk and derivatives, accounted for a larger amount and proportion of fluid intake than plain water. Sixty-five percent of adult males and 66% of adult females consumed more than 10% of their estimated daily caloric intake from fluids. Fluid intake did not differ significantly by gender, but showed a declining trend with age.**

Conclusion: **Our findings may have important implications for policy recommendations, as part of comprehensive strategies to promote the adoption of healthy life styles, in this case, promoting consumption of plain water while discouraging excessive consumption of caloric beverages.**

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Key words: *Fluid intake. Water. Sugar sweetened beverages. Adults. Mexico.*

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INGESTA DE LÍQUIDOSPOR ADULTOS MEXICANOS; UN ESTUDIO TRANSVERSAL

Resumen

Introducción: **Un adecuada hidratación resulta fundamental para el buen funcionamiento de diversas funciones orgánicas, incluyendo la regulación de la temperatura corporal, la eliminación de metabolitos por los riñones, y el funcionamiento adecuado de diversas funciones físicas y cognitivas. Algunas instituciones han establecido recomendaciones para una ingesta adecuada de agua y otros líquidos, pero estas recomendaciones varían ampliamente.**

Objetivo: **Estimar el consumo diario usual de líquidos (incluyendo agua otras bebidas), en una muestra seleccionada de adultos mexicanos.**

Métodos: **Estudio transversal de 1.492 hombres y mujeres adultas con edades entre 18-65 años, reclutados en 16 ciudades distribuidas a lo largo de todo el país. Se recolectó información auto-reportada sobre la ingesta de líquidos a lo largo de un período consecutivo de 7 días, registrando el consumo de agua, leche y derivados, bebidas calientes, bebidas azucaradas, bebidas alcohólicas, y otras bebidas.**

Resultados: **Encontramos que el 87,5% de los hombres y el 65,4% de las mujeres registraron una ingesta de líquidos por debajo de la recomendación vigente para estos grupos, que es de 3 L/día para hombres y 2 L/día para mujeres. Además, en el 80% de la población participante la ingestión de bebidas azucaradas, no incluyendo la leche y derivados ni las bebidas calientes, fue mayor que la de agua simple. El 65% de los hombres y el 66% de las mujeres consumieron más de la recomendación del 10% de energía correspondiente a su requerimiento calórico estimado a partir de bebidas. La ingestión de líquidos no mostró diferencias estadísticamente significativas de acuerdo al género, pero mostró una tendencia significativa a declinar con la edad.**

Conclusión: **Nuestros resultados tiene importancia para orientar políticas publicas como parte de recomendaciones integrales que promuevan la adopción de estilos saludables de vida, particularmente en lo que concierne a fomentar el consumo de agua simple y a desaconsejar el consumo exagerado de bebidas con contenido calórico.**

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Palabras clave: *Ingesta de líquidos. Agua. Bebidas azucaradas. México.*

Introduction

An adequate hydration is critical for a series of body functions, including proper regulation of core body temperature, elimination of waste metabolites by the kidney and maintenance of normal physical and cognitive functions[1-3]. Some institutions have set an adequate intake (AI) for total water intake (water from food and from fluids), but these recommendations vary widely. For example, the European Food Safety Agency[4] set the AI for total water intake at 2.5 L/day for men older than 14 years and 2 L/d for women older than 14 years[4], while AI for total water intake set by the Institute of Medicine (IOM) of the United States of America is 3.7 L/day for men and 2.7 L/day for women[5]. In Mexico, a panel of experts convened by the Ministry of Health recommends to consume 0.75-2 L (6-8 glasses) of water per day. As for other fluids, the panel specifically recommends that consumption of higher energy content beverages, mainly coming from sugar-sweetened beverages (SSB), should be discouraged[6]. This group laid specific emphasis on the promotion of consumption of water and low-calorie beverages, strongly arguing against consumption of high-energy beverages, and in general terms followed the recommendation for total fluid intake set forth by IOM[5]. The differences in recommendations may, in part, be due to the wide individual variation found in response to hydration needs, as fluid loss is affected by environmental factors such as ambient temperature and humidity, as well as individual factors, such as age, body size and level of physical exercise[2].

Even though AI for total water has seen set, methods to estimate daily ingestion and adequacy of water and other fluids at a population level remain elusive in the literature. A wide-extended practice that nutritionists and public health specialists have resorted to, is accounting for ingestion of fluids as part of dietary intake methods, commonly the 24-hour intake recall. While this –and other– methods have estimated that approximately 20% of total water intake comes from food, while the remaining 80% comes from fluids[7], it has also become evident that 24-hr recall methods greatly underestimate fluid intake, by as much as 0.5 L/day[8]. Recently, a fluid-specific dairy has been proposed, to collect information about fluid consumption over a 24-hour period over a 7-consecutive day span, supported by photographs or drawings of commonly used recipients of different sizes for fluids[8,9]. A proper assessment of the intake of water and other beverages is important from a public health point of view for many reasons, including the need to promote adoption of healthy life styles in order to counter the growing epidemics of chronic diseases, many of which are related to unhealthy habits of consumption of different foods and beverages[6,10-13].

The objective of this paper was to estimate the usual daily consumption of fluids (water and all other beverages) by a selective sample of Mexican population. Evaluating the quantity of fluid intake and understanding the contribution of each fluid type to total fluid intake is critically needed in order to draw conclusions about the adequacy of drinking habits. This information may help to shape up public health policies and programs oriented to the promotion of the adoption of healthy life-styles.

Methods

A cross-sectional study was carried out between the months of april and may, 2012, when the average ambient temperature in the country is around 18°C. The quota based sample was drawn from 16 cities throughout Mexico, including Chihuahua, Culiacan, Guadalajara, Hermosillo, Leon, Merida, Monterrey, Morelia, Oaxaca, Puebla, Queretaro, San Luis Potosi, Tijuana, Toluca, Mexico City and surrounding peri-urban area, and Veracruz. Quotas were set in term of age, gender, region and socio-economical levels, to allow us to identify mean fluid consumption with a confidence level of 95%, based on previous studies[14,15]. Houses to be visited were chosen at random based on the sampling frame provided by the Mexican National Institute of Geography. Inclusion criteria were defined as a healthy, male or female consenting adult, between the ages of 18-65 years old, who could read and write, and had been a regular resident of the area for the past year. Exclusion criteria included being under any kind of diet or medical treatment that may affect or modify his/her eating or drinking habits. Elimination criteria included a mean reported fluid intake below 0.4 L/day or above 6 L/day.

To register daily ingestion of water and any other fluid throughout the day the study resorted to a fluid specific intake dairy that had been previously used in similar populations (i.e., literate, Spanish-speaking adults)[15]. Participants were asked to record in the diary what type of beverage they consumed, in what size of container, what amount was consumed, and the time of day when consumption took place. Data recording went on for 7 consecutive days. To increase reporting accuracy of the consumed volume of fluids, the dairy was supported by a photographic booklet illustrating commonly used drinking containers and their volume. Upon recruitment and oral consent, a study interviewer explained how to fill in the diary, and went over the first day of beverage intake with the study participant to familiarize him/her with data entry. Interviewers visited the house again half-way through the study, to address any questions participants may have about how to register the information, and again at the end of the 7-day period, to collect the dairies and thank participants for their participation. No monetary incentive was offered for taking part in the study. Throughout the study there was a telephone hot-line available to address any question participants may have.

The beverages consumed were grouped into six broad categories: water, milk and derivatives, hot be-

verages, sugar sweetened beverages (SSB), alcoholic beverages and others. The specific beverages under each category are listed in table I. Total fluid intake was defined as the sum of these 6 categories. To calculate the proportion of participants having an inadequate fluid intake, total fluid intake provided by beverages of each subject was compared to the fluid recommendations in Mexico, based on recommendations of a group of expert nutritionists[16]. Table I also indicates which fluids were taken into consideration to calculate energy intake from added sugar coming from fluids. Information regarding the energy content of fluids was extracted from Mexican food composition tables[17]. Additions (by hand) to each beverage (e.g. sugar, honey) were not taken into account. To be able to calculate the proportion of participants consuming ≥ 10% of the energy requirements as free sugars,[13] associated with fluid intake, the assumption had to be made that men and women have on average a daily energy intake of respectively 2400 kcal/day and 1800 kcal/day[18].

