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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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NORMAS DE PUBLICACIÓN PARA LOS AUTORES DE NUTRICIÓN HOSPITALARIA

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).

IMPORTANTE: A la aceptación y aprobación definitiva de cada artículo deberán abonarse 150 euros, más impuestos, en concepto de contribución parcial al coste del proceso editorial de la revista. El autor recibirá un comunicado mediante correo electrónico, desde la empresa editorial, indicándole el procedimiento a seguir.

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Los trabajos se remitirán por vía electrónica a través del portal www.nutricionhospitalaria.com. En este portal el autor encontrará directrices y facilidades para la elaboración de su manuscrito.

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

1.1 Carta de presentación

Deberá indicar el Tipo de Artículo que se remite a consideración y contendrá:

- Una breve explicación de cuál es su aportación así como su relevancia dentro del campo de la nutrición.
- Declaración de que es un texto original y no se encuentra en proceso de evaluación por otra revista, que no se trata de publicación redundante, así como declaración de cualquier tipo de conflicto de intereses o la existencia de cualquier tipo de relación económica.
- Conformidad de los criterios de autoría de todos los firmantes y su filiación profesional.
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- Nombre completo, dirección postal y electrónica, teléfono e institución del autor principal o responsable de la correspondencia.
- Cuando se presenten estudios realizados en seres humanos, debe enunciarse el cumplimiento de las normas éticas del Comité de Investigación o de Ensayos Clínicos correspondiente y de la Declaración de Helsinki vigente, disponible en: http://www.wma.net/s/ index.htm.

1.2 Página de título

Se indicarán, en el orden que aquí se cita, los siguientes datos: título del artículo (en castellano y en inglés); se evitarán símbolos y acrónimos que no sean de uso común.

Nombre completo y apellido de todos los autores, separados entre sí por una coma. Se aconseja que figure un máximo de ocho autores, figurando el resto en un anexo al final del texto.

Mediante números arábigos, en superíndice, se relacionará a cada autor, si procede, con el nombre de la institución a la que pertenecen.

Podrá volverse a enunciar los datos del autor responsable de la correspondencia que ya se deben haber incluido en la carta de presentación.

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).

1.3 Resumen

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.

1.4 Palabras clave

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

1.5 Abreviaturas

Se incluirá un listado de las abreviaturas presentes en el cuerpo del trabajo con su correspondiente explicación. Asimismo, se indicarán la primera vez que aparezcan en el texto del artículo.

1.6 Texto

Estructurado en el caso de originales, originales breves y revisiones, cumplimentando los apartados de Introducción, Objetivos, Métodos, Resultados y Discusión (Conclusiones, en su caso).

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

Material suplementario que sea necesario para el entendimiento del trabajo a publicar.

1.8 Agradecimientos

Esta sección debe reconocer las ayudas materiales y económicas, de cualquier índole, recibidas. Se indicará el organismo, institución o empresa que las otorga y, en su caso, el número de proyecto que se le asigna. Se valorará positivamente haber contado con ayudas.

Toda persona física o jurídica mencionada debe conocer y consentir su inclusión en este apartado.

1.9 Bibliografía

Las citas bibliográficas deben verificarse mediante los originales y deberán cumplir los Requisitos de Uniformidad del Comité Internacional de Directores de Revistas Médicas, como se ha indicado anteriormente.

Las referencias bibliográficas se ordenarán y numerarán por orden de aparición en el texto, identificándose mediante números arábigos en superíndice.

Las referencias a textos no publicados ni pendiente de ello, se deberán citar entre paréntesis en el cuerpo del texto.

Para citar las revistas médicas se utilizarán las abreviaturas incluidas en el Journals Database, disponible en: http://www. ncbi.nlm.nih.gov/entrez/query.fcgi?db=journals.

En su defecto en el catálogo de publicaciones periódicas en bibliotecas de ciencias de la salud españolas: http://www.c17.net/c17/.

▶▶▶

1.10 Tablas y Figuras

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.

Se clasificarán con números arábigos, de acuerdo con su orden de aparición, siendo esta numeración independiente según sea tabla o figura. Llevarán un título informativo en la parte superior y en caso de necesitar alguna explicación se situará en la parte inferior. En ambos casos como parte integrante de la tabla o de la figura.

Se remitirán en fichero aparte, preferiblemente en formato JPEG, GIFF, TIFF o PowerPoint, o bien al final del texto incluyéndose cada tabla o figura en una hoja independiente.

1.11 Autorizaciones

Si se aporta material sujeto a copyright o que necesite de previa autorización para su publicación, se deberá acompañar, al manuscrito, las autorizaciones correspondientes.

2. TIPOS Y ESTRUCTURA DE LOS TRABAJOS

2.1 Original: Trabajo de investigación cuantitativa o cualitativa relacionado con cualquier aspecto de la investigación en el campo de la nutrición.

2.2 Revisión: Trabajo de revisión, preferiblemente sistemática, sobre temas relevantes y de actualidad para la nutrición.

2.3 Notas Clínicas: Descripción de uno o más casos, de excepcional interés que supongan una aportación al conocimiento clínico.

2.4 Perspectiva: Artículo que desarrolla nuevos aspectos, tendencias y opiniones. Sirviendo como enlace entre la investigación y la sociedad.

2.5 Editorial: Artículo sobre temas de interés y actualidad. Se escribirán a petición del Comité Editorial.

2.6 Carta al Director: Observación científica y de opinión sobre trabajos publicados recientemente en la revista, así como otros temas de relevante actualidad.

2.7 Carta Científica: La multiplicación de los trabajos originales que se reciben nos obligan a administrar el espacio físico de la revisa. Por ello en ocasiones pediremos que algunos originales se reconviertan en carta científica cuyas características son:

- Título
- Autor (es)
- Filiación
- Dirección para correspondencia
- Texto máximo 400 palabras
- Una figura o una tabla
- Máximo cinco citas

La publicación de una Carta Científica no es impedimento para que el artículo in extenso pueda ser publicado posteriormente en otra revista.

2.8 Artículo de Recensión: Comentarios sobre libros de interés o reciente publicación. Generalmente a solicitud del Comité editorial aunque también se considerarán aquellos enviados espontáneamente.

2.9 Artículo Especial: El Comité Editorial podrá encargar, para esta sección, otros trabajos de investigación u opinión que considere de especial relevancia. Aquellos autores que de forma voluntaria deseen colaborar en esta sección, deberán contactar previamente con el Director de la revista.

2.10 Artículo Preferente: Artículo de revisión y publicación preferente de aquellos trabajos de una importancia excepcional. Deben cumplir los requisitos señalados en este apartado, según el tipo de trabajo. En la carta de presentación se indicará de forma notoria la solicitud de Artículo Preferente. Se publicarán en el primer número de la revista posible.

EXTENSIÓN ORIENTATIVA DE LOS MANUSCRITOS

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

Eventualmente se podrá incluir, en la edición electrónica, una versión más extensa o información adicional.

3. PROCESO EDITORIAL

El Comité de Redacción acusará recibo de los trabajos recibidos en la revista e informará, en el plazo más breve posible, de su recepción.

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Los autores puden sugerir revisores que a su juicio sean expertos sobre el tema. Lógicamente, por motivos éticos obvios, estos revisores propuestos deben ser ajenos al trabajo que se envía. Se deberá incluir en el envío del original nombre y apellidos, cargo que ocupan y email de los revisores que se proponen.

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Previamente a la publicación de los manuscritos, se enviará una prueba al autor responsable de la correspondencia utilizando el correo electrónico. Esta se debe revisar detenidamente, señalar posibles erratas y devolverla corregida a su procedencia en el plazo máximo de 48 horas. *Aquellos autores que desean recibir separatas deberán de comunicarlo expresamente. El precio de las separatas (25 ejemplares) es de 125 euros + IVA.*

Abono en concepto de financiación parcial de la publicación. En el momento de aceptarse un articulo original o una revision no solicitada se facturará la cantidad de 150 € + impuestos para financiar en parte la publicación del articulo (vease Culebras JM y A Garcia de Lorenzo. El factor de impacto de Nutrición Hospitalaria incrementado… y los costes de edición también. *Nutr Hosp* 2012; 27(5).

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SENPE

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continuación ►►►

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Artículo especial

Document of standardization of enteral nutrition access in adults

Lorena Arribas[1], Laura Frías[2], Gloria Creus[3], Juana Parejo[4], Carmen Urzola[5], Rosana Ashbaugh[6], Cleofé Pérez-Portabella[7] and Cristina Cuerda[2]

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Abstract

The group of standardization and protocols of the Spanish Society of Parenteral and Enteral Nutrition (SENPE) published in 2011 a consensus document SENPE/SEGHNP/ANECIPN/SECP on enteral access for paediatric nutritional support. Along the lines of this document, we have developed another document on adult patients to homogenize the clinical practice and improve the quality of care in enteral access in this age group. The working group included health professionals (nurses, dietitians and doctor) with extensive experience in enteral nutrition and access. We tried to find scientific evidence through a literature review and we used the criteria of the Agency for Health-care Research and Quality (AHRQ) to classify the evidence (Grade of Recommendation A, B or C).

Later the document was reviewed by external experts to the group and requested the endorsement of the Scientific and Educational Committee (CCE) and the group of home artificial nutrition (NADYA) of the SENPE.

The full text will be published as a monograph number in this journal.

(*Nutr Hosp.* 2014;30:1-14)

DOI:10.3305/nh.2014.30.1.7446

Key words: *Enteral nutrition. Adult. Enteral access. Gastrostomy.*

DOCUMENTO DE ESTANDARIZACIÓN SOBRE LAS VÍAS DE ACCESO EN NUTRICIÓN ENTERAL EN ADULTOS

Resumen

El grupo de estandarización y protocolos de la Sociedad Española de Nutrición Parenteral y Enteral (SENPE) publicó en el año 2011 un Documento de Consenso SENPE/SEGHNP/ANECIPN/SECP sobre vías de acceso en nutrición enteral (NE) pediátrica. Siguiendo las líneas de este documento, hemos querido realizar un documento similar centrado en los pacientes adultos que sirva para homogeneizar la práctica clínica y mejorar la calidad de los cuidados de las vías de acceso en NE en este grupo de edad. El grupo de trabajo incluyó a profesionales (enfermeras, dietistas y médico) con extensa experiencia en NE y vías de acceso Se intentó buscar la evidencia científica mediante una revisión bibliográfica y se utilizaron los criterios de la Agency for Health-care Research and Quality (AHRQ) para clasificar la evidencia (grados de recomendación A-B-C).

Posteriormente el documento fue revisado por expertos externos al grupo y se solicitó el aval del Comité Científico Educacional (CCE) y del Grupo de Nutrición Artificial Domiciliaria y Ambulatoria (NADYA) de la SENPE.

El texto completo se publicará como número monográfico.

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Palabras clave: *Nutrición enteral. Adultos. Acceso enteral. Gastrostomía.*

Introduction

Enteral nutrition (EN) is a safe and effective technique of specialized nutritional support (SNS). Its development has been possible thanks to the advances that have occurred in recent decades, both in the chemical definition of the formula and the different routes for enteral access.

In recent years significant progress has being made to improve the security of the access and materials used in enteral nutrition, to make them incompatible with other routes of administration (essentially the intravenous access, incompatible with Luer-lock systems)[1], hoping these changes will decrease the connection errors for the administration of enteral formulas, which can be lethal to the patient if given IV.

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All this has made it possible for many patients to maintain an adequate nutritional status with the exclusive administration of EN. In addition, this treatment can be provided long term in the patient's home with many advantages to their quality of life and saving hospital costs.

Although EN is the technique of SNS of choice, there are no conclusive prospective randomised studies to demonstrate superior efficacy compared to parenteral nutrition (PN). However, EN offers many advantages over the PN: it is more physiological, is associated with fewer and less severe complications, and costs less. Furthermore, the EN has a trophic effect on the intestinal mucosa, to maintain the structural and functional integrity of the wall and collaborates in the barrier function, preventing the passage of germs and toxins inside the body[2].

Indications for EN

EN is indicated in patients who cannot, should not or do not want to eat by mouth to maintain a functioning intestine.

It is not essential that the digestive tract is fully functioning in order to initiate EN, it is sufficient to maintain a minimal functional activity, with absorptive capacity.

Before starting EN the following should be considered[3,4]:

- The nutritional status of the patient at the time the nutritional support begins.
- What percentage of the recommended intake is met orally.
- Duration of the inadequate intake prior to commencing nutritional support.

The indications and contraindications of EN are summarized in table I.

Gastrointestinal access in EN

EN enables the administration of chemically defined formulas, by mouth or through enteral tubes.

The administration of EN orally is the most physiological route because it respects the normal progression of nutrients through the gastrointestinal tract, although it requires the collaboration of the patient, a stable situation, swallowing reflex and functioning gastrointestinal transit.

The formulas used must have a pleasant taste and smell, to avoid patient rejection. In these cases the EN may be used as complete nutrition or as a supplement. This access can be useful in patients with chronic and stable processes to meet daily nutritional requirements. When the above conditions are not met, we will request EN using a different technique. The techniques used are classified into two groups: non-invasive and invasive.

Non-invasive techniques

Nasogastric tube (NGT)

The NGT is the simplest method for short-term or extended enteral access. Nasogastric feeding should never be started without checking if the distal end is located in the stomach. The most reliable method is the realization of an X-ray covering chest and abdomen before removing the guide wire and initiating nutrition. (B)[5-7].

EN through NGT is indicated in the short-term in patients whose stomach is anatomically and functionally conserved and with vomiting reflex intact. The main advantages and disadvantages of EN through an NGT are described below:

– *Advantages:*

- Can be used for the administration of medication.

Table I
Indications and contraindications of EN

EN indications	*EN contraindications*
• Undernourished patient that is not going to be able to eat in a period of time > 5-7 days and has a minimal functional absorptive capacity of the small intestine.	• *Absolute:* uncontrollable vomiting, gastrointestinal bleeding, ileus, intestinal obstruction, intestinal perforation.
• Well-nourished patient that is not going to be able to eat in a period of time > 7-9 days and has a minimal functional absorptive capacity of the small intestine.	• *Relative:* high jejunal fistulas, inflammatory bowel disease in acute phase, short < 50 cm bowel syndrome, severe acute pancreatitis.
• Patients in stage adaptation of a short bowel syndrome.	
• Patients after surgery, trauma or severe burn.	

- Low cost.
- Minimum knowledge required for their placement.

– *Disadvantages:*

- Can be unsightly and uncomfortable for the patient.
- Possibility of sores and nasal erosion.
- Frequent involuntary removal.
- The placement can be difficult in patients with mechanical dysphagia.
- Tubes can become blocked.
- Easily misplaced.
- Increases the chances of gastroesophageal reflux (GER) and therefore may increase the risk of aspiration.

Nasoenteric tube:
nasoduodenal (NDT)
and nasojejunal (NJT)

These types of tubes are indicated for short-term nutrition in patients who require a postpyloric approach. NDT feeding is the process of placing a tube through the nose into the duodenum. NJT feeding is placing a tube in the jejunum, through the nostril.

Sometimes the use of endoscopy or fluoroscopy techniques are required for the placement of these tubes[8]. It is mandatory to ensure a radiological control to check its location.

The nasogastric tube-nasojejunal feeding allows you to decompress the stomach while maintaining the nutrient intake in the intestine[5]. These are indicated in patients with gastric ileus of any aetiology, with bowel functioning.

The main advantage of post pyloric nasoenteral tubes is that it decreases the GER and minimizes the risk of aspiration, as well as the incidence of misplacements.

Invasive techniques

Gastrostomy

It involves placing a tube in the stomach through the abdominal wall. The performance of this technique requires the following preconditions:

- Stomach not affected by primary disease
- Gastric emptying and absence of distal obstruction
- Minimal or non-existent GER
- Vomiting reflex intact

It is indicated in patients who need enteral nutrition for more than 4-6 weeks and the digestive system is anatomical and functional (C). Also in patients with severe oesophageal stenosis that impede the placement of a nasogastric tube or in those oesophageal lesions in which the passing of the tube has a high risk of oesophageal perforation.

Contraindications of gastrostomy placement are:

- *General:* expected survival of the patient < 6-8 weeks, serious blood clotting disorders, severe infections or sepsis, heart or respiratory failure.
- *Local:* ascites, portal hypertension, peritonitis, inflammatory process or tumour along the GI tract.
- *Relative:* GER and erosive esophagitis. In patients with oesophageal stricture not dilatable, obesity and important history of gastric or abdominal surgery may be contraindications for a percutaneous endoscopic gastrostomy.

1. Surgical gastrostomy (SG)

The SG consists of the placement of a tube into the stomach through surgery. It is indicated in those patients who require long term nutritional support, when less invasive techniques, such as endoscopic or radiological placement cannot be performed or when it's done during the surgery itself.

2. Percutaneous endoscopic gastrostomy (PEG)

The PEG involves placing a tube into the stomach through the abdominal wall by endoscopy. It is simpler and cheaper than the SG. It offers the possibility of jejunal feeding (J-PEG) and gastric decompression. The most common technique of placement is the so-called "pull-through".

The contraindications of the PEG are[9-11]:

- Gastric tumours.
- Oesophageal obstruction (which prevents the passage of the endoscope).
- Severe obesity.
- Ascites, peritoneal dialysis, portal hypertension, pregnancy (relative).

3. Percutaneous radiological gastrostomy (PRG)

The PRG is the insertion of a feeding tube by direct puncture of the stomach through a guide with fluoroscopic control. This procedure is considered safe, effective and fast, which does not require general anesthesia. In addition, it is a procedure that does not require gastroscopy, and can be performed in patients with an oesophageal stricture. It is contraindicated in patients with hiatus hernia, gastric volvulus or colonic interposition.

Jejunostomy

The jejunostomy is indicated in patients who require long term enteral nutrition and a gastrostomy can not be performed as well as in the early postoperative period after major abdominal surgery. It is contraindicated in cases of complete bowel obstruction, upper GI fistula, morbid obesity, massive ascites and peritoneal dialysis.

Two different techniques can be used:

- Witzell surgical jejunostomy and fine catheter
- Jejunal access through percutaneous endoscopy or radiology

The surgical jejunostomy can be temporary or permanent. Access to the jejunum can be through a PEG or PRG with jejunal extension or directly (direct percutaneous endoscopic jejunostomy or D-PEJ, direct percutaneous radiological jejunostomy or D-PRJ).

Equipment

Nasoenteric and enterostomy tubes

In the selection of the type of feeding tube it will be necessary to take into account the materials used in its composition, length, size, the use of guide wire, type of connections, characteristics of the proximal end, characteristics of the distal end, existence of positioning marks, lubrication, cost, ease of placement, and security. At present, the two materials that are considered most appropriate are the silicone and polyurethane (PUR) to comply with all the required conditions.

As part of a program of continuous improvement and in response to the demands of the healthcare community, the Medical Nutrition International Industry (MNI) introduced in Europe, a new system of connections for EN in order to avoid incorrect connections between systems of enteral and intravenous access, which are available from September 2012 and that are adapted to the European standard UNE-IN 1615. These new systems of connection ENLock and ENPlus are specific for enteral nutrition and have been designed to be incompatible with the systems of administration with intravenous Luer connection. Some enteral nutrition companies have already incorporated these new systems of secure connection in nasogastric or nasoenteral tubes. There are also feeding tubes on the market with another type of secure connections Superlock, Nutrisafe whose downside is the lack of connectivity between equipment of different companies. Some companies maintain connections less secure (Luer or reverse Luer) that should be avoided.

Table II and III show the different types of nasoenteral and enterostomy feeding tubes respectively.

Containers for the formula

A container is a vesicle in which the formula of EN is decanted. It is recommended to use the "ready-to-use" formula made by the manufacturers.

Original container or package itself

This is the container that comes out of the manufacturing process containing the EN feed. These containers can be glass bottles or plastic airtight packaging.

This packaging of the product has several benefits:

- Reduces the risk of contamination because there is no manipulation.
- Saves costs as it doesn't need preparation.
- It is easily identified and allows the management of accurate volumes.
- The possibility of confusion with the products of PN is minimal.

Empty container

This container is used to decant the feed from the original package. They are made of polyvinyl chloride (PVC) or ethylene-vinyl acetate (EVA) and many of them are latex-free and phthalate and di(2-ethylhexyl) phthalate (DEHP).

The container may be flexible or semi-rigid. It is recommended to change the container every 24 hours.

Enteral infusion giving sets

They are manufactured in plastic and are transparent and flexible. The proximal end is adapted to the container and the distal to the feeding tube. To avoid errors in the connection of the giving sets with the formulas and catheters of intravenous infusion, some manufactures have developed secure connections incompatible with the intravenous route, both in the proximal end of the giving set (ENPlus connection) and in the distal end (connection ENLock, Nutrisafe, Superlock), unsuitable with intravenous connections Luer-lock type. In addition the side ports of these giving sets support only entry of syringes with termination ENLock connections unsuitable for intravenous infusion systems Luer-lock.

At the present time, there are universal enteral giving sets suitable for different EN containers and interchangeable between different commercial manufactures. There are two types of enteral giving sets: for administration by gravity and for administration with feeding pump. In turn, the giving sets consist of the following elements: header, filter, drip chamber, flow regulator and connector.

Table II
Type of nasoenteral feeding tube

	Abbott	*Fresemius*		*Nestlé Health Science*			*Nutricia*		*Grifols*
Brand	FLEXIFLO	FREKA TUBE ENLock	FREKA ENDOLUMINIA	FREKA TRELUMINIA	COMPACT Soft and ENLock	COMPACT STAY PUT	FLOCARE PUR	NASO-INTESTINAL BENGMARK FLOCARE	CORFLO
Material	PUR	PUR	PUR	PUR	PUR	PUR	PUR	PUR	PUR
Radiopaque	YES	YES	YES	YES	YES	YES	YES	YES	YES
Connector	Y-Port	Y-Port 8/10/12 Fr *ENLock:* 15 Fr	ENLock	ENLock jejunal nutrition Gastroic ventilation lumen with funnel connector	ENLock	ENLock jejunal nutrition Funnel connector for aspiration/gastric decompression	ENLock	ENLock	Y-Port
Guarantor (Wire introducer)	With/ Whithout	With	With	Preinstalled	With	Preinstalled	With	With	With/without
Weighted tip	YES/NO	NO	NO	NO	NO	NO	NO	NO	NO
Terminal holes	1 terminal hole 2-4 side holes	2 holes at the distal tip	4 holes for jejunal feed 1 distal hole 4 side holes	2 holes for jejunal feed 5 side holes for aspiration 5 holes for gastric ventilation		3 holes for jejunal feed 4 holes for gastric decompression	3 holes (1distal hole and 2 side holes)	At the distal end (spiral Bengmark)	1 distal hole
Caliber (Fr) Length (cm)	- 8 Fr/91-114 cm with wire introducer and weighted tip - 12 Fr/91-114 cm without wire introducer or weighted tip	8/10/12 FR/120 cm with wire introducer and without weighted tip 15 Fr/100 cm with wire introducer nd without weighted tip	8 Fr/270 cm	9 Fr jejunal feeding lumen with 16 Fr/150 cm gastric decompression lumen The jejunal end protrudes 44cm from the end gastric located 95 cm	8/10/12 Fr/ 120 cm	9Fr jejunal feeding lumen with 18 Fr/150 cm gastric decompression lumen The jejunal end protrudes 35cm from the end gastric located 115 cm	6/8/10/12/ 14 Fr/110 cm	8/10 Fr/145 cm	Guarantor: 10/12 Fr/109 cm Guarantor : 10 Fr/91 cm Guarantor : 8 Fr/91/109 cm Guarantor : 6 Fr/38/56/91 cm Without guarantor : 12 Fr/109 cm
Marking intervals	50 and 76 cm	5 cm	5 cm	5 cm	10 cm	10 cm	2 cm	cm	cm

PUR: Polyurethane; French: Caliber.
Modified from reference[12].

Table III
Type of enterostomy feeding tube

	Model	*G/PEG/J-PEG/J*	*Material*	*Connector*	*Internal retention*	*Caliber (fr) Length (cm)*	*Placement technique*	*Endoscopical removal*	*Maximum recommended usage*
Fresenius Kiabi	Freka PEG	PEG	PUR	ENLock	Bumper	9-15-20 Fr	Endoscopical	Yes	6 months
	Freka PEXACT	B	SIL	Funnel	Ballon	15 Fr	Direct puncture method with gastropexy	No	6 months
	Freka GASTROTUBE	G	SIL	Funnel	Ballon	15 Fr / 13 cm	Replacement for PEG	No	6 months
	Freka INTESTINAL TUBE	J- PEG	PUR	ENLock	Bumper	9-12 Fr/ 120 cm	Endoscopical	Yes	6 months
	Freka FCJ	JeJunostomy	PUR	ENLock	Surgical fixation plate	9 Fr/ 70 cm	Surgical	No	6 months
Nestlé Health Science	Compat NUPORT PEG	PEG	SIL	Y-Port	3-leaf internal bolster	22 Fr	Endoscopical	No	3-6 months
	Compat PEG	PEG	PUR	Y-Port	Bumper	15 Fr	Endoscopical	No	3-6 months
	Compact GASTROTUBE	Replacement for PEG	SIL	Funnel	Balloon	14-20-22 Fr	Replacement for PEG	No	3 months
	Compat Jejunalcath	Surgical jejunostomy	PUR	Luer-Lock	–	9 Fr / 70 cm	Surgical	No	90 days
	Compat J-Line	PEG	PUR	Funnel with luer-lock adaptor	–	9 Fr / 120 cm	Mediante Compat GEP 15 Fr	No	3-6 months
Nutricia	PEG Flocare	PEG	PUR+SIL	ENLock	Bumper	10-14-18 Fr/ 40 cm	Endoscopical	Yes	6 months
	J-PEG Flocare (Sonda Bengmark)	PEG-J	PUR	ENLock/Luer-Lock / Y-Port	Retention ring	9 Fr / 105 cm	Endoscopical	Yes	6 months
Grifols	MIC-Key Gastrostomy	B	SIL	Funnel / Y-Port	Balloon	12-14-16-18-20-24 Fr (0,8 to 4,5 cm)	Replacement for PEG	No	4-6 weeks
	MIC-PEG Gastrostomy	PEG	SIL	Y-Port	Bumper	14-20-24 Fr	Endoscopical	No	6 months
	MIC-G Gastrostomy	G	SIL	Y-Port	Balloon	12-14-16-18-20-22-24-26-28-30 Fr	Replacement for PEG	No	3-6 months
	MIC-B Gastrostomy (Bolus)	G	SIL	Y-Port	Balloon	12-14-16-18-20-22-24 Fr	Replacement for PEG	No	3-6 months
	MIC-KEY transgastric-jejunal	B	SIL	Funnel / Y-Port	Balloon	16/18/22 Fr/Stoma length 1 to 3,5 cm Jejunal length (15,22, 30 and 45 cm)	Endoscopical/Radiological	No	6 months
	MIC transgastric-jejunal	Jejunostomy	SIL	Y-Port	Balloon	16-18-22 Fr/ Jejunal length (15,.22, 30 and 45 cm)	Endoscopical/Radiological/ Surgical	No	6 months
	MIC Gastro-enteric	Jejunostomy	SIL	Y-Port	Balloon	16-18-20-22-24-26-28-30 Fr Jejunal length (25, 56,5 cm)	Endoscopical/Radiológical	No	6 months
	MIC Jejunal	JeJunostomy	SIL	Y-Port	–	14 Fr	Surgical	No	6 months

G: Gastrostomy tube; PEG: Percutaneous endoscopical gastrostomy; J: JeJunostomy tube; B: Button or Low profile system; SIL: Silicone; PUR: Polyurethan; FR: French (Caliber); J-PEG: Percutaneous endoscopical gastrostomy with jejunal extensión; NS: non-specified by the manufacturer. Modified from reference[12].

It is recommended that enteral giving sets are changed every 24 hours in the hospital to decrease the risk of contamination (B)[7], but in reality with good hygiene and conservation of the giving set, in our experience in the home care setting, it is possible to extend its use for a period of time greater than that[12].

Feeding pumps

Current feeding pumps are accurate, reliable and allow the management of exact volumes of feed within a given time.

There are two types of feeding pumps (table IV): peristaltic and volumetric.

In adults, it is recommended that feeding pumps have an accuracy of 10% of the volume administered (B) and it needs to be calibrated periodically (B). In the homecare setting the feeding pumps should be used safely and should not interfere with the patient`s night rest (B)[7].

Forms of administration of the EN

Place of infusion

The enteral feeding route determines the starting rate of the nutritional feeding regimen and the progression. When the infusion is in the stomach, the capacity for tolerance of the volume is much greater, allowing use of intermittent or cyclic infusion regimes delivered with a syringe or by gravity. In contrast to this, if the infusion is into the duodenum or jejunum then the volume of the nutrition administered and the infusion rate should be limited since high rate of infusion may increase the risk of feed intolerance with diarrhoea and dumping syndrome.

Initiation of enteral nutrition

The initiation of enteral nutrition will progress by following the guidelines as per-protocol according to the place of infusion and the technique of the feeding tube used. *In the non-invasive techniques EN may be start immediately* after verifying the proper placement of the feeding tube. *In the surgical techniques* (gastrostomy or jejunostomy) EN may be started between 24-48 h following the intervention (A)[7]. *In endoscopic and radiological techniques,* it is usual to start the enteral nutrition at 6 h after the technique. In the endoscopic technique recent studies indicate that it is possible to advance the start without increasing the risk of complications (B)[7].

It is not recommended to dilute the formula with water to avoid contamination and to reach as soon as possible the nutritional goals (C)[4,7].

Infusion regime

Once the correct tolerance of the EN is verified, the regime of infusion will help us to optimize the tolerance and the compliance.

The infusion regime depends on the place of infusion (gastric or intestinal), on the pattern prescribed (full or mixed), individual tolerance (diarrhoea, abdominal distension, nausea) and the needs of each patient (nutritional requirements, timetables, treatments and individual preferences).

There are different feeding regimes [9,13,14]:

- *Continuous EN:* The EN is administered continuously throughout the day at a consistent rate with a feeding pump.
- *Cycled EN:* The EN is administered on a continuous basis in a period of 8-12 hours with a feeding pump.
- *Intermittent EN:* The EN is administered not administered continuously but in short periods of time (usually according to the mealtimes), the administration can be with feeding pump, gravity or by bolus.

Monitoring

In general, during nutritional support with EN, it is recommended to monitor:

- The NGT site.
- The insertion site in case of ostomy.
- The daily amount given of EN.
- Oral intake (if any).
- Hydration status.
- Fluid balance in some cases.
- Gastric residual volume.

Method of infusion

There are three methods of infusion to deliver the EN:

1. *Syringe:* it is used for bolus enteral feeding.
2. *Gravity:* is administered through a giving set that allows regulating the infusion rate of the EN.
3. *Feeding pump:* indicated for patients who require a constant infusion rate over an established number of hours during the day and/or at night. Continuous feeding are often well tolerated and is commonly used for duodenal or jejunal infusion.

Transition of EN

1. *From EN to oral feeding:* the swallowing capacity of the patient needs to be taken into

Table IV
EN feeding pumps

Brand	*Model*	*Type of pump*	*Portable*	*Flow rate (ml/h)*	*Accuracy of flow rate*	*Size (cm) = height × length × depth*	*Battery runtime*	*Weight*
ABBOTT	Flexiflo Companion	Volumetric	Yes	5-300 ml/h 1 by 1 ml	± 10%	Only pump 10.92 × 15.24 × 4.32 Only charger 15.24 × 17.02 × 8.38	8 h to 150 ml/h	675 g Charger: 1,125 g
	Flexiflo Companion Clear Star	Volumetric	Yes	1-300 ml/h 1 by 1 ml	± 10% ± 0.5 ml/h	Only pump 10.92 × 15.24 × 4.32 Only charger 15.24 × 17.02 × 8.38	24 h	Pump: 600 g Charger: 1,125 g
	Flexiflo Quantum	Volumetric with automatic flush set	No	1-300 ml/h 1 by 1 ml Automatic flush set 25 ml of water every hour	± 10% ± 0.5 ml/h	20.96 × 19.05 × 15.24	8 h to 125 ml/h	3,270 g
	Flexiflo Patrol	Peristaltic	No	1-300 ml/h 1 by 1 ml	± 10% ± 0.5 ml/h	21.59 × 16.51 × 12.19	8 h to 125 ml/h	3,000 g
NESTLE NUTRITION	Compat Standard	Peristaltic	No	1-295 ml/h 1 by 1 ml	± 10% ± 0.5 ml/h	14 × 18 × 10	8 h to 100 ml/h	2,500 g
	Compat Go	Peristaltic	Yes	1-600 ml/h 1 by 1 ml If < 100 ml 10 by 10 ml Si > 100 ml	± 10% ± 0.5 ml/h	12.8 × 11.4 × 4.3	24 h to 125 ml/h	480 g
GRIFOLS	Nutriflow II	Peristaltic	No	1-300 ml/h 1 by 1 ml	± 10%	17 × 26 × 14	10 h to 150 ml/h	2,750 g
	Nubo	Peristaltic	Yes	1-400 ml/h 1 by 1 m	± 10%	15.5 × 10.5 × 4.5	24 h to 125 ml/h	530 g
NUTRICIA	Flocare Infinity	Peristaltic	Yes	1-400 ml/h 1 by 1 m	± 5%	9.5 × 14 × 3.5	24 h to 125 ml/h	392 g
COVIDIEN	Kangaroo cPump	Peristaltic	Yes	1-300 ml/h 1 by 1 m	± 10%	16.8 × 16.3 × 11.7	15 h to 125 ml/h	1,100 g
FRESENIUS KABI	Applix Smart	Peristaltic	Yes	1- 600 ml/h 1 by 1 ml	± 10%	12.8 × 11.4 × 4.3	24 h to 125 ml/h	480 g

account. If any alterations, a swallowing test should be performed to assess the volume and texture suitable for starting oral feeding.