Individuals who agreed to be part of the study received a detailed information about the study and its objectives, what was expected from them, as well as a disclosure of the study's provisions to preserve confidentiality, risks and benefits, and a clear explanation about their option to participate voluntarily or not in the

Table I
Description and classification of fluids consumed by Mexican adults

Classification of fluids	*Detailed fluid types*	*Fluids considered for analysis of energy intake*
Water	Still water, unflavored sparkling water, tap/filtered/ boiled water	
Milk and derivatives	Packaged (fermented milk, milk (ready-to-drink), flavored milk, yogurt milk), *atole*/*champurrado*, raw milk, powder milk, powder/syrup flavored milk, fruit shake with milk	Packaged (fermented milk, milk (ready-to-drink), flavored milk, yogurt milk), *atole*/*champurrado*, powder/syrup flavored milk, fruit shake with milk
Hot beverages	Coffee, Coffee from coffee maker (e.g.: homemade coffee, dolce gusto, others), powder coffee, vending machine coffee, restaurant/franchise coffee, homemade hot/cold tea (from tea bags), Infusions (herbal)	Coffee, Coffee from coffee maker (e.g.: homemade coffee, dolce gusto, others), vending machine coffee, restaurant/franchise coffee, powder coffee, homemade hot/cold tea (from tea bags)
Sugar sweetened beverages (SSB)	• Regular sweet beverages: flavored packaged water, flavored sparkling water, flavored water slightly fizz, flavored waters made with powder or concentrate/ syrup, fruit shake with water powder, packaged tonic/ quinine water, vitamin/ functional water, electrolyte/ saline solution beverages, sport/isotonic drinks, energetic drinks, nutritional supplement, non carbonated refreshing drinks (e.g.: Frutsi®, Boing®,…), packaged coffee ready-to-drink (canned or boxed coffee), packaged tea, powder food supplement, cola carbonated drinks, flavored carbonated drinks • Juices & derivatives: Packages fruits & vegetables juices (packages juices (fruits or vegetables), packaged orangeade, packages nectars, Eskimos/smoothies), *aguas frescas*, natural fruits & vegetables juices (natural fruit/ vegetable juices, restaurant lemonade/orangeade) • Diet sweet beverages: Packaged light juices, diet/light/zero cola carbonated drinks, diet/light/ zero flavored carbonated drinks	• Regular sweet beverages: flavored packaged water, flavored sparkling water, flavored water slightly fizz, flavored waters made with powder or concentrate/ syrup, fruit shake with water powder, packaged tonic/quinine water, vitamin/functional water, electrolyte/saline solution beverages, sport/isotonic drinks, energetic drinks, nutritional supplement, non carbonated refreshing drinks (e.g.: Frutsi®, Boing®,…), packaged coffee ready-to-drink (canned or boxed coffee), packaged tea, powder food supplement, cola carbonated drinks, flavored carbonated drinks • Juices & derivatives: Packages fruits & vegetables juices (packages juices (fruits or vegetables), packaged orangeade, packages nectars, Eskimos/ smoothies), *aguas frescas*, • Diet sweet beverages: Packaged light juices, diet/light/zero cola carbonated drinks, diet/light/zero flavored carbonated drinks
Alcoholic beverages	Beer, Wine, Aperitifs and digestives straight, packages/canned alcoholic beverages, alcoholic beverages straight (not mixed like vodka, tequila, rum, ….), aperitifs and digestives with other beverages, *clamato*-type, beer/*michelada*	Beer, Wine, Aperitifs and digestives straight, packages/canned alcoholic beverages, alcoholic beverages straight (not mixed like vodka, tequila, rum, ….), aperitifs and digestives with other beverages, *clamato*-type, beer/*michelada*
Other beverages	*Agua de arroz*, Alcohol-free beer, packaged soy drinks	Packaged soy drinks

study. After offering a full-informed description of the study, following the principles of informed consent, participants were asked for their oral approval to participate.

Statistical analysis

Analyses were performed using the SPSS software version 17.0 (SPSS Inc., Chicago, IL). Values of continuous variables are presented as the mean and standard error of mean (SEM) and values of dichotomous variables as percentages. Group comparisons were made using χ^2 tests for categorical variables or Student's t-tests or analysis of variance (ANOVA) as appropriate for the continuous variables. All statistical tests were two-tailed and the significance level was set at $p < 0.05$.

Results

The initial recruited sample consisted of 1,502 participants before applying elimination criteria. Ten participants were removed from the sample because they reported drinking either less than 0.4 L/day or more than 6 L/day, for a final sample size of 1,492 participants. The baseline characteristics of the sample population may be seen in table II.

Mean total fluid consumption of the total population was 1.85 L/day (table III). Figure 1 shows the distribution of mean total fluid intake by gender. Among men, 87.5% of the sample drank less than the recommended 3 L/day of total fluids, while 65.4% of women, drank less than the recommended 2 L/day (16). Moreover, 6% of adults did not report drinking water, while 50% of the sample consumed 0.5 L/day, and 75% of the sample consumed 1 L/day (fig. 2). Thirty-eight percent of the sam-

Table II
Socio-demographic characteristics of study sample

	Total sample n = 1,492	*Males n = 520 (35%)*	*Females n = 972 (65%)*	*P-value*
Age categories, % (n)				< 0.001
18-24 years	22 (335)	26 (137)	20 (198)	
25-35 years	23 (338)	20 (106)	24 (232)	
36-45 years	20 (300)	15 (80)	23 (220)	
46-55 years	19 (280)	21 (109)	18 (171)	
56-65 years	16 (239)	17 (88)	16 (151)	
Socio-Economic Level*, % (n)				< 0.001
ABC+	27 (402)	37 (192)	22 (210)	
C	26 (382)	27 (142)	25 (240)	
D+/D	47 (708)	36 (186)	54 (522)	
Nielsen Regions, % (n)				0.08
Region 1 (Pacific)	16 (234)	17 (86)	15 (148)	
Region 2 (North)	19 (277)	16 (83)	20 (194)	
Region 3 (Central lowlands)	16 (241)	15 (78)	17 (163)	
Region 4 (Central plateau)	17 (253)	18 (95)	16 (158)	
Region 5 (Valle of Mexico)	17 (250)	19 (98)	16 (152)	
Region 6 (Southeast)	16 (237)	15 (80)	16 (157)	

Data expressed as percentage (n).
P values for comparisons between groups were tested by 2.
* The highest level is A.

Table III
Total daily consumption of different types of fluids (ml/day) in all population and stratified by gender

Variables	*All population n = 1,492*	*Males n = 520*	*Females n = 972*	*P-value*
Water	717 (17)	672 (28)	741 (22)	0.059
Milk and derivatives	175 (5)	175 (9)	175 (6)	0.987
Hot beverages	150 (5)	150 (8)	150 (6)	0.803
Sugar sweetened beverages	583 (15)	608 (24)	566 (19)	0.152
Alcoholic beverages	37 (4)	64 (9)	22 (4)	< 0.001
Other beverages	5 (1)	3 (1)	3 (1)	0.788
Total fluid intake	1851 (25)	1847 (41)	1853 (31)	0.899

Data expressed as mean (SEM).
[a] P values for comparisons between gender were tested by student's t-test.

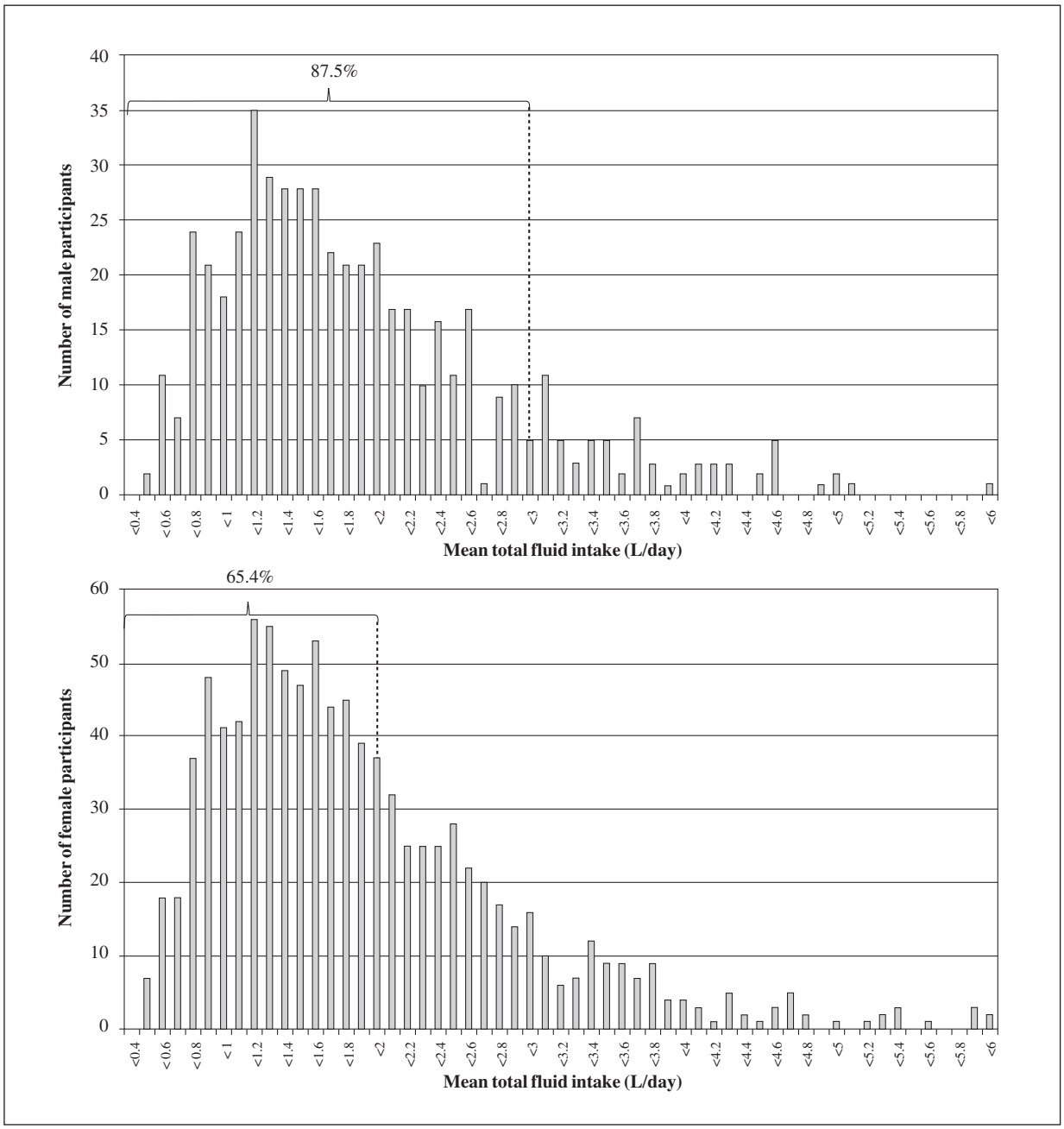


Fig. 1.—Distribution of mean total fluid intake (L/day) by adult male and female participants, indicating the proportion of participants drinking less than the recommendation on total water intake/fluid intake/water intake[16].

ple consumed 0.5 L/day of SSB, and 75.5% consumed 1 L/day. For 80% of the sample the consumed volume of SSB was larger than the volume of water (fig. 2).

There were no statistically significant differences in the mean total fluid intake and the volume of the different fluid type according to gender, with the exception of alcohol, which was consumed more by men (respectively 0.06 *vs* 0.02 L/day; p = 0.001) (table III). Males consumed an average of 0.314 L/day of SSB while females consumed an average of 0.315 L/day.

Table IV shows the mean total fluid intake and the volume of the different fluid types according to age groups. Overall, fluid consumption showed a decreasing trend by age: the highest total fluid intake was reported in the 2 youngest age groups (18-24 years 1.95 L/day; 25-35 years 1.99 L/day; $p < 0.001$ compared to any of the subsequent age groups) and the lowest mean total fluid intake was reported by the oldest age group 56-65 years 1.61 L/day; $p < 0.001$ compared to the 2 youngest groups). Not only the total fluid intake changed with age, also the volume of fluid types consumed was statistically significant different between the age groups. The consumption of hot beverages increased with age, whereas the consumption of SSB decreased (table IV).

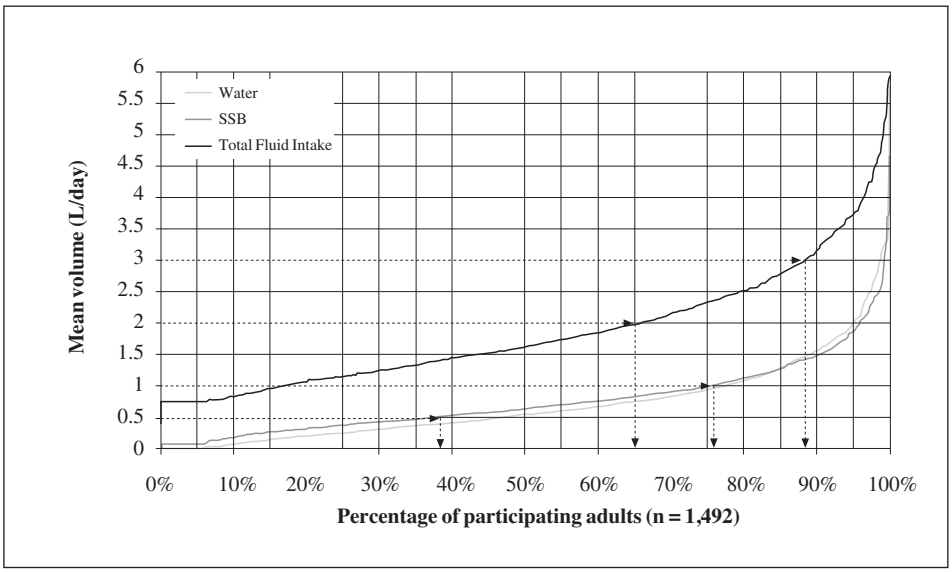


Fig. 2.—Cumulative distribution of total fluid intake, water intake and sugar sweetened beverages intake by participating adults.

Table IV
Total daily consumption of different types of fluids (ml/day) stratified by age range

Variables	*18-35 years (n = 335)*	*25-35 years (n = 338)*	*36-45 years (n = 300)*	*46-55 years (n = 280)*	*56-65 years (n = 239)*	*P value*[a]
Water	697 (35)	794 (40)	715 (38)	721 (42)	632 (36)	0.027
Milk and derivatives	205 (11)	195 (12)	158 (10)	156 (11)	151 (12)	0.017
Hot beverages	103 (9)[b]	129 (9)[d]	148 (10)[f]	180 (12)[c]	212 (16)[c,e,g]	< 0.001
Sugar sweetened beverages	693 (36)[b]	624 (30)[d]	559 (31)	513 (32)[c]	389 (33)[c,e]	< 0.001
Alcoholic beverages	48 (11)	33 (7)	37 (9)	32 (7)	33 (12)	0.003
Other beverages	5 (2)	6 (2)	3 (1)	5 (2)	8 (2)	0.420
Total fluid intake	1948 (55)[b]	1986 (53)[b,d]	1806 (56)[e]	1822 (57)	1612 (53)[c]	< 0.001

Data expressed as mean (SEM). [a]P values for comparisons between groups were tested by bivariate analysis of variance (ANOVA) followed by *post hoc* tests with the Bonferroni correction. P < 0.01 for differences between letters ([b] versus [c]; [d] versus [c]; [f] versus [g]).