2. *From PN to EN:* Rates for initiating enteral feeding after bowel rest should be slow and progressive. The current clinical situation of the patient and the progressive tolerance will establish the time from PN to EN.
3. *Trophic feeding:* Minimal quantities of enteral nutrition can have beneficial effects on the preservation of the intestinal epithelium, improves immune function and prevents the bacterial translocation in spite of not covering the daily nutritional requirements[15].

Care of enteral feeding access in adults

Common care guidelines for EN

Hand hygiene

Is the most effective method for the prevention and control of infections. The caregiver or patient should wash their hands with running water, liquid soap and dried with disposable paper towels when preparing the nutrition or when handling any part of the set.

At the hospital, after the washing of hands, it is recommended to use disposable gloves during the administration (A)[7].

Patient position during the administration of EN

The patient must be seated or at an angle of 30-45 degrees during the administration of the EN (A)[7] and between half an hour to an hour after the administration, except when it is delivered into the jejunum[16].

Oral hygiene

Although there is no oral intake, the patients must maintain a good oral hygiene: brushing with fluoride toothpaste twice a day[16] (B) and mouthwash without alcohol The toothpaste must be washed out and it is preferable not to rinse the mouth with water (B).

The consumption of foods, drinks or drugs rich in refined sugars should be avoided (C). The lips should be hydrated[17].

Water administration

Institutionalized patients must use sterile water for irrigation of the feeding tube before and after the administration of EN or medications (B)[7], while in the home setting the type of water will depend on the patient's environment. If there is an increased risk of infection or GI barrier disorder, sterile water must be used since it loses the bactericidal effect of the gastric barrier (C)[16].

Care of the EN formula

Should be stored in a clean dark place, between 15-25 degrees, avoiding extreme temperatures[18] (B).

Handling should be avoided. It is recommended that, whenever possible, use products ready to use and not powdered formulations to reconstitute (A)[7]. Handling should be done in a clean environment, using aseptic techniques and by trained personnel (A)[18] and reconstituted with sterile or purified water (B).

Hang time of enteral feeds needs to be closely monitored and depends on the type of formula presentation[3,17,19,20]:

- Airtight Packaging of plastic (semi-rigid or packs): 24 hours.
- Glass bottle: 8 hours.
- Powdered formula in a container: 4 hours.

Blockage prevention of the feeding tubes

The tube size depends on the site of the GI tract that EN will be delivered. Viscosity and drug interactions need to be taken into account[16].

Feeding tubes for intermittent feeds should be flushed with 20-30 ml of warm water before and after delivering the enteral feed. In continuous feeds water should be flushed every 4-6 hours[7] or when the formula is replaced. Maximise prevention of blockage in naso-jejunal or jejunostomy tubes. It is necessary to flush the feeding tubes before and after every medication (C)[16] even if not used.

Administering medications

Enteral guidelines should be followed to minimize complications of the enteral nutrition and medication. Medication should never be mixed directly with the enteral formula (B) or mixing different drugs together (B). The drugs should be administered separately crushed into fine powder and mixed with sterile water (B). Medication given via a feeding tube should be in liquid form whenever possible. Before the administration of the medication, EN should be stopped and the feeding tube should be flushed with 15 ml of water before and after the administration (A). In some cases, it is necessary to wait over 30 minutes to avoid the reduction of the bioavailability of the drug (A). Only syringes of oral/enteral administration (> 30 ml) should be used for the administration of medications (B).

Care of nasogastric and nasointestinal feeding tube

Silicone or polyurethane feeding tubes are flexible and have a duration of 4-6 weeks[16] (C). PVC tubes should only be used for gastric aspiration and must be changed every 3-4 days. Once the tube is placed, the guide wire should not be reintroduced[17].

Tube fixation

The nostril should be rotated, use hypoallergenic tape, change the area of the skin where it is fixed and maintain good hygiene and hydration of the skin and the nostrils at least once a day with a cotton swab or moistened gauze [17].

Control of the position of the feeding tube

Before starting the EN, the location of the feeding tube should be with abdominal X Ray. For subsequent tests, in addition to the location mark in the feeding tube, the measurement of gastric pH can be used (less than 5.5)[19,21]. This method most closely matches the effectiveness of radiation test, it is important to bear in mind those patients who are receiving treatment with antacids or continuous EN.

Care of gastrostomy and jejunostomy tubes

The replacement of the gastrostomy and jejunostomy tubes shall be carried out once a year, and in the balloon button tube every 3- 6 months.

Gastrocutaneous fistula

Accidental removal of the gastrostomy tube before the 3-4 weeks is an emergency because gastrocutaneous fistula has not formed and there is a high risk of peritonitis. If the removal is later in time, the stoma can close in 1-2 hours, so a replacement feeding tube must be introduced or a Foley catheter and return quickly to the reference hospital[21]. The caregivers and the patient must have an action plan and enough training to address this complication. At this stage you should never use a balloon button, gastrostomy or jejunostomy tube at home unless you are sure of the correct position.

Skin care stoma

The care will aimed to prevent infections, excoriations, wounds and granulomas[17]. Daily cleaning with a sterile gauze, during the first two weeks with a gauze soaked in saline water or hydrogen peroxide. From the third week the skin stoma should be clean with soap and water, rinse and dry the stoma and the surrounding area with another gauze and apply an antiseptic solution[21]. The skin of the stoma needs to kept clean, dry and hydrated[17]. It must be cleaned once a day, but if there are secretions it should be cleaned more often.

Control of feeding tube positioning

There will be daily checking reference marks, fixing systems and external length of the tube. In case of doubt the position will be confirmed by radiography, ultrasound, or measuring the gastric or intestinal pH with a colorimetric strip[17].

Specific care of button gastrostomy

Monitor the volume of the balloon at least once a month or if there are signs that it had ripped. Replacement of the button is performed every 6 months.

Specific care of the percutaneous radiologic gastrostomy (PRG)

The three anchor buttons[22,23] (three points of gastropexy and the surrounding area) must be cleaned daily with saline. To do this, the retaining plate need to be lifted carefully and cleaned with cotton swab, dried and an antiseptic solution applied. Finally a sterile gauze can be placed to cover the area.

The buttons of the gastropexy will fall between one week and three months. It is recommended to keep one for at least three weeks.

Specific care of the surgical gastrostomy and jejunostomy feeding tubes

Daily cleaning with saline in the periostomal area and attachment points is needed. Subsequently the stoma needs to be dry, apply an antiseptic and cover with a dressing[23]. It is essential to monitor presence of exudates, bleeding, or irrigation[22].

Care after enterostomy feeding tube removal

The most common complication after enterostomy feeding tube removal is the persistence of the fistula that depends on the time that it has been inserted[23].

If the duration was less than 11 months, the fistula will close spontaneously.

When a PEG or gastrostomy balloon is removed it is sufficient to make an approach with Steri-Strips® to close the stoma. If after 7-15 days has not been closed, we can cauterize the area with silver nitrate,

return to bring the ends with Steri-Strips® and treat the patient with antacids. If after 3-4 weeks of the cauterizing is not closed, it is a convenient surgical closure or by endoscopy combining cauterization and metal clips[9, 24].

EN complications

Classically they are classified as mechanical, infectious, gastrointestinal, metabolic and psychological (table V).

Table V
Potential complications associated with EN

Mechanical complications	*Action*
Type of feeding tube: **Nasoentetic**	
• Nasofaringeal discomfort	➪ Mouth higiene. ➪ Use of analgesia.
• Nasal irritation or erosion	➪ Tape tube securely to avoid pressure on nose. ➪ Use smaller tube.
Type of feeding tube: **Ostomy**	
• Leakage around tube and skin scoriation	➪ Replace the feeding tube to adapt it to the stoma. ➪ Pull back on tube gently until resistance felt to ensure intestinal securing device is flush to stomach wall. ➪ Tape tube securely to abdomen ➪ Consider changing the feeding tube. . ➪ Use creams/ointments only as indicated if skin is irritated or infected.
• Buried bumper syndrome	➪ Consult with endoscopist or surgeon.
• Granulation tissue	➪ Carefully mobilise the feeding tube. ➪ Stabilize the tube. ➪ Prescribe silver nitrate, if necessary.
Type of feeding tube: **Nasoenteric / Ostomy**	
• Tube displacement	➪ Tape tube securely after position verified. . ➪ Mark with fixed marker the right position of the tube.
• Internal digestive erosions	➪ Mobilise the tube with rotary movements. ➪ Check the position of the fixation.
• Involuntary tube removal	➪ Assess changing the Access. ➪ Secure and properly protect the tube. ➪ Replaced the PEG with a replacement kit or for another PEG as soon as possible.
• Blocked tube	➪ Flush with water every 4-6 hrs with continuous feeding and after each intermittent feeding.. ➪ Dilute medication according to pharmacy, in liquid form if possible. ➪ Flush with warm water or carbonated beverage.
Mechanical complications	*Action*
Type of feeding tube: **Nasoenteric**	
• Nasal septal abscess • Sinusitis • Otitis	➪ Careful and regular mobilization. ➪ With fever and pain, remove the tube and treat. ➪ Evaluate the placement of a gastrostomy.
• Infections	➪ Daily care and cleaning stoma. ➪ Avoid placing post trauma. ➪ Use appropriate hygiene measures (hand washing, use of disposable gloves) to prevent skin infections.
• Aspiration pneumonia	➪ Check the position of the tube prior to administration. ➪ Position the patient at more than 30 º or upright even once the enteral feed is finished. ➪ Evaluate a transpiloric access. ➪ Evaluate the placement of jejunostomy.

Table V *(cont.)*
Potential complications associated with EN

Gastrointestinal complications	*Action*
Type of feeding tube: **Nasoenteric / Ostomy**	
• Nausea, vomiting, regurgitation and abdominal distension	➪ Check gastric residuals ➪ Decrease the flow rate or change to continuous feeding. ➪ Room temperature of the enteral feed. ➪ Evaluate antiemetics. ➪ Decrease the fluid intake (< 30-40% of the total calories). ➪ Isotonic formula administration.
• Constipation	➪ Regular fluid intake. ➪ Fibre-containing formula. ➪ Increase physical activity when possible. ➪ Assess all the medication. Consult pharmacy for alternative. Use of laxatives if possible.
• Diarrhoea	➪ Increase higiene measurements. Check the time of infusion and the temperature. ➪ Decrease osmolality of the formula and evaluate the need of alternative medication. ➪ Use isotonic formula. . ➪ Decrease or modify the type of fibre used. . ➪ Decrease the flow rate of the enteral feed. ➪ Remove dietary components not tolerated. ➪ Room temperature enteral feed to be administrated. ➪ Check or modify the position of the tube.
Gastrointestinal complications	*Action*
Type of feeding tube: **Nasoenteric/ Ostomy**	
• Difficulties in adapting to the new situation	➪ Psycological support. ➪ Evaluate an individual suitable enteral access. ➪ Allow to remain in certain patients food in their mouth to taste it.
Metabolic complications	*Action*
Type of feeding tube: **Nasoenteric/ Ostomy**	
• Hyperglycemia	➪ Adjust the input according to glycemia. Assess specific formula. ➪ Assess hypoglycemic agents. ➪ Blood sugar control until stabilization.
• Hypoglycemia	➪ Gradual withdrawal of the enteral feed. ➪ Keep glucose infusion or intake.
• Dehydration	➪ Replace fluids as indicated. Check electrolites, fluid balance, osmolality and renal function. ➪ Provide an adequate amount of liquid and control the abnormal fluid losses. ➪ Evaluate the use of isotonic formula.
• Inadequate serum electrolites	➪ Check blood levels and adequate the composition of the feed if possible. ➪ Treat the cause of excess losses.

Criteria of care at discharge

The possibility to administer enteral nutrition in the patient's home (HEN), has great advantages as it allows the patient to remain in their family and social environment, and reduces health care costs associated with hospitalization.

But for greater safety and effectiveness for patients with HEN, an appropriate training program for both the patient and the primary caregivers with periodic follow-up is necessary.

HEN indications

Not all patients may be candidates to receive HEN support, to ensure the effectiveness of this treatment the patient must meet a number of requirements[25,26]:

- The patient's clinical condition should allow their discharge.
- Expectations should be made for improvement of quality of life.
- The family and/or caregivers must accept nutritional therapy.
- The patient should not be discharged until enteral nutritional tolerance is assured with the same HEN regimen that will be at home.
- The patient and/or caregivers must follow a training program that includes demonstration of their ability in handling the administration of enteral nutrition and action on the most frequent complications.
- The family and social environment of the patient should be favorable, the family of the patient must be willing to collaborate and help the patient in the administration of the enteral nutrition.

Program of education and training of the patient and /or caregivers[25,27,28]

When the need for HEN is established it is necessary to carry out a program of education and training for both the patient and primary caregivers to provide management of the nutritional support at home minimizing complications and ensuring the patient's maximum independence

The staff responsible for the education in this program at discharge should assess the acquirement of knowledge necessary for the administration of the HEN.

Contents of the education and training program

- What is HEN and the objectives to be achieved with this support.
- Enteral access: should include the most common complications and how to avoid them. In the case of the nasogastric tube, it should describe the length of the tube visible to assess possible mobilizations.
- Equipment required for the administration of the enteral nutrition.
- Characteristics and management of the prescribed formula: the conditions of conservation, storage and handling (hygiene, temperature, expiration...), as well as knowledge about how to detect possible alterations of the preparation.
- Method of administration: shall state the amount and timing of administration of prescribed formula and water, as well as time of administration.
- Nursing care: frequency and how to perform oral and nasal hygiene as well as care both of the feeding tube and the stoma.

Conflict of interest

The authors declare that they have participated in activities funded by the pharmaceutical industry for the marketing of nutritional products (clinical studies, educational programmes and attendance to scientific events). No pharmaceutical industry has participated in the preparation, discussion, writing, and establishing of evidences in any phase of this article.

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Revisión

Aplicaciones móviles en nutrición, dietética y hábitos saludables; análisis y consecuencia de una tendencia a la alza

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Resumen

Una aplicación móvil o app, es un software diseñado para funcionar en teléfonos inteligentes y otros dispositivos móviles. En los últimos años, estas apps han sufrido un auge en ofertas a sus usuarios y diversidad, entrando en el campo de la medicina, tanto para profesionales como para pacientes. De todas las "health apps", hay una parte destinada al campo de la nutrición. Se estima que en la categoría de "diet and fitness" hay más de 5.400 apps.

Objetivo: **Revisar las apps, para hacer un diagnóstico de la calidad y validez, así como revisar estudios que incorporen apps como parte de la metodología de trabajo.**

Metodología: **Búsqueda bibliográfica en las principales bases de datos científicas, PubMed, SciELO, Embase (últimos 5 años). Por otro lado, se realizó una búsqueda en el APPs Store de Android, además se introdujeron 7 palabras clave en el buscador de APPs Sotre, para analizar las 5 primeras de cada búsqueda.**

Resultados: **95 apps fueron analizadas, además de las revisadas en los estudios de investigación. Las apps resultaron ser una opción en la elección de estrategias de mejora y prevención de ciertas enfermedades relacionadas con la nutrición, el ejercicio y los hábitos diarios, tanto desde el punto de vista individual, como por profesionales, aunque cabe destacar la poca fiabilidad de la gran mayoría. De las 95 apps analizadas, el 51,57% se calificaron como "calidad baja".**

Conclusión: **Aunque la mayoría de las aplicaciones no son útiles ni seguras, si en un futuro se normalizan y mejoran, podrían suponer una herramienta de gran utilidad para la sociedad y el sistema sanitario.**

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Palabras clave: *App. TIC. Móvil. Nutrición. Dietética.*

MOBILE APPLICATIONS FOR NUTRITION, DIETETICS AND HEALTHY HABITS; ANALYSIS AND CONSEQUENCES OF AN INCREASING TREND

Abstract

A mobile application or app, is a software designed for smartphones and other mobile devices. Nowadays these have undergone a boom in its users offer and diversity, entering the field of medicine, for both professionals and patients. In "health apps" category, there is a part for the field of nutrition. It is estimated that in the category of "diet and fitness" more than 5,400 apps.

Aim: **Reviewing apps, to make a diagnosis of the quality and validity, and review studies witch incorporating apps as part of the project s methodology.**

Methods: **Literature search in major scientific databases, PubMed , SciELO , EMBASE (last 5 years) . In the other hand, a search was conducted in the Android APPs Store, 7 Key words were introduced in the form of APPs Sotre to analyze the top 5 of each search.**

Results: **95 Apps were analyzed, and others used from research studies. The apps found to be an option as strategies for improvement and prevention of certain diseases related to nutrition, exercise and daily habits, both from the individual used or as professionals, but include the unreliability of the majority. From the 95 apps analyzed, 51.57% were classified as "low quality".**

Conclusion: **Although most applications are not useful or safe, if in the future are normalized and improved, they could provide a useful tool for the healthcare system and society.**

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Key words: *App. ITC. Phone. Nutrition. Dietetics.*

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Abreviaturas

APP: Aplicación informática.
GPS: Sistema de posicionamiento global.
IMC: Índice de masa corporal.
Kcal: Kilo calorías.
PDA: Asistente digital personal.

Introducción

Una aplicación móvil o app, es un software o programa informático, que está diseñado para funcionar en teléfonos inteligentes (smartphones), tablets y otros dispositivos móviles[1].

Aunque originalmente las apps fueron concebidas como herramientas de trabajo y ofertaban información general, como el correo electrónico o el calendario, ha habido un rápido incremento de su desarrollo y su variabilidad, debido al desarrollo de las nuevas tecnologías y, en parte, a que cada vez más porcentaje de la población tiene smartphones u otros dispositivos capaces de soportar estas aplicaciones. Estas apps pueden ser de pago o gratuitas[1].

Además de como herramientas de trabajo, también han entrado en el campo de la medicina[2]. Debido al aumento de tablets y smartphones, hay una mayor posibilidad de usar estas nuevas tecnologías y apps en la práctica clínica[3].

En una revisión reciente de artículos que trataban sobre el desarrollo y la evaluación de aplicaciones para smartphones, se hizo una clasificación que separaba las apps para profesionales y apps para pacientes. Para profesionales en concreto, el uso de la tecnología resultó ser beneficiosa, dado que permite tomar decisiones de manera más rápida, con una menor tasa de error y un aumento en la calidad de la gestión y la accesibilidad a los datos[2].

La tecnología moderna ha revolucionado la habilidad de tener una gran cantidad de fuentes de información con sólo un movimiento de dedo y ha dado a los profesionales sanitarios la capacidad de combinar sus recursos de información y comunicación en un sólo instrumento portátil[4]. Se estima que en el Reino Unido, el 79% de los estudiantes de medicina y el 75% de los postgraduados poseen smartphones[5]. Y en este contexto, un uso importante de los smartphones, es que son capaces de ayudar en el diagnóstico, y tratamiento de varias enfermedades, gracias a que hay apps con referencias, o con funciones para apoyar decisiones que requieren menos esfuerzo para el profesional, y se considera que tienen una baja tasa de error[6].

Por su parte, las apps para pacientes son capaces de mejorar la educación, el manejo de las enfermedades crónicas de forma autónoma y en gran medida, permite la monitorización a distancia de los pacientes[2].

Sin embargo, pese a este beneficio, también nos encontramos varios desafíos. Por una parte los problemas de software, que rápidamente cambian. En segundo lugar, que el contenido y la información en esas apps no siempre es fiable, puesto que normalmente se desarrollan por profesionales no expertos en salud. Este último tema, ha dado inicio a varias iniciativas y trabajos para solventar dicho problema y para evaluar la calidad de estas apps[2].

De todas las "health apps", hay una parte destinada al campo de la nutrición: dietas, balance energético, consejos, ejercicio, etc. De hecho, las aplicaciones médicas más solicitadas son las que ayudan a controlar el peso y las que ofrecen consejos sobre una correcta nutrición[7]. Aunque también hay otras apps destinadas a otros colectivos con necesidades especiales, como alérgicos o intolerancias a alimentos, como por ejemplo "FoodLinkers" de Android, cuyo contenido está relacionado con las alergias o la app que lanzó el ministerio de salud de Buenos Aires, destinada a personas que padecen celiaquía: "BA sin T.A.C.C.", la APP "mobiCeliac[Scanner]"; o "iGLU info gluten para celiacos", de la *Asociación de Celiacos de Madrid*, en colaboración con la *Universidad de Alcalá* y *Fundación Vodafone España*.

Hoy en día, sólo en la plataforma iTunes, hay más de 650.000 apps, y el número continua creciendo. Esta "sobrecarga" de apps en el mundo de la salud, plantea 2 problemas:

1. Dificultad para encontrar la app adecuada a cada necesidad o situación[2].
2. Fragmentación de la información: Hay que usar varias aplicaciones para poder generar una mayor confianza y cantidad de los datos[2].

En este sentido, el estudio "patient apps for improving healthcare"[8], planteó uno de los análisis más completos hasta la fecha. Este estudio analizó 43.689 apps y los resultados fueron que 20.007 (45,8%) no estaban realmente relacionadas con la salud, eran más bien "trucos" sin unos beneficios reales; 7.407 (16,9%) eran fiables, y estaban dirigidas a profesionales; 16.275 (37,3%) eran fiables, y dirigidas a pacientes. A pesar de que aproximadamente el 50% sí tenían algo de fiabilidad, la mayoría de las apps eran simplemente una fuente de información (no diferente a las encontradas en libros, revistas especializadas o internet). Lo único de especial que tienen, es la forma de acceso a los usuarios, usando un canal en lugar de otro, pero sin ser nada innovador ni con una utilidad mayor. Había muy pocas dónde se pudieran hacer registros, muy pocas guías y apenas había apps para comunicarse con profesionales. Sin embargo, el informe refleja que hay una mayor conciencia sobre la salud, y la gente se involucra más en el manejo de la misma desde que la tecnología está permitiendo el rápido y fácil acceso a la información.

Se estima que en la categoría de "diet and fitness" hay más de 5.400 apps, vemos así que la cantidad de apps prima frente a la calidad del contenido y de su función, siendo además, responsabilidad del usuario elegir la adecuada. Esto se convierte en uno de los grandes problemas y retos, puesto que el usuario no tiene por

qué tener los conocimientos necesarios para saber si una app es de alta o baja calidad.

Además, mantener registros de alimentos y actividad precisos durante un tiempo prolongado es difícil y, hay varios errores de medición. Por ejemplo, las personas tienden a subestimar sistemáticamente la ingesta de alimentos y sobreestimar el nivel de actividad[9]. Es importante solventar esto, debido a que numerosos estudios a lo largo de la última década, han demostrado que el uso de las tecnologías puede ser muy eficiente para que la gente empiece a cuidarse más, pudiendo ser una posible solución a enfermedades de carácter epidemiológico, como la obesidad en occidente[10].

Sobre el ejercicio, al igual que con las apps de salud, también han ido publicándose revisiones y trabajos sobre el tema. En dos publicaciones recientes, podemos ver la dualidad de posibilidades que aún representa este tema en la comunidad científica. En uno de los trabajos[11], tras examinar 127 apps de la categoría "Health and fitness" concluye que carecen de mucha información; y en el segundo trabajo[12], se diseñó una app destinada a la promoción del ejercicio físico, y resultó tener una gran utilidad, que podría aumentar tanto el uso de las apps, así como la preocupación por la salud.

A medida que entramos en la tercera década de internet, varios artículos demuestran que estamos empezando a ver los beneficios de las primeras investigaciones sobre educación en salud, con la introducción de esta herramienta como parte de los mismos. Y a la vez que se expanden y aumentan los medios de comunicación y los canales para la comunicación electrónica, también lo hace el potencial de usar estas herramientas para crear programas para una correcta educación para la salud. Tampoco debemos menospreciar los programas a distancia, que facilitan el seguimiento de los datos propios del paciente para controlar enfermedades y promover la salud y el bienestar[10].

Las apps para contar kcal son otro de los reclamos populares, especialmente en países como Estados Unidos, las cuales aportan herramientas rápidas para calcular el contenido calórico de platos y menús completos, incluidos los de cadenas de restauración muy populares. Dos ejemplos son "Calorie Counter by FatSecret" y "Fast Food Calorie Counter", esta última cuenta con más de 70 restaurantes de comida rápida conocidos a nivel internacional y más de 9.100 menús y platos de estos establecimientos.

Objetivos

Revisar la tecnología de las apps, para hacer un diagnóstico de la calidad y validez, de aquellas relacionadas con el ámbito de la nutrición, la dietética y la salud, dentro del *Apps Store* de Android. Así como revisar en la literatura científica, aquellos estudios que incorporen apps como parte de la metodología de trabajo y propuesta de valor, en la recomendación de profesionales de la salud y la nutrición.

Metodología

Parte del presente estudio se centra en la revisión de la literatura científica sobre las diferentes apps destinadas al usuario en materia de salud, nutrición y deporte. Para ello, se ha llevado a cabo una búsqueda bibliográfica en las principales bases de datos científicas, *PubMed*, *SciELO*, *Embase*.

Para recuperar los estudios más relevantes se diseñaron distintas estrategias de búsqueda combinando las palabras clave según el tipo de estudio que se deseaba encontrar. La búsqueda se limitó a un periodo de manuscritos publicados que en su gran mayoría no superan los 5 años, y aproximadamente el 63% de los mismos han sido publicados en el últimos año. Se excluyeron de la revisión, los estudios que superaban esas fechas, debido a que el tema del estudio: apps, cambian rápido y avanzan de manera que las más antiguas no tienen mucha validez ni utilidad comparadas con las más nuevas.

La estrategia de búsqueda en *PubMed* fue la siguiente: (medical[All Fields] AND apps[All Fields] AND smartphones[All Fields]) AND ("2009/02/27"[PDat] : "2014/02/25"[PDat] AND "humans"[MeSH Terms]), para cada uno de los términos y palabras claves seleccionados de interés (medical, nutritional, diet, dietetic, nutrition, fitness, eHealth, mHealth, eDiet, app, phone, ITC, software, etc) adaptado a cada motor de búsqueda de las bases de datos analizadas, expuestas anteriormente.

Por otro lado, se realizó una búsqueda en el *APPs Store* de *Android*. Lo primero que hicimos fue acceder a la lista de aplicaciones bajo la categoría de "Salud y bienestar". Tras ello, descargamos las 40 más posicionadas en este canal y categoría, para proceder a su evaluación. Las agrupamos en 2 categorías: 1ª) Dietas, menús, recetas, pérdida de peso. 2ª) Ejercicio, balance energético, kcal, monitorizar entrenamiento, etc.

Para encontrar apps que tuvieran que ver con el manejo de enfermedades, pusimos varias etiquetas en el buscador del *APPs Store*, hasta descargar otras 20 y constituir así una tercera categoría: 3ª) apps sobre enfermedades relacionadas con la nutrición, dieta equilibrada, guías (clínicas y para pacientes).

Por último, tratando de evitar un posible sesgo de las aplicaciones que el *Apps Store* puede posicionar en cada categoría en primeras posiciones por razones meramente comerciales, se introdujeron palabras clave en el buscador, para analizar las 5 primeras de cada búsqueda.

Para el análisis se uso un score *ad hoc*, valorando los siguientes ítems: 1) Nombre de la app (¿corresponde con el contenido que aporta?); 2) categoría donde se encuentra la app (¿Es la correcta?); 3) Fácil manejo para el usuario al que va dirigido; 4) Funcionalidad (¿Grado de evidencia de los contenidos de la app?), siendo esta última la característica evaluada de mayor importancia.

Resultados

Respecto a la búsqueda de las apps, lo primero que podemos observar cuando navegamos en la categoría "salud y fitness" desde el sitio web del *APPs Store* (https://play.google.com/store/apps?hl=es) o desde el *APPs Store* de *Android,* aparecen gran cantidad de apps que no tienen nada que ver con dicho tema. Esto dificulta la búsqueda de las apps que son realmente útiles para cada usuario, sus necesidades y su situación.

Análisis de las apps más descargadas en las categorías descritas

Las apps que encontramos para la *primera categoría* fueron: Dietas para adelgazar (Tanish Pradhan); Dietas para reducir el abdomen (Clark Beggage); Dietas para adelgazar (STR Labs); 101 tips para bajar de peso (King apps); Peso ideal IMC (Mmapps mobile); IMC calculadora (Smayer.net); Dieta fitness (Gimca); Monitorea tu peso (Husain al-bustan); Dieta fácil y sana (Ismado); Dietas (CMR Paradise); Bajar la panza (Deviris); Peso perfecto (Team Geny); Dieta por puntos (JPLSoft); Dieta quema grasas (Sustore); Dieta relámpago (Lawstore); Recipes for fat burning (Tops apps 247); Diet point español (Dietpoint LTD.); Recetas (Eroski consumer); Peso asistente (Kevin Tung); Mi peso ideal (Oltrevista mobile).

El 40% (8) de las apps ofrecían dietas milagro (según la definición y los criterios del consenso del "Grupo de Revisión, Estudio y Posicionamiento de la Asociación Española de Dietistas-Nutricionistas" (GREP-AED-N), 2012[13]), el 10% (2) teoría sobre nutrición, y el 30% (6) se basaban en ofrecer una clasificación del peso del usuario, en función de su Índice de Masa Corporal (IMC). El 10% (2) ofrecían dietas ajustadas a la constitución, IMC y el peso que deseado, sin embargo estaban mal estructuradas y con una sola opción de menú, por lo que resulta difícil de adherirte, sin conocer los gustos del usuario. Sólo un 5% (1) adjuntaba una lista de la compra para el menú que ofrecía. En el 10% (2), se podía hacer un registro diario de peso y ejercicio para ver tu evolución a través del tiempo. Sorprendentemente, sólo un 5% (1) añadía ejercicios para hacer a la vez que se seguía la dieta.

Para la *segunda categoría:* Runtastic (Runtastic); Adelgazar los abdominales (Vairen); Runtastic pedometer (Runtastic); Runtastic heart rate (Runtastic); Runtastic sit-ups (Runtastic); Runtastic pull-ups (Runtastic); Runtastic squarts (Runtastic); Runtastic push-ups (Runtastic), Contador de calorias (My Fitness Pal INC.); Sports tracker (Sport tracking technologies); Runkeeper GPS (Fitness keeper INC.); Lifesum (dhapeUP AB); Perder peso. Adelgazar (Cryofy.com); Ejercicios y rutinas para adelgazar (Proxit apps); Gym trainer (DuritzHTC); Cardiógrafo (Macropinch); Ejercicios en casa (Deviris); Ejercicios para glúteos (Lawstore); Entrenamiento en circuito (Riana); Endomondo (Endomondo.com).

Sólo la mitad de las apps (10) permitían conservar tus datos para ir conformando un registro de los progresos. Un 25% (5), incorporaban una opción para usar el GPS y obtener tu circuito. El 45% (9) te indicaban las Kcal medias que gastabas en hacer un ejercicio. Aunque en la mitad de las apps, te decían qué ejercicios hacer y cómo llevarlos a cabo, las bases teóricas de los mismos, sólo estaban presentes en 2 apps (10%). Otro 10% (2) eran apps para medir tu frecuencia cardíaca. Tan sólo 2 apps (10%) relacionaban el ejercicio con la alimentación y aportaban una base de datos con alimentos, para que fueras añadiendo lo que comes cada día. El 10% (2) ofrecían dietas para llevar a cabo con un número predeterminado de kcal diario, en función de si querías ganar peso, perderlo o mantenerlo.

Para la *tercera categoría:* Osteoporosis diet (Primera sangre); Salud responde (Junta de Andalucía); Mini atlas VIH-SIDA (EC EUROPE); VIH-AIDS medical dictionary (Focus Medica India pvt); On track diabetes (Medivo); Diabetes diario (Suderman Solutions); Peso corporal. Obesidad cheque (Heycloud); Monitoreo obesidad (Carlos Alberto Veloz Vidal); Obesity management (CIMS Hospital PVT LTD); Cancer (Historia LLC); Cancer.net mobile (ASCO); Elderly care (SCIAB); Lower cholesterol tips (Bigo); Dislipemias (EC EUROPE); Health assistant (WSMRSoft); Metabolism (Guides); Liver disease synthoms (Pedestal apps); Eye diseases (Mobile apps for cahs flow); Alzheimer disease evaluation (Volca digital INC.) Optimum nutrition (Magzter INC.).