The largest contributor to energy intake from fluids was SSB (256 kcal/day or 80-83% of energy intake from fluids), followed by milk and derivatives (men: 37 kcal/day or 12% of energy intake from fluids; women 47 kcal/day or 15% of energy intake from fluids; $p < 0.05$), and hot beverages (14 kcal/day or 5% of energy intake from fluids). In the total population, 81.5% of the participants consumed more than 10% energy from added sugars coming from fluids. Compared to men, a higher percentage of women exceed the recommendation for 10% energy from added sugars (73.6% *versus* 85.7%; $p < 0.001$) (fig. 3).

Discussion

This is the first comprehensive description of habitual fluid intake by a large sample of Mexican adults, including main fluid categories as plain water, milk and derivatives, hot beverages, SSB, alcoholic beverages, and 'others'. The main findings of this paper include that 87.5% of adult males and 65.4% of adult females drink below their recommended daily fluid intake (3 L for males and 2 L for females), and that in 80% of the population SSB, accounted for a larger contribution to total fluid intake than water. This intake brings along a substantial contribution to daily energy intake from SSB, such that 65% of adult males and 66% of adult females exceeded this recommendation. We also found that fluid intake did not differ significantly by gender, but showed a declining trend with age.

There are several methodological strengths supporting our findings. The sample was drawn from different geographic locations, across different ages and socioeconomic strata, both genders, and was large enough to identify the mean fluid consumption by any of these stratification variables with statistical significance. The use of a self-reported fluid-drinking diary kept by study participants for a seven-day consecutive period was supported by an initial supervised one-to-one training period, and data collection was supported throughout the seven day period by a hot-line service to

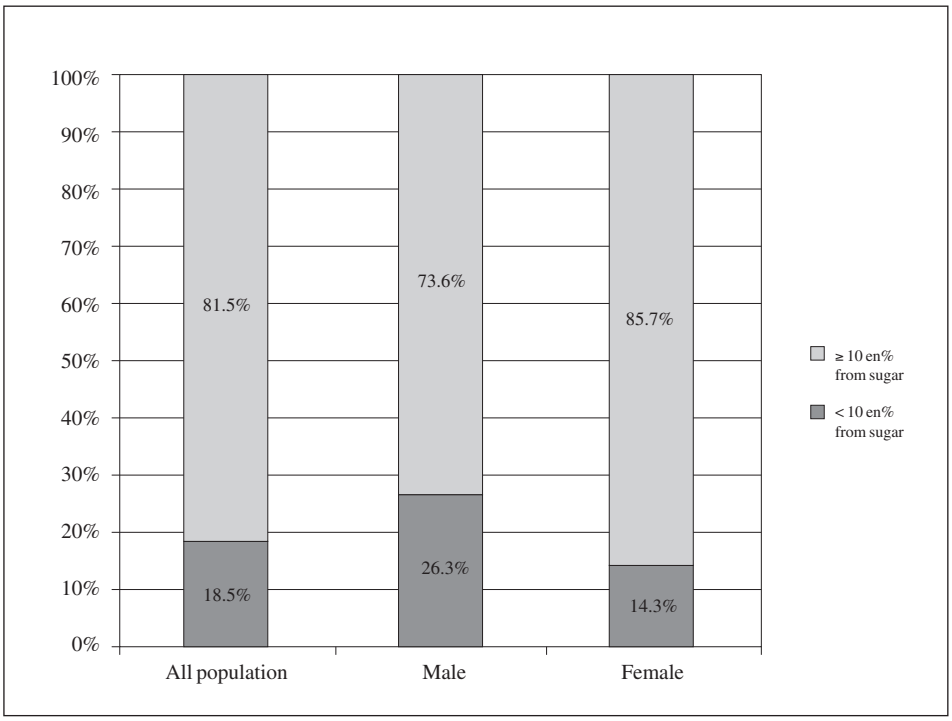


Fig. 3.—Proportion of participants reporting an energy intake from sugar associated to fluid consumption, above or below the recommended 10% of total energy intake[6,13].

address any questions participants may have, plus a mid-term home visit by team staff. This careful data collection method is more likely to capture the habitual ingestion of fluids than other methods used in previously published studies, like the 24-hour recall[8,19].

We do recognize, however, that our study was also subject to several limitations. Different authors have recognized that an accurate registry of drinking habits is difficult in free-living conditions (as opposed to the closed environment provided by laboratory conditions)[20], although we believe that the use of a self-registration fluid-drinking diary may offer a more accurate description of fluid intake[8,19]. The possibility of bias in self-reported data is always present, but the large sample collected, spread across age, socio-economic level and geographic region, greatly reduces the possibility of systematic biases across the whole sample. We did not collect any measure on hydration status, so we can not make any inference regarding the adequacy of fluid intake towards maintenance of hydration status. Therefore, we can only compare reported fluid intake *vs*. fluid intake recommendations. Data on body weight, height and physical activity level was not collected either and therefore we estimated average energy requirements for our population, by gender. Our sample was not a statistically representative sample of adult Mexican population, as we did not have a sampling frame from where to draw our sample. However, we did make an attempt to cover the range of socio-economic and geographic (as a proxy for climate) conditions found throughout the country, stressing that our sample was drawn from 16 major cities distributed widely throughout the country, covering the main geographic regions, i.e., Pacific, North, Central lowlands, Central highland plateau, Valley of Mexico and Southeast. Our study was carried out in the months that represent the transition from the dry to the rainy season (April to May), with an average ambient temperature well in the "comfort zone" of 18°C, the diversity of climate in the country may have provided for warmer and cooler ambient temperatures, which were not accounted for. Also, contextual variables such as availability of specific drinks in the local market, influence of advertising, peer pressure or family preferences for specific types of beverages at home could not be accounted for.

Keeping these strengths and limitations in mind may help to interpret the significance of our data. As mentioned, this is the first comprehensive study about overall fluid consumption in a sample of Mexican adults from throughout the country. Previously, some attempts had been made to characterize water and fluid intake of the population. The Mexican National Institute of Public Health carried out national nutrition surveys in 1999 and 2006 (the latest national nutrition survery in Mexico, conducted in 2012, has not released data on calorie intake nor fluid consumption), and noticed that *per capita* consumption of bottled sodas showed an increasing trend among adults, with over half the population consuming these beverages in the 2006 survey[21,22]. Even though the consumption of milk and other derivatives decreased among the adult population, the overall consumption of SSB increased, to an average 0.155 L/day by 2006[23]. This same survey found that fluid intake provided 22.3% of total caloric intake among the adult population[21]. In our study, conducted in 2012, we found an average consumption of SSB of

0.324 L/day by men and 0.315 L/day by women. Also in the 2006 survey, total fluid intake by the adult population showed an average of 1.721 L/day, with water contributing with 0.889 L/day[6]. In comparison, our study found an average consumption of 1.85 L/day of fluid consumption, with water contributing a mean of 0.711 L/day. As has been noted previously, with our methodology we can not make assumptions about the hydration status of the population. However, it should be noted that, in this sample of adult Mexicans, 65% of women and 88% of men reported consuming less than the daily recommended amount of fluids, and mean fluid consumption tended to decrease with age.

With regards to the consumption of SSB, it was noticeable that only 3% of participating adults reported not consuming this type of beverages. About two out of three adults in our sample (65%) drank more than 0.5 L/day of SSB, and about one out of four (26%) adults consumed more than 1 L/day. The World Health Organization has recommended that no more than 10% of the recommended daily calorie requirement should come from beverages, and the panel of experts convened in Mexico by the Ministry of Health also supports this recommendation[6,13]. On average, a healthy male adult such as those included in our study population should consume no more than 240 kcal/day from fluids, and a healthy female adult should consume no more than 180 kcal/day from fluids[6,13]. In our sample, there were 65% of adult males and 66% of adult females who exceeded this recommendation.