Dentro de las apps de la tercera categoría, encontramos mayor variabilidad, dirigidas a distintas enfermedades a las que estaban destinadas. Predominaban las que eran bases de datos con teoría en formato texto, tanto destinadas a pacientes, como a profesionales. La búsqueda resultó tan heterogénea que no se pudieron agrupar por sub-funciones. Destacamos algunos de los usos más frecuentes: citaciones en centros de salud, definiciones de términos médicos, apps que redireccionaban a soportes externos como guías, webs, o videos del portal de videos *Youtube*, etc.

- *"Nutrición":* Las 5 primeras apps que aparecen con esta etiqueta, son bastante correctas. Incluían tablas de composición de alimentos, ayudan a entender el significado de la clasificación del usuario de su IMC, acompañaban las funciones de información adicional teórica, ayudaban a hacer una dieta equilibrada según los consensos aceptados para la misma, etc. Podrían calificarse de alta o media calidad.
- *"Dietética":* dentro de esta etiqueta, 2 respondían al patrón de "dieta milagro". Las otras 3 eran aceptables: una sobre recetas (perfectamente detalladas, con kcal, ingredientes, una lista negativa y positiva sobre alergias o enfermedades, etc), otra era sobre ejercicio y registros de cambios de peso,

y la otra era teórica, pero muy bien estructurada, por alimentos, nutrientes y enfermedades, y podías buscar por cualquiera de los 3 apartados. Las apps que aparecieron en esta categoría, las puntuamos en conjunto con un valor de calidad media.

– *"Ejercicio":* La mayoría bastante simples, dado que te explicaban cómo hacer sólo ejercicios concretos. Varias tenían como función ayuda para hacer tu propio *planning*, y además añadían como información adicional algunos consejos sobre alimentación. El conjunto de estas apps resultó ser de calidad media y baja.
– *"Salud y nutrición":* sin duda los resultados han sido los peores, y más simples (sin ningún valor añadido, como elección de una de sus apps, frente a otros canales habituales para el usuario. Apenas hablaban sobre estos dos conceptos, introducidos. Referían más puntos de venta de libros o test sin ninguna validez. La puntuación es: calidad baja.
– *"Dietetic":* Variabilidad para las 5 seleccionadas. Una hablaba de alimentos, otra era de ejercicios, otra de recetas, y 2 ofrecían consejos sobre nutrición y belleza. Dada la pobreza de las 5 apps que aparecieron, este conjunto también fue categorizado de calidad baja.
– *"Sport and health":* Eran apps para hacer deporte. Algunas llevaban el GPS para hacer el recorrido, el tiempo, distancia, velocidad, etc. y en una, había una pequeña base de datos donde tu elegías el musculo que querías ejercitar y te daba una lista de movimientos y ejercicios caseros que podías hacer. Puntuación: alta calidad o calidad media.
– *"Nutrition":* Eran bastante útiles, una daba consejos, otra era un diario nutricional, dos eran tablas de composición de alimentos y la otra era información teórica pero muy bien explicada sobre consejos, ejercicios, calculadora de necesidades, enfermedades, etc. La puntuación que se le dio al conjunto de las apps que aparecieron con esta palabra clave, también fue de alta calidad o calidad media.

A continuación vamos a ver en forma de tabla, imágenes de las apps que aparecieron al escribir las distintas palabras clave en el buscador.

En cuanto a la puntuación llevada a cabo con el score, observamos (tabla II), que el 83,15% de las APPs analizadas tenían una calidad media o baja, y más de la mitad (51,57%), calidad baja).

Discusión

Como hemos visto en el apartado anterior, una búsqueda rápida en APPs Store de un Smartphone o tablet, puede arrojarnos apps con un perfil muy dispar en cuanto al lugar en el que se visualizan y su funcionalidad.

Uno de los aspectos a comentar, es que, incluso a pesar de la variabilidad y fiabilidad de los contenidos, la

Tabla I
Análisis de las 5 primeras apps por palabras claves

Palabras clave	*APPs*
Nutrición	Dietas y nutrición (Nature Soft Games); informe nutricional (ArmDevelopers), guía nutricional gratuita (Thiago Neves); soporte nutricional (Prestaciones médica RCCC); valores nutricionales (Nature Soft Games).
Dietética	Diet point español (DietPoint LTD); Recetas (Eroski consumer); nexercise (Nexercise), la dieta de los 90 días (Sussane kessler); jeepfit (Total wireless solutions)
Ejercicio	Ejercicios caseros (Dmastore); belleza. Ejercicio abdominal (Domobile health); ejercicios para glúteos (Lawstore); ejercicios cintura hermosa (Domobile health), Ejercicios y rutinas para adelgazar (Proxit apps)
Salud y nutrición	Libros de salud y medicina (VP. EN), Ayurveda: salud y belleza (My ayurveda); Calculadora nutricional (Paganini mobile & social dev); nutrición ayuda (Mindmapping); anytime health mobile (Anytime fitness).
Dietetic	Wellness dietetic (JDSoft); Wellness detetic guide (Quality guides LTD.); Recetas (Eroski consumer); acadroid culturismo (G5 develper); FoodQuery (GFactor).
Sports and health	Sport tracker (Sport tracking technologies); Endomondo sport tacker (Endomondo); Endomondo pro (Endomondo); Gym sport (Gymca); entrenador de deportes (Amalgame)
Nutrition	Health and nutrition guide (Naveeninfotech); Nutrition tracker (Meuuha apps); nutrition facts (Yuku); recipes & nutrition (Edamam); nutrition facts (starApps).

Nombre de las 5 apps (y sus creadores), localizadas en primer lugar tras realizar la búsqueda con las palabras claves indicadas.

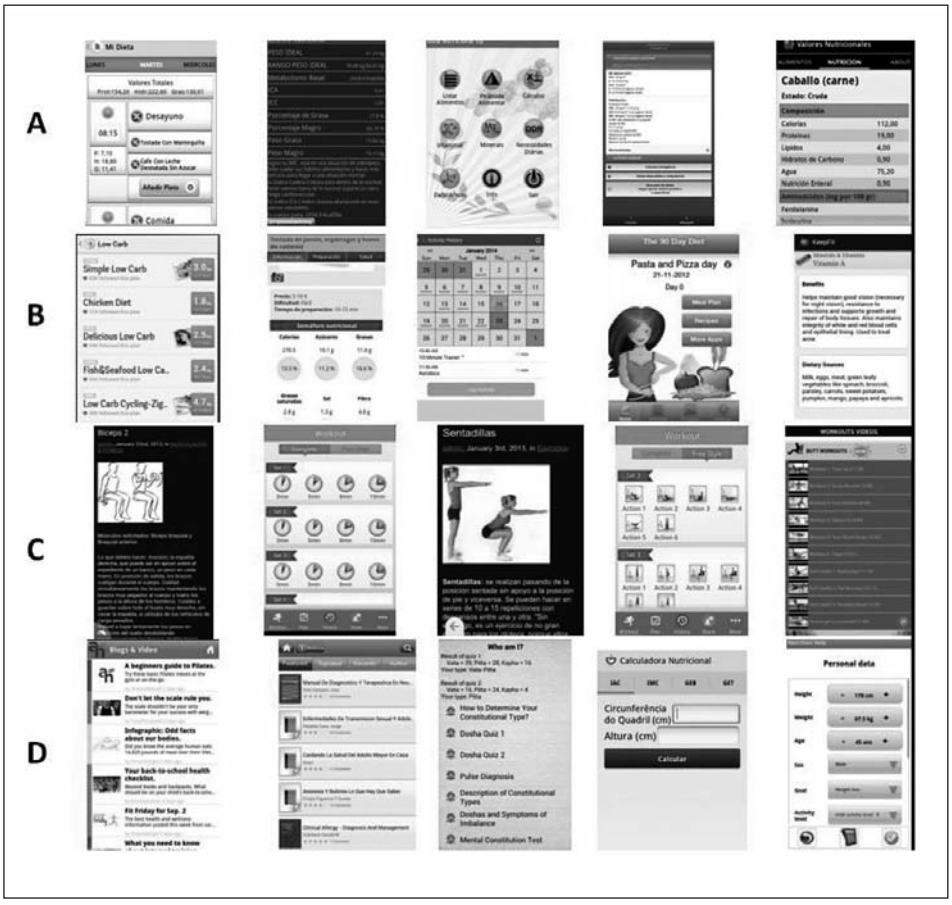

Fig. 1.—Cinco primeras APPs encontradas por palabras clave I (4 primeras palabras). A: Nutrición. B: Dietética. C: Salud y nutrición. D: Ejercicio.

Fig. 2.—Cinco primeras APPs encontradas por palabras clave II (3 últimas palabras). A: Dietetic. B: Sports and health. C: Nutrition.

Tabla II
Puntuación del score para la valoración de las 95 APPs analizadas

Grupo de APPs	*APPs valoradas*	*Calidad alta*	*Calidad media*	*Calidad baja*
Categoría 1 (20 APPs)	Dietas para adelgazar; Dietas para reducir el abdomen; Dietas para adelgazar; 101 tips para bajar de peso; Peso ideal OMC; IMC calculadora; Dieta fitness*; Monitorea tu peso*; Dieta fácil y sana; Dietas; Bajar la panza; Peso perfecto; Dieta por puntos; Dieta quema grasas; Dieta relámpago; Recipes for fat burning; Diet point español; Recetas*; Peso asistente; Mi peso ideal	3	7	10
Categoría 2 (20 APPs)	Runtastic*; Adelgazar los abdominals*; Runtastic pedometer; Runtastic heart rate; Riunstatic sit-ups; Runtastic squarts; Runtastic push-uyps; Contador de calorías*; Sports tracker*; Runkeeper GPS*; Lifesum*; Perder peso. Adelgazar; Ejercicios y rutinas para adelgazar; Gym trainer*; Cardiografo; Ejercicios en casa; Ejercicios para glúteos; Entrenamiento en circuito; Endomondo*	8	3	9
Categoría 3 (20 APPs)	Osteoporosis diet; Salud responde; Mini atlas VIH-SIDA; VIH-AIDS medical dictionary; On track diabetes; Diabetes diario; Peso corporal. Obesidad cheque; Monitoreo obesidad; Obesity management; Cancer; Cancer.net mobile*; Elderly care; Lower cholesterol tips; Dislipemias; Health assitant; Metabolism; Liver disease synthoms; Eye diseases; Alzheimer disease evaluation; Optimum nutrition	1	3	16
Palabra 1 (5 APPs)	Dietas y nutrición; informe nutricional; guía nutricional gratuita; soporte nutritional; valores nutritionales	0	5	–
Palabra 2 (5 APPs)	Diet point español; Recetas*; nexervise), la dieta de los 90 días; keepfit*	2	1	2
Palabra 3 (5 APPs)	Ejercicios caseros; belleza. Ejercicio abdominal; ejercicios para glúteos; ejercicios cintura hermosa; Ejercicios y rutinas para adelgazar	–	2	3
Palabra 4 (5 APPs)	Libros de salud y medicina; Ayurveda; slaud y belleza; Calculadora nutricional; nutrición ayuda; anytime health mobile	–	–	5
Palabra 5 (5 APPs)	Wellness dietetic; Wellness dietetic guide; Recetas*; acadroid culturismo; Foodquery	1	0	4
Palabra 6 (5 APPs)	Sport tracker; Endomondo sport tacker; Endomondo pro; Gym sport; entrenador de deportes	0	5	–
Palabra 7 (5 APPs)	Health and nutrition guide*; Nutrition tracker; nutrition facts; recipes & nutrition; nutrition facts	1	4	–
TOTAL		**16**	**30**	**49**

Clasificación de las puntuaciones obtenidas de las 95 APPs analizadas con el APP Store, usando el score usado, para cada una de las categorías o palabras clave, en 3 grupos: Calidad alta, media o baja. *APPs puntuadas como "Calidad Alta".

utilización que se le dé, por parte del usuario puede ser nefasta, teniendo en cuenta que el usuario no tiene por qué conocer el significado de cierta terminología o textos introducidos de libros o estudios científicos. Por ejemplo, no saber lo que es el IMC o lo que significa su clasificación, o no entender la relación entre un nutriente, su función en el organismo y cómo va a ayudarle en su enfermedad o situación, a pesar de que esté muy bien documentado (basado en medicina y nutrición en la evidencia). Además, no toda la teoría mostrada o en la que se basa la funcionalidad de las apps, es correcta, como otros autores han puesto también de manifiesto[14].

De todas las apps que encontramos en el App Market, la gran mayoría eran destinadas a pacientes, por lo que la información que obtuvimos no se puede extrapolar al grupo de apps para profesionales, que fueron revisadas en la búsqueda, en bases de datos científicas.

De la revisión en las bases de datos, se recuperaron 27 estudios relacionando las APPs y nutrición, mayoritariamente como estrategia de programas de intervención realizadas por profesionales de la nutrición. También los estudios estaban enfocados a los pacientes, por lo que las conclusiones obtenidas, sólo tienen validez a la hora de hablar del comportamiento de los pacientes, respecto a las apps.

La mayoría de los estudios revisados, iban encaminados a reforzar la idea de que las apps y las nuevas tecnologías, son elementos con gran potencial para mejorar la situación de personas enfermas, prevenir enfermedades en personas sanas y, en definitiva, mejorar el sistema sanitario. Sin embargo coinciden en que no todas las apps son útiles, y que aunque así lo sean, el usuario necesita saber manejarlo correctamente, además de necesitar estrategias, para que el uso de las apps tenga continuidad en el tiempo.

Dentro de los estudios revisados, el más antiguo e incluido como excepción, es el estudio de *Tsai CC* y cols. 2007. Los investigadores crearon una aplicación en la que los usuarios registraban lo que habían comido y la actividad física que habían realizado para obtener así información sobre su balance energético. La plataforma se conectaba con un servidor externo y así los usuarios podían ver en internet sus datos guardados con más detalles. En la web se guardaban también los datos sobre la ingesta y la actividad física, además podían enviar mensajes de recordatorio al usuario. Tras desarrollar la aplicación crearon 3 grupos: un grupo de pacientes iba a usar papel y lápiz para su registro diario, otro grupo haría un registro diario en la aplicación y los pacientes pertenecientes al tercero, harían 3 registros al día en la aplicación. Al final del estudio se midieron 2 parámetros: en primer lugar el software y en segundo la viabilidad en función de la satisfacción y el cumplimiento (ambos evaluados por los usuarios). Los resultados mostraron que los usuarios de la aplicación piloto daban puntuaciones más altas en satisfacción, utilidad y cumplimiento frente a aquellos que habían hecho el estudio con lápiz y papel; mostrando así, que una app podría ser muy útil para mejor control de la ingesta calórica, y una mayor adherencia[15].

En cuanto a la percepción de uso de las apps, existen varios reportes en la literatura. En el estudio de *Hebden L* y cols. 2012, se evaluó la satisfacción del manejo de una app, con una población adulta joven (18-35 años). Los sujetos que participaron la valoraron positivamente, y las pocas quejas que se manifestaron fueron referidas a aspectos de menor relevancia, por ejemplo que hacía falta meter usuario y clave para entrar, que el tiempo de carga a veces era lento, o que la app se quedaba "congelada"[16].

Pero no sólo se piensa en gente joven, también en las personas más mayores, siendo el fundamento de otro proyecto[17]. Los resultados fueron que los hombres estaban dispuestos a usar internet para mejorar sus hábitos, siempre que fueran programas rápidos y fáciles de usar. Este estudio piloto sugiere que existen posibilidades viables para involucrar a hombres de mediana edad en el entorno de las apps y nuevas tecnologías. Aunque también aclara, que para tener éxito, estas intervenciones tienen que ser hechas a medida. Teniendo en cuenta la prevalencia de multipatologías que frecuentemente encontramos en esta población, esta nueva posibilidad, podría ser una gran aliada.

En el estudio de *Mattila E* y cols. 2013, se desarrolló "*Wellness diary*", para que el usuario fuera registrando sus cambios de peso y aprender sobre su comportamiento, mejorarlo y mantenerlo. Sin embargo, el compromiso a largo plazo, sólo se demostró si el diario era paralelo a otra intervención, sin embargo, si se usaba de forma independiente no tenía suficiente motivación para que la gente lo usara. Por lo tanto, se necesitaba identificar cómo se podría personalizar y en general como podría mantenerse la motivación de los usuarios, para que su uso se diera a largo plazo. De aquí podemos extraer, que la motivación para la continuación es esencial para cualquier app que requiera resultados a largo plazo, como pueden ser la relación y supervisión de uno o varios profesionales, que acompañen en estas intervenciones[14].

En cuanto a aplicaciones para el manejo del peso y composición corporal, varios estudios fueron encontrados: *Lee W* y cols. 2010, crearon *SmartDiet*, que analizaba diariamente la ingesta de alimentos y patrones diarios de ejercicio. Con ello, proporcionaba un perfil dietético personalizado, y la técnica que se usó para fomentar los conocimientos sobre nutrición, fue hacerlo mediante un juego. Evaluaron la efectividad según la información adquirida, el control del peso y la satisfacción de los usuarios. Fue llevada a cabo mediante un estudio de casos-controles. Y los resultados fueron significativos; los individuos que usaron la aplicación tuvieron una reducción significativa de masa grasa, peso e IMC con respecto al grupo que no la usó, que no tuvieron bajadas significativas de esos 3 parámetros[18].

Otro estudio[19], también se creó una app para monitorizar un programa de reducción de peso. Se hizo un estudio aleatorizado en el que se dividió a los usuarios en

3 grupos para comprobar qué era más efectivo a la hora de bajar peso: una app, un programa online o un diario escrito. Y los resultados fueron favorables a la utilización de la app. El compromiso y adherencia con la intervención fue el más grande con respecto a los otros 2 grupos, y además pareció causar una mayor satisfacción y aceptabilidad que los otros dos métodos.

El grupo de *Oliver E* y cols. 2013, facilitó a varios niños de entre 9 y 15 años una PDA para hacer registros diarios, dentro de un tratamiento para el sobrepeso. Concluye que la PDA es un sistema fiable, que permite al clínico confiar en los datos registrados por los niños respecto a la ingesta y a la actividad física[20]. Por lo que resulta interesante, teniendo en cuenta la tasa de obesidad infantil y en la adolescencia que sufrimos en España actualmente[21].

Además de para tratar enfermedades, se podrían usar las apps, como promoción de hábitos saludables (entre los que se encontraría el ejercicio) y disminuir así la tasa de sedentarismo, como ayuda en la prevención de la obesidad y el sobrepeso. Las nuevas tecnologías pueden ayudar en ello, debido a todos los "exergames" o juegos para el ejercicio que se están desarrollando basados en la ubicación y el GPS. Así los individuos podrían estar más en este tipo de ocio activo, en lugar de sedentarismo con videojuegos tradicionales[22].

Otra posibilidad de esta tecnología, que han aprovechado varios autores, es en el manejo de enfermedades relacionadas con nutrición y que precisan una educación y seguimiento de los pacientes:

Arsand E y cols. 2010, presentó una app para controlar y monitorizar la diabetes tipo II de una muestra de sujetos. Reportando que varios de los usuarios, aprendieron a ajustar mejor su medicación, mejoraron sus hábitos alimenticios y su ejercicio físico[23]. Sin embargo, otros autores advierten que en el manejo de la diabetes, y a pesar del creciente número de apps para este fin en los últimos años, los usuarios carecen de las habilidades suficientes para encontrar información relevante acerca de su salud, situación concreta y su manejo[24].

Las apps, pueden ser por lo tanto una opción en la elección de estrategias, mejora y prevención de ciertas enfermedades relacionadas con la nutrición, el ejercicio y los hábitos diarios, tanto desde el punto de vista individual, como a nivel global o salud pública. Donde quizás sea primordial conocer que si los objetivos requieren un compromiso a largo plazo, como es el caso de la nutrición (cambios de hábitos de alimentación) y la actividad física, se necesitarán estrategias de apoyo adicionales para prolongar la motivación de usar estas apps[15], como podría ser la supervisión de un profesional de la salud y la nutrición.

Conclusión

Las apps suponen un avance social, y a priori una ventaja en el mundo de la salud. Por otro lado, queda patente el problema de que la mayoría de las aplicaciones que hay en el mercado, no son útiles (desde el punto de vista de su funcionalidad), ni seguras (desde el punto de vista de la evidencia científica), pero cuando hay supervisión profesional, puede acompañarse de resultados muy beneficiosos. Su mal uso, podría derivar en una falta de información en la salud pública. Lo que es seguro, es que si se normalizan y mejoran, podrían suponer una herramienta de gran utilidad para la sociedad y el sistema sanitario.

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Hypertriglyceridemic waist phenotype: association with metabolic disorders and visceral fat in adults

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Abstract

Objective: **To evaluate the association of Hypertriglyceridemic waist with metabolic disorders and visceral fat in adults.**

Methods: **Cross-sectional study with 191 individuals of both sexes. Subjects were grouped according to Waist Circumference (WC) ratings (Men: > 90 cm; Women: > 80 cm) and triglycerides (TG) (> 150 mg/dl) in Group 1 (HTW Phenotype): elevated WC and TG; Group 2 (absence of HTW Phenotype): elevated WC and normal TG or normal WC and elevated TG or normal WC and TG. Metabolic alternations, visceral adipose tissue (VAT) and visceral/subcutaneous fat index (VF/SF) measured by computed tomography were evaluated as cardiovascular risk factors between the groups.**

Results: **Individuals with HTW phenotype, 82% had three or more cardiovascular risk factors. The association between cardiovascular risk factors with HTW phenotype revealed that among men 73.7% had hypercholesterolemia, 94.9% elevated non-HDLc and 78.9% excess of VAT area (p = 0.001). Among women, 65% had elevated Sistolic Blood Plessure, 80% hypercholesterolemia and 90% elevated non-HDLc (p < 0.02).**

Conclusion: **The HTW phenotype associated with the metabolic alternations and VAT excess. Individuals with HTW had higher number of cardiovascular risk factors. The Hypertriglyceridemic waist can be used in clinical practice for investigating cardiovascular risk and visceral adipose tissue in individuals.**

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Key words: *Hypertriglyceridemic waist. Metabolic profile. Visceral adipose tissue. Tomography computed. Cardiovascular diseases.*

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FENOTIPO CINTURA HIPERTRIGLICERIDÉMICA: RELACIÓN ENTRE CAMBIOS METABÓLICOS Y GRASA VISCERAL EN ADULTOS

Resumen

Objetivo: **Evaluar la relación entre Cintura Hipertrigliceridémica (CHT) con cambios metabólicos y grasa visceral en adultos.**

Métodos: **Estudio transversal con 191 personas de ambos sexos. Los participantes fueron agrupados según clasificación de Circunferencia de Cintura (CC) (Hombres: > 90 cm; Mujeres: > 80 cm) y triglicéridos séricos (TG) (>150 mg/dl) en el Grupo 1 (Fenotipo CHT): Elevación en CC y TG; Grupo 2 (ausencia del Fenotipo CHT): Aumento en CC y TG normal, o CC normal y TG elevado o CC y TG normales. Cambios metabólicos, área del tejido adiposo visceral (TAV) y índice de grasa visceral/subcutáneo (GV/GS), medidas por tomografía computadorizada, fueron evaluados como factores de riesgo cardiovascular entre los grupos.**

Resultados: **De los participantes con el Fenotipo CHT, 82% presentaban tres o más factores de riesgo cardiovascular. La relación entre los factores de riesgo cardiovascular y el Fenotipo CHT demostró que entre los hombres 73,7% presentaban hipercolesterolemia, 94,9% no-HDLc elevado y 78,9% exceso de área TAV (p = 0,001). Entre las mujeres, 65% presentaban presión arterial sistólica alta, 80% hipercolesterolemia y 90% no-HDLc elevado (p < 0,02).**

Conclusión: **El Fenotipo CHT se relacionó con cambios metabólicos y exceso de TAV. Personas con CHT presentaron más factores de riesgo cardiovascular. La Cintura Hipertrigliceridémica puede ser utilizada en la práctica clínica para investigar el riesgo cardiovascular y el depósito del tejido adiposo visceral en las personas.**

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Palabras clave: *Cintura hipertrigliceridémica. Perfil metabólico. Tejido adiposo visceral. Enfermedades cardiovasculares.*

Abbreviations

TG: Triglycerides.
LDLc: LDL Cholesterol.
WC: Waist circumference.
VAT: Visceral adipose tissue.
HTW: Hypertriglyceridemic waist.
CVD: Cardiovascular disease.
UFBA: Universidade Federal da Bahia (Federal University of Bahia).
BMI: Body Mass Index.
SBP: Systolic Blood Plessure.
DBP: Diastolic Blood Plessure.
Non-HDLc: Non-HDL cholesterol.
TC: Total Cholesterol.
HDLc: HDL cholesterol.
Group 1 (HTW Phenotype): elevated WC and TG.
Group 2 (Absence of HTW Phenotype): Elevated WC and normal TG or normal WC and elevated TG or normal WC and TG.
CT: Computerd Tomography.
TAT: Total Adipose Tissue.
SAT: Subcutaneous Adipose Tissue.
VF/SF: visceral fat/subcutaneous fat index.
MS: Metabolic Syndrome.

Introduction

Hypertriglyceridemia is a factor known as potentially risk for cardiometabolic alterations, since triglycerides level (TG) is a good marker of LDL cholesterol (LDLc) particles size, these potentially atherogenic and components of the metabolic triad (characterized by increased levels of insulin, apolipoprotein B and a predominance of small and dense particles of LDLc)[1-4]. The Waist Circumference (WC) is used as a simple tool to identify individuals with high cardiovascular risk (CV), by its association with visceral adipose tissue (VAT) and concentrations of insulin and Apo B[4-6].

The hypertriglyceridemia and an elevated WC, known as Hypertriglyceridemic Waist (HTW) could represent a simple clinical phenotype to identify individuals with excess visceral adipose tissue. Indeed, the presence of HTW identifies individual characterized by metabolic triad[4,7-9]. On the other hand, little has been revealed whether individuals without the phenotype also express such consequences.

In clinical practice, measurement of the metabolic triad elements and VAT precise quantification, through image methods, presented limitations of use due to the high cost and time spent, on the other hand, HTW is easily obtained and offers possibility of diagnosis in screening and follow-up to identify potentially risk individuals for cardiovascular disease (CVD).

In order to contribute for the adoption of a viable method to estimate accurately the global cardio metabolic risk, the objective of this study was to evaluate the association of hypertriglyceridemic waist with metabolic disorders and visceral fat in adults.

Methods

Sample and Study Design

Cross-sectional study conducted by the School of Nutrition of the Universidade Federal da Bahia (UFBA) during the first quarter of 2009, conducted by the team of the Center of Studies and Intervention in Aging of UFBA in Salvador, the third largest city of Brazil.

Two-hundred individuals were randomly selected through equal inclusion by sex, age and body mass (estimated by BMI: Body Mass Index), based on the inclusion criteria: age ≥ 20 years and BMI < 40 kg/m^2. For this study, 9 individuals were excluded as they have value of TG ≥ 400 mg/dL and individuals with VAT area equal to or lesser than 10cm^2, remaining a total of 191 evaluated individuals.

The non-inclusion criteria were: severely malnourished and suffering from dystrophy and neural sequel; patients with amputation or any other physical or postural problem that compromise the verification of anthropometric measurements and abdominal fat; that had recently undergone abdominal surgery, pregnant women or who gave birth during the last six months; patients with abdominal injuries and tumors, hepatomegaly and/or splenomegaly and ascites.

All subjects underwent anthropometric, biochemical and imaging assessments by computed tomography for measurements of abdominal adipose tissue areas.

The measurement of systolic (SBP) and diastolic (DBP) blood pressure followed the technique recommended by the VIth Brazilian Guidelines in Hypertension[10].

Anthropometric evaluation-indicator of abdominal fat

It has been performed by a properly trained staff and consisted in the measurement of WC, collected using tape measure of inelastic synthetic material (TBW Importing Ltda), measured at the midpoint between the lower costal margin and the iliac crest[11], with a reading taken at the time of expiration.

Laboratory Evaluation

The lipid profile and uric acid were measured in serum using a colorimetric system, dry chemistry method using kits manufactured by Ortho-Clinical Diagnostics®, collected in a private laboratory, with patients in a 12-hour overnight fast. The LDLc value was measured by the Friedewald[12] equation and the non-HDL cholesterol value (non-HDLc) was obtained by calculating the difference between total cholesterol (TC) and HDL cholesterol (HDLc)[3].

Ratings of waist circumference, triglyceride level, the hypertriglyceridemic waist phenotype (HTW phenotype)

The WC was classified according to criteria suggested by the International Diabetes Federation (IDF)[13] for the South-American ethnic groups, being considered high when > 80 cm for females. For TG classification, it was considered high when the serum level > 150 mg/dL[3,13]. Thus, subjects were stratified in 2 groups: Group 1 (HTW Phenotype): elevated WC and TG; Group 2 (Absence of HTW Phenotype): Elevated WC and normal TG or normal WC and elevated TG or normal WC and TG.

CT scans- an indicator of visceral adipose tissue

Computed tomography was performed in the Department of Radiology of the University Hospital of the UFBA and analyzed by a radiologist. To perform the exam it was necessary to complete the 4-hours fasting, with the subject in supine position and the arms extended overhead. No barium or organoiodine contrast medium were administered.

A single CT cut was taken at the level of L4-L5 vertebrae for delineation of total adipose tissue (TAT), visceral (VAT) and subcutaneous (SAT) areas. With the free electronic cursor, the external edges that limit the abdominal circumference were delimited, and the total abdominal area calculated. Then, the visceral abdominal area was delimited through the abdominal cavity marking; using as limits the muscles of the rectus abdominis, internal oblique and square lumbar[14]. The tomography program was used with X-ray CT scanner parameters 140 kV and 45 mA; being used the density of -50 and -150 Hounsfields units for the identification of adipose tissue.

Cardiovascular risk factors

The following metabolic alternations and in the visceral fat area were considered as cardiovascular risk factors, according to criteria already established in the literature[3,13,15,16]: SBP > 120 mmHg; DBP > 80 mmHg; TC > 200 mg/dl; LDLc > 160 mg/dl; HDLc < 40 mg/dL for men and < 50 mg/dL for women, non-HDL-C > 130 mg/dl, uric acid > 8.5 mg/dl for men and > 6.2 mg/dl for women; VAT area > 130 cm^2; visceral fat/subcutaneous fat index (VF/SF) > 0.4. For analysis of cardiovascular risk factors the number of metabolic alternations that individuals presented was considered, being categorized into: no factor, 1-2 factors, 3-4 factors and > 5 risk factors for development of CVD.

Statistical analysis

Analyses were performed with the Statistical Package for Social Science (SPSS), version 16.0. In order to characterize the study population, the variables were expressed by descriptive analysis of data, with the frequency distribution, calculation of central tendency and dispersion, analyzes stratified according to the sex and HTW Phenotype classification (Group 1 and 2). The coefficient of variation was calculated to assess inter and intra examiner variability of anthropometric measures (Inter-class coefficient > 0.90). Data normality was verified by the Kolmogorov-Smirnov's test for all the analyzed variables. The *t-student's* test has been used for independent samples, to compare the mean results of the variables of normal distribution and the *chi-square* test to verify the existence of an association between the number of cardiovascular risk factors and the presence and absence of HTW Phenotype. The significance level was less than 5%.

Ethic Aspects

This study was approved by the Ethic Committee (Committee of Ethics in Research of the Federal University of Bahia, School of Nutrition - CEPNUT/UFBA), declaration number 01/09, and all participants provided their written informed consent to participate in this study, after approval of the process by the ethics committee.

Results

The study included 191 individuals, of both sexes, aged between 21 and 95 years old. Among the participants, women had a higher percentage of elevated WC (74.2% *versus* 52.1% in men, p = 0.002). Hypertriglyceridemia was present in 28.7% and 25.8% of men and women, respectively, with no statistically significant difference. HTW Phenotype was similar between both sexes (men - 20.2% and women - 20.6%; p > 0.05). Men had higher means of uric acid, VAT area, VF/SF index and WC than women (p<0.01) (data not shown).

The analysis comparing the means of variables considering cardiovascular risk factors between groups 1 and 2 (table I) showed that, for both sexes, individuals with HTW phenotype (Group 1) showed higher means (p < 0.01). Among men, the mean values of TC (223.9 mg/dl), non-HDLc (182.6 mg/dl) and VAT area (187.2 cm^2) were higher than the cut-offs points established in the literature. Among women, the same was observed for SBP (130.0 mmHg), TC (240.2 mg/dl), LDLc (151 mg/dl), non-HDLc (190.9 mg/dl) and VAT area (133.7 cm^2).