The evidence provided by this study related to drinking practices of an adult population is relevant in order to provide guidance for public health policies that aim to promote healthy drinking practices. Water should suffice to provide for all the hydration needs of a healthy human, so there is no need to complement the recommended daily fluid intake by drinking caloric beverages. In reality, however, different factors contribute to the ingestion of fluids other than water to satisfy thirst or to accompany food intake or even as part of social interaction, including taste, availability, convenience, marketing, peer pressure, cultural practices, etc. However, an excessive ingestion of calories provided by beverages may lead to an excessive increase in caloric intake[24], and there is evidence that physiological mechanisms related to satiety regulation are less effective when calories are provided in fluid form in contrast to calories provided by foods[25]. Some authors dispute the role that calories provided by beverages may have in the onset of overweight and obesity, but a recent systematic review looking into this relationship has found enough evidence to support the recommendation that consumption of SSB should be discouraged as part of the public health interventions aimed at promoting a healthy lifestyle[26]. Along these lines, the World Health Organization has identified the consumption of SSB as a "probable contributor" to the obesity epidemic[13]. Therefore, our findings may have important implications for policy recommendations, as part of comprehensive strategies to curve the obesity epidemic currently affecting Mexico and other developing countries, as well as to promote the adoption of healthy lifestyles that may have an impact on decreasing morbidity and mortality related to chronic diseases such as type-2 diabetes mellitus, stroke, cardiovascular disease and different types of cancer[6,27,28].

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Original / *Otros*

Sweets and fats tasting in patients with anorexia nervosa; the role of the thought-shape fusion cognitive distortion

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Abstract

Introduction: **It has been found that the olfactory-gustatory function is altered in patients with eating disorders, with an impairment affecting the perception of olfactory and gustatory stimuli.**

Objective: **The aim was to explore the subjective reactivity after the exposure and tasting of foods with different gradient of sweetness and different fats textures. In addition, changes in the thought-shape fusion (TSF) cognitive distortion were assessed after tasting those different presentations as well as the correlations between the initial scores on TSF-Questionnaire (TSF-Q) and the different responses after that tasting.**

Method: **A total of 15 healthy controls and 23 outpatients with anorexia nervosa underwent two sessions of tasting (sweets with different gradient of sweetness and fats with different textures) and they filled several questionnaires (pre- and post-tasting) to measure their responses after tasting.**

Results: **Participants showed less "self-control" after tasting sweets. The score on TSF-Q increased significantly after the sweets tasting in the patients group. Patients had the worst response after tasting presentations with more quantity of glucose (less gradient of sweetness) than after tasting those with more amount of sucrose (much more sweetness). With respect to the fats, patients showed the worst reaction after tasting the most unfamiliar texture. Pre fats tasting TSF-Q scores correlated significantly with all responses in the patients group.**

Discussion: **Both psychological and biological (e.g. genetic) factors could be involved in the reactions of patients with anorexia nervosa after tasting sweets and fats.**

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Key words: *Taste responsiveness. Sweets taste. Fats taste. Thought-shape fusion. Anorexia nervosa.*

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CATA DE DULCES Y GRASAS EN PACIENTES CON ANOREXIA NERVIOSA; EL PAPEL DE LA DISTORSIÓN COGNITIVA FUSIÓN PENSAMIENTO-FORMA

Resumen

Introducción: **Se ha encontrado que la función olfativa-gustativa está alterada en pacientes con trastornos de la alimentación, con una alteración que afecta la percepción de los estímulos olfativos y gustativos.**

Objetivo: **El propósito fue explorar la reactividad subjetiva tras la exposición y prueba de alimentos con distintos gradientes de dulzor y diferentes texturas grasas. Además, se evaluaron los cambios en la distorsión cognitiva de la fusión idea-forma (FIF) tras probar diferentes presentaciones así como las correlaciones entre las puntuaciones iniciales del Cuestionario FIF (C-FIF) y las distintas respuestas tras esa prueba.**

Método: **Un total de 15 controles sanos y 23 pacientes ambulatorios con anorexia nerviosa se sometieron a dos sesiones de pruebas (dulces con distintos grados de dulzor y grasas con distintas texturas) y rellenaron varios cuestionarios (pre y post-prueba) para medir sus respuestas tras la prueba.**

Resultados: **Los participantes mostraron menos "autocontrol" tras las pruebas con dulces. La puntuación del C-FIF-Q aumentó de forma significativa tras las pruebas con dulces en el grupo de pacientes. Los pacientes tuvieron una peor respuesta tras las pruebas con aquellos alimentos con mayor contenido en glucosa (menor gradiente de dulzor) que tras probar aquellos alimentos con una mayor cantidad de sucrosa (mucho más dulzor). Con respecto a las grasas, los pacientes mostraron una peor reacción tras probar la textura menos familiar. Las puntuaciones del C-FIF pre-prueba se correlacionaron significativamente con todas las respuestas en el grupo de pacientes.**

Discusión: **Tanto factores psicológicos como biológicos (p. ej., genéticos) podrían estar implicados en las reacciones de los pacientes con anorexia nerviosa tras las pruebas con dulces y grasas.**

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Palabras clave: *Respuesta al sabor. Cata de dulces. Cata de grasas. Fusión pensamiento-forma. Anorexia nerviosa.*

Introduction

It has been found that the olfactory-gustatory function is altered in patients with eating disorders (ED), with an impairment affecting the perception of olfactory and gustatory stimuli[1]. Patients with restrictive-type anorexia nervosa (AN) have shown significant lower pleasantness scores for pleasant taste stimuli compared with controls, these differences being greatest for a lower concentration of sucrose, umami and sodium chloride[2]. Prospective studies have reported that compared to healthy controls and bulimic patients, anorectic patients show lowered olfactory and gustatory sensitivities that may be improved by increasing body mass index and decreasing eating pathology during the treatment[3]. Considering taste as a hereditary trait, the number of fungiform papillae of the tongue has been explored in anorectic patients. As a result, a reduced number of papillae has been associated with a decreased 6-n-propylthiouracil sensitivity. In this regard the variation of the papillae number and 6-n-propylthiouracil sensitivity might influence the pathophysiology of eating behaviour and taste perception, and consequently this might be involved in the development of ED[4].

Changes in taste responsiveness (sweet, salty, sour and bitter tastes) have been assessed during behaviour therapy of anorectic patients. As result, lower taste responsiveness at admission has been observed when compared to controls. That responsiveness was found out to be improved significantly over the course of treatment and that improvement occurred prior to increase in body weight. In fact no significant correlation was noted between weight gain and improvement in taste responsiveness. Those patients who reached 1,600 kcal/day earlier showed more rapid improvements in taste responsiveness, these results suggesting that decreased taste responsiveness in AN patients could rapidly improve and such early improvement might result in better progression of treatment[5].

Despite having been reported different alterations with respect to the taste sensitiveness and to some extent in the olfactory-gustatory function, the topic seems to remain controversial. In fact, a recent study suggests that individuals with AN do not have a markedly greater ability to taste fat than controls, so fat avoidance would be likely based primarily on cognitive factors. In this case, a taste case was performed by means of three different presentations of cream cheese (fat-free, low fat and regular). There were not observed main effects of the fat content but a significant main effect of the trial was found out. The post hoc findings of this study suggested that with repeated exposure (i.e., over three trials), AN patients' ratings of the fat-free cream cheese improved. Reasons for this were unclear, but authors stated that personal experience with fat-free products would had made it easier for these patients to recognize some taste or sensory characteristics associated with a fat-free food[6].

The relationship between specific thoughts related to food and feelings related to body image have been described as thought-shape fusion (TSF)[7]. In a previous study we explored the subjective reactivity and the TSF cognitive distortion after thinking about eating fattening foods, as opposed to anxiety-inducing thoughts in general[8]. As far as we know, there are no studies based on the subjective reactivity and the TSF distortion after tasting different gradients of sweetness and fat textures.

The aim of the current study was to explore the subjective reactivity after the exposure and tasting of foods with different gradient of sweetness (cupcakes) and different textures (olive oil in its natural state, olive oil as mayonnaise and olive oil as meringue). In addition, changes in the TSF cognitive distortion were assessed after tasting those different presentations as well as the correlations between the initial scores on TSF-Q and the different responses after that tasting.

Method

Participants

The sample comprised of 48 females, 15 healthy controls (students recruited from the Pablo de Olavide University, Seville) and 23 outpatients with anorexia nervosa (AN). These outpatients were receiving treatment in the ED Unit of the Behaviour Sciences Institute in Seville and they fulfilled the DSM IV-TR[9] criteria for AN. The sample mean age was 21.34 ± 4.96. There was not significant difference between the two subsamples. With respect to the students, they did not have any psychiatric history, this being assessed by means of a brief questionnaire at the moment of obtaining the informed consent.

Materials

Meals

1. Sweets: the idea was to offer three cupcakes with a gradient of sweetness without changing significantly the texture and the calorie content.
2. Fats: The idea was to offer three preparations using the same amount of extra virgin olive oil (EVOO) but with three different textures. In order to use a common way to take the EVOO we chose the presentation of "bread with oil and tomato", a usual breakfast in our Spanish context. Initially, four possible presentations were designed: a) The oil without any treatment; b) The oil emulsified as mayonnaise; c) The oil as a foam or meringue type mouse and d) The oil as solid form like a typical Christmas sweet ("polvorón"). After a pilot test, the latter form was removed due to difficulties to maintain it for several hours

(keeping in mind that most of the tastings were made in a place other than where preparations were ellaborated) and because it was a presentation served on top of bread, it produced an unfortunate marriage.

Ingredients

1. Sweets: All data will be expressed in g, except the eggs, which were classified in units (having a "L" category: 63-73 g). Flour with a chemical propellant (added in order to obtain more homogeneous repetitions) was used. "Bizcochona" flour (HARIMSA brand) was used. The sugar was a refined beet one ("White Sugar Azucarera" brand). Glucose powder was used ("Sosa" brand). Natural unsweetened yogurt ("Danone" brand) was chosen. As a result, the three preparations were:

Ingredients	Preparation 1 (P1) (No glucose)	Preparation 2 (P2) (Glucose 40 g)	Preparation 3 (P3) (Glucose 80 g)
Flour	150	150	150
Sucrose	167	127	87
Glucose	0	40	80
Natural yogurt	83	83	83
Lemon zest	3.5	3.5	3.5
EVOO	43	43	43
Eggs (L)	2	2	2

2. Fats: The oil was the Arbequina EVOO. For the different presentations the following products were used: a) Canned crushed tomatoes ("Orlando" brand); b) Salt; c) "Gelespesa" thickener gel based on xanthan gum ("Sosa" brand); d) A emulsifier paste based on mono- and diglycerides of fatty acid esters of glycerol ("Sosa" brand); e) Powder of albumin ("Sosa" brand). The emulsifier paste comprised of water, mono- and diglycerides of fatty acids (E471), polyglycerol esters (E475), oxyethylenated sorbitan esters (E435), sorbitol, dextrose, citric acid (E330) and sorbic acid (E200). The thickener gel consisted of maltodextrin and xanthan gum (E415). For the presentation, "BIMBO" brand bread without crust was used.

Preparation

1. Sweets (cupcakes): The ingredients were weighed with a precision balance (Tanita KD320WH33; 0.1 g accuracy). Eggs were beaten with a hand mixer and sugars (table sugar alone or mixed with glucose) were incorporated. The mixture was beaten until smooth and whitish mixture was achieved. Yogurt, oil and lemon zest were incorporated and beaten until becoming homogeneous. Flour was gradually incorporated while beating it until getting a homogeneous mixture. A plum cake-type silicon mold was filled with the mixture. It was baked for 33 minutes at 175 °C with forced air and with the heat source from both above and below (an oven of forced convection Teka mark was used). After cooling, the cupcakes, they were taken out of the mold and cut into portions of 15 g (with similar size and always with one of its edges with bark) thus giving it a look as consistent as possible.
The reason to use mixed sugar (sucrose) and glucose was that sugar not only adds flavour but also influences the physical characteristics (appearance, texture, etc.) of the final preparation. Glucose, having the same caloric content than sucrose, has a lower sweetening power than sucrose (about 30% lower). With mixtures of sucrose/glucose isocaloric cupcakes are obtained, containing the same amount of sugar but with less sweetness (the smaller the quantity of sucrose is, the lower the sweetness will be). With this we also tried to minimize the differences in texture and appearance they may have, although there may remain some minor differences.
2. Fats: All textures of oil were served on homogeneous 5 g-slices of bread without crust ("BIMBO" brand). In all cases the amounts of tomato and oil were the same (1.2 g), regardless the total weight of the preparation. The three presentations were:

   a) Bread with oil and tomato: 1.2 g of Arbequina EVOO, 1.2 g of canned crushed tomatoes and salt (this mixture is made using 50 g of tomato and 0.5 grams of salt), and 5 g of bread without crust.
   b) Bread with tomato mayonnaise: The tomato mayonnaise comprised of 70 g of Arbequina EVOO, 70 g of canned crashed tomatoes, 1.2 g of thickener gel, 1.2 g of emulsifier paste and 0.7 g of salt. The tomato, salt, emulsifier and paste were mixed by means of a hand blender. The oil was added gradually until getting the mayonnaise texture. Finally, 2.46 g of the tomato mayonnaise were placed on the 5 g-portions of white bread.
   c) Bread with olive oil and tomato meringue: The tomato meringue comprised of 100 g of Arbequina EVOO, 100 g of canned crashed tomatoes, 18 g of albumin powder and 1 g of salt. Oil, tomato, salt and albumin were mixed and then the mixture was placed in a bowl of a food processor (a Kitchen Aid robot). It was beaten by means of special rods to mount until a meringue texture was reached (8/9 power). Finally, 2.62 g of tomato meringue were placed on the 5 g-portions of white bread.

Instruments

The following scales/questionnaires were applied:

1. Subjective Reactivity to the exposure of food: this was assessed by means of a list of adjectives (7 positive and 7 negative) modified from Rodriguez (2005)[10]. For each adjective, participants rated their feelings from 0 to 100. The positive adjectives were self-controlled, self-assured, happy, valuable, motivated, satisfied and relaxed. On the contrary, the negative adjectives were depressed, embarrassed, anxious, overwhelmed, vulnerable, guilty and angry.
2. Ten cm-Visual Analogue Scales (VAS): This self-report instrument gathers information about mood, anxiety, likelihood of weight gain, feelings of fatness, and moral wrong-doing, all of them marked from 0 to 10 (0 = the lowest level on each variable, 10 = the highest level on each variable). These scales have been used in previous studies[8,11,12].
3. Thought Shape Fusion questionnaire (TSF-Q): It is a 34-item, self-report questionnaire, which measures the fusion between thought and body shape or image. TSF-Q comprises of two sections, identified by its authors as conceptual (TSF conceptual) and interpretative (TSF interpretative). The Spanish version was used, which has shown adequate psychometric properties[7,13,14].
4. The Positive and Negative Affect Schedule (PANAS): This is a 20-item self-report questionnaire to measure affectivity by means of two dimensions (positive and negative affect). The Spanish version was applied, which has shown adequate psychometric properties[15].

Procedure

Foods were prepared at the kitchen of the Nutrition and Bromatology Area (Pablo de Olavide University, Seville). The experiment was run at that kitchen in the case of students. In the case of patients, they underwent the experiment in the Behaviour Sciences Institute. In both cases a Nutritionist was in charge to conduct the experiment. The experiment comprised of two different sessions: a) Sweet presentations tasting and b) Fat presentations tasting. During the sweet tasting, participants were invited to try the three above-mentioned presentations (1, 2 and 3). In the case of the fat tasting, participants tried bread with oil and tomato, bread with tomato mayonnaise and bread with olive oil and tomato meringue. Before each session (one for the sweets and another for the fats) participants filled the list of adjectives, the TSF-Q and the PANAS. Immediately after each presentation (three for the sweets and three for the fats) they responded to the VAS. Finally, at the end of each session (one for the sweets and another for the fats) they filled again the list of adjectives, the TSF-Q and the PANAS.

In the case of patients, individual sessions were held, coinciding with their regular appointments. In the case of students, individual sessions were held after previous appointment specifically established for the experiment. After obtaining informed consent for the study, the participants completed the questionnaires in individual sessions with no time limit; this was done in the therapeutic context (patients) or in the University (students) in similar conditions and with the nutritionist present during the sessions. That nutritionist gave participants instructions both about how to complete the questionnaires and how to proceed during food presentations.. After making sure that they had understood him, the experiment started. All participants (both clinical participants and students) volunteered to take part in the study and none of them received any kind of recompense for completing the experiment. In order to counterbalance the possible carryover effects, the three presentations in each case (sweets and fats) were randomly assigned.