In figure 1 the cardiovascular risk factors frequency was presented among individuals with or without HTW phenotype. It was observed that among individuals with HTW phenotype (Group 1), 82% had three or more cardiovascular risk factors, 53.8% had 3-4 risk

Table I
Comparison between means of metabolic risk factors in the presence and absence of HTW Phenotype, by gender

	Men		
	Group 1	*Group 2*	*p-value*
SBP	133.2 (20.8)	127.3 (17.9)	0.225
DBP	84.7 (12.6)	80.5 (13.4)	0.221
TC	223.9 (31.1)	188.2 (36.1)	0.000
LDLc	139.3 (28.1)	117.5 (32.3)	0.008
HDLc	41.3 (5.5)	49.7 (12.9)	0.001
Non-HDL	182.6 (30.0)	138.4 (37.4)	0.000
Uric Acid	6.6 (0.9)	5.4 (1.2)	0.000
TAT	736.4 (109.5)	582.5 (151.3)	0.000
VAT	187.2 (62.0)	112.3 (77.3)	0.000
SAT	549.2 (100.9)	470.3 (98.1)	0.002
Rate VF/SF	0.35 (0.12)	0.23 (0.14)	0.001
	Women		
	Group 1	*Group 2*	*p-value*
SBP	135.0 (23.3)	122.2 (13.4)	0.002
DBP	82.0 (12.4)	78.9 (8.2)	0.182
TC	240.2 (68.9)	203.5 (41.1)	0.003
LDLc	151.5 (70.6)	123.2 (38.0)	0.017
HDLc	49.3 (9.7)	60.2 (14.6)	0.002
Non-HDL	190.9 (70.8)	143.2 (42.5)	0.000
Uric Acid	5.8 (1.4)	4.2 (0.9)	0.000
TAT	684.5 (119.6)	592.4 (155.2)	0.015
VAT	133.7 (40.6)	88.3 (51.6)	0.000
SAT	550.8 (95.8)	504.2 (128.6)	0.133
Rate VF/SF	0.24 (0.07)	0.18 (0.10)	0.001

Data presented in Mean (Standard Deviation).
Group 1 (HTW Phenotype):Elevated WC and TG; Group 2 (Absence of HTW Phenotype): elevated WC and normal TG or normal WC and elevated TG or normal WC and TG.
* Independent Samples *t-test*
SBP: Systolic Blood Pressure (mmHg); DBP: Diastolic Blood Pressure (mmHg); TC: Total Cholesterol (mg/dL); LDL: Low Density Lipoprotein (mg/dL); HDL: High Density Lipoprotein (mg/dL); TG: Triglycerides (mg/dL); TAT: Total area of Adipose Tissue (cm²); VAT: Total area of Visceral Tissue (cm²); SAT: Total area of Subcutaneous Tissue (cm²); VF/SF: Visceral Fat/Subcutaneous Fat index.

factors and 28.2% had five or more risk factors. While from individuals without the HTW phenotype (Group 2), 37.5% had 3 or more risk factors, and 7.2% had five or more risk factors, with statistically significant difference between groups ($p < 0.000$).

The association between cardiovascular risk factors with the HTW phenotype showed high percentage of individuals, of both sexes, having changes of cardiovascular risk factors (table II). Among men with the phenotype, 73.7% had hypercholesterolemia, 94.9% high non-HDLc and 78.9% excess VAT area, when compared with men without the phenotype ($p < 0.01$). Among women with the phenotype, 65% had elevated SBP, 80% hypercholesterolemia and 90% high non-HDLc ($p < 0.02$).

Discussion

HTW phenotype, the indicator used in this study, had an association with metabolic alternations and VAT excess, which are cardiovascular risk factors, in men and women. There are few researches on this topic using computed tomography as an imaging method for quantification of VAT, which underscores the relevance of this study.

In the present study, the HTW phenotype prevalence was 20.2% in men and 20.6% in women, this data agrees with other studies conducted with adults of both sexes, with the prevalence ranging from 12.7% to 36.5%[2,17-19]. It is noteworthy that studies in Brazil are scarce, with a prevalence of HTW ranging from 4.5% to 33%[20-22]. Note that variations in prevalence may be due to the use of different cut-offs for WC and serum TG levels, as well as ethnic differences and use of hypolipidemic.

For both sexes, individuals with HTW phenotype (Group 1) had higher means for metabolic variables and adipose tissue area ($p < 0.01$), with mean values higher than the cutoffs points established in literature. This result was similar to that demonstrated by Sam et

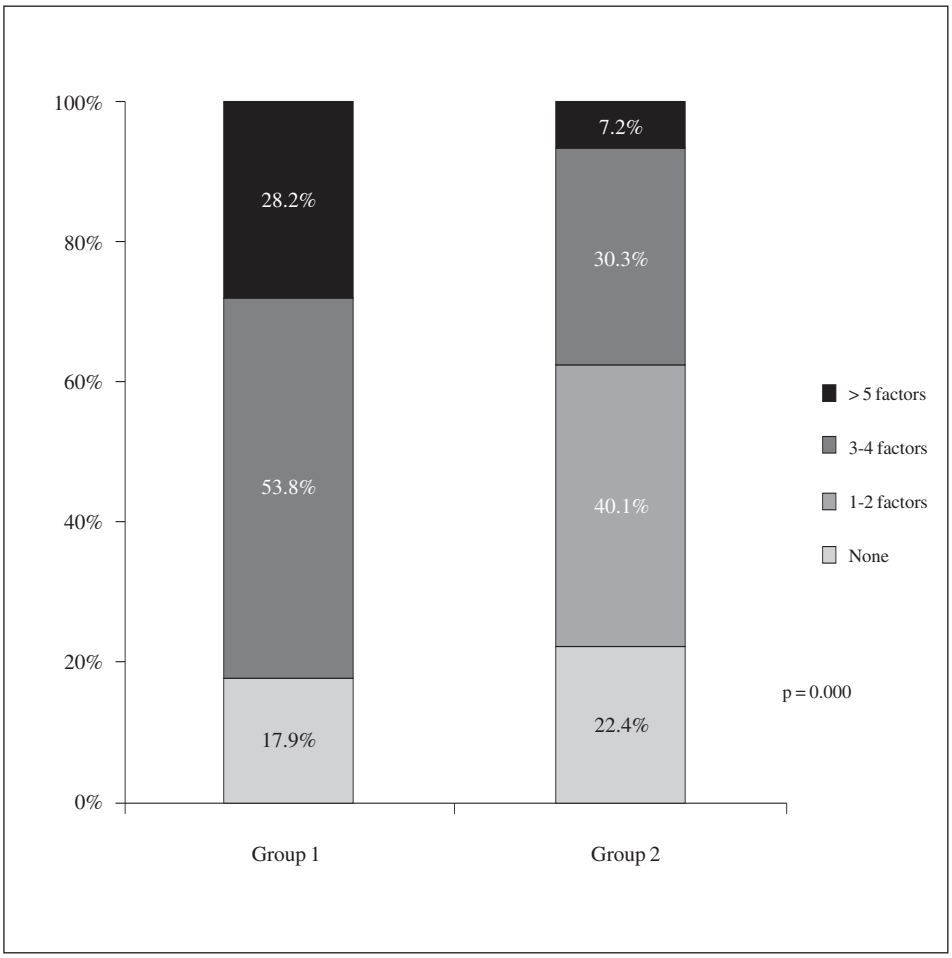

Fig. 1.—Frequency of cardiovascular risk factors according to the presence and absence of HTW Phenotype. Group 1 (HTW Phenotype): Elevated WC and TG; Group 2 (Absence of HTW Phenotype): elevated WC and normal TG or normal WC and elevated TG or normal WC and TG.

al.[7] who found statistically significant difference in the means of components of the lipid profile and adipose tissue volume among different groups of classification on WC and TG of individuals with type 2 diabetes, so that those ones with HTW had higher mean.

Blackburn et al.[23], compared the HTW ability in relation to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) in predicting the CVD risk in women (32-82 years) and Solati et al. [24], analyzing cardiovascular risk factors in men (18 to 70 years old) with HTW, also found similar results, although these authors had developed the study only with female and male subjects, respectively, and using other parameters and criteria of cardiovascular risk factors classification. These results show that the metabolic profile of individuals with HTW phenotype predispose the development of metabolic syndrome (MS) and increased cardiovascular risk.

Solati et al.[24] observed that 75% of individuals with WC and high TG had four or more cardiovascular risk factors. In the present study it has been observed that 82% of individuals in Group 1 had three or more cardiovascular risk factors, thus, highlighting the importance of the simultaneous analysis of WC and TG in clinical nutritional screening of individuals at risk for developing cardiovascular and metabolic alternations.

Most evaluated risk factors in the present study are part of the MS and when the percentage of individuals that had alternations in these risk factors has been analyzed, it was observed that most individuals who possessed the HTW phenotype had significant changes in lipid profile (especially TC and non-HDLc) and VAT area, with a percentage higher than 70% for men and women ($p < 0.01$).

Hypercholesterolemia and its association with HTW has also been observed in other studies, as in the one performed by Tankó et al.[25], which found that 76.1% of individuals with HTW had hypercholesterolemia ($p < 0.01$). In other studies, also performed in Brazil, there was a percentage ranging from 64.3% and 80.6% of the studied population with high levels of CT with significant association with HTW[20,21].

Non-HDL cholesterol is composed of potentially atherogenic lipoproteins rich in TG, making it a good TG predictor of the "worst" profile and is therefore associated with the VAT excess and increased cardiovascular risk[26]. This result is similar to the one found by Bos et al.[27] who found that the risk associated with HTW increased in 50% in the presence of

Table II
Association between metabolic alterations and visceral adipose tissue with HTW phenotype by gender

	Men		
	Group 1	*Group 2*	*p-value*
SBP > 120 mmHg	12 (63.2)	32 (42.7)	0.110
DBP > 80 mmHg	7 (36.8)	17 (22.7)	0.243
TC ≥ 200 mg/dl	14 (73.7)	22 (29.3)	0.011
LDL ≥ 160 mg/dl	3 (15.8)	8 (10.7)	0.689
HDL < 40 mg/dl	11 (57.9)	17 (22.7)	0.005
Non-HDL > 130mg/dl	18 (94.7)	44 (58.7)	0.002
Uric acid ≥ 8.5 mg/dl	0 (0.0)	3 (4.0)	1.000
VAT ≥ 130 cm²	15 (78.9)	27 (36.0)	0.001
VF/SF ≥ 0.4	7 (36.8)	12 (16.0)	0.043
	Women		
	Group 1	*Group 2*	*p-value*
SBP > 120 mmHg	13 (65.0)	26 (33.8)	0.020
DBP > 80 mmHg	6 (30.0)	14 (18.2)	0.351
TC ≥ 200 mg/dl	16 (80.0)	36 (46.9)	0.001
LDL ≥ 160 mg/dl	6 (30.0)	14 (18.2)	0.351
HDL < 50 mg/dl	9 (45.0)	21 (23.7)	0.174
Non-HDL > 130mg/dl	18 (90.0)	44 (57.1)	0.008
Uric acid ≥ 6.2 mg/dl	6 (30.0)	2 (2.6)	0.001
VAT ≥ 130 cm²	9 (45.0)	18 (23.4)	0.090
VF/SF ≥ 0.4	0 (0.0)	2 (2.6)	1.000

Data presented in Absolute Value (Frequency)
Group 1 (HTW Phenotype):Elevated WC and TG; Group 2 (Absence of HTW Phenotype): elevated WC and normal TG or normal WC and elevated TG or normal WC and TG.
*Chi-Square Test
SBP: Systolic Blood Pressure (mmHg); DBP: Diastolic Blood Pressure (mmHg); TC: Total Cholesterol (mg/dL); LDL: Low Density Lipoprotein (mg/dL); HDL: High Density Lipoprotein (mg/dL); VAT: Total area of Visceral Tissue (cm^2); VF/SF: Visceral Fat/Subcutaneous Fat index.

high concentrations of non-HDLc, for men and women ($p < 0.05$).

Solati et al.[24] also observed a higher percentage of metabolic changes in individuals with characteristics similar to the present study, however different cut-off points were used for the analyzed biochemical variables.

In the same way that the present study did, other authors[7,28,29] demonstrated an association between the VAT and the presence of HTW phenotype, which confirms the principle of HTW in identifying viscerally obese subjects, with metabolic alternations and with the risk of developing CDV.

Individuals with high WC not always had excess in VAT or high cardiovascular risk, because the accumulation of adipose tissue can be subcutaneous. Data presented here corroborates with scientific literature when describing high serum levels of TG as a marker for a variety of atherogenic lipoprotein disorders and insulin resistance[2,4,28], especially when associated with high WC, strengthen the use of HTW as a global cardio metabolic risk.

The hypertriglyceridemic waist has a low cost, thus making it an available and easily applicable indicator in clinical practice. Thus, WC and TG standardization for acceptable values brings positive and beneficial effects on cardio metabolic risk factors.

The use of HTW can be useful for health professionals to identify individuals with high cardiovascular risk who may benefit from early intervention. Therefore, further researches should be conducted, whether of epidemiological studies, so that larger samples can be analyzed in order to assess the HTW.

Potential Conflict of Interest

No potential conflict of interest relevant.

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Original / *Obesidad*

Psychological well-being in a sample of obese patients compared with a control group

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Abstract

Introduction: **The literature has found that obese patients usually report more depression and anxiety than normal weight individuals. However, not many investigations have studied the relationship between obesity and quality of life from a Positive Psychology approach.**

Objective: **In this study it is analyzed if obese patients have less psychological well-being than a control group (normal weight participants).**

Method: **A total of 221 participants (111 obese individuals and 110 controls) were selected to conduct the study. To measure psychological well-being, the Spanish version of the Ryff's Scales was used. To measure mental health, the Spanish version of the mental health component of the Short Form 36 Health Survey (SF-36) was used.**

Results: **It was found that obese participants reported less psychological well-being than normal weight individuals, but that there were not statistically significant differences in the case of mental health measured with the SF-36.**

Discussion: **According to the results, it can be concluded that reports of psychological well-being problems were much more common in participants with weight problems than in the control group.**

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Key words: *Obesity. Psychological well-being. Mental health. SF-36.*

BIENESTAR PSICOLÓGICO EN UNA MUESTRA DE PACIENTES OBESOS COMPARADOS CON UN GRUPO CONTROL

Resumen

Introducción: **La literatura ha puesto de manifiesto que los pacientes obesos suelen padecer más depresión y ansiedad que los individuos de peso normal. Sin embargo, no son muchas las investigaciones que han estudiado la relación entre obesidad y calidad de vida a partir del enfoque de la Psicología Positiva .**

Objetivo: **En este estudio se analizó si los pacientes obesos tienen menor bienestar psicológico que los de un grupo de control (participantes de peso normal).**

Método: **Se seleccionaron un total de 221 participantes (111 individuos obesos y 110 de control) para realizar el estudio. Para medir el bienestar psicológico, se utilizó la versión española de las escalas de Ryff. Para medir la salud mental, se utilizó la versión española del componente de salud mental de la Forma Abreviada de la Encuesta de Salud (SF- 36).**

Resultados: **Los participantes obesos mostraron menos bienestar psicológico que las personas de peso normal, pero que no hubo diferencias estadísticamente significativas en el caso de la salud mental medida con el SF- 36.**

Discusión: **De acuerdo con los resultados, se puede concluir que la expresión de problemas acerca del bienestar psicológico es mucho más común en los participantes con problemas de peso que en los del grupo de control.**

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Palabras clave: *Obesidad. Bienestar psicológico. Salud mental. SF-36.*

Introduction

Obesity is a medical condition in which excess body fat produces a negative effect on health, reduces life expectancy and increases the likelihood of several illnesses, among others, heart disease, breathing difficulties during sleep, type 2 diabetes, certain types of cancer and osteoarthritis[1]. For all these reasons, nowadays the authorities in advanced societies (e.g. the World Health Organization, WHO) consider obesity as one of the highest risks to public health (WHO, 2011)[2]. For example, in Spain, the country where this study has been carried out, obesity has increased significantly in the last few years, reaching currently a prevalence rate of 23%[3].

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The fact that obesity is predominantly a life-long condition emphasizes the importance of quality of life research in this field. For example, obese patients have an increased risk for symptoms of depression and anxiety and some studies have shown that weight loss may lead to significant relief of such symptoms[4]. Additionally, several meta-analyses show that obesity is related with less quality of life. For example, it has been found that obese individuals suffer more depression[5] and anxiety[6] than normal weight people. However, according to the WHO definition[7], health is considered as a state of complete physical, mental, and social well-being and not just the simple absence of disease. For this reason, it is important to study also the positive psychological human functioning, and not just focus on the negative aspects of the disease[8]. Unfortunately, the Positive Psychology[9] is not an approach very common in the obesity field[10]. For this reason, in this study we will focus on the positive aspects related with obesity, rather than depression and anxiety.

As we have pointed out before, although several investigations have studied the relationship between depression, anxiety and obesity, not many researchers have focused on the positive aspects related to obese patients' quality of life (see for example Böckerman et al. 2013)[11]. The common approach in this field of study is to measure quality of life with the Short Form 36 Health Survey (SF-36)[12], one of the most widely used and evaluated generic health-related quality of life questionnaires. However, the SF-36 does not take account of the different components of well-being and it has been suggested that SF-36 is not broad enough to assess specific domains as comprehensively like other instruments[13]. Additionally, a meta-analysis conducted recently shows that obese patients, compared with a normal weight control group, do not report less mental health, measured with the SF-36, especially in the case of men with weight problems[14]. For this reason, we believe that it is important to measure the positive aspects of quality of life with other type of instruments.

Eudaemonism, the tradition started by Aristotle, is reflected by the concept of psychological well-being (PWB). Eudaimonic view of well-being focuses on feeling fully functioning, self-coherent, and with a deep sense of wellness, and vitality, rooted on the idea of fulfilling or realizing one's daimon or true nature. Experts suggest that although people report being happy, it does not necessarily mean that they are psychologically well[15]. Thus, from this perspective a person is considered to be psychologically well when developing his/her true potential, or there is congruence between the proposed goals and his/her true self or daimon. From this approach, according to Ryff's model, six core domains for optimal functioning are identified: Self-Acceptance, Environmental Mastery, Positive Relations, Purpose in Life, Personal Growth and Autonomy[16]. Therefore, PWB is a dynamic concept that includes subjective, social, and psychological dimensions as well as health-related behaviors. PWB is usually measured with the Ryff's Scales of Psychological Well-Being[17] that is a theoretically grounded instrument that specifically focuses on the multiple facets of well-being. Therefore, in this study PWB will be measured in a sample of obese patients comparing the results with the SF-36 to see if there are any differences between the instruments.

There are some studies about the relationship between obesity and PWB[18] that show the negative link that exists between PWB and obesity, although more studies need to be conducted to confirm this pattern. According to these authors, weight change at 12 months was associated with higher overall PWB and weight loss was associated with positive changes in PWB in overweight and obese patients[18]. However in this study, Ryff's scales were not used[17] and there was not a control group to compare the results.

In order to better understand obesity and well-being, the present paper focuses on the relationship between quality of life from a Positive Psychology approach and weight. Therefore, the aim of the present study is to analyze whether obese patients suffer less PWB than normal weight participants, and compare the results with the mental health component of the SF-36. According to the reviewed literature, it is expected that obese individuals will report less PWB than a normal weight group used as a control[18]. However, we do not expect to find differences in the case of mental health problems[14]. To study the relationship between obesity and PWB a cross-sectional study will be conducted with obese and normal weight groups. We believe that our work is innovative because a Positive Psychology approach has been used rarely in the field of study. Additionally, Ryff's scales[17] have not been used before with obese patients, and the studies that have measured PWB in obese patients have not used a control group[18].

Method

Sample

Participants (n = 221) were obese outpatients from the Valme Spanish Hospital (Seville) and students from the Spanish Open University (UNED). The average Body Mass Index (BMI) was 38.34 kg/m^2 (SD = 4.52) in the obese group and 22.51 kg/m^2 (SD = 2.23) in the control group. Mean age was 43.99 years (SD = 12.97) in the obese group and 31.99 years (SD = 10.45) in the control group. There were 37 men and 74 women in the obese group and 52 men and 58 women in the case of the control group.

With respect to the characteristics of the clinical sample, 63 participants had completed primary school studies (56.75%), 34 of them had finished secondary school studies (30.63%) and the rest had university studies (12.62%). A total of 106 patients lived in urban areas (95.49%). The criterion considered to distinguish rural from urban areas was to define rural as a geographic area, which is located outside cities and towns with

an economy mainly based on agricultural productions. With regards to the income level, it was 15,250 € ± 7.250 €/year (which is the normal range in Andalucía), the average income level being 23.000 € in Spain.

Among the patients there were not any cases of specific eating disorders associated to their obesity. With respect to other clinical characteristics, the patients attended the Clinical Nutrition Unit (CNU) with the main objective to lose weight so no other data were collected for the proposal of this study.

Procedure

All participants of the obese group attended the Valme Spanish Hospital where they were treated by the CNU. After having obtained the Unit Headmaster's permission and the patients' informed consent, participants completed the questionnaires and scales individually without time limits. A nutritionist supervised the procedure, instructing the participants about how to complete the questionnaires and scales until they were completely sure about their fully understanding of the instructions. Data collection was developed in a suitable setting so the attainment of the task could be reached easily. All the participants volunteered to take part in the study and none of them received any kind of reward after fulfilling the task. The anthropometric measures (weight, height) were taken by the members of the Unit who treated the patients so with enough experience of working in this type of studies.

With respect to the inclusion/exclusion criteria, all patients who were attending the CNU regularly and with a good adherence were invited to participate. Due to the fact that more than 50% had primary school studies only those patients who understood the content of the questionnaires were accepted. Patients with other diagnostics (for example eating disorders) were excluded as well as those who were not able to follow the treatment as outpatients due to medical complications or difficulties to go on a diet.

The participants of the control group were Spanish students of the UNED (Spanish Open University) who were enrolled in a psychology course and who received extra credit for their participation. To recruit participants from the control group, students of the School of Psychology (UNED) were contacted during class period. Students were informed on the general purposes of the research and those who voluntarily wanted to participate filled out a booklet with the different questionnaires after time class. With respect to their weight and height (in order to obtain the BMI), in this case these measures were self-reported.

Instruments

To measure PWB the Spanish version of the Ryff's Scales of Psychological Well-Being was used [17,19]. This scale is a 39-items self-report instrument which is based on six dimensions that point to different aspects of positive psychological functioning: self-acceptance (6 items), positive relations with others (6 items), autonomy (8 items), environmental mastery (6 items), purpose in life (6 items), and personal growth (7 items). Items are scored on a 7-point scale ranging from 0 (strongly disagree) to 6 (strongly agree). Six scores were computed, one for each dimension, by averaging the corresponding items for each of these dimensions. The following are example statements from each of the areas of well-being measured by the Ryff inventory: "I like most aspects of my personality" (self-acceptance), "People would describe me as a giving person, willing to share my time with others" (positive relation with others", "I have confidence in my opinions, even if they are contrary to the general consensus" (autonomy), "In general, I feel I am in charge of the situation in which I live" (environmental mastery), "Some people wander aimlessly through life, but I am not one of them" (purpose in life) and "I think it is important to have new experiences that challenge how you think about yourself and the world" (personal growth). A person with a high score on the Ryff inventory possesses a positive attitude toward the self (self-acceptance), has warm, satisfying, trusting relationships with others (positive relation with others), is self-determining and independent (autonomy), has a sense of mastery and competence in managing the environment (environmental mastery), has goals in life and a sense of directedness (purpose in life) and has a feeling of continued development (personal growth). Alpha coefficients obtained for present study were: 0.81 for self-acceptance, 0.79 for positive relations with others, 0.68 for autonomy, 0.71 for environmental mastery, 0.73 for purpose in life, and 0.73 for personal growth.

To measure mental health the Spanish version of the mental health component of the SF-36 was used[12,20]. The SF-36 consists of 36 items distributed by eight domains (physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health) that comprise two summary measures: the physical component summary (the first four domains) and the mental component summary (the last four domains). The following are example items from the mental health component measured by the SF-36: "How much of the time during the past 4 weeks... Have you been a very nervous person?" and "How much of the time during the past 4 weeks... Did you feel worn out?". A score was computed by averaging the items of the last four domains (mental health component). Each scale is directly transformed into a 0-100 scale according to the authors[12]. However, in this research after the calculation of the scores of the mental health component of the SF-36 with the algorithm proposed by the authors[12], the results were transformed into a 7-point scale ranging from 0 to 6 to compare them with the Ryff's Scales of Psychological Well-Being.

Higher scores on the mental component reflect greater mental health. Alpha coefficient obtained for present study was 0.93.

Participants supplied also information about their height and weight, sex, level of education and working situation.

Results

To test for possible differences between men and women, sex group comparisons were examined. Having checked that the sample fit a normal distribution by means of the Kolmogorov-Smirnoff test, T test showed that there were no statistically significant differences in any of the analyzed variables (PWB and mental health) between both groups. To test whether these variables varied as a function of age, Pearson's correlations between age and all variables analyzed were also calculated, but these were not statistically significant. Since no differences were found on the analyzed variables either in terms of gender or age, all data were analyzed together.

An Analysis of Variance (ANOVA) was conducted with the 6 sub-scales of the PWB as a dependent variable and group (2 levels: obesity and control) as an independent variable to test whether participants with obesity have less PWB and mental health, measured with the SF-36, than the control group. It was found, as it can be seen in table I, that the control group had the highest scores on the PWB subscales, except for self-acceptance. The differences were statistically significant in the case of positive relations with others, autonomy, environmental mastery, purpose in life and personal growth.

Additionally, it was found that the control group did not score more than obese participants on the SF-36. The differences were not statistically significant.

Cohen's ds[21] were also calculated as indexes of effect size. Cohen (1988) defined *d* as the difference between means divided by standard deviation of either group (ds ≥ .2 are considered medium effect sizes and ds ≥ .8 large effect sizes) [21]. According to this criterion, most of the sub-scales of PWB are of large size, except for purpose in life that is just medium.

Discussion

The results of the current research give support to our hypothesis: obese patients report less PWB than participants for the control group. However, the differences in self-acceptance were not statistically significant. In the case of mental health, as expected, there were no differences between the groups of the study, a result congruent with a meta-analysis about the relationship between obesity and quality of life measured with the SF-36[14].

Specifically, it was found that the control group had the highest scores on most of the different PWB subscales. Normal weight individuals reported more positive relations with others, autonomy, environmental mastery, purpose in life and personal growth than obese patients. It is important to remark that large effect sizes were found, except for purpose in life that it was just medium.

These results are similar to previous research[18]. According to these authors, there was a negative relationship between obesity and PWB. However, these authors did not measure PWB with the Ryff's scales[17] and they did not include a control group. For this reason, we believe that our results expand literature.

As it has been said, not statistically significant differences were found in the case of self-acceptance. This result suggests that both groups, obese and normal weight, do not feel dissatisfied with their self. This is an unexpected finding because usually obese patients score more on self-acceptance scales when they have lost weight[22].

We believe that this work is innovative because investigations in the obesity topic have traditionally focused on psychological symptoms, like depression and anxiety, rather than PWB. As we have seen, the results show that there is an important impairment in PWB in obese patients compared to normal population. According to our results, no differences have been found with the SF-36, which gives an idea of the importance of not just focus on negative aspects of quality of life.

The current study is subject to some limitations that deserve mention. First of all, in the research self-reports has been used. Additionally, subjectively measured height and weight for BMI calculation were used

Table I
Means (standard deviation) of the variables of the study and size effects

Variables	*Obese*	*Control*	$F_{1,219}$	*p*	*d*
Self-acceptance*	3.60 (.80)	3.61 (.81)	.08	> .05	-.01
Positive relations*	2.99 (1.21)	4.01 (1.10)	42.39	< .01	.88
Autonomy*	2.66 (.88)	4.11 (.92)	140.41	< .01	1.61
Environmental*	2.83 (1.44)	4.99 (.74)	195.02	< .01	1.88
Purpose in life*	3.04 (1.10)	3.79 (1.38)	20.15	< .01	.60
Personal growth*	3.94 (.71)	4.75 (.75)	66.41	< .01	1.10
Mental health**	3.81 (.78)	3.82 (79)	.01	> .05	-.01

* Measured with Ryff's Scales of Psychological Well-Being ** Measured with SF-36.

in the case of the control group. In the second place, it is a cross-sectional study. However, only longitudinal studies can provide insight into how obesity, PWB and mental health interact with different daily life stressful experiences. Although no causal relationship can be stated, the results of our study showed that obese individuals report less PWB than normal weight individuals. In the third place, subjective well-being has not been measured[11]. In the fourth place, the lack of a randomly controlled study design. In the fifth place, due to the small sample sizes, some results of this study are of limited explanatory power. However, the size effects calculated are of a high magnitude. Despite these limitations, the study provides new data with potential applications.

We believe that knowledge of quality of life from a Positive Psychology approach may contribute to a better understanding of the patients' needs, an improvement in care, and a better evaluation of treatment. According to some authors, an important improvement in quality of life can be a compensation for not fully achieving weight loss and it can be helpful for maintaining the motivation to continue lifestyle modifications with obese patients[23].

The present findings suggest that future research using longitudinal designs should continue to address quality of life from a Positive Psychology approach. Additionally, it would be interesting to include obesity-specific measures of quality of life (see for example, Kolotkin et al. 2001[24]). Finally, the assessment of medical comorbidities, a variable likely to be associated with obesity, should be assessed in future studies analyzing obesity from a Positive Psychology approach.

These limitations considered, the current study offers new directions for the study of obesity and quality of life. With the growing prevalence of obesity, it is becoming increasingly important to understand the ways in which obese people suffer less quality of life than normal weight individuals.

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Original / *Obesidad*

Beliefs, attitudes and phobias among Mexican medical and psychology students towards people with obesity

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Abstract

Background: **A high prevalence of stigmatizing attitude among healthcare personnel towards obese people has been reported.**

Objective: **To evaluate the beliefs, attitudes and phobias that Mexican medical and psychology students have towards obese people.**

Methods: **A cross-sectional study was conducted with 528 students enrolled at the Autonomous University of Baja California in psychology and medical schools. Weight, height and waist circumference were evaluated. Beliefs about obesity were assessed with the BAOP scale, attitudes towards obese people by the ATOP scale and obesity phobias by the F-scale.**

Results: **Participants achieved a mean F-scale score of 3.4. Only seven per cent showed neutral or positive attitudes towards obesity (≤ 2.5). Less fat phobia was associated with beliefs that obesity was not a result of the person's self-control (p = 0.0001) and had better attitudes towards obese people (p = 0.0001). Men had higher risk of fat phobia (OR = 1.5).**

Conclusions: **High prevalence of phobias and negative attitudes towards obesity was observed. Men had higher stigma.**

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Key words: *Obesity. Stigmatization. Attitudes. Phobia. Medical students. Psychology students.*

CREENCIAS, ACTITUDES Y FOBIAS HACIA LA OBESIDAD ENTRE ESTUDIANTES MEXICANOS DE LAS CARRERAS DE MEDICINA Y PSICOLOGÍA

Resumen

Introducción: **Se ha observado una alta frecuencia de estigmatización entre el personal de salud hacía las personas con obesidad.**

Objetivo: **Evaluar las creencias, actitudes y fobias que los estudiantes de medicina y psicología tienen hacía las personas con obesidad.**

Métodos: **Se realizó un estudio transversal en 528 estudiantes de las carreras de psicología y medicina de la Universidad Autónoma de Baja California. Se evaluó el peso, la estatura y la circunferencia de cintura. Las creencias sobre obesidad fueron valoradas con la escala BAOP, las actitudes hacía las personas con obesidad mediante la escala ATOP, y la fobia hacía la obesidad con la escala F.**

Resultados: **Los participantes obtuvieron una calificación media de la escala F de 3,4. Solamente siete por ciento presentaron una actitud neutral o positive (≤ 2,5). Se observó una asociación entre menos fobia con el hecho de considerar que la obesidad no es el resultado absoluto del auto control de las personas (p = 0,0001) y también con una mejor actitud hacía las personas con obesidad (p = 0,0001). Los hombres presentaron más fobia hacía la obesidad que las mujeres (OR = 1,5).**

Conclusiones: **Se observó una alta prevalencia de fobia y actitudes negativas hacía las personas con obesidad. Los hombres presentaron mayor grado de estigmatización.**

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Palabras clave: *Obesidad. Estigmatización actitudes. Fobia. Estudiantes de medicina. Estudiantes de psicología.*

Introduction

Obesity (O) is a global public health problem and is especially severe in Mexico.[1-4] The O is also related to psychological and psychiatric disorders such as low self-esteem, depression, anxiety, bipolar disorder and panic attacks.[5-8] Several studies have investigated prejudice, negative attitude, phobia, stigma and discrimination that exist towards people with O among professionals and students in the area of health[9-13], schoolchildren[14-16], and teachers and parents[17].

Studies have shown that most of the participants believe O is caused by lack of exercise or excessive food intake[11,18,19]. Discrimination has also been documented due to body weight in various life areas such as education, employment, health care and interpersonal rela-

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tionships[20,21]. These negative attitudes increase the likelihood that people with O adopt or maintain poor eating habits and a reduction of physical activity[22].

The purpose of this study is to evaluate the beliefs, attitudes and phobias that medical and psychology students from a Mexican city bordering USA have towards people with obesity.

Methodology

Design and study sample. A cross-sectional study was conducted with 528 students from the first and last year of the School of Medical and Psychology at the Autonomous University of Baja California (UABC).

Ethical considerations

The project was approved by the Ethics Committee of the Medical and Psychology School from UABC. All participants signed an informed consent.

Recruitment and training

Three students were trained to take anthropometric measurements and apply the questionnaires.