The study protocol was approved by the institution review board of the Behaviour Sciences Institute (Seville, Spain).

Data analysis

All data were analysed by means of the statistical package, SPSS 17.0. (SPSS, Inc.)[16]. Differences were considered significant for $p < 0.05$. Values were expressed as mean values (M) with standard deviation (SD). The variables "magnitude of change" (Post-tasting minus Pre-tasting) were calculated for several variables and the normality of these transformed variables was checked by the Kolmogorov-Smirnov test. As a result, the parametric Student's *t*-test was applied (despite the small sample size, *t*-test is considered as appropriate when variables fit the normal distribution) for both dependent (intra-group differences) and independent samples (inter-groups differences). In the case of correlations, the Pearson's *r* coefficient was calculated.

Results

Healthy control group

There were not any significant differences pre- and post-tasting of sweet presentations with respect to the VAS. As far as the adjectives were concerned, a significant difference was found in the case of "self-controlled" (pre-tasting = 67.33, post-tasting = 56.00; $p < 0.05$). Taking into account the TSF-Q and the PANAS, no differences were found.

The fats tasting revealed a significant difference in the VAS related to the "likelihood of weight gain" with the highest score obtained after tasting the presentation "oil

with bread and tomato" ($p < 0.05$). The fats tasting also yielded a significant difference in the adjective "guilty" (pre-tasting = 14, post-tasting = 20; $p < 0.05$). Considering the TSF-Q, the difference was not statistically significant (pre-tasting = 15.53, post-tasting = 19.07). There were not any significant differences respecting the PANAS.

Patients group

Respecting to the sweets tasting, there were found some significant differences in the case of VAS. While the score on "mood" decreased (P1 = 5.40; P2 = 4.88; P3 = 4.20; $p < 0.05$), the scores on "likelihood of weight gain" (P1 = 1.81; P2 = 2.53; P3 = 2.86), "feeling of fatness" (P1 = 1.91; P2 = 2.56; P3 = 2.83) and "moral wrong doing" (P1 = 2.47; P2 = 2.93; P3 = 2.98) increased ($p < 0.0001$, $p < 0.05$ and $p < 0.05$, respectively). In the case of the adjectives, the score on "self-controlled" decreased significantly (35.30 *vs* 23.52; $p < 0.05$).

There were not any significant differences with respect to the PANAS. With regards to TSF-Q, a significant difference was obtained (pre-tasting = 44.78, post-tasting = 56.30; $p < 0.05$)

The fats tasting did not reveal any differences considering the VAS. The score on "self-controlled" increased (22.17 *vs* 27.61) during the tasting with the highest score after taking the bread with olive oil and tomato meringue. Finally there were not significant differences with regards to TSF-Q and PANAS.

Patients group vs *Control group*

Tables I and II show the differences between the two groups after sweets and fats tasting. In order to analyse the magnitude of change with respect to the TSF-Q and PANAS, the variable "post minus pre" was obtained for TSF-Q, PANAS positive and PANAS negative. As a result, the magnitude of change was significantly different in the case of TSF-Q after sweets tasting: while in the control group the mean change was -1.4 (that means that TSF-Q score decreased), in the patients group the mean change was + 11.52 (the TSF-Q score increased clearly). No significant differences were found with respect to TSF-Q after fats tasting and PANAS (sweets and fats) considering the magnitude of change.

Table I
Differences between CG and PG after sweets tasting (M ± SD)

	Control group (CG)			*Patients group (PG)*		
	Post-P1	*Post-P2*	*Post-P3*	*Post-P1*	*Post-P2*	*Post-P3*
Mood	8.16 ± 1.02**	8.04 ± 1.22**	8.44 ± 1.04**	5.40 ±1.67**	4.88 ± 1.03**	4.20 ± 1.22**
Anxiety	2.21 ± 0.83	2.09 ± 1.02	2.25 ± 0.97	3.05 ± 1.03	3.67 ± 1.44	3.90 ± 1.03
Guilty	1.03 ± 0.19	1.10 ± 0.77*	1.15 ± 0.88**	2.48 ± 0.98	3.40 ± 1.07*	3.77 ± 1.34**
Likelihood weight gain	1.65 ± 1.03	1.32 ± 0.42	1.27 ± 0.08*	1.81 ± 0.99	2.53 ± 1.01	2.86 ± 0.98*
Feeling fatness	1.78 ± 0.98	1.10 ± 0.21	0.92 ± 0.11*	1.90 ± 0.67	2.56 ± 0.96	2.83 ± 0.78*
Moral wrong doing	0.41 ± 0.11	0.44 ± 0.09**	0.48 ± 0.12*	2.47 ± 1.03	2.93 ± 0.66**	2.99 ± 1.01*

* $p < 0.05$.
** $p < 0.01$.
P1-P2-P3 = Preparations/presentations 1-2-3.

Table II
Differences between CG and PG after fats tasting (M ± SD)

	Control group (CG)			*Patients group (PG)*		
	Post-O	*Post-M*	*Post-Me*	*Post-O*	*Post-M*	*Post-Me*
Mood	8.38 ± 1.07**	8.37 ± 0.99**	8.37 ± 0.65**	4.95 ± 1.21**	4.40 ± 1.07**	4.26 ± 1.20**
Anxiety	1.32 ± 0.76	1.27 ± 0.99	1.22 ± 0.21	2.53 ± 0.87	2.63 ± 0.76	2.76 ± 1.01
Guilty	0.97 ± 0.11	0.90 ± 0.22*	0.79 ± 0.31*	2.36 ± 0.23	2.34 ± 0.89*	2.62 ± 1.10*
Likelihood weight gain	1.21 ± 0.17	1.00 ± 0.32	0.95 ± 0.43*	1.65 ± 0.98	1.91 ± 0.12	2.23 ± 0.75*
Feeling fatness	1.12 ± 0.45	0.98 ± 0.55	1.00 ± 0.23*	1.97 ± 0.76	2.00 ± 0.55	2.52 ± 0.77*
Moral wrong doing	0.28 ± 0.02**	0.33 ± 0.08**	0.23 ± 0.07**	1.93 ± 0.89**	2.00 ± 0.91**	2.44 ± 0.32**

* $p < 0,05$.
** $p < 0.01$.
O = Oil.
M = Mayonnaise.
Me = Meringue.

Correlations between the score on TSF-Q pre-tasting and the results after tasting

In the control group, pre sweets tasting TSF-Q correlated significantly with "guilty" and "likelihood of weight gain" after sweets tasting P1 (0.63 and 0.55; $p < 0.01$) and P3 (0.60 and 0.66; $p < 0.01$). Pre sweets tasting TSF-Q also correlated significantly with post sweets tasting TSF-Q (0.92; $p < 0.01$) and with post sweets tasting PANAS positive (-0.61; $p < 0.01$). Pre fats tasting TSF-Q correlated with "likelihood of weight gain" and "feeling fatness" after oil tasting (0.53 and 0.58; $p < 0.01$) and with "feeling fatness" after mayonnaise tasting (0.78; $p < 0.01$). Again pre fats tasting TSF-Q correlated with post fats tasting TSF-Q (0.98; $p < 0.01$) and with post fats tasting PANAS positive (-0.71; $p < 0.01$).

The correlations in the patients group with respect to the VAS are shown in table III. In addition, pre fats tasting TSF-Q correlated significantly with post fats tasting PANAS negative (-0.56; $p < 0.01$) and with post fats tasting TSF-Q (0.99; $p < 0.01$).