Data collection

Anthropometry

A portable scale (Tanita model Corp, Tokyo, Japan, adjusted to 0.1 kg with a precision of 100 g, and a range of 0.1-130 kg), a stadiometer (Model 214 Road Rod, Seca Corp, Hanover, MD, USA) and a flexible measuring tape (Seca brand with a range of 0-200 cm) were used to determine weight, height and waist circumference (WC) respectively. The measurements and the application of the questionnaires were conducted during the school year from August to December 2013 in the classrooms. WC values were compared to WHO criteria[24] where the waist ≥ 94 cm in men is considered abdominal obesity (AO) and ≥ 80 cm in women. The body mass index (BMI) was calculated using the formula BMI = weight in kg/height in meters^2. BMI values were compared to WHO criteria[23]. Underweight, BMI < 18.5 kg/m^2; normal weight, BMI 18.5-24.99 kg/m^2; overweight, BMI 25-29.99 kg/m^2; class I obesity, BMI 30-34.99 kg/m^2, class II obesity, BMI 35-39.99 kg/m^2 and class III obesity BMI ≥ 40 kg/m^2.

Standardization of measurements

Three evaluators were trained for assessing inter and intra-individual variation for weight, height and WC. Results were considered homogeneous when the measurements were higher than 0.90.

Questionnaires

Participants were invited to complete the BAOP (Beliefs About Obese People) scale[24], the ATOP (Attitudes Toward Obese People) scale[24] and the F-scale (Fat Phobia Scale)[25]. The BAOP scale was used to evaluate explicit beliefs regarding O and contains eight items that are scored on a six-point scale (-3 = I strongly disagree, +3 = I strongly agree). Responses were scored according to the instructions reported by Allison[24]. A score ranging from 0 to 48 was obtained. Higher scores indicate a stronger belief that O is not under an obese person's self-control. Explicit attitudes toward O were evaluated through the ATOP scale, which contains 20 items rated on a six-point scale (-3 = I strongly disagree to +3 = I strongly agree). Responses were also scored according to the instructions reported by Allison[24]. A score ranging from 0 to 120 was obtained. Higher scores indicate stronger positive attitudes towards people with O. The F-scale was used to evaluate fat phobic attitudes, and contains 14 items that are used to describe people with O. Participants indicated on a scale of 1 to 5, which one was the best adjective that described their beliefs about people with O. Responses were scored according to instructions published by Bacon et al.[25] which provides a possible score from 1 to 5. Higher scores indicate greater phobias. Based on the design of the scale, a score of 2.5 would indicate a neutral attitude, a score less than 2.5 would indicate a positive attitude and a score greater than 2.5 would indicate a negative attitude. The participants were also asked how much contact they had with obese people at school or in their personal life, and they were given four options: 1 = much contact, 2 = some contact, 3 = hardly any contact and 4 = no contact (question adapted from Kerby, 2008)[26].

Data collection procedure

Recruitment of participants and data collection was performed during the 2013-2014 school year. Before taking the anthropometric measures and applying the questionnaires, the purpose of the study was explained to the students being careful not to prejudice the results.

Statistical analysis

Data capture was carried out by two members of the research group. All data were analyzed using SPSS version 22. Variables were examined for normality, means, standard deviations, frequencies and quartiles of parametric and nonparametric variables were calcu-

lated. Spearman's correlation was used to assess the association between scales. Logistic regression was performed to see the probabilities of having a higher score on the scales with the variables sex and contact with people with O. The level was set at < 0.05.

Reproducibility and reliability

The BAOP scale showed a Spearman's of 0.63-0.91 and a Cronbach's alpha reliability of 0.70. The ATOP scale produced a Spearman's of 0.67-0.98 and a Cronbach's alpha reliability of 0.84. The F-scale produced a Spearman's of 0.75-0.97 and a Cronbach s alpha reliability of 0.85.

Participants

All the students from first and final year enrolled in the School of Psychology and Medical were selected. Three hundred and two psychology students and 315 medical students were enrolled. Two hundred and fifty (83%) medical students and 278 (88%) psychology students for a total of 528, agreed to participate (56.3% were women). The participants' average age in years was 20.7 ± 3.0.

According to WHO classification criteria[23], 7% were underweight, 53% had normal weight, 25% had OW, 16% had O and 34% of the participants had AO. Forty eight percent of women in psychology had AO and 39% of female medical students; 27% of male psychology students had AO and 17 % of male medical students. On average the WC was higher in female psychology students (+3 cm) compared to women in medical school (p = 0.038). No significant differences in age, BMI, OW and O among medical and psychology students were observed.

Results

Psychology students achieved a mean (SD) BAOP score of 18.6 (5.7) and medical students 16.6 (5.5); a mean (SD) ATOP score of 75.6 (14.4) and 69.6 (17.3) in psychology and medical students respectively, and a mean (SD) F-scale score of 3.25 (0.5) in psychology and 3.5 (0.5) in medical students. Higher F-scale scores were observed in older medical students (p = 0.0001).

The BAOP and the ATOP scales were correlated (Rho = 0.3, p = 0.0001), and also a negative correlation between the BAOP and the F-scale (Rho = -0.34, p = 0.0001) was observed. No significant correlations were found with age, BMI or WC.

The ATOP scale with the F- Scale had a negative correlation of -0.49 (p = 0.0001). Students who had more contact with persons having excess fat, were more likely to have a better attitude (OR = 2.8, 95% CI 1.26, 6.11, p = 0.012) towards people with obesity.

The F-scale, had a negative correlation (Rho = -0.10, p = 0.021) with BMI. Men were more likely to have fat phobias (OR = 1.5, 95% CI, 1.04, 2.08, P = 0.029).

Spearman's correlations of the BAOP, the ATOP and the F-scale with other variables among psychology and medical students are presented in table I.

Men in medical school were more likely to have fat phobias (OR = 3.0, 95% CI, 1.76, 5.24, P = 0.0001) than those in psychology school, and women in medical school were 2.7 more likely to have fat phobias (OR = 2.7, 95% CI, 1.70-4.40, P = 0.0001) than those in psychology.

Participants of both schools achieved a mean (SD) F-scale score of 3.4 (0.53), which represented an average level of fat phobia, 12 (2.3%) students showed a high level (≥ 4.4 points) of fat phobia[26]. Only 36 (6.8%) students demonstrated positive or neutral attitudes towards people with O, score ≤ 2.5. The distribution of students with negative attitudes towards people with excess fat is presented in table II.

The 5 most frequently mentioned adjectives by psychology and medical students about people with obesity were; likes food, overeats, slow, poor self-control and inactive. The less reported adjectives were; having no endurance, weak, self-indulgent, lazy and unattractive.

Discussion

The results of this study indicate that students from the psychology and medical school at the Mexico-US border have little knowledge about the causes of O, have negative attitudes towards people with O and a high level of fat phobias. Psychology students achieved a mean BAOP score of 18.6 and medical ones of 16.6. These are consistent with those reported in medical students (16.5 and 17.5) in New Jersey and North Caroli-

Table I
Spearman's correlations of BAOP, ATOP and F-scale with other variables

Variables	*Psychology*	*Medical*
BAOP	rs (p)	rs (p)
ATOP	0.34 (0.0001)	0.25 (0.0001)
F-scale	-0.30 (0.0001)	-0.31 (0.0001)
Age	0.10 (0.126)	-0.19 (0.001)
WC	-0.06 (0.326)	-0.08 (0.191)
BMI	-0.04 (0.571)	-0.11 (0.073)
ATOP		
F-scale	-0.43 (0.0001)	-0.50 (0.0001)
Age	0.12 (0.060)	-0.16 (0.006)
WC	-0.06 (0.370)	0.11 (0.076)
BMI	0.00 (0.944)	0.08 (0.205)
F-scale		
AGE	0.03 (0.617)	0.14 (0.018)
WC	-0.01 (0.840)	-0.15 (0.015)
BMI	-0.03 (0.700)	-0.17 (0.006)

WC: Waist circumference. BMI: Body Mass Index.

Table II
Students who agreed with negative adjetives is the F-scale

	Psychology N = 250			*Medical N = 278*	
Adjectives	*N*	*%*	*Adjectives*	*N*	*%*
Likes food	198	(79.2)	Likes food	232	(83.5)
Overeats	163	(65.2)	Overeats	216	(77.7)
Slow	143	(57.2)	Inactive	187	(67.3)
Poor self-control	113	(45.2)	Slow	183	(65.8)
Inactive	107	(42.8)	Shapeless	167	(60.1)
Insecure	107	(42.8)	Low self-esteem	158	(56.8)
Shapeless	103	(41.2)	Insecure	157	(56.5)
Low self-esteem	100	(40.0)	No will power	156	(56.1)
No will power	91	(36.4)	Poor self-control	147	(52.9)
Lazy	74	(29.6)	Unnattractive	134	(48.2)
Unnattractive	72	(28.8)	Lazy	115	(41.4)
Self-indulgent	58	(23.2)	Weak	77	(27.7)
Weak	41	(16.4)	Self-indulgent	72	(25.9)
Having no endurance	27	(10.8)	Having no endurance	30	(10.8)

na[27,28] and higher than those reported among trainee dietitians, doctors and nurses (13.4) in the United Kingdom[10]. The mean ATOP scores are similar to those reported by medical students in New Jersey[27]. No differences in attitudes were observed between genders, which is consistent with those observed in Virginia[29]. However, in New York, the attitudes of male graduates in psychology towards people with O were more positive[30]. Participants who have more contact with people with excess fat showed a better attitude towards them. The level of phobias of medical students was consistent with those reported by Swift et al.[10] in medical students from the United Kingdom and by Wolf[31] in physician assistant students from New York.

Additionally, this study found that psychology students have better knowledge about the causes of O, less negative attitudes and phobias towards people with O. The positive correlation between the BAOP and the ATOP scales suggests that a better understanding of the causes of O leads to more positive attitudes towards people with OW and O. This suggests the need to increase the knowledge about the causes of the O and improve the attitudes that health professionals have towards people with OW and O.

On the BAOP scale no differences were observed in the results according to age, WC, BMI, gender or contact with persons with O. On the F-scale, men had higher phobias towards people with excess fat, which was not consistent with the study reported in students of USA medical assistants[32]. A lower BMI associated with greater fat phobia was observed, which was not consistent with those reported by Swift et al.[10] in trainees in the health field and in medical students in New Jersey[27]. No significant correlations were observed on the BAOP scales and on the F-scale with gender or age. These results probably mean that due to cultural reasons and lack of knowledge, men and normal weight students have less tolerance towards people with excess fat. This also indicates the need for specific content in medical and psychology school curriculums about the multiple causes of O[32] and more information about the stigmatization of O and its implications[9-17].

The BAOP scale was associated with the ATOP scale in psychology and medical students. The ATOP and the BAOP scales were negatively associated with the F-scale. Psychology students showed no significant correlations with age, WC and BMI. These results are consistent with those reported by Allison et al.[30] in undergraduate and graduate students in psychology.

On the other hand, in medical students the ATOP and the BAOP scales were negatively associated with age, and was related to their year of study. The F-scale was positively associated with age and negatively with WC and BMI. These results suggest the need to focus course content on nutrition on the multi-causality of O and the causes of stigmatization toward individuals with O in nutrition, internal medicine, surgery and endocrinology clinics for medical students.

Students of both schools achieved a mean F-scale score of 3.4, which represents an average level of fat phobias. Twelve (2.3 %) showed a high (≥ 4.4 points) level of fat phobias and 36 (6.8%) students demonstrated positive or neutral attitudes towards people with O, having a score ≤ 2.5. These results were lower than those reported by Bacon et al.[25] However, that study was conducted between1984-1991. In 1999 a lower mean among nursing students and nurses[33] was also observed. Trends of stigmatization of O might have changed since the early 2000's in countries where changes in the curriculum of medical schools have been made. Nonetheless, the results of these Mexican students show less stigmatization than those observed in recent studies in students in health professional[10,31,34]. The five most frequently variables measured referring

to people with O by psychology and medical students were: likes food, overeats, is slow, has poor self-control and is inactive. These results are similar to those reported in a study of dietetic[34] and physician assistant students[31] in New York.

Among the limitations of this study the participants were in the first and last year of their careers, so it cannot be determined whether the change is continuous or limited to a year, because it is a cross-sectional study and the cause and effect cannot be assessed. The BAOP, the ATOP and the F-scale evaluated explicit bias towards O. However it has been suggested that assessments of implicit or indirect attitude are better indicators because some people are hesitant to respond honestly[35].

Among the strengths of the study it might be mentioned that this is the first study in Latin America that assesses these attitudes of medical and psychology students using validated scales, such as the BAOP, ATOP and the F-scale. The reproducibility and internal consistency of the three questionnaires in the study population were adequate and the participation of the students was higher than 80%.

In conclusion a high frequency of fat phobias and negative attitudes towards O was found. Men and those having little or no contact with people with O demonstrated a higher stigma towards the obese. It is recommended that in pediatrics, nutrition, internal medicine and endocrinology courses in psychology and medical schools, should include content on the causality of O and the effects of stigmatization towards O.

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Original / *Obesidad*

Genome-wide screen of promoter methylation identifies novel markers in diet-induced obese mice

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Abstract

Objective: **To investigate the genome-wide promoter methylation and gene expression for the identification of methylation markers in obesity.**

Methods: **Using a high-fat, diet-induced obese mouse model, we performed comprehensive DNA methylation profiling of gene promoters to determine the differentially methylated genes using methylated DNA immunoprecipitation followed by hybridization to the NimbleGen MM8 CpG plus Promoter Microarray. We further integrated epigenomics data with gene expression profiling to identify promoters exhibiting an association between methylation status and the expression of downstream genes.**

Results: **A total of 24 hypermethylated promoters and 42 hypomethylated promoters in epididymal fat were selected as methylation markers, which were associated with downregulated and upregulated gene expression, respectively. The promoter methylation and differential gene expression of three markers (Mmp2, Foxj3 and Ube2q2) in the fat were validated by sequencing bisulfite-modified DNA and real-time reverse transcriptase PCR. The genes with these differentially methylated promoters and the associated transcriptional expression in the fat were primarily involved in biological activities in lipid metabolism and storage, cellular differentiation, immunity and the pathogenesis of obesity-related complications.**

Conclusions: **This study represents the first effort to determine methylation markers in obese mice that may regulate gene transcription in obesity. Our approach has potential relevance for clinical applications by identifying markers useful in elucidating the mechanisms of obesity pathogenesis and its complications.**

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Key words: *Obesity. Genome-wide DNA methylation. Gene expression. High-fat diet. Mouse.*

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EL CRIBADO PANGENÓMICO DE LA METILACIÓN DEL PROMOTOR IDENTIFICA MARCADORES NUEVOS EN RATONES CON OBESIDAD INDUCIDA POR LA DIETA

Resumen

Objetivo: **Investigar la metilación pangenómica del promotor y la expresión génica para la identificación de los marcadores de metilación en la obesidad.**

Métodos: **Empleando un modelo de ratón con obesidad inducida por la dieta con alto contenido en grasa, realizamos un perfil exhaustivo de la metilación del ADN de los genes promotores para determinar los genes metilados diferencialmente utilizando la inmunoprecipitación del ADN metilado seguida de la hibridación del NimbleGen MM8 CpG y el Promoter Microarray. Posteriormente, integramos los datos de la epigenómica con el perfil de expresión génica para identificar los promotores que mostraban una asociación entre el estado de metilación y la expresión de los genes sucesivos.**

Resultados: **Se seleccionó un total de 24 promotores hipermetilados y 42 promotores hipometilados en la grasa epididimaria como marcadores de la metilación, que se asociaron con la expresión génica regulada al alza y a la baja, respectivamente. La metilación del promotor y la expresión génica diferencial de tres marcadores (Mmp2, Foxj3 y Ube2q2) de la grasa se validaron mediante secuenciación del ADN modificado por bisulfito y por PCR de la transcriptasa reversa en tiempo real. Los genes con estos promotores metilados de forma diferencial y la expresión transcripcional asociada en la grasa estaban implicados primariamente en las actividades biológicas del metabolismo y almacenamiento de los lípidos, la diferenciación celular, la inmunidad y la patogenia de las complicaciones relacionadas con la obesidad.**

Conclusiones: **Este estudio representa el primer intento por determinar los marcadores de la metilación en los ratones obesos que pueden regular la transcripción génica en la obesidad. Nuestro abordaje tiene una relevancia potencial por sus aplicaciones clínicas al identificar marcadores útiles en la dilucidación de los mecanismos de la patogenia de la obesidad y sus complicaciones.**

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Palabras clave: *Obesidad. Metilación pangenómica del ADN. Expresión génica. Dieta rica en grasa. Ratón.*

Introduction

In recent years, epigenetic modifications such as DNA methylation and histone modifications have been highlighted in chronic non-communicable diseases due to their role in chromatin structure and gene expression related to physiologic and pathologic processes and their potential use as markers for disease onset, progression, diagnosis and prognosis[1-4]. DNA methylation is the only known modification that targets the DNA itself. Compared to histones, which undergo a variety of post-translational modifications under different conditions, DNA methylation is relatively stable over a longer period. The methylation of cytosine residues at CpG dinucleotides in gene promoters or CpG islands is well described and known to have profound effects on the regulation of gene expression[1,3,5].

Emerging evidence indicates that epigenetic changes are closely associated with obesity and related complications. The candidate gene methylation studies in animal models and humans have demonstrated methylation changes in promoters of varied genes implicated in obesity, appetite control and/or metabolism, insulin signaling, immunity, growth and circadian clock regulation[6-9]. Genome-wide analyses in human peripheral blood cells have detected obesity-associated differentially methylated sites of genes with a wide diversity of functions, such as immune response, cell differentiation and the regulation of transcription[9]. Additionally, the methylation profiles of obese individuals can be modified by reductions in body weight/fat mass. For example, promoter methylation levels of the leptin and tumor necrosis factor-alpha (TNF-α) genes may predict the susceptibility to weight loss as well as comorbidities such as hypertension or type 2 diabetes[10,11]. Thus, the role of epigenetic modifications in obesity is a fruitful area for further research. Thus far, the epigenome-wide association with gene expression in obesity has never been explored.

The methylation microarrays and high-throughput sequencing technologies allow for large-scale epigenome-wide association studies (EWASs) and the determination of epigenomic events in the development of metabolic diseases[12]. In the present study, we used the methylated DNA immunoprecipitation (MeDIP) approach, which generates an enrichment of methylated genomic fragments by means of an anti-5-methylcytosine antibody combined with the hybridization of the fragments to a whole-genome promoter array. We then performed the MEDME (modeling experimental data with MeDIP enrichment) post-processing routine to determine the methylation levels in diet-induced obese (DIO) mice. Finally, an analysis of the potential methylation markers, along with additional gene expression experiments, revealed promoter features that appeared to be relevant for transcriptional regulation. The identification of methylation changes in specific genes will provide important targets for further study into the underlying mechanisms and the therapeutic potential for obesity and its comorbidities.

Materials and methods

Diets and animals

Based on the high-fat diet formula (D12492) for DIO mice from Research Diets Inc. (New Brunswick, NJ), a high-fat diet (HFD) (34.9% fat by wt., 60% kcal) with soy oil and lard oil as the main sources of fat was designed with a standard diet (SD) (4.3% fat by wt; 10% kcal) as a control. Forty male C57BL/6J mice at 3 to 4 weeks of age were obtained from the Laboratory Animal Center, Hospital 304 affiliated with the General Hospital of the People's Liberation Army in China. All mice were housed at the animal facilities in a temperature-, light- and humidity-controlled room with a 12-h (h) light/12-h dark cycle. After one week of recovery from transportation, mice were classified into two groups (20 mice in each group) and fed with one of the two types of diets for 4 months. The body weight was measured weekly to confirm that the HFD-fed mice gained more weight than the SD-fed mice. At the end of the experiment, fasted mice were anesthetized by an intraperitoneal injection of Avertin (2,2,2-tribromoethanol, T-4840-2; Sigma-Aldrich Chemie GmbH, Steinheim, Germany; 125 mg/kg) to obtain blood samples by heart puncture. An evaluation of blood triglyceride levels and leptin concentration was performed at the end of the experiment to confirm that the HFD-fed mice developed an obese phenotype. The mice were then immediately euthanized by decapitation. The epididymal fat and the brain were dissected free of the surrounding tissue, immediately frozen in liquid N_2 and stored at -80°C until analysis. All of the animal experiments were conducted in accordance with the guidelines of the Animal Care and Use Committee of Hospital 304 affiliated with the General Hospital of the People's Liberation Army in China.

Gene-expression microarrays and data analysis

Total RNA from the adipose tissue or the brain hypothalamus was quantified using a NanoDrop ND-1000 spectrophotometer, and the RNA integrity was assessed using standard denaturing agarose gel electrophoresis. For microarray analysis, an Agilent Array platform was employed. The sample preparation and microarray hybridization were performed based on the manufacturer's standard protocols. Briefly, 1 μg of total RNA from each sample was amplified and transcribed into fluorescent cRNA using Agilent's Quick Amp Labeling protocol (version 5.7, Agilent Technologies). The labeled cRNAs were hybridized onto the Whole Genome Oligo Array (4×44K, Agilent Technologies) with over 39,000 mouse genes and trans-

cripts represented. After the slides were washed, the arrays were scanned with an Agilent Scanner G2505B.

Agilent Feature Extraction software (version 10.7.3.1) was used to analyze the acquired array images. Quantile normalization and subsequent data processing were performed using the GeneSpring GX v11.5.1 software package (Agilent Technologies). After quantile normalization of the raw data, differentially expressed genes with statistical significance were identified through Volcano Plot filtering between the two groups, with a threshold of fold change at ≥ 1.5 and P ≤ 0.05. Pathway analysis and GO analysis were applied to determine the roles of these differentially expressed genes in these biological pathways or GO terms. Finally, hierarchical clustering was performed to determine the distinguishable gene expression pattern among samples.

DNA methylation microarrays and data analysis

Genomic DNA extraction

Genomic DNA (gDNA) was extracted from samples using a DNeasy Blood & Tissue Kit (Qiagen, Fremont, CA). A total of 10 µg gDNA of each sample was sonicated to approximately 200 – 1000 bp with a Bioruptor sonicator (Diagenode) on "Low" mode for 10 cycles of 30 seconds "ON" and 30 seconds "OFF." The gDNA and each sheared DNA were agarose analyzed.

Immunoprecipitation

Then, 1 µg of sonicated gDNA was used for immunoprecipitation using a mouse monoclonal anti-5-methylcytosine antibody (Diagenode). For this procedure, DNA was heat-denatured at 94°C for 10 min, rapidly cooled on ice and immunoprecipitated with 1 µL primary antibody overnight at 4°C with rocking agitation in 400 µL immunoprecipitation buffer (0.5% BSA in PBS). To recover the immunoprecipitated DNA fragments, 200 µL of anti-mouse IgG magnetic beads was added and incubated for an additional 2 h at 4°C with agitation. After immunoprecipitation, a total of five immunoprecipitation washes were performed with ice-cold immunoprecipitation buffer. The washed beads were resuspended in TE buffer with 0.25% SDS and 0.25 mg/mL proteinase K for 2 h at 65°C and then allowed to cool to room temperature. MeDIP DNA was purified using Qiagen MinElute columns (Qiagen).

Whole-genome amplification

The MeDIP-enriched DNA was amplified using a GenomePlex® Complete Whole Genome Amplification (WGA2) kit from Sigma-Aldrich. The amplified DNA samples were then purified with a QIAquick PCR purification kit (Qiagen).

DNA labeling and array hybridization

The NimbleGen Dual-Color DNA Labeling Kit (NimbleGen Systems, Inc., Madison, WI, USA) was used for labeling according to the manufacturer's guidelines. Briefly, 1 µg DNA of each sample was incubated for 10 min at 98°C with 1 OD of Cy3-9mer primer (IP sample) or Cy5-9mer primer (Input sample). Then, 100 pmol of deoxynucleoside triphosphates and 100 U of the Klenow fragment (New England Biolabs, USA) were added, and the mix was incubated at 37°C for 2 h. The reaction was halted by adding 0.1 volume of 0.5 M EDTA, and the labeled DNA was purified by isopropanol/ethanol precipitation and hybridized to genomic promoter arrays. For array hybridization, a NimbleGen MM8 CpG plus Promoter Microarray was used, which is a single array design containing all known CpG islands annotated by UCSC and all well-characterized RefSeq promoter regions (from approximately -1300 bp to +500 bp of the TSSs) entirely covered by approximately 385,000 probes. Scanning was performed with the Axon GenePix 4000B microarray scanner.

Raw data were extracted as pair files using NimbleScan software. We performed median-centering, quantile normalization and linear smoothing using the Bioconductor software packages Ringo, limma and MEDME, respectively. After normalization, normalized log2-ratio data were created for each sample. From the normalized log2-ratio data, a sliding-window peak-finding algorithm provided by NimbleScan v2.5 aodrqEW (Roche-NimbleGen) was applied to determine the enriched peaks with specified parameters (sliding window width: 750 bp; mini-probes per peak: 2; P value minimum cutoff: 2; maximum spacing between nearby probes within peak: 500 bp). The identified peaks were mapped to the following genomic features: transcripts and CpG Islands.

Promoters or regions were further classified into three categories to distinguish strong CpG islands, weak CpG islands and sequences with a low abundance of CpG sites[13]. High CpG promoters/regions (HCP) contain a 500-bp sequence with GC content above 55%, a CpG ratio above 0.75 and a CpG observed to expected ratio greater than 0.6. Intermediate CpG promoters/regions (ICP) contain a region below 500 bp and have moderate CpG richness (GC content less than 55%) with a CpG ratio between 0.48 and 0.75 and a CpG observed to expected ratio between 0.4 and 0.6. Low CpG promoters/regions (LCP) do not have a region of 500 bp with a CpG ratio above 0.48 or a CpG observed to expected ratio above 0.4[14].

Identification of biomarkers

Overlapping between gene expression and DNA methylation was conducted using the R gplots package

(cran.r-project.org) to screen the possible biomarkers involved in the pathogenesis of obesity. Only promoters whose downstream gene was differentially expressed at least 1.5-fold ($P < 0.05$) through Volcano Plot filtering were considered. For the last filter, methylation markers in adipose tissue of DIO mice were required to display an inverse relationship to gene expression, i.e., hyper- and hypomethylated states being down- and upregulated, respectively.

Sequencing of bisulfite-modified DNA

The methylation levels of the selected site-specific CpG sites from the three genes (Ube2q2, Foxj3 and Mmp2) were determined by bisulfite sequencing. The target regions of the relevant genes and the primers used for amplification are listed in table I. Briefly, DNA from the epididymal fat was isolated and purified with the DNA Purification Kit (cat. no. DN 1008, Biofuture Group Inc., Beijing, China) and modified with bisulfate using the Methylamp TM DNA Modification Kit (cat. no. P-1001, Epigentek Group Inc., Brooklyn, NY). The methyl-modified DNA was amplified by nested PCR, and products were sequenced directly. DNA methylation was calculated from the amplitude of cytosine and thymine within each CpG dinucleotide, C/(C+T), as described by Lewin et al. [15].

Gene expression by quantitative RT-PCR

Total RNA was extracted from mouse epididymal fat using TRIzol Reagent (cat. no. 15596-026, Invitrogen, Carlsbad, CA, USA), and cDNA was prepared from the total RNA using the SuperScriptTM III First-Strand Synthesis System for RT-PCR (cat. no. 18080-051, Invitrogen, Carlsbad, CA, USA) according to the procedures provided by the manufacturer. The genes' mRNA levels in the fat were measured using real-time quantitative RT-PCR with an ABI PRISM 7300 sequence detection system (Applied Biosystems, Foster City, CA, USA). The oligonucleotide primers were designed with the assistance of PrimerExpress software: Ube2q2 (NM_180600) (Forward: GACCAAACCTGCTTCCTG; Reverse GTGCCAACCATTCCATAA), Foxj3 (NM_172699) (Forward: AGGTCCTCAGTAGTTTGC; Reverse: AGACTGCGATACTCCAAC), Mmp2 (NM_008610) (Forward: CCCCGATGCTGATACTGA; Reverse: CTGTCCGCCAAATAAACC), beta-actin (NM_007393) (forward: ACCAGTTCGCCATGGATGAC; reverse: TGCCGGAGCCGTTGTC). The co-amplification of mouse beta-actin mRNA, an invariant internal control, was performed in all the samples. The assays were performed in triplicate, and the results were normalized to the beta-actin mRNA levels using the $2^{-\Delta CT}$ method.

Statistical analysis

All statistical analyses for gene expression microarray and DNA methylation microarray were conducted with R statistical packages v2.15.0 (www.r-project.org) and SPSS (Statistical Package for the Social Sciences) version 11.5 for Windows. For site-specific CpG sites from the three genes, Student's *t*-test was used to investigate whether their methylation or expression levels differ between the obese and the lean group. The two-sided level of significance was set at $P < 0.05$.

Results

Differences in promoter methylation between obese mice and lean mice

DNA methylation was determined using MeDIP followed by hybridization to the NimbleGen MM8 CpG plus Promoter Microarray, which probes 385,000 RefSeq mouse promoters. In adipose tissues between the obese mice and the control mice, 626 differentially methylated promoters were found, with 277 gene promoters hypermethylated and 349 hypomethylated

Table I
Bisulfite sequencing primers used in this study

Gane Name	*Forward (F) and Reverse (R) Primers*	
Ube2q2	Outer F:	(-499) TATAAGTTTGGAGAGAAGGATTTTT (-475)
	Inner F:	(-472) GGAGTTATATTTAGAAAAGTGGTG (-449)
	R:	(-212) AAAATAAACCTAAACTCCCCTAC (-234)
Foxj3	Outer F:	(-566) GTTTTATTTGTTGATAGTGAGGTTA (-542)
	Inner F:	(-535) GGTTAGTTAATTTGAGATGGAG (-514)
	R:	(-293) AAATTCCAACTCCTAAAAAATAC (-315)
Mmp2	Outer R:	(+473) AAACCAACATAACAACTTACCAC (+451)
	Inner R:	(+453) CACTACCAACTCTTTATCTATTTTA (+429)
	F:	(+255) ATAGTTAGAGATTTTAGGGTGATA (+278)

Table II
The number of differentially methylated gene promoters in the DIO mice compared with the lean mice

	Adipose tissu			*Hypothalamu*		
	Hypermethyl	*Hypomethyl*	*Total*	*Hypermethyl*	*Hypomethyl*	*Total*
HCP	185	207	392	157	189	346
ICP	53	93	146	72	62	134
LCP	39	49	88	103	63	166

in obese mice. In the brain hypothalamus of obese mice, 646 differentially methylated promoters were found, with 332 hypermethylated and 314 hypomethylated compared to that of control mice (table II).

Identification of gene methylation markers in obesity

Gene expression was evaluated for each methylation profile to assess the promoter methylation relevant to transcriptional repression. An analysis of the gene expression microarray showed that compared to the lean mice, there were 3284 genes transcriptionally upregulated and 3390 genes downregulated in the adipose tissue; in the brain, 275 genes were transcriptionally upregulated and 120 genes were downregulated. An overlapping analysis of gene expression and promoter methylation provided a list of differently methylated genes whose transcriptional expressions were associated with their promoter methylation profiles in the adipose tissue of DIO mice compared to the control mice (table III and table IV). A total of 24 hypermethylated promoters and 42 hypomethylated promoters in adipose tissue were selected as methylation markers. In the brain hypothalamus, only the promoter of gene tmem204 was hypermethylated and that of gene olfr485 was hypomethylated, which were associated with downregulated and upregulated gene expression, respectively.

Then, gene expression was evaluated for each methylation profile to assess promoter CpG content relevant to transcriptional repression. The results indicated that the expression levels of genes under the control of HCPs is negatively related to the promoter methylation levels (trend P value 0.009), whereas no significant correlation was found between the methylation levels of ICPs or LCPs and gene transcriptional expression (P = 0.364 and 0.677, respectively) (fig. 1). These filters increased the likelihood of identifying promoters with a dysregulated methylation pattern causally related to the differential expression of downstream genes.

GO and Pathway analysis indicated the specific roles of these differentially methylated and expressed genes in the biological pathways or GO terms. The genes with hypermethylated promoters and underexpression were potentially relevant to metabolic processes (GO: 0008152) including lipid metabolism and storage (Abhd5, 4921517L17Rik); the insulin-like growth receptor signaling pathway (Atxn7); obesity-linked diseases such as diabetes mellitus (Foxj3, Hmg20a) and thrombosis (Zfp161); cellular processes (GO: 0009987) including protein modification, such as lipidation and ubiquitination (Atxn7, Hecw2, Ube2q2, Dpm1); nuclear import/export pathways (Xpo4, Npm1) and transcription activator/repressors (Cebpd, Mamstr); cellular component organization (GO: 0071840), including nucleosome and cell junction assembly (Nap111, Pard3), spliceosome (Clk4), telomere organization and maintenance (Tnks2) and microtubule cytoskeleton organization (Npm1); and growth (GO: 0040007), including cell differentiation of the epidermis, lung alveolus, neural crest cell and bone (Lamas, Npm1, Errfil, Co19a1); and gland morphogenesis (Lama5). The genes that were hypomethylated in promoters with transcriptional overexpression were associated with metabolic processes (GO: 0008152), including lipid metabolism (Asah1, Acaa2); biological regulation (GO: 0065007), including the positive regulation of fat cell differentiation (Sh3pxd2b) and the negative regulation of T and B cell proliferation and immunity (Pawr, Trpm4, Usp25); signaling (GO: 0023052), including the insulin-like growth receptor signaling pathway (wdr11) and the TLR4-dependent innate immune response (Usp25); response to stimulus (GO: 0050896), including the response to estradiol stimulus (Mmp2), macrophage colony stimulating factor (csflr), tumor from hypoxia (Car9) and ischemic stroke (Arl6ip6); and localization (GO: 0051179), including activating delayed rectifier K+ current (Kcnh2) and the G2/M transition checkpoint (Fzr1).

Further validation of promoter methylation and gene expression

Three genes (Ube2q2, Foxj3 and Mmp2) were chosen for further validation of promoter methylation and gene expression in the adipose tissue. The methylation status of the promoters of these three genes was evaluated by sequencing the bisulfite-converted DNA. An increased total averaged methylation level of CG sites was found in promoters of the Ube2q2 and Foxj3 genes in DIO mice compared to the control mice. The total averaged CG site methy-

Table III
The screened genes transcriptionally upregulated by their promoters' hypomethylation

Gene Name	*Classification*	*Accession No.*
G protein-coupled receptor 137B, pseudogene (Gpr137b-ps)	HCP	NR_003568
RIKEN cDNA 2610524H06 gene (2610524H06Rik)	HCP	NM_181075
transmembrane protein 189 (Tmem189)	HCP	NM_145538
collagen, type IV, alpha 1 (Col4a1)	**HCP**	**NM_009931**
MKL (megakaryoblastic leukemia)/myocardin-like 1 (Mkl1)	HCP	NM_001082536
potassium voltage-gated channel, subfamily H (eag-related), member 2 (Kcnh2)	**HCP**	**NM_013569**
membrane bound O-acyltransferase domain containing 7 (Mboat7)	HCP	NM_029934
PRKC, apoptosis, WT1, regulator (Pawr)	HCP	NM_054056
fizzy/cell division cycle 20 related 1 (Drosophila) (Fzr1)	HCP	NM_019757
Williams-Beuren syndrome chromosome region 17 homolog (human) (Wbscr17)	HCP	NM_145218
ring finger protein 26 (Rnf26)	HCP	NM_153762
protein phosphatase 1, regulatory (inhibitor) subunit 16A (Ppp1r16a)	HCP	NM_033371
SH3 and PX domains 2B (Sh3pxd2b)	HCP	NM_177364
asparagine-linked glycosylation 13 homolog (S. cerevisiae) (Alg13)	HCP	NM_026247
growth factor receptor bound protein 2 (Grb2)	**HCP**	**NM_008163**
potassium channel tetramerisation domain containing 5 (Kctd5)	HCP	NM_027008
RIKEN cDNA 1810058I24 gene (1810058I24Rik)	**HCP**	**NR_027875**
ubiquitin specific peptidase 25 (Usp25)	HCP	NM_013918
ADP-ribosylation factor-like 6 interacting protein 6 (Arl6ip6)	HCP	NM_022989
AFG3(ATPase family gene 3)-like 1 (yeast) (Afg3l1)	HCP	NM_054070
adaptor-related protein complex AP-1, mu subunit 1 (Ap1m1)	HCP	NM_007456
round spermatid basic protein 1-like (Rsbn1l)	HCP	NM_001080977
transient receptor potential cation channel, subfamily M, member 4 (Trpm4)	ICP	NM_175130
N-acylsphingosine amidohydrolase 1 (Asah1)	ICP	NM_019734
colony stimulating factor 2 receptor, alpha, low-affinity (granulocyte-macrophage) (Csf2ra)	ICP	NM_009970
UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 4 (B3galt4)	ICP	NM_019420
zinc finger protein 7 (Zfp7)	ICP	NM_145916
RIKEN cDNA 5730508B09 gene (5730508B09Rik)	**ICP**	**NM_027482**
signal sequence receptor, beta (Ssr2)	ICP	NM_025448
histocompatibility 2, Q region locus 10 (H2-Q10)	ICP	NM_010391
Rab acceptor 1 (prenylated) (Rabac1)	ICP	NM_010261
Sjogren's syndrome/scleroderma autoantigen 1 homolog (human) (Sssca1)	**ICP**	**NM_020491**
WD repeat domain 11 (Wdr11)	ICP	NM_172255
aldo-keto reductase family 1, member A4 (aldehyde reductase) (Akr1a4)	ICP	NM_021473
ubiquitin-conjugating enzyme E2E 1, UBC4/5 homolog (yeast) (Ube2e1)	ICP	NM_009455
acetyl-Coenzyme A acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase) (Acaa2)	ICP	NM_177470
ryanodine receptor 2, cardiac (Ryr2)	**ICP**	**NM_023868**
colony stimulating factor 1 receptor (Csf1r)	**LCP**	**NM_001037859**
carbonic anhydrase 9 (Car9)	LCP	NM_139305
solute carrier family 6 (neurotransmitter transporter, GABA), member 1 (Slc6a1)	LCP	NM_178703
spondin 2, extracellular matrix protein (Spon2)	**LCP**	**NM_133903**
matrix metallopeptidase 2 (Mmp2) *	**LCP**	**NM_008610**

Bold font indicates genes whose promoter methylation has been studied in cancers.
* chosen for further validation of promoter methylation and gene expression.

lation level in the Mmp2 promoter was significantly lower in DIO obese mice than in the control mice (fig. 2). Quantitative real-time RT-PCR validated the inverse correlation between gene expression (fig. 3) and promoter methylation.

Discussion

Recent studies have demonstrated that DNA methylation in promoters of varied genes is closely associated with obesity and its complications[6-9]. In the present study, we performed comprehensive DNA methylation profiling of gene promoters in DIO mice and control lean mice to determine the differentially methylated genes using MeDIP followed by hybridization to the NimbleGen MM8 CpG plus Promoter Microarray. We further integrated epigenomic data with gene expression profiling to identify promoters that exhibited an association between methylation status and the expression of downstream genes. We identified 66 methylation markers in the adipose tissue of DIO mice, of which 24 were hypermethylated and 42 were hypomethylated.

Table IV
The screened genes transcriptionally downregulated by their promoters' hypermethylation

Gene Name	*Classification*	*Accession No.*
ataxin-7 (Atxn7)	HCP	NM_139227
CCAAT/enhancer-binding protein delta (Cebpd)	**HCP**	**NM_007679**
RIKEN cDNA 4921517L17 gene (4921517L17Rik)	**HCP**	**NM_027585**
splicing factor, arginine/serine-rich 4 (Srsf4)	HCP	NM_020587
abhydrolase domain containing 5 (Abhd5)	**HCP**	**NM_026179**
HECT, C2 and WW domain containing E3 ubiquitin protein ligase 2 (Hecw2)	HCP	NM_172655
exportin-4 (Xpo4)	**HCP**	**NM_020506**
ERBB receptor feedback inhibitor 1 (Errfi1)	HCP	NM_133753
RIKEN cDNA 1700096K18 gene (1700096K18Rik)	**HCP**	**NR_027388**
forkhead box J3 (Foxj3) *	HCP	NM_172699
cDNA sequence BC049762 (BC049762)	**HCP**	**NM_177567**
zinc finger protein 161 Gene (Zfp161)	**HCP**	**NM_009547**
tankyrase, TRF1-interacting ankyrin-related ADP-ribose polymerase 2 (Tnks2)	HCP	NM_001163635
nucleosome assembly protein 1-like 1 (Nap1l1)	**HCP**	**NM_015781**
Rap1 interacting factor 1 homolog (yeast) (Rif1)	**HCP**	**NM_175238**
ubiquitin-conjugating enzyme E2Q (putative) 2 (Ube2q2) *	HCP	NM_180600
par-3 (partitioning defective 3) homolog (C. elegans) (Pard3)	**HCP**	**NM_001122850**
CDC like kinase 4 (Clk4)	HCP	NM_007714
CDC like kinase 4 (Clk4)	HCP	NM_007714
nucleophosmin 1 (Npm1)	**HCP**	**NM_008722**
dolichol-phosphate (beta-D) mannosyltransferase 1 (Dpm1)	HCP	NM_010072
MEF2 activating motif and SAP domain containing transcriptional regulator (Mamstr)	**ICP**	**NM_172418**
high mobility group 20A (Hmg20a)	ICP	NM_025812
laminin, alpha 5 (Lama5)	ICP	NM_001081171
collagen, type IX, alpha 1 (Col9a1)	**LCP**	**NM_007740**

Bold font indicates genes whose promoter methylation has been studied in cancers.
* chosen for further validation of promoter methylation and gene expression.

Previous experiments have indicated that the relationship between promoter methylation and gene expression is related to the CpG density of the promoter[14]. To examine this relationship, we divided promoters into three types according to CpG content: high CpG promoters (HCPs), low CpG promoters (LCPs) and intermediate CpG promoters (ICPs). A stronger correlation was shown between DNA methylation levels and transcriptional repression in HCPs compared with ICPs and LCPs. Weber et al. reported that LCPs show no significant correlation between gene activity and the abundance of methylated cytosines, implying that low concentrations of methylated cytosines do not preclude gene activity, whereas the activity of ICPs and HCPs was negatively correlated with their DNA methylation status[14].

The GO and Pathway analyses suggested that the genes with differentiated methylation and transcriptional expression were associated with biological activities in lipid metabolism and storage, adipocyte differentiation, immunity and the pathogenesis of obesity-related complications. However, the epigenetic control and involvement in obesity have not yet been established for any of the methylation markers found in this study. Interestingly, among these markers, there were 11 hypomethylated and 13 hypermethylated promoters that have been previously studied, almost all of which are involved in the pathogenesis of cancers such as follicular lymphoma and Burkitt's lymphoma, breast cancer, neuroblastoma, myeloid leukemia and others[16-18]. This finding implies that these differentially methylated genes most likely play important roles in the abnormal adipocyte proliferation and differentiation in obese individuals, which should be further studied.

We assessed the methylation status of Mmp2, Foxj3 and Ube2q2 in the adipose tissue of DIO mice and found a significant methylation change between the obese and control groups. The protein encoded by the Mmp2 gene is a matrix metalloproteinase, which degrades type IV collagen, the component of the basement cellular membrane, and is essential for proper extracellular matrix remodeling in adipose tissue[19]. It has been reported that Mmp2 may facilitate the hypertrophic development of adipocytes, the formation of adipose clusters[20], and the early phase of murine preadipocyte differentiation[21]. Moreover, preadipocyte treatment with MMP inhibitors or antibodies markedly decreases adipocyte differentiation by inhibiting the lipogenesis of triglycerides and its hydrolysis[22]. In addition, Mmp2 is strongly upregulated by macrophage-secreted factors, inducing a major inflammatory response in human adipocytes[23]. In the current study, the methylation fraction of the Mmp2 promoter

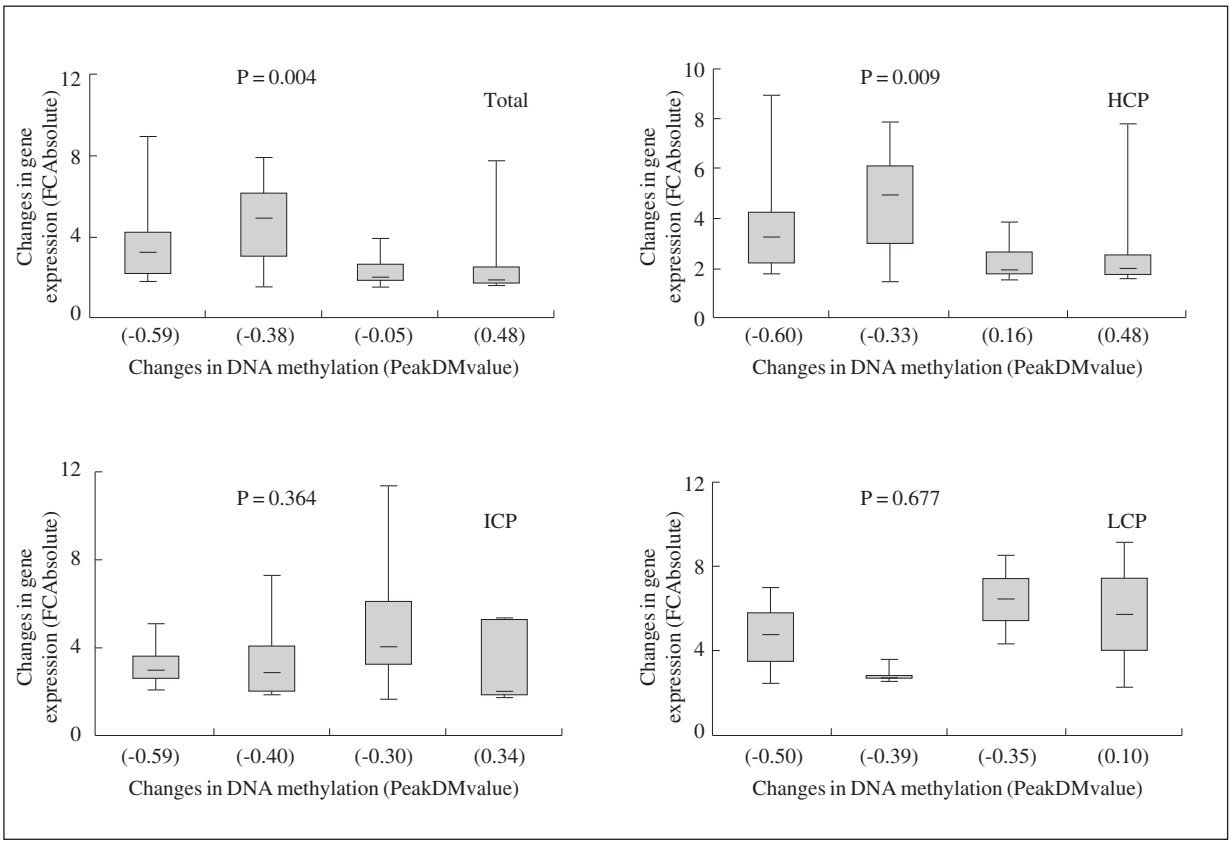

Fig. 1.—Association of transcriptional changes with DNA methylation. Promoters or regions were further classified into three categories: HCPs, ICPs and LCPs. P values were determined by the linear regression to analyze the correlation between promoter methylation levels and gene transcriptional changes.

was reduced with the correlated upregulation of transcription in DIO mice, which is consistent with the findings that the increased expression of Mmp2 is associated with overweight/obese subjects[24,25].

The product of the Foxj3 gene is a forkhead/winged helix transcription factor that functions to regulate cellular fate determination, proliferation and differentiation[26]. Foxj3 may regulate a network of zinc finger proteins (ZFPs)[27], which is a key transcriptional regulator involved in adipocyte proliferation and differentiation[28]. Additionally, Foxj3 activates the transcriptional expression of the Mef2c (myocyte enhancer factor) gene involved in adipogenesis[29]. Grant et al. reported that the knockdown of Foxj3 and Foxk1 eliminated cell cycle-dependent oscillations and resulted in decreased cell proliferation rates[30]. In response to feeding with a high-calorie diet, Foxj3 expression is downregulated, with a concomitant decrease in Mef2c expression[31]. In keeping with this finding, we found that high-fat feeding to mice downregulated the expression of Foxj3, most likely by enhancing the methylation level of the Foxj3 promoter.

The Ube2q2 protein, one of the functional ubiquitin-conjugating enzymes, is responsible for the intermediate phase of the ubiquitination pathway, which is fundamental in the regulation of protein stability and turnover. In adipocytes, the ubiquitin-dependent proteasomal pathway controls several highly regulated proteins, such as fat-specific protein 27 (Fsp27), peroxisome proliferator-activated receptor-gamma (Ppargamma) and pigment epithelium-derived factor (Pedf), which participate in lipid storage, adipocyte development and insulin sensitivity, respectively[32-34]. Transcriptome analysis has demonstrated that the expression of several genes in the hypothalamus, including Ube2q2, is modulated by high fat intake[35]. In the present study, our findings showed that the expression of Ube2q2 in the adipose tissue of DIO mice was decreased, which may be attributable to the higher methylation of its promoter.

In summary, we have shown that the integration of high-throughput data from the genome-wide integrative analysis of promoter methylation and gene expression in DIO mice, compared to the lean controls, can identify new DNA methylation markers related to obesity. The aberrant methylated promoters reported here have potential relevance in clinical applications as markers for elucidating the mechanisms of obesity pathogenesis (abnormal lipid metabolism, storage and adipocyte proliferation and differentiation, etc.) and its complications.

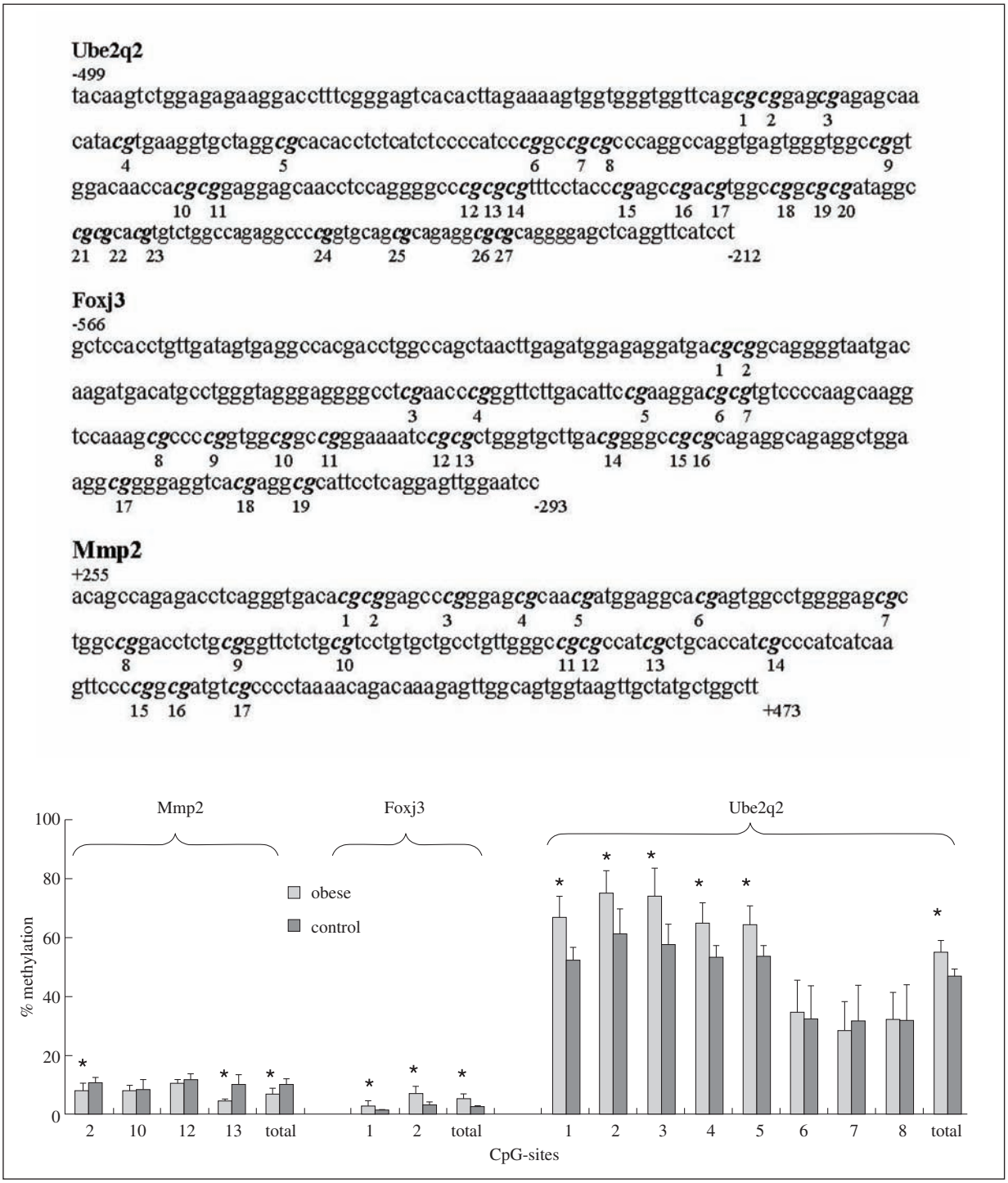

*Fig. 2.—Validation of promoter methylation for the selected markers. Genomic DNA isolated from the epididymal fat was analyzed for the methylation levels of CpG sites at the indicated positions of the gene promoters (the upper panel). Except for the methylated CpG sites shown in the lower panel, the rests were all completely demethylated. The total indicated the averaged methylation levels from the CpG sites shown. Data represent means±SD determined from 15 mice in each group. * Compared to the control group, P < 0.05.*

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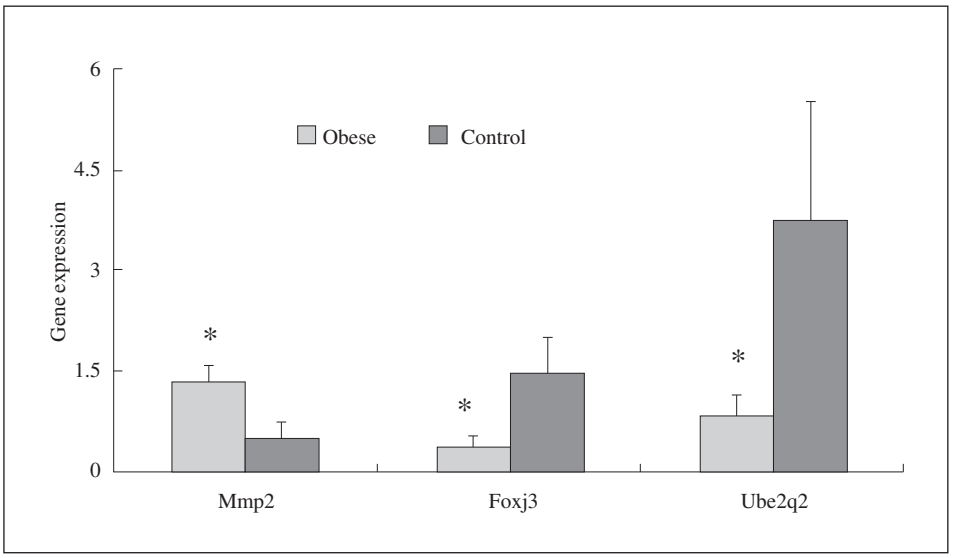

*Fig. 3.—The mRNA expression of the selected gene markers. Gene transcripts in the epididymal fat were measured by real-time RT-PCR, and the expression levels were normalized to that of beta-actin using $2^{-\Delta CT}$ method. Data represent the mRNA levels determined from 15 mice in each group. *Compared to the control group, $P < 0.05$.*

Conflict of Interest

There are no competing financial interests related to the work described.

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Original / *Obesidad*

Short term low-calorie diet improves insulin sensitivity and metabolic parameters in obese women

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Abstract

Obesity and insulin resistance are associated with an increase of cardiovascular risk factors, including adipocytokines. The aim of this study was to investigate the effect of low-calorie diet on serum lipids, adipokines, insulin resistance and body composition in obese women. It was a clinical trial with class I obese women aged 30-45 years submitted to hypocaloric diet for 90 days. Dietary intake, anthropometric parameters, body composition, serum lipids, glucose, insulin, leptin, adiponectin, HOMA-IR and QUICKI indexes were evaluated at the baseline, 30, 60 and 90 days. There was 30% significant decrease in energy intake, and also decrease in body weight, body mass index and waist circumference ($p < 0.01$) throughout the treatment period. Despite the amount of lean body mass (kg) reduced in average, it was observed that lean body mass (%) had increased ($p < 0.01$) and that the amount of fat body mass (kg) had decreased significantly in the third month ($p < 0.05$). Systolic blood pressure reduced up to -5mmHg ($p < 0.05$) after 90 days. Was observed a decrease ($p < 0.05$) on serum insulin and HOMA-IR until the 60th day, while the serum adiponectin increased ($p < 0.01$) during treatment. Corroborating with the reduction of fat body mass and weight, serum leptin also reduced ($p < 0.01$). These results suggest that the short-term low-calorie diet reduces total body fat, mainly found in the abdominal region, and efficiently improve insulin sensitivity decreasing cardiovascular risk in obese women.

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LA DIETA BAJA EN CALORÍAS A CORTO PLAZO MEJORA LA SENSIBILIDAD A LA INSULINA Y LOS PARÁMETROS METABÓLICOS EN LAS MUJERES OBESAS

Resumen

La obesidad y la resistencia a la insulina se asocian con un aumento de los factores de riesgo cardiovascular, incluyendo las adipocitocinas. El propósito de este estudio fue investigar el efecto de una dieta baja en calorías sobre los lípidos séricos, las adipocinas, la resistencia a la insulina y la composición corporal en mujeres obesas. Se trataba de un estudio clínico en mujeres con obesidad de clase I, con edades entre 30-45 años, sometidas a una dieta hipocalórica durante 90 días. Se evaluaron basalmente y a los 30, 60 y 90 días la ingesta dietética, los parámetros antropométricos, la composición corporal, los lípidos séricos, la glucosa, la insulina, la leptina, la adiponectina y los índices HOMA-IR QUICKI. Hubo un descenso significativo del 30 % en el consumo de energía y un descenso del peso corporal, el índice de masa corporal y la circunferencia de la cintura ($p < 0,01$) durante todo el periodo de tratamiento. A pesar de que se redujo en promedio la masa magra corporal (kg), se observó que la masa magra corporal (%) se incrementó ($p < 0,01$) y que la cantidad de masa corporal grasa (Kg) disminuyó significativamente al tercer mes ($p < 0,05$). La presión sanguínea sistólica se redujo en 5 mmHg ($p < 0,05$) a los 90 días. Observamos un descenso de la insulina sérica y del HOMA-IR en el día 60 ($p < 0,05$), mientras que la adiponectina sérica aumentó ($p < 0,01$) durante el tratamiento. Como corroboración de la reducción de la masa corporal grasa y del peso, la leptina sérica también se redujo ($p < 0,01$). Estos resultados sugieren que la dieta hipocalórica a corto plazo reduce la grasa corporal total, fundamentalmente en la región abdominal y mejora de forma eficiente la sensibilidad a la insulina disminuyendo el riesgo cardiovascular en mujeres obesas.

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Palabras clave: *Obesidad. Dieta hipocalórica. Insulina. Adiponectina. Peso corporal.*

List of abbreviations

BMI: Body mass index.
CVD: Cardiovascular disease.
DBP: Diastolic blood pressure.
HDL: High-density lipoprotein.
FBM: Fat body mass.
HOMA-IR: Homeostatic Model Assessment-Insulin Resistance.
95% CI: 95% confidence interval.
IR: Insulin resistance.
LBM: Lean body mass.
LDL: Low-density lipoprotein.
OR: Odds ratio.
SBP: Systolic blood pressure.
VLDL: Very-low-density lipoprotein.
WC: Waist circumference.

Introduction

Obesity is defined by an accumulation of adipocytes throughout the body and is also associated with a variety of metabolic diseases[1]. To improve the adverse metabolic condition it is necessary to create a negative balance in energy intake, thereby leading to weight loss[2]. Obesity and insulin resistance are associated with an increase of cardiovascular risk factors, including inflammatory markers and adipocytokines[3].

The incidence of obesity and associated comorbidities is clearly increasing worldwide. In the past few years, this epidemiologic evidence has led to increased interest in adipose tissue as an active participant of physiologic and pathological processes[4,5]. Adipose tissue, then, can be considered as an active secretory organ able to send and respond to signals that modulate appetite, insulin sensitivity, energy expenditure, and inflammation. Regarding obesity and type 2 diabetes, it is well established that the association between visceral adipose tissue and insulin resistance is associated with increased cardiovascular risk[6].

Adiponectin, an adipose-specific plasma protein, possesses insulin-sensitizing and anti-atherogenic properties[7]. It has been well documented that plasma adiponectin is lower in obese subjects than in lean subjects and is negatively correlated with body weight, visceral fat mass and resting level of insulin[8]. Leptin is produced by adipocytes and its action occurs through the receptor in the hypothalamic nucleus. Leptin concentration is proportional to the total body fat[9].

Energy restriction followed by weight loss is important for reducing the risk of type 2 diabetes in individuals with obesity and impaired glucose homeostasis as well as for improving dyslipidemia and reducing blood pressure[2]. The purpose of this study was to evaluate the effect of short term low calorie diet on serum lipids, adipokines, insulin resistance and body composition in obese women.

Methods

Study participants

Thirty volunteers obese women; aged 30 to 45 years with a body mass index (BMI) of 30 to 34.9 kg/m^2 participated in the study at the Josué de Castro Institute of Nutrition, University of Rio de Janeiro (Rio de Janeiro, Brazil). Exclusion criteria were: diabetes mellitus; non-treated thyroid disease; treatment with lipid-lowering drugs and glucocorticoids; and weight loss treatment within the previous three months. All volunteers gave their written informed consent and this study was approved by the Ethics Committee of the State University of Rio de Janeiro (Rio de Janeiro, Brazil) (Protocol number 007.3.2008).

Energy requirement and composition of diets

The daily energy requirement was estimated by Dietary Reference Intakes[10]. The subjects were then prescribed a daily energy intake of 500 kcal lower than the estimated energy requirement. The dietary target for fat content was 25 to 30% of energy (E%), 15 to 20 E% from protein and 50 to 60 E% from carbohydrates[11]. The subjects were given dietary instructions consisting of isoenergetic interchangeable servings. Instructions were given to minimize differences in the amount of fruit and vegetables eaten, type of fat, amount and type of fibers, type of carbohydrates and frequency of meals.

Study design

A 3-month clinical trial was performed. All recruited women underwent a screening visit for selection before enrolling in the study. A dietitian supervised weight loss and diet compliance every month, until the third month. At the beginning and on 30, 60 and 90 days were evaluated meal records, anthropometric measures and laboratory assessment.

Dietary intake

All enrolled subjects received instructions to record their dietary intake for three days including a weekend day of each month completed during the intervention. Records were reviewed by a dietician and analyzed with a computerized dietary assessment program (Food Processor ESHA Research, Salem, Oregon, 1998). USDA composition food table were used as a reference[12].

Anthropometric measurements

Body weight, BMI and waist circumference (WC) were measured. Tetrapolar body electrical bioimpe-

dance was used to determine body composition[13]. An electric current of 0.8 mA and 50 kHz was produced by a calibrated signal generator (model 410e, Biodynamics, Seattle, WA, USA) and applied to the skin using adhesive electrodes placed on the right hand and foot. Fat body mass (FBM), and lean body mass (LBM) were estimated by body electrical bioimpedance. Blood pressure was measured twice in the right arm by the trained investigator, with a mercury sphygmomanometer and stethoscope after subjects had rested for a minimum of 10 minutes[14].

Laboratory assessment

Blood samples were obtained after 12 hour overnight fasting and were collected into tubes (Vacutainer, Becton Dickinson, USA) to obtain serum samples, respectively. Aliquots of serum were separated by centrifugation at 4,000 rpm for 15 minutes at room temperature (Excelsa Baby I, model 206, FANEM®, São Paulo, Brazil) and were individually kept at –20°C until assaying.

Serum concentrations of total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, glucose and uric acid were determined by enzymatic colorimetric assay (commercial kit BioSystems S.A, Barcelona, Spain), using an A15 Automatic Analyzer (BioSystems S.A., Barcelona, Spain). Low-density lipoprotein (LDL) was calculated[15]. Serum glucose and uric acid were measured by spectrophotometry using the glucose oxidase/peroxidase and uricase/peroxidase methods, respectively (A15 Automatic Analyzer, BioSystems S.A., Barcelona, Spain)[16]. Serum insulin was measured by a radioimmunoassay (RIA) kit (ImmuChem™ Coated Tube, MP Biomedicals®, LLC, USA)[17], with an assay sensitivity of 4.6 µU/mL and 12.2% of intra-assay coefficients of variation. Serum leptin was measured using a commercially available RIA assay kit (LINCO Research®, Missouri, USA), with 0.5 ng/mL assay sensitivity and < 8.3% intra-assay coefficient of variation. Finally, serum adiponectin was also measured by available a RIA assay kit (MILLIPORE®, Missouri, USA), with 2 ng/mL assay sensitivity and < 3.59% intra-assay coefficient of variation. To count samples of RIA assays a 2470 WIZARD^2 Automatic Gamma Counter (Perkin-Elmer Inc.) was used.

Homeostasis Model Assessment for insulin resistance (HOMA-IR) and Quantitative Insulin-Sensitivity Check Index (QUICKI) were calculated[18,19].

Statistical analysis

Data were presented as mean ± standard error mean. To check the distribution of continuous variables of interest, Kolmogorov-Smirnov adhesion test was performed. The comparisons of mean values over time were made using the paired Student's *t*-test and One-way ANOVA for comparison of fatty acids intake at baseline. Statistical analyzes were conducted, using the statistical package SPSS Statistics 17.0 and GraphPad Prism 5.0. Differences were considered significant at $p < 0.05$.

Results

Table I shows the general characteristics of the women studied. The mean age was 39.1 ± 0.8 years, and BMI and WC were 32.7±0.4 kg/m^2 and 99.2 ± 1.4 cm, respectively. Basal assessment of nutritional intake showed high variability, as it can be seen in table II.