Discussion

According to the results, the participants of both the control group and the patients group showed less "self-control" after tasting sweets. This result confirms other similar findings related with the fact that sweet foods are the most craved[17-19]. In the laboratory context, Martin et al., have reported an association between food cravings and consumption of specific foods in a taste test[20]. With respect to the sweets, patients showed a decrease of the "mood" state as well as an increase of "likelihood of weight gain", "feeling of fatness" and "moral wrong doing" after tasting sweets. In a previous study[8] a TSF-induction condition caused more "guilt", more "feelings of fatness", more "likelihood of weight gain", and higher degree of "moral wrong doing" compared with participants in both anxiety and control induction conditions. The results of the current study are based not on thoughts related with food but on an experimental food tasting. The TSF cognitive distortion emerges not only after thinking about eating some foods but after tasting them, thus possibly closing a pathological circle which maintains the core symptoms of the anorexia nervosa. In fact, in this experiment the score on TSF-Q increased significantly after the sweets tasting in the patients group. In addition, the pre sweets tasting TSF-Q score correlated significantly with all VAS scores (negatively with "mood" and positively with the rest of scales). After fats tasting the participants of the control group felt more "guilty" than prior, which is a result coherent with other data previously reported[12]. This was not the case in the patients group, in which the participants showed less "self-control" after tasting "bread with olive oil and tomato meringue". Paradoxically, while patients did not change their scores on the VAS scales after fats tasting, the participants of the control group showed an increase in the "likelihood of weight gain" after tasting "olive oil with bread and tomato". The texture of these presentations seems to be relevant regarding the participants' reaction. The patients' less control after tasting "bread with olive oil and tomato meringue" could be explained by the unfamiliarity of this presentation, which is not usual in their usual diet. While "olive oil with bread and tomato" is a normal breakfast in Spain, especially in Andalucía, the "meringue" presentation is rare in our context. During the patients' nutritional treatment "olive oil with bread and tomato" becomes familiar with a progressive reduction of fear regarding this presentation. In the case of the "meringue", this form of fat intake remains unusual so it is something new and a possible reason for the feeling of less control. In fact, the tendency to dislike some high-fat foods in anorexia nervosa patients has been reported[21]. The increasing of "likelihood of weight gain" after tasting "olive oil with bread and tomato" is not surprising taking into account the irrational food beliefs widely spread in Western populations. In this regard, the healthy/unhealthy categorization of foods leads to prefer/avoid certain foods and distinguishing between guiltless and guilty eating. A variable related to guilty eating is the calorie content and the fat content of the food and the likelihood of

Table III
Correlations (Pearson's r coefficient) between pre TSF-Q and VAS after sweets and fats tasting in patients group

	Post-P1	*Post-P2*	*Post-P3*	*Post-O*	*Post-M*	*Post-M3*
Mood	-0.49*	-0.52*	-0.53**	-0.54**	-0.46*	-0.64**
Anxiety	0.43*	0.45*	0.42*	0.56**	0.53**	0.46*
Guilty	0.53**	0.55**	0.69**	0.63**	0.65**	0.50*
Likelihood weight gain	0.45*	0.52*	0.51*	0.54**	0.49*	0.42*
Feeling fatness	0,47*	0.50*	0.53**	0.60**	0.51*	0.43*
Moral wrong doing	0,58**	0.57**	0.59**	0.63**	0.54**	0.47*

* $p < 0.05$.
** $p < 0.01$.
O = Oil.
M = Mayonnaise.
Me = Meringue.

weight gain after eating that type of high-calorie/high-fat food[22]. Again the TSF cognitive distortion is clearly involved in the results. Despite not having observed a significant difference pre fats tasting/post fat tasting with respect to the TSF-Q, either in the control group or in the patients group, the pre fats tasting TSF-Q scores correlated significantly with all VAS scores in the patients group.

Besides the psychological facets of the participants' responses it must be noted some results considering the gustatory function in these patients. While the control group's participants showed higher "likelihood of weight gain" and more "feeling fatness" scores after tasting the cupcake with the highest gradient of sweetness (P1), patients showed a different response: the more amount of glucose the presentations had the higher scores were obtained on the previously mentioned two VAS scales. Due to the proportions glucose/sucrose, the result indicates that patients have a worse response after tasting more quantity of glucose (less gradient of sweetness) than after tasting more amount of sucrose (much more sweetness). Several methods for measuring sweet taste preferences have been developed but the results seem to be different depending on the technique. Thus Holt et al.[23] found that liking for sweetness in an aqueous solution did not predict the degree of liking for sweetness in orange juice, custard or shortbread biscuits. Approximately half of the variation in liking for sweet solution and liking and use-frequency of sweet foods is explained by genetic factors, whereas the rest of variation is due to environmental factors[24]. In an experimental study it has been shown that leptin selectively suppresses gustatory neural and behavioural responses to sweet compounds without affecting responses to other taste stimuli. In addition it seems that taste recognition threshold for sweets compounds is independent of changes in blood glucose[25]. We have currently no persuasive explanation for this result considering that a lower level of leptin should be correlated with lower taste recognition threshold for sweets, which was not the case.

Taste perception is highly related to functional metabolic status and body adiposity, so it has been reported that calorie restriction could alter the sweet taste perceptions[26]. In order to explore whether patients recovered from anorexia nervosa had an abnormal physiological response to sugar, a pleasant taste, or water, a neutral contrast taste, in the primary or in secondary taste-modulation cortical regions, Wagner et al.[27] designed a study based on fMRI. As a result, authors reported that participants recovered from anorexia nervosa had disturbances of gustatory processing in the central nervous system. They had a significantly reduced fMRI signal response to the blind administration of sucrose or water in the insula, anterior cingulate and striatal regions. In addition individuals failed to show any relationship in these regions to self-reporting of pleasant response to a sucrose taste. Comparing anorexia nervosa patients with those suffering from bulimia nervosa some authors have reported that bulimic patients had an exaggerated anterior ventral striatum response for the cream/water contrast in comparison to anorectic patients[28]. Operndorfer et al.[29] reported that women recovered from anorexia nervosa had significantly diminished and women recovered from bulimia nervosa had significantly elevated hemodynamic response to tastes of sucrose in the right anterior insula. Anterior insula response to sucrose compared with sucralose was exaggerated (lower in patients recovered from anorexia nervosa and higher in women recovered from bulimia nervosa). These altered insula responses have been suggested to be linked to disgust sensitivity[30]. Finally, animal models of activity-based anorexia suggest that a history of anorexia could enhance food avoidance learning and retard its extinction in female rats[31].

In the case of fats tasting the control group did not show any significant differences based on the different textures. On the contrary, patients showed the worst responses after tasting the "meringue" form and the best after tasting the "olive oil with bread and tomato". That indicates that anorectic patients could exhibit different responses depending on fat presentations (textures). In fact these patients seem not to have greater ability to taste fat content than healthy individuals[6]. It seems that their responses with respect to the fats are based more on the texture than on the fat content per se, despite having observed that these patients tend to associate calories with fat content[21].

From a clinical point of view, it has been reported that taste responsiveness in patients with anorexia nervosa improves with the treatment prior to increase the body weight[5]. Apart from the origin of some gustatory alterations in patients with anorexia nervosa, the problem remains controversial in general. In fact some authors have reported that there is no systematic sensory-perceptual deficits in these patients, and specifically, not in gustatory function. The differences observed might be due to fear of food-related stimuli or comorbidity[32].

The present study has some limitations. With respect to the patients, the sample did not comprise of either cases of bulimia nervosa or other type of eating disorders. Bearing in mind some previous studies, the inclusion of different types of patients would be interesting. Consequently a bigger sample size would be necessary. Another point to be considered in future studies would be the different period of time under treatment, this being a variable that was not considered in here. Whether the worst reaction after tasting more concentration of glucose (instead of sucrose) is due to a special sensitivity or not should be carried out in another study. May be that the fact of being something different (so unfamiliar) would have been the reason for that reaction. The specific associations learnt by the participants of the control group during the period of time of their illness were not taken into account and they might be a variable interesting to be considered in a future line of study. Besides these limitations, the present study has some strengths. First of all the use

of habitual foods (olive oil, tomato, bread, cupcakes), which is not the case in other studies based on different products (or different dilutions, etc.) a bit less familiar in our context. With respect to the control group, the participants had not special knowledge of nutrition and had not participated in similar studies. The use of different textures for the same calorie content would be a limitation but at the same time is a clear strength due to the fact that patients normally eat different textures (foods and meals) and not pure tastes. In this regard this study shows a naturalistic approach to the problem.

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