Table I
Baseline characteristics of obese women (n = 30)

Measurements	*Mean*	*Minimum*	*Maximum*
Age (years)	39.1	30	45
Body weight (kg)	86.0	67.6	103.0
BMI (kg/m^2)	32.7	29	37
WC (cm)	99.2	89	116
LBM (kg)	53.2	44.6	62.8
LBM (%)	62.0	56.1	67.3
FBM (kg)	32.1	19.0	44.2
FBM (%)	37.2	21.7	43.1
SBP (mmHg)	120.3	110	140
SBP (mmHg)	80.5	60	100
Total cholesterol (mg/dL)	182.4	124	239
HDL-c (mg/dL)	53.9	32	80
LDL-c (mg/dL)	106.2	51.6	161.4
Triglycerides (mg/dL)	110.9	45	272
Uric acid (mg/dL)	4.2	69	99
Fasting glucose (mg/dL)	83.8	2.9	7.8
Insulin (µU/mL)	34.0	12.4	92.0
Leptin (ng/mL)	25.4	15.0	59.0
Adiponectin (ng/mL)	4.9	1.2	13.9
HOMA-IR	7.4	2.6	23.0
QUICKI	0.361	0.255	0.477

BMI: Body mass index, WC: waist circumference, LBM: lean body mass, FBM: fat body mass, SBP: systolic blood pressure, DBP: diastolic blood pressure.

Table II
Baseline characteristics of dietary intake of obese women

Parameters	*Mean*	*Minimum*	*Maximum*
Total energy intake (KJ)	7253.4	2655.9	15372.6
Carbohydrates (% TEI)	54.0	34.0	77.0
Protein (% TEI)	18.9	8.0	28.0
Lipids (% TEI)	27.3	12.0	43.0
SFA (% TEI)	10.0	2.0	21.0
MUFA (% TEI)	9.0	2.0	13.0
PUFA (% TEI)*	4.1*	1.0	8.0
Trans FA (g/day)	3.1	0.0	26.9
Cholesterol (mg/day)	211.7	16.3	591.3
Dietetic fiber (g/day)	21.9	5.3	62.2
Soluble fiber (g/day)	5.2	0.8	14.8

*$p < 0.0001$ compared to PUFA and MUFA, TEI: total energy intake, SFA: saturated fatty acid, PUFA: polyunsaturated fatty acid, MUFA: monounsaturated fatty acid, FA: fatty acid.

Was observed PUFA intake lower than MUFA and SFA ($p < 0.0001$).

Table III describes the effect of hypocaloric diet on dietary consumption. Energy intake decreased during the total time of treatment with low-calorie diet compared to baseline. There was a significant decrease in energy intake of about -31%, -23%, -28% at 1st, 2nd and 3rd months, respectively. The women had lower intake of carbohydrates and higher intake of lipids in the first (-9.0% $p < 0.01$ and +5.7%, $p < 0.05$, respectively) and third month (-10.3 % and +8.8%, $p < 0.01$, respectively), while the consumption of *trans* FA was lower during the total time of treatment. They had an important decrease in fiber ingestion ($p < 0.05$) in the first month of treatment, which continued to drop during treatment.

Table IV shows the effect of hypocaloric diet on anthropometric, body composition and blood pressure measures. Body weight loss and consequent reduction of BMI and WC were significant ($p < 0.01$) throughout the treatment period. Despite the percentage of LBM had increased significantly ($p < 0.01$) during treatment, it is observed that the amount of LBM (kg) reduced in average and that the quantity of FBM also decreased; however, it became significant ($p < 0.05$) in the 3rd month. Systolic blood pressure also reduced significantly ($p < 0.05$) during the treatment period, while diastolic blood pressure reduction was not significant.

Table V describes the effect of low-calorie diet on lipid profile, insulin resistance and adipokines. Serum lipids did not change significantly with a reduced calorie diet. The treatment showed a decrease in serum insulin and in HOMA-IR in the first two months ($p < 0.05$). On the contrary, serum concentrations of adiponectin increased significantly ($p < 0.01$) during treatment. Corroborating with the reduction of body fat and weight, serum leptin levels also reduced significantly during treatment ($p < 0.01$), showing a 32% decline in the second month compared to baseline. In the 3rd month, energy intake was related do weight loss (r 0.564, $p < 0.05$) and adiponectin was inversely related to HOMA-IR (r -0.365, $p < 0.05$).

Table III
Dietary consumption by each month of treatment with hypocaloric diet

Parameters	*1st month* Δ ± *SEM*	*2nd month* Δ ± *SEM*	*3rd month* Δ ± *SEM*
Total energy intake (KJ)	-2236.6 ± 848.8*	-1680.2 ± 771.6*	-2083.4 ± 881.9*
Carbohydrates (% TEI)	-9.0 ± 2.8**	-5.2 ± 2.8	-10.3 ± 3.3**
Protein (% TEI)	3.3 ± 1.6	2.1±1.8	1. 5 ± 1.5
Lipids (% TEI)	5.7 ± 2.7*	3.1±2.3	8.8 ± 2.9**
SFA (%TEI)	3.1 ± 1.6	1.6±1.6	5.6 ± 2.0*
MUFA (%TEI)	1.6 ± 1.1	-0.1±1.0	1.9 ± 1.3
PUFA (%TEI)	0.7 ± 0.4	0.5±0.6	0.8 ± 0.6
Trans FA (g/day)	-3.1 ± 1.3*	-3.4±1.5*	-3.2 ± 1.6
Cholesterol (mg/day)	-11.7 ± 34.3	-15.6±38.3	40.4 ± 55.4
Dietetic fiber (g/day)	-6.7 ± 3.2*	-4.5±3.9	-6.9 ± 4.1
Soluble fiber (g/day)	-1.5 ± 1.0	-1.1±1.0	-1.5 ± 1.1

*p < 0.05. **p < 0.01. Δ: mean difference compared to the baseline, TEI: total energy intake, SFA: saturated fatty acid, PUFA: polyunsaturated fatty acid, MUFA: monounsaturated fatty acid, FA: fatty acid.

Table IV
Effect of hypocaloric diet on anthropometric measures, body composition and blood pressure parameters

Measurements	*1st month* Δ ± *SEM*	*2nd month* Δ ± *SEM*	*3rd month* Δ ± *SEM*
Body weight (kg)	-2.0 ± 0.2**	-2.7 ± 0.4**	-3.0 ± 0.5**
BMI (kg/m²)	-0.8 ± 0.1**	-1.0 ± 0.2**	-1.1 ± 0.2**
WC (cm)	-1.7 ± 0.4**	-2.2 ± 0.5**	-3.2 ± 0.6**
LBM (kg)	-0.1 ± 0.3	-0.7 ± 0.3	-0.6 ± 0.4
LBM (%)	1.4 ± 0.4**	1.3 ± 0.4**	1.6 ± 0.4**
FBM (kg)	-0.8 ± 0.7	-1.3 ± 0.7	-1.7 ± 0.7*
FBM (%)	-0.1 ± 0.8	-0.4 ± 0.7	-0.8 ± 0.7
SBP (mmHg)	-5.7 ± 2.1*	-3.8 ± 1.8*	-5.0 ± 1.9*
DBP (mmHg)	-1.7 ± 2.2	-3.8 ± 2.0	-2.8 ± 2.2

*p < 0.05; **p < 0.01. Δ: mean difference compared to the baseline, BMI: Body mass index, WC: waist circumference, LBM: lean body mass, FBM: fat body mass, SBP: systolic blood pressure, DBP: diastolic blood pressure.

Table V
Effect of hypocaloric diet on lipid profile, insulin resistance and adipokines

Measurements	*1st month* Δ ± *SEM*	*2nd month* Δ ± *SEM*	*3rd month* Δ ± *SEM*
Total cholesterol (mg/dL)	-0.9 ± 4.6	-10.8 ± 6.6	4.5 ± 4.5
HDL-c (mg/dL)	-1.2 ± 1.5	-1.0 ± 2.6	-1.8 ± 2.3
LDL-c (mg/dL)	2.0 ± 4.6	-5.0 ± 5.3	5.3 ± 3.7
Triglycerides (mg/dL)	-7.7 ± 9.9	-4.8 ± 10.2	4.8 ± 10.7
Uric acid (mg/dL)	-0.1 ± 0.2	-0.3 ± 0.1	-0.1 ± 0.1
Fasting glucose (mg/dL)	-1.6 ± 2.3	-3.1 ± 1.6	1.0 ± 1.8
Insulin (μU/mL)	-6.7 ± 2.9*	-6.6 ± 3.0*	1.0 ± 3.2
Leptin (ng/mL)	-5.8 ± 1.8**	-8.3 ± 1.5**	-5.7 ± 1.9**
Adiponectin (ng/mL)	0.8 ± 0.3**	1.1 ± 0.5*	1.0 ± 0.4**
HOMA-IR	-1.7 ± 0.8*	-1.8 ± 0.8*	0.1 ± 0.8
QUICKI	0.019 ± 0.009*	0.009 ± 0.008	-0.015 ± 0.009

*p < 0.05; **p < 0.01. HDL-c: high-density lipoprotein cholesterol, LDL-c: low-density lipoprotein cholesterol, VLDL-c: very-low-density lipoprotein cholesterol, HOMA-IR: Homeostatic Model Assessment - Insulin Resistance.

Discussion

This study showed that obese women submitted to a low-calorie diet treatment loosed weight, improved insulin resistance and other metabolic abnormalities characteristic of obesity.

Adherence to dietary treatment is very important. In the present study there was reduction of energy intake during the three-month intervention, with greater emphasis in the first month. These data confirm previous studies that also reported success in adherence to dietary treatment for weight loss[20,21]. The progressive increase in energy intake after the initial reduction may have occurred due to adaptive thermogenesis. The decreased energy expenditure when the intake is limited is a counter-productive response during a hypocaloric diet, contributing significantly to lower efficacy of long-term treatment for obesity.

As a consequence of lower caloric intake, mainly carbohydrates, there was a reduction in body weight and BMI of these women, both reaching 3.5% in the last month. The percentage of LBM increased during the study, but mainly due to the reduction of FBM, which remained significant in the third month.

The low-calorie diet alone has been an intervention strategy for weight loss in several studies[22,23]. In a systematic review of 21 studies, in which the diet was the main intervention, we observed that diet alone promoted greater weight loss up to 36 months from the start of the intervention, compared to nutritional guidelines only. Lofgren et al.[24] evaluated in premenopausal women, the response of a hypocaloric diet for 10 weeks with a reduction of 26.6% of VET and observed a reduction of 4.6% of body weight, slightly higher than our study. However, the amount of weight loss varies widely among studies due to different strategies, duration of interventions, age, degree of overweight, etc[22].

The present study showed that a significant percentage of weight loss could promote improvement in some clinical and metabolic parameters. Although other studies did not show higher percentages of weight loss, they showed that even small weight losses contribute to important health benefits[20,21,24,25]. This is probably due to a decrease in WC, which was gradual and reached a higher percentage in the last month of treatment. It is well known that the excess adiposity in the abdominal region is more frequently associated with metabolic abnormalities, such as insulin resistance and atherosclerosis[26]. These findings about treatment with hypocaloric diet and decreased in WC are in agreement with other studies[24,27].

Generally, treatments with low-calorie diets lead to body weight loss. Regarding body composition, there is loss of both adipose tissue and LBM, depending on physical activity. However, in this study, was observed that the loss of body fat promoted relative increase in LBM, i.e., the increase in the percentage of LBM leads to a misconception of its increase. In fact, fat mass has decreased more than lean mass. It is recommended that the loss of lean mass does not exceed 30% of the weight lost. Therefore, maintaining the largest possible amount of lean mass is essential[28]. Thus, this study agrees with these recommendations.

Systolic blood pressure reduced during the study. Our results corroborate with those reported by Al-Sarraj et al.[29], which showed a decrease in both SBP and DBP after treatment with calorie-restricted diet for six weeks, followed by fat-restricted diet for six weeks. In addition, weight loss greater than 5% showed a significant reduction in SBP[25]. The decrease in SBP showed possible relationship with reduced serum insulin, since high concentrations of serum insulin is a contributing factor in the pathophysiological mechanism of systemic arterial hypertension. Therefore, it is likely that a significant reduction in serum insulin had contributed to reduction in SBP.

Insulin resistance in obese subjects markedly increases the risk of coronary artery disease[30]. As expec-

ted, was found that the amount of weight lost had a significant effect on the degree of improvement in insulin sensitivity. The women in this study showed a significant reduction in insulinemia in the first two months of treatment. Regarding insulin concentrations, the mean HOMA-IR was also reduced in the same period, while QUICKI, which evaluates sensitivity to insulin, showed an effect opposite to HOMA-IR in the first month. These results corroborate with the study conducted by Samaha et al.[20], which showed an improvement in insulin sensitivity in obese subjects, after six months of a carbohydrate-restricted diet. Thus, despite the greater weight loss at the end of our study, adherence to treatment and increased serum adiponectin seem to be the main factors related to improve insulin sensitivity.

Adiponectin, a protein secreted by adipocytes, is related to improved insulin sensitivity[31]. It increases insulin sensitivity by increasing fatty acid oxidation and glucose uptake in skeletal muscle and adipose tissue and decreased hepatic glucose release[32].

Adiponectin levels increased during the study, in agreement with reduction of HOMA-IR, weight and WC, which means that insulin resistance reduced with the treatment. The data of adiponectin levels are in agreement with those of Al-Sarraj et al.[29], which showed an increase in adiponetin average (1.58 mg/L) after 12 weeks of treatment with fat-restricted diet. Considering that adiponectin also acts as a protective effect on cardiovascular function[33], the increase observed in this study can be considered a good perspective of the effect of low-calorie diet.

Leptin is another hormone secreted by adipose tissue and is directly related to BMI[34]. Leptin production and its action maintain a regulatory control of energy balance in the body. Insulin is the major regulator of leptin production by adipose tissue in the healthy state. Insulin infusions increase circulating leptin concentrations in humans. Insulin-stimulated leptin production appears to involve increased glucose metabolism while blockade on glucose transport or glycolysis inhibits leptin expression and secretion in isolated adipocytes. Insulin and leptin concentrations decrease during fasting and energy-restricted diets, independent of body fat changes, ensuring that feeding is triggered before body energy stores become depleted[35].

The reduction in leptin after weight loss is variable. Some authors reported reductions of 22%[36] and 45%[37] on serum. While other authors have reported minor loss (5.9%) but significant and simultaneous loss of 7.5% of BFM (kg) and 6.5% of WC (cm)[24]. Still, De Luis et al.[25] showed that regardless of the amount of body weight lost, leptin significantly reduced in groups with weight loss greater and lesser than 5%. Throughout the treatment, the women had significantly lower concentrations of leptin, which is consistent with the reduction of BMI and WC and confirms previous studies[24,25].

In conclusion, the results suggest that short-term nutritional treatment with a balanced hypocaloric diet, in relation to macronutrients, reduces body weight and total body fat, mainly found in the abdominal region, and efficiently improves insulin sensitivity decreasing cardiovascular risk in obese women.

Authors' contributions

GVBH – Followed the subjects, carried out immunoassays, statistical analyses and draft the manuscript; SKU - Followed the subjects, carried out immunoassays, participated to draft the manuscript; FNN - Carried out biochemistry assessment; EGM - Participated in study design;

GR - Participated in study design, statistical analyses and to draft the manuscript; MCFP - Participated in study design, statistical analyses and to draft the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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Original / *Obesidad*

The relationship between dental caries and obesity among primary school children aged 5 to 14 years

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Abstract

Background: **Previous study revealed that the link between dental caries and obesity has been controversial. The purpose of this research is to investigate the association between dental caries and obesity among primary school children in Wannan area, China.**

Methods: **A cross-sectional study was designed to collect the routine health screening data for primary school children aged 5-14 years inWannan area,China, Overweight and obesity status were determined using the International Obesity Task Force standard (IOTF) BMI cut-off points. Caries status was recorded based on WHO recommendations.**

Results: **Our results revealed that the overall caries prevalence of the subjects was 44.9%, Maximum number of caries affected children belonged to underweight and normal group, followed by overweight, and the least number was obesity. These differences were statistically significant (chi-square test, P < 0.001). Children with obesity were 1.908 times (OR =1.908; CI95%=1.750, 2.079) more likely have caries than children with underweight or health weight. Overweight children were 1.547 times (OR = 1.547; CI95% = 1.479, 1.618) more likely to have caries than children with underweight or health weight. After adjusted the gender and age, a statistically significant association was also observed between body mass index categories and caries.**

Conclusions: **Obesity may have a significant effect on caries prevalence of primary school children in Wannan area, China. The importance of obesity should not only be emphasized with respect to general diseases but also with regard to carious lesions.**

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LA RELACIÓN ENTRE CARIES DENTAL Y OBESIDAD EN LOS NIÑOS DE ESCUELA PRIMARIA CON EDADES ENTRE 5 Y 14 AÑOS

Resumen

Antecedentes: **Un estudio previo reveló que la asociación entre la caries dental y la obesidad es controvertida. El propósito de esta investigación fue investigar la asociación entre la caries dental y la obesidad en niños de escuela primaria en el área de Wannan, China.**

Métodos: **Se diseñó un estudio transversal para recoger los datos del chequeo rutinario de salud de los niños de escolarización primaria con edades de 5-14 en el área de Wannan, China. Se determinó el estado de sobrepeso y obesidad utilizando los puntos de corte estándar del IMC del Grupo de Trabajo Internacional en Obesidad (GTIO). El estado de las caries se registró de acuerdo con las recomendaciones de la OMS.**

Resultados: **Nuestros resultados revelaron que la prevalencia global de caries en los sujetos fue del 44,9%. El máximo número de niños afectados por las caries estaba en los grupos normal y con peso bajo, seguido por el grupo con sobrepeso y por último en el grupo de obesidad. Estas diferencias fueron estadísticamente significativas (test Chi-cuadrado, P < 0,001). Los niños con obesidad fueron 1.908 times (OR = 1,908; IC 95% = 1,750, 2,079) más probable tener la caries que los niños con bajo peso o de peso de salud. Los niños con sobrepeso tenían una probabilidad 1,547 veces superior (OR = 1,547; IC al 95% = 1,479, 1,618) de tener caries dental que los niños con un peso bajo o normal. Tras ajustar por sexo y edad, también se observó una asociación estadísticamente significativa entre el índice de masa corporal y la caries.**

Conclusiones: **La obesidad puede tener un efecto significativo sobre la prevalencia de caries en niños en escolarización primaria en el área de Wannan, China. No sólo se debería poner el énfasis de la importancia de la obesidad en relación con las enfermedades generales sino también en relación con las lesiones cariales.**

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Palabras clave: *Caries dental. Niños de escuela primaria. Obesidad. Sobrepeso. China.*

Introduction

Dental caries and obesity constitute important health problems worldwide and have been associated with a great number of negative health outcomes[1-3]. Dental caries is a chronic disease which can affect us at any age. If untreated, it can lead to pain and discomfort and finally loss of teeth. Dental caries has a multifactor etiology. The risk of dental caries can be evaluated by analyzing and integrating several causative factors such as fluoride, microbial plaque, diet, bacterial and salivary activity, and social and life style related behavioral factors[4,5] .

In recent decades, the prevalence of obesity risen steeply world wide[6,7], Obesity is associated with breast cancer[8], asthma[9,10], diabetes mellitus[11,12], hypertension[13], coronary artery disease[14], and dental caries[15-17]. Previous study showed that the prevalence of obesity in Chinese children and adolescents was considered to be still relatively low[18]. However, research recently found that rapid increasing of both obesity and overweight, in both urban and rural areas would arouse special attention[19,20].

However, there have been little studies documented in literature in this part of China assessing the prevalence of dental caries in relation to obesity. Thus, cross-sectional study was designed to assess the prevalence of dental caries in relation to obesity in 5- 14 year-old school children in Wannan area, China.

Methods

Subjects and Methods

Participants

A population-based cross-sectional study was conducted among primary school children for routine health screening from 2009 to 2013. A total of 67956 subjects (36,664 male and 31,292 female) aged 5-14 years were recruited in this study. All subjects agreed to provide their personal information regarding the purpose and the procedures of our study. This study was approved by local ethics committee.

Anthropometric measurements

Height was measured to the nearest 0.1 cm with a standard stadiometer following study protocols, and weight in kilograms was measured in light clothing to the nearest 0.1 kg on an electronic scales. All anthropometric data were collected by trained staff and supervised by the school nurse. BMI was computed using the following standard equation: BMI = Weight in kg/height squared in meter.

Definitions

Overweight and obesity were defined using the International Obesity Task Force standard (IOTF) body mass index cut-off points established for children[21]. These cut-off points are based on health related adult definitions of overweight (≥ 25 kg/m^2) and obesity (≥30 kg/m^2) but are adjusted to specific age and sex categories for children[21]. Caries status was recorded based on WHO recommendations[22]. A single trained and calibrated examiner performed comprehensive clinical examination with the assistance of one recorder. Children were made to sit on the chair and examination was conducted under bright daylight.

Ethical consideration

All respondents agreed to take part in this study. According to local and international guidelines on ethics considerations in research involving human participants, this study was approved by local ethics committee.

Statistical analysis

Excel software was performed to describe the characteristics of study population. The difference in caries prevalence of children according to year, age, grade and body mass index categories was tested using chi-square test. Relationships between year, grade, body mass index categories and dependent variable dental caries were assessed using multivariate logistic regression. Adjusted odds ratios (OR) and their 95% confidence intervals (CI) were calculated. In evaluating the association, we adjusted for the following confounders: gender and age. A line graph was drawn for caries prevalence of boys and girls among children by age and year. A value of $P < 0.05$ was considered statistically significant.

Results

A total of 67,956 subjects (36,664 male and 31,292 female) aged 5-14 years were recruited in this study.

The characteristics of study population are shown in table I.

Caries prevalence of children according to year, age, grade and body mass index categories are shown in table II. The overall caries prevalence of the subjects was 44.9%, caries prevalence of boys and girls are showed in figure 1 and figure 2. Maximum number of caries affected children belonged to underweight and normal group, followed by overweight, and the least number was obesity. These differences were statistically significant (chi-square test, $P < 0.001$).

Table I
Characteristics of study population

Variable		Male		Female		Total
		n	%	*n*	%	
Year	2009	9054	24.7	7778	24.9	16832
	2010	9166	25.0	7814	25.0	16980
	2011	9248	25.2	7870	25.2	17118
	2012	9196	25.1	7830	25.0	17026
Age years	5	13	0.0	34	0.1	47
	6	3116	8.5	3082	9.8	6168
	7	5561	15.2	4855	15.5	10416
	8	5855	16.0	4901	15.7	10756
	9	6111	16.7	5317	17.0	11428
	10	6267	17.1	5443	17.4	11710
	11	6571	17.9	5489	17.5	12060
	12	2934	8.0	2021	6.5	4955
	13	204	0.6	125	0.4	329
	14	32	0.1	25	0.1	57
Grade						
	one	5541	15.1	4828	15.4	10369
	two	5724	15.6	4836	15.5	10560
	three	5916	16.1	4982	15.9	10898
	four	6172	16.8	5291	16.9	11463
	five	6472	17.7	5530	17.7	12002
	six	6839	18.7	5825	18.6	12664
Caries						
	Yes	16307	55.5	14196	54.6	30503
	No	20357	44.5	17096	45.4	37453
Body mass index categories						
	Underweight or health weight	28265	77.1	27536	88.0	55801
	overweight	6485	17.7	3180	10.2	9665
	obesity	1914	5.2	576	1.8	2490

Table III provide unadjusted and adjusted ORs of dental caries by year, grade and body mass index categories. Subjects recruited in 2009, 2010 and 2011 had less likely to have caries than subjects conducted in 2012, the OR (95%CI) was 0.44, 0.871 and 0.996, respectively. Children from low grade have more likely have caries than children from high grade. Children with obesity were 1.908 times (OR =1.908; CI 95% = 1.750, 2.079) more likely have caries than children with underweight or health weight.Overweight children were 1.547 times (OR = 1.547; CI95% = 1.479, 1.618) more likely have caries than children with underweight or health weight. After adjusted the gender and age, a statistically significant association also observed between year, grade, body mass index categories and caries.

Discussion

The main objective of the present study was to determine the prevalence of dental caries in relation to obesity of 5-14 year-old school children of Wannan area, China. Our study found high caries prevalence (44.9%), a statistically significant association was observed between obesity and caries. Similar results were obtained in a systematic review and meta-analysis conducted by Hayedn et al.[23] showed that, overall, there was a significant relationship between childhood obesity and dental caries. However, this relationship between dental decay and BMI was not significant for the study by Pinto et al[24]. Kopycka-Kedzierawski et al.[25] even found an inverse association between BMI and caries experience: overweight children were less likely to have caries experience than normal weight children aged 6-11 years. The possible explaition was that both obesity and dental caries are multifactorial in aetiology and various genetic and environmental factors have an impact on them. Another possible reason was that high sugar intake is risk factor common to both obesity and dental caries[26]. The role of high sugar intake in the prevalence of obesity and dental caries should be further researched.

Recent evidence suggests that the nutrition transition is accelerating and the outcome of this trend is a rapid increase in obesity and chronic diseases[27]. Lifestyle transition and socio-economic improvement have con-

Table II
The prevalence of caries for children according to year, age, grade and body mass index categories

Variable		*Caries free*		*Caries*		*p*
		n	*%*	*n*	*%*	
Year	2009	11459	68.1	5373	31.9	0.00
	2010	9024	53.1	7956	46.9	
	2011	8510	49.7	8608	50.3	
	2012	8460	49.7	8566	50.3	
	Total	37453	55.1	30503	44.9	
Age years	5	29	61.7	18	38.3	
	6	3249	52.4	2949	47.6	0.00
	7	4958	47.6	5458	52.4	
	8	4839	45.0	5917	55.0	
	9	5341	46.7	6087	53.3	
	10	6428	54.9	5282	45.1	
	11	8498	70.5	3562	29.5	
	12	3809	76.9	1146	23.1	
	13	259	78.7	70	21.3	
	14	43	75.4	14	24.6	
Grade						
	one	5308	51.2	5061	48.8	0.00
	two	4780	45.3	5780	54.7	
	three	4911	45.1	5987	54.9	
	four	5614	49.0	5849	51.0	
	five	7276	60.6	4726	39.4	
	six	9564	75.5	3100	24.5	
Body mass index categories						
	Underweight or health weight	29604	53.1	26197	46.9	0.00
	overweight	6148	63.6	3517	36.4	
	obesity	1701	68.3	789	31.7	

[#]*P* for linear-by-linear association.

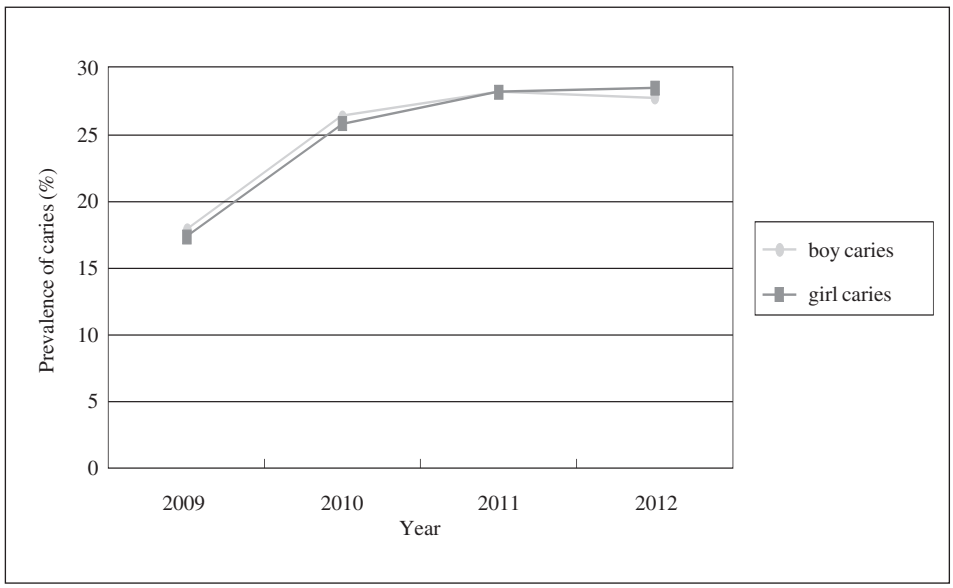

Fig. 1.—The prevalence of caries for children by year.

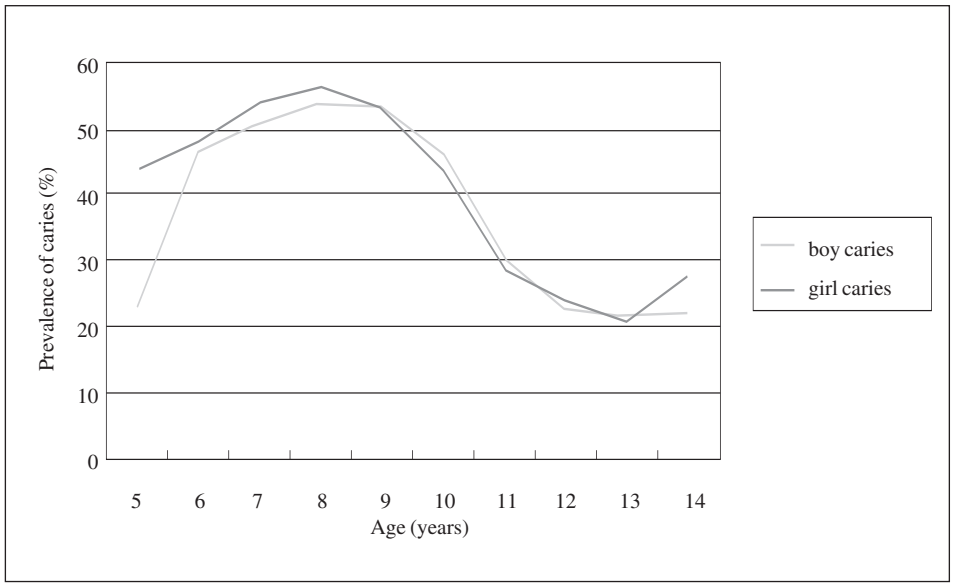

Fig. 2.—The prevalence of caries for children by age.

Table III
The results of association between year, grade, and body mass index categories and dependent variable dental caries

Variable		*Unadjusted OR (95% CI)*		*P*	*Adjusted OR (95%CI)*[#]		*P*
Year	2009	0.440	(0.420,0.460)	0.000	0.446	(0.426,0.466)	0.000
	2010	0.871	(0.834,0.910)	0.000	0.893	(0.855,0.933)	0.000
	2011	0.996	(0.954,1.041)	0.873	1.000	(0.958,1.045)	0.992
	2012	1			1		
Grade	one	2.948	(2.785,3.120)	0.000	1.979	(1.707,2.295)	0.000
	two	3.823	(3.613,4.046)	0.000	2.688	(2.377,3.041)	0.000
	three	3.927	(3.712,4.154)	0.000	2.914	(2.639,3.218)	0.000
	four	3.310	(3.132,3.499)	0.000	2.705	(2.503,2.924)	0.000
	five	2.022	(1.913,2.137)	0.000	1.829	(1.720,1.945)	0.000
	six	1			1		
Body mass index categories	Obesity	1.908	(1.750,2.079)	0.000	2.092	(1.917,2.184)	0.000
	Overweight	1.547	(1.479,1.618)	0.000	1.515	(1.448,1.586)	0.000
	Underweight or health weight	1			1		

[#]Adjusted for gender, age.

tributed enormously to the escalating problem in developing countries[28]. Especially, lifestyle[29] and food variety[30] may have an influence on obesity. Thus, the eating pattern among overweight or obese children my be a common risk factor in overweight children and dental caries. Lack of oral health education and less physical training to primary school children may also be linked to high obesity and dental caries prevalence.

Conclusions

Obesity may have a significant effect on caries prevalence of primary school children in Wannan area, China. The importance of obesity should not only be emphasized with respect to general diseases but also with regard to carious lesions.

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Conflict of Interest

None declared.

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Original / *Pediatría*

Association between nutritional status, C-reactive protein, adiponectin and HOMA-AD in Brazilian children

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Abstract

Introduction: **In children, the presence of obesity is a major risk factor for the occurrence of cardiovascular diseases on the adulthood.**

Objective: **To evaluate the association of anthropometry, body composition, clinical variables and biochemical profile with C-reactive protein and adiponectin levels, and insulin resistance in children in the municipality of Nova Era, Brazil.**

Methods: **Nested case-control study following a cross-sectional study. We evaluated 178 children, 57 of them classified as obese and 121 as normal-weight from a population of 1024 schoolchildren 6 to 10 years old: Blood samples were collected after 12-hour fast to obtain serum and plasma. We collected anthropometric and body composition measures, systolic and diastolic blood pressure data. Sexual maturation was assessed according to the stage of sexual development. We performed Student's t-test, Mann-Whitney U test, Pearson's correlation, Spearman's test and multiple linear regression analysis. Independent variables with $p < 0.05$ were included in the multiple regression model. Residual analysis was performed to assess model validity.**

Results: **Among obese children, C-reactive protein levels were associated with triacylglycerol levels and body fat percentage estimated by skinfold thickness ($R^2_{adjusted}$ = 27.6%, $p < 0.001$). Adiponectin was associated with HOMA-IR, HOMA-AD and body fat percentage estimated by skinfold thickness ($R^2_{adjusted}$ = 75.5%, $p < 0.001$). HOMA-AD index was associated with HOMA-IR, adiponectin, systolic blood pressure and weight ($R^2_{adjusted}$ = 90.7%, $p < 0.001$).**

Conclusion: **Significant associations were found between body composition, anthropometry, clinical variables, biochemical profile and adiponectin and C-reactive protein levels and insulin resistance in obese and normal-weight children.**

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ASOCIACIÓN ENTRE ESTADO NUTRICIONAL, PROTEÍNA C REACTIVA, ADIPONECTINA Y HOMA-AD EN NIÑOS BRASILEÑOS

Resumen

Introducción: **En niños, la obesidad es um factor de riesgo para enfermedades cardiovasculares en la edad adulta.**

Objetivos: **Asociaciar la antropometría, composición corporal, variables clínicas y bioquímicas con la proteína C reactiva (PCR), adiponectina y resistencia a la insulina en niños de Nova Era, Brasil.**

Métodos: **Estudio de casos y controles anidado en un transversal. Se evaluaron 178 niños, 57 obesos y 121 eutróficos en una población de 1.024 escolares de 6 a 10 años. Las muestras de sangre se recogieron después de 12 horas de ayuno. Recogimos las medidas antropométricas, de composición corporal y presión arterial. La madurez sexual fue evaluada de acuerdo con el desarrollo sexual. Se realizo las pruebas t de Student y U de Mann-Whitney, las correlaciones de Pearson y Spearman y el análisis de regresión lineal múltiple. Se incluyeron en el modelo de regresión, las variables independientes con $p < 0,05$. Se realizo el análisis residual para evaluar la validez del modelo.**

Resultados: **Entre los niños obesos, los niveles de PCR se asociaron con los triglicéridos y el porcentaje de grasa corporal (%GC) estimada por los pliegues cutáneos ($R^2_{ajustado}$ = 27,6%, $p < 0,001$). La adiponectina se asoció con HOMA-IR, HOMA-AD y % GC estimada por los pliegues cutáneos ($R^2_{ajustado}$ = 75,5%, $p < 0,001$). El HOMA-AD se asoció con HOMA-IR, adiponectina, presión arterial sistólica y peso ($R^2_{ajustado}$ = 90,7%, $p < 0,001$).**

Conclusiones: **Se encontraron asociaciones entre la composición corporal, antropometría, variables clínicas, perfil bioquímico, adiponectina, PCR y la resistencia a la insulina en niños obesos y eutróficos.**

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Palabras clave: *Inflamación. Niño. Resistencia a la insulina. Obesidad. Marcadores biológicos.*

Abbreviations

BF: Body Fat.
BIA: Bioelectrical Impedance Analysis.
BMI: Body Mass Index.
BP: Blood Pressure.
C INDEX: Conicity Index.
CRP: C-Reactive Protein.
DP: Standard Deviation.
HDL-C: High-Density Lipoprotein Cholesterol.
HOMA-AD: Homeostatic Model Assessment-Adiponectin.
HOMA-IR: Homeostatic Model Assessment for Insulin Resistance.
IL-1: Interleukin 1.
IL-10: Interleukin10.
IL-6: Interleukin 6.
LDL-C: Low-Density Lipoprotein Cholesterol.
MUAC: Mid-Upper Arm Circumference.
ND: Not Detected.
SBP: Systolic Blood Pressure.
SST: Subscapular Skinfold Thickness.
TBIA: Tetrapolar Bioelectrical Impedance.
TC: Total Cholesterol.
TFM: Trunk Fat Mass.
TNF-α: Tumor Necrosis Fator-alpha
TST: Triceps Skinfold Thickness.
VIF: Variance Inflation Factor.
WC: Waist Circumference.

Introduction

Obesity is a chronic multifactorial and complex disease, a low-grade chronic inflammatory state resulting from altered secretion of cytokines, chemokines and hormones[1]. Studies show that prevalence of overweight and obesity in children has increased significantly in many countries, including Brazil[2].

Importantly, excess body fat is a possible risk marker for cardiovascular disease, metabolic syndrome, insulin resistance, and dyslipidemia. It is noteworthy that atherosclerotic process arising from the combination of endothelial dysfunction and inflammation may begin with the development of fatty streaks in childhood[3].

It is essential to analyze obesity as an inflammatory state, as research proves its direct association with markers of angiogenesis and inflammation even in children and adolescents[4].

Thus, studies associate measures of adiposity and biochemical profile with cytokines that modulate the inflammatory state, such as IL-1, IL-6, IL-10, TNF-α, C-reactive protein (CRP), leptin, resistin and adiponectin even in apparently healthy individuals[5]. CRP, an acute phase protein produced primarily in hepatocytes, has been used in clinical and epidemiological studies as inflammation marker and risk factor for acute myocardial infarction, ischemic stroke, and death from various cancers and pulmonary diseases[6,7].

Even a low-grade inflammatory process is probably related to CRP levels in overweight or obese children[8].

Among adipokines, adiponectin stands out as one of the most abundant hormones secreted by adipocytes, and its expression decreases as adipose tissue increases. In addition, adiponectin levels are inversely proportional to insulin resistance, type 2 diabetes, cardiovascular diseases, hypertension, atherosclerosis and triglycerides, and directly proportional to HDL cholesterol levels[9].

Adiponectin has antiatherogenic, anti-inflammatory and insulin sensitizer properties. Thus, this hormone protects vascular endothelium against processes involved in the pathogenesis of atherosclerosis and diabetes[10]. In addition, hypoadiponectinemia may be considered an independent biomarker of metabolic syndrome and atherosclerosis even in overweight young people[11].

As nutritional status is correlated with inflammatory markers, studies indicate that weight reduction in children can decrease CRP and increase adiponectin levels[12].

Since insulin resistance plays a major role in obesity complications, it should also be investigated for being associated with central adiposity, lipid profile and blood pressure in various age groups[13].

From the assumptions mentioned above, this study evaluated associations of body composition, anthropometry, clinical and biochemical variables with adiponectin and C-reactive protein levels and insulin resistance in children aged 6 to 10 years old.

Materials and methods

Study design and subjects

In 2009 we conducted a nested case-control study following a cross-sectional study with 1024 children aged 6 to 10 years old from public municipal schools in Nova Era, state of Minas Gerais, Brazil. In the first stage of the study we found a prevalence of 2.3% underweight, 11.2% overweight and 6.4% obesity by calculating z-score of body mass index for age (BMI-for age)[14] (fig. 1).

In the second stage we selected two normal-weight children (n = 130) for each obese child (n = 65) making a total sample of 195 students.

Children with acute, chronic, degenerative diseases, changes in the gastrointestinal tract (e.g. diarrhea), weight loss in the past six months, under special diets, medication that alters metabolism or affects inflammation pathways, showing values of C-reactive protein above 10 mg/L and elite athletes were excluded from the study. Finally we included 57 obese and 121 normal-weight children in the sample.

The study followed the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the Federal University of Ouro Preto (2007/93).

Consent was written and signed in duplicate by those responsible.

Anthropometry and blood pressure

Students were instructed not to perform intense workouts before anthropometry and body composition assessment, to attend school with light clothing, not to ingest large volume of water in the 24 hours before the tests, and be fasting for at least 4 hours. All measurements were performed on the right side of the students' bodies.

Weight (Tanita® BC554 Ironman, Illinois, USA) and height (Alturexata®, Belo Horizonte, Brazil) were measured and body mass index (BMI) was calculated by dividing weight by the square of height. Circumferences were measured with a tape measure to the nearest 0.1 cm. Mid-upper arm circumference (MUAC) was measured in duplicate at the midpoint between the acromion process of the scapula and the olecranon. Waist circumference (WC) was measured in triplicate at the midpoint between the anterior superior iliac crest and the last rib, then we calculated the Conicity index (C index)[15].

$$\text{Conicity index} = \frac{\text{Waist circumference (m)}}{0.109\sqrt{\frac{\text{Weight (kg)}}{\text{Height (m)}}}}$$

We also measured triceps skinfold thickness (TST) and subscapular skinfold thickness (SST) using a Cescorf® skinfold caliper (Cescorf Equipamentos Ltda, Porto Alegre, Brazil) in triplicate and not consecutively. TST was measured at the midpoint between acromion and olecranon on the posterior arm, and SST on the 45° diagonal line formed by the skinfold, 2 cm below the inferior angle of the scapula. Trunk fat mass (TFM) was obtained with the formula TFM = SST (mm)/TST (mm)[16].

Blood pressure (BP) was measured by oscillometry and Doppler ultrasound with Omron® HEM 705 CP and Doppler DV 610. The procedure was performed three times at 2-minute intervals and after a 5-minute rest period before the first blood pressure measurement. Values were replaced by averages.

Body Composition Assessment

Body fat percentage (% BF) was assessed by bipolar bioelectrical impedance analysis (bipolar BIA) using a Tanita® BC554 scale with body fat rate 0.1% and tetrapolar bioelectrical impedance (TBIA) using the Bioscan Maltron® BF-916. We also used an equation to predict body fat percentage by summing triceps and subscapular skinfolds (Body fat from skinfold)[17].

Biochemical Assessment

After a 12-hour fast, 10 mL blood was collected from the median cubital vein into disposable tubes, then fractionated in vials either containing sodium fluoride for glucose analysis or no anticoagulant for assessing total cholesterol and its fractions.

Samples were processed using an Excelsa Baby® 206-2 centrifuge (FANEM, São Paulo, Brazil). After centrifugation, serum was aliquoted into three amber microtubes and stored at -80°C for later analysis.

Blood glucose was measured by the enzymatic-colorimetric method and insulin by chemiluminescence. Levels of triglycerides and total cholesterol (TC) were determined in an CM 200 analyzer (WIENER LAB, Rosario, Argentina) by the enzymatic colorimetric method using Triglycerides Liquicolor mono and Cholesterol Liquicolor test kits (Human do Brazil, Itabira, Brazil). High-density lipoprotein cholesterol (HDL-C) was measured by the enzymatic colorimetric direct HDL-PP method (Analisa, Gold Analisa Diagnóstica Ltda, Belo Horizonte, Brazil) and levels of Low-density lipoprotein cholesterol (LDL-C) were calculated using the Friedewald equation. Subsequently, the atherogenic index was obtained by dividing Total cholesterol by HDL-C[18].

Levels of C-reactive protein were assessed with an Immage® 800 analyzer (Beckman Coulter, Fullerton, California, USA) by nephelometry with a detection limit of 0.1 mg/dL. Adiponectin levels were measured by the sandwich ELISA method in a Human Adiponectin ELISA kit (Liconplex Kit, EZHADP-61K, Linco Research - St Charles Missouri-USA).

Subsequently, we calculated the homeostatic model assessment for insulin resistance (HOMA-IR) from the equation HOMA-IR = (fasting insulin (μUI/mL) × fasting glucose (mmol/mL)/22.5).[19] Homeostatic model assessment-adiponectin (HOMA-AD) was obtained by using the formula HOMA-AD = insulinemia (mU/L) × glicemia (mg/dL)/adiponectina (μg/mL).[20]

Pubertal development

Development stages of the children's pubic hair were analyzed, based on the stages proposed by Tanner. Students were classified as prepubertal (stage 1), pubertal (stages 2, 3 and 4) and postpubertal (stage 5).

Statistical analysis

Identification of probability distributions is relevant, as depending on the distribution that best fits the data set choices concerning which inferential procedures will be applied may vary. In this study the Anderson-Darling test was employed. This test examines whether a data sample comes from a population with specific distributions. For the present study, tests were conduc-

ted to verify whether the data came from a normally distributed population. A normal distribution was obtained for the samples, whereas for others it was not. Variables were presented as mean ± standard deviation for the samples with normal distribution and median and interquartile range for samples was not. For comparison between groups were performed T-tests and Wilcoxon-Mann-Whitney a test fitting non-parametric data. For this study an α-level of 0.05 was used across all statistical tests.

As dependent variable we consider the concentrations of CRP, adiponectin and HOMA-AD. Tests were performed Pearson correlation and Spearman, to verify the associations between each of the independent variables and the dependent. Multiple linear regression models were estimated, and the independent variables that showed p-value less than 0.05 were considered significant, which were the "biological plausibility" and "epidemiological relevance"[21].

Analyses of waste each model in order to check the validity of the assumptions of normality, homoscedasticity and independence between observations. The statistics "Cook's distance" and "Variance Inflation Factor (VIF)", were used to identify outliers and verification of possible multicollinearity of the independent variables. For statistical analyzes we used the statistical software R. 2.13.1.

Results

We evaluated a sample of 178 children, 104 females (58.4%) and 74 males (41.6%). Comparing the two groups of obese and normal-weight children, there were no statistical differences between medians of age, HDL-C, adiponectin, and systolic blood pressure (SBP Omron). However, obese children had significantly higher mean and median values of the other variables compared to normal-weight group (table I).

Table I
Demographic, anthropometric, body composition, biochemical and clinical characteristics of schoolchildren 6-10 years of city of Nova Era, Minas Gerais, Brazil, 2009

	All (n = 178)	*Normal (n = 121)*	*Obese (n = 57)*	*p-value*
Age (years)	8.0 (7.0-9.0)[b]	8.0 (7.0-9.0)[b]	8.0 (7.0-9.0)[b]	0.618
Weight (kg)	29.80 (25.40-37.30)[b]	27.7 (24.0-30.6)[b]	40.9 (36.1-48.3)[b]	**<0.001**
Height (cm)	132.2 ± 9.68[a]	130.83 ± 9.52[a]	135.98 ± 9.45[a]	**0.006**
MUAC (cm)	20.05 (18.5-23.92)[b]	19.3 (18.0-20.2)[b]	25.7 (24.05-27.65)[b]	**<0.001**
Waist circumference (cm)	60.52 (56.98-71.5)[b]	58.4 (55.7-61.0)[b]	76.5 (70.87-83.0)[b]	**<0.001**
Triceps skinfold (mm)	10.20 (7.77-17.57)[b]	8.63 (7.13-10.56)[b]	21.13 (16.23-24.11)[b]	**<0.001**
Subscapular skinfold (mm)	7.43 (5.68-16.57)[b]	6.03 (5.23-7.6)[b]	19.46 (12.83-24.86)[b]	**<0.001**
BF from skinfolds (%)	16.41 (13.02-27.46)[b]	14.22 (11.96-17.33)[b]	32.08 (27.11-36.94)[b]	**<0.001**
BF bipolar (%)	19.25 (16.67-29.77)[b]	17.61 (15.2-19.7)[b]	32.67 (30.4-35.00)[b]	**<0.001**
BF tetrapolar (%)	19.24 (15.35-26.63)[b]	16.79 (13.89-20.67)[b]	29.45 (23.80-32.24)[b]	**<0.001**
BF tetrapolar (kg)	5.47 (3.86-9.38)[b]	4.24 (3.40-5.83)[b]	12.34 (8.58-15.58)[b]	**<0.001**
BMI (kg/m^2)	16.55 (15.4-20.75)[b]	15.7 (15.1-16.6)[b]	22.4 (21.05-25.25)[b]	**<0.001**
Conicity index	1.19 (1.16-1.24)[b]	1.17 (1.14-1.20)[b]	1.26 (1.22-1.29)[b]	**<0.001**
Trunk adiposity index	0.79 (0.67-0.90)[b]	0.76 (0.65-0.84)[b]	0.92 (0.77-1.06)[b]	**<0.001**
Fasting glucose (mg/dL)	84.33 ± 7.42[a]	83.48 ± 7.45[a]	86.14 ± 7.08[a]	**0.002**
Fasting insulin (µU/mL)	5.42 (3.85-7.81)[b]	4.72 (3.25-6.42)[b]	7.61 (5.34-13.13)[b]	**<0.001**
Total cholesterol (mg/dL)	152.26 ± 28.96[a]	147.75 ± 27.08[a]	161.84 ± 30.68[a]	**0.004**
HDL cholesterol (mg/dL)	56.0 (49.0-65.0)[b]	57.0 (50.0-66.0)[b]	54.0 (48.0-64.0)[b]	0.159
LDL cholesterol (mg/dL)	78.84 ± 23.94[a]	74.82 ± 23.00[a]	87.38 ± 23.86[a]	**0.001**
Triacylglycerols (mg/dL)	69.5 (53.0-108.25)[b]	63.0 (48.5-99.0)[b]	94.0 (65.0-118.5)[b]	**<0.001**
Atherogenic index	2.69 ± 0.53[a]	2.58 ± 0.50[a]	2.94 ± 0.49[a]	**<0.001**
C-reactive protein (mg/dL)	ND (ND-0.172)[b]	ND (ND-0.051)[b]	0.148 (ND-0.449)[b]	**<0.001**
Adiponectin (µg/mL)	26.75 (18.95-38.28)[b]	26.89 (18.23- 39.66)[b]	26.30 (19.74-35.11)[b]	0.471
HOMA-IR index	1.14 (0.83-1.68)[b]	0.96 (0.69-1.32)[b]	1.64 (1.13-2.76)[b]	**<0.001**
HOMA-AD index	16.97 (9.95-29.83)[b]	14.01 (8.42-24.21)[b]	25.21 (16.37-51.0)[b]	**<0.001**
Systolic BP Dopller (mmHg)	94.84 (89.25-103.33)[b]	92.67 (87.33-98.34)[b]	103.33 (94.84-111.67)[b]	**<0.001**
Systolic BP Omron (mmHg)	102 (96.59-112.0)[b]	102.0 (96.33-107.84)[b]	104.50 (98.67-114.67)[b]	0.097
Diastolic BP Omron (mmHg)	58.00 (54.67-62.54)[b]	58.0 (53.83-60.0)[b]	62.0 (56.0-68.50)[b]	**<0.001**

a: Values presented as mean ± standard deviation. b: Values presented as median and interquartile range. T-tests and Test of Mann-Whitney U significant with p-value less than 0.05.
Abbreviations used: MUAC: Mid-upper arm circumference, BF: body fat, BMI: body mass index, HDL: high-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, HOMA-IR: homeostatic model assessment for insulin resistance, HOMA-AD: homeostatic model assessment-adiponectin. BP: blood pressure, ND: not detected.

Sexual maturation assessment based on pubic hair growth 55% of children diagnosed with obesity were prepubescent, 43.3% pubescent and 1.7% postpubescent. Regarding normal-weight children, 66.9% were classified as prepubertal and 33.1% as pubescent. No statistical differences were found between degree of sexual maturation between obese and normal-weight groups (data not shown).

We performed Pearson's correlation and Spearman's correlation tests with independent variables. CRP and adiponectin levels and HOMA-AD index are shown in table II.

Transformations were performed on dependent variables for constructing the final multiple regression model. These changes were necessary to ensure that residual assumptions were met.

Among normal-weight children, variables associated with CRP levels were blood glucose, age, arm circumference, HDL-C and weight ($R^2_{adjusted}$ = 16.1%, p < 0.001), whereas in the group of obese children associations occurred with body fat percentage estimated by skinfold thickness and triacylglycerol levels ($R^2_{adjusted}$ = 27.6%, p < 0.001) (table III).

In normal-weight children, adiponectin was associated with HOMA-AD (log) HOMA-IR and height ($R^2_{adjusted}$ = 87.4%, p < 0.001), whereas in obese children adiponectin levels were associated with HOMA-IR, HOMA-AD (log) and body fat percentage estimated by skinfold thickness ($R^2_{adjusted}$ = 75.5%, p < 0.001) (table IV).

HOMA-AD was associated with adiponectin and waist circumference ($R^2_{adjusted}$ = 55.5%, p < 0.001) in normal-weight children. Among obese children, associated independent variables were HOMA-IR, adiponectin, systolic blood pressure (Doppler) and weight ($R^2_{adjusted}$ = 90.7%, p < 0.001) (table V).

Discussion

In this study, body composition, anthropometry, biochemical and clinical profiles of normal-weight and obese children were associated with adiponectin, C-reactive protein levels and HOMA-AD.

As noted, CRP levels were associated with blood glucose levels, age, arm circumference, HDL-C, and weight in normal-weight children ($R^2_{adjusted}$ = 16.1%, p < 0.001). Among obese children, association was found with triacylglycerol levels and body fat percentage estimated by skinfold thickness ($R^2_{adjusted}$ = 27.6%, p < 0.001) thus highlighting the role of adipose tissue in subclinical inflammation.

Progressive increases in body adiposity may result in cellular hypoxia, adipocyte death by necrosis or apoptosis, and increased secretion of cytokines and proinflammatory chemokines, which favors states of insulin resistance. High levels of insulin and blood glucose increase free fatty acid levels, which are associated with high levels of triglycerides and low HDL-C levels[22].

CRP has been used in studies with different age groups as a marker of inflammatory processes. In a 2004 study with children and adolescents, Lambert et al. showed that BMI and insulin levels were the main determinants of altered CRP levels. In addition, individuals with the highest quartile of CRP levels had 1.4, 1.7, and 2.3 times higher chance of having high systolic blood pressure, high triglycerides, and low HDL-C levels compared with those with levels below the 75th percentile[23].

A study of obese and normal-weight adolescents found a positive association between CRP levels and obesity. Along with the sum of skinfolds, the z-score of BMI explained 42.1% of variation in protein levels[24].

Furthermore, another cross-sectional study showed relationship between adipose tissue and inflammation in children and adolescents. Overweight and obese individuals had lower HDL-C and higher triglycerides, CRP, and insulin levels. Thus, the authors concluded that overweight and obese adolescents had higher prevalence of cardiovascular risk factors shown by early signs of atherosclerosis[25].

In the present study, we found no statistical difference in adiponectin levels between obese and normal-weight groups. This result can also be explained by the low number of postpubertal children since this stage has significant influence on adiponectin levels, which decrease with sexual maturation[26].

However, adiponectin was associated with HOMA-AD, HOMA-IR and height in normal-weight children ($R^2_{adjusted}$ = 87.4%, p < 0.001) and HOMA-AD, HOMA-IR and body fat percentage estimated by skinfold thickness in obese children ($R^2_{adjusted}$ = 75.5%, p < 0.001).

Through intracellular signaling pathways, adiponectin promotes activation of glucose transport, fatty acid oxidation in muscles, and inhibition of liver gluconeogenesis, which decreases blood glucose levels thus reducing insulin[27]. In addition, adiponectin inhibits the expression of cell adhesion molecules, scavenger receptors, and inflammatory proteins such as TNFα, IL-6 and IL-1[28].

A cross-sectional study evaluated obese and overweight children. The authors found that HOMA-IR index, age, and HDL-C were associated with adiponectin levels[29]. When comparing obese children and adolescents, and their respective controls, Panagopoulou et al in 2008 found that gender and body fat percentage measured by tetrapolar bioimpedance were important determinants of adiponectin levels[30].

Reinehr et al. in 2004 evaluated influence of age, gender, puberty, weight loss, and adiponectin levels. The authors concluded that adiponectin levels in obese children were negatively correlated with age, body fat, and insulin resistance, and decreased at puberty. Conversely, significant weight loss increased adiponectin levels and improved insulin resistance[10].

In our study, HOMA-AD was associated with adiponectin and waist circumference among normal-weight children ($R^2_{adjusted}$ = 55.5%, p < 0.001) and with

Table II

Correlation between concentrations of C-reactive protein, adiponectin and HOMA-AD with anthropometric, body composition, biochemical, clinical and demographic in children aged 6 to 10 years of city of Nova Era, Mina Gerais, Brazil, 2009

	CRP (mg/dL)			*Adiponectin (µg/mL)*			*HOMA-AD*		
	All	*Normal*	*Obese*	*All*	*Normal*	*Obese*	*All*	*Normal*	*Obese*
	r	r	r	r	r	r	r	r	r
Age (years)	0.149	**0.207***	0.111	-0.089	-0.060	-0.137	**0.198***	**0.287***	0.186
Weight (kg)	**0.375***	0.081	**0.425***	-0.127	-0.021	**-0.391***	**0.474***	**0.345***	**0.436***
Height (cm)	0.120	0.057	0.060	-0.146	-0.540	**-0.331***	**0.244***	0.160	**0.281***
MUAC (cm)	**0.432***	0.174	**0.428***	**- 0.151***	-0.110	**-0.397***	**0.465***	**0.339***	**0.417***
Waist circumference (cm)	**0.423***	0.121	**0.469***	-0.104	-0.025	**-0.349***	**0.434***	**0.256***	**0.442***
Triceps skinfold (mm)	**0.419***	0.140	**0.422***	-0.055	-0.085	**-0.365***	**0.372***	0.118	**0.466***
Subscapular skinfold (mm)	**0.441***	**0.204***	**0.445***	-0.096	-0.004	**-0.409***	**0.410***	**0.198***	**0.510***
BF from skinfolds (%)	**0.432***	0.169	**0.483***	-0.065	0.074	**-0.393***	**0.384***	0.136	**0.508***
BF bipolar (%)	**0.380***	0.052	**0.272***	-0.066	0.024	**-0.322***	**0.379***	0.158	**0.351***
BF tetrapolar (%)	**0.387***	0.094	**0.381***	-0.042	0.083	**-0.339***	**0.373***	0.170	**0.393***
BF tetrapolar (kg)	**0.407***	0.112	**0.426***	-0.081	0.028	**-0.392***	**0.453***	**0.313***	**0.453***
BMI (kg/m^2)	**0.399***	0.069	**0.489***	-0.107	-0.050	**-0.362***	**0.428***	**0.244***	**0.468***
Conicity index	**0.362***	0.028	**0.310***	-0.040	0.077	-0.216	**0.253***	-0.049	**0.310***
Trunk adiposity index	**0.294***	0.107	0.215	-0.115	-0.077	-0.199	**0.241***	0.080	**0.270***
Fasting glucose (mg/dL)	**0.177***	**0.211***	0.092	0.031	0.006	0.156	0.036	-0.001	-0.011
Fasting insulin (µU/mL)	**0.221***	-0.011	0.241	-0.107	-0.097	-0.052	**0.779***	**0.738***	**0.770***
Total cholesterol (mg/dL)	0.006	-0.122	-0.066	-0.119	-0.109	-0.094	**0.168***	0.117	0.123
HDL cholesterol (mg/dL)	**-0.203***	**-0.180***	-0.124	-0.097	-0.158	-0.022	0.028	**0.188***	-0.172
LDL cholesterol (mg/dL)	0.076	-0.100	0.054	-0.125	-0.111	-0.157	0.108	0.091	0.075
Triacylglycerols (mg/dL)	0.127	0.111	-0.196	0.117	**0.247***	-0.157	0.140	-0.004	0.209
Atherogenic index	0.142	0.033	0.039	-0.042	0.039	-0.156	0.090	-0.056	0.123
C-reactive protein (mg/dL)	–	–	–	0.049	0.096	0.033	**0.147***	-0.049	0.141
Adiponectin (µg/mL)	0.049	0.096	0.033	–	–	–	**-0.651***	**-0.691***	**0.610***
HOMA-IR index	**0.244***	0.016	0.248	-0.112	-0.102	-0.037	**0.787***	**0.749***	**0.758***
HOMA-AD index	**0.147***	-0.049	0.141	-0.651	**-0.691***	**-0.610***	–	–	–
Systolic BP Dopller (mmHg)	**0.268***	0.031	**0.269***	0.047	**0.181***	**-0.284***	**0.157***	-0.068	-0.068
Systolic BP Omron (mmHg)	0.007	-0.040	0.162	0.062	0.139	-0.103	0.046	-0.050	-0.050
Diastolic BP Omron (mmHg)	**0.185***	0.006	0.194	-0.051	-0.038	-0.061	0.140	0.107	0.107

Abbreviations used: MUAC: Mid-upper arm circumference, BF: body fat, BMI: body mass index, HDL: high-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, CRP: C-reactive protein, HOMA-IR: homeostatic model assessment for insulin resistance, HOMA-AD: homeostatic model assessment-adiponectin. BP: blood pressure, Obese (n = 57), Normal (n = 121). * Significant correlations with p-value less than 0.05.

Table III
Multiple linear regression analysis of the association between concentrations of C-reactive protein (mg/dL) and demographic, anthropometric, body composition and biochemical in schoolchildren 6-10 years of city of Nova Era, Minas Gerais, Brazil, 2009

	Normal (n = 121)	
	β ± SE	*p-value*
Constant	-1.1652 ± 0.3616	**0.002***
Glucose (mg/dL)	0.005771 ± 0.002731	**0.037***
Age (years)	0.06287 ± 0.02192	**0.005***
MUAC (cm)	0.07001 ± 0.02164	**0.002***
HDL-c (mg/dL)	-0.004973 ± 0.001803	**0.007***
Weight (kg)	-0.027750 ± 0.008352	**0.001***
	Obese (n = 57)	
	β ± SE	*p-value*
Constant	-0.1416 ± 0.1355	0.301
BF from skinfolds (%)	0.018483 ± 0.003871	**< 0.001***
Triacylglycerols (mg/dL)	-0.0022375 ± 0.0009861	**0.027***

Unstandardized coefficients (β) and P values are presented. Abbreviations used: MUAC: Mid-upper arm circumference, HDL-c: high-density lipoprotein cholesterol, BF: body fat. $R^2_{adjusted}$ Normal = 16.1%; $R^2_{adjusted}$ Obese = 27.6%. *p< 0.001, α of 0.05.

Table IV
Multiple linear regression analysis of the association between concentrations of Adiponectin (μg/mL) and anthropometric, body composition and biochemical in schoolchildren 6-10 years of city of Nova Era, Minas Gerais, Brazil, 2009

	*Normal (n = 121)***	
	β ± SE	*p-value*
Constant	1.8895 ± 0.1023	**< 0.001***
HOMA-AD (log)	-0.90026 ± 0.03171	**< 0.001***
HOMA-IR	0.32761 ± 0.01962	**< 0.001***
Height (cm)	0.0017363 ± 0.0008174	**0.036***
	Obese (n = 57)	
	β ± SE	*p-value*
Constant	74.052 ± 3.885	**< 0.001***
HOMA-IR	9.0229 ± 0.9629	**< 0.001***
HOMA-AD (log)	-39.459 ± 3.645	**< 0.001***
BF from skinfolds (%)	-0.24045 ± 0.09465	**0.014***

Unstandardized coefficients (β) and P values are presented. Abbreviations used: HOMA-IR: homeostatic model assessment for insulin, HOMA-AD: homeostatic model assessment-adiponectin, BF: body fat. $R^2_{adjusted}$ Normal = 87.4 %; $R^2_{adjusted}$ Obese = 75.5%; *p< 0.05, α of 0.05 **Log adiponectin.

Table V
*Multiple linear regression analysis of the association between HOMA-AD** and anthropometric, biochemical and clinical in schoolchildren 6-10 years of city of Nova Era, Minas Gerais, Brazil, 2009*

	Normal (n = 121)	
	β ± SE	*p-value*
Constant	0.5095 ± 0.2408	**0.037***
Adiponectin (μg/mL)	-0.016429 ± 0.001497	**< 0.001***
WC (cm)	0.019297 ± 0.003984	**< 0.001***
	Obese (n = 57)	
	β ± SE	*p-value*
Constant	1.3413 ± 0.1513	**< 0.001***
HOMA-IR	0.21589 ± 0.01268	**< 0.001***
Adiponectin (μg/mL)	-0.018188 ± 0.001350	**< 0.001***
Systolic BP Dopller (mmHg)	0.003466 ± 0.001366	**0.014***
Weight (kg)	-0.004666 ± 0.001485	**0.003***

Unstandardized coefficients (β) and P values are presented. Abbreviations used: HOMA-IR: WC: Waist circumference, homeostatic model assessment for insulin, BP: blood pressure. $R^2_{adjusted}$ Normal = 55.5 %; $R^2_{adjusted}$ Obese = 90.7%; *p< 0.05, α of 0.05 **LogHOMA-AD.

HOMA-IR, adiponectin, systolic blood pressure, and weight in obese children ($R^2_{adjusted}$ = 90.7%, p < 0.001).

Few published studies have used HOMA-AD to assess insulin resistance. However, Makni et al. in 2012 found a significant correlation between HOMA-AD and waist circumference, blood glucose, HDL-C, and blood pressure in obese Tunisian children[31].

We emphasized the association of waist circumference with HOMA-AD in normal-weight children. Abdominal obesity, assessed in our study by measuring waist circumference, is associated with visceral fat accumulation, insulin resistance, elevated blood glucose, dyslipidemia, and hypertension[32].

Adiponectin levels are inversely proportional to body fat, and low levels promote lower glucose oxidation and increased activation of hormone-sensitive lipase[33].

Regarding blood pressure, adiponectin increases nitric oxide production by activating endothelial nitric oxide synthase. Moreover, low adiponectin levels reduce nitric oxide production and vasoconstriction. Also, high insulin levels stimulate endothelin, a powerful vasoconstrictor[9].

The present study has some limitations. Our sample consists of children aged 6 to 10 years from a specific municipality, which limits generalizability of results outside this population. In addition, the study design allowed associations to be determined, but not cause-effect results. Therefore, longitudinal studies are needed.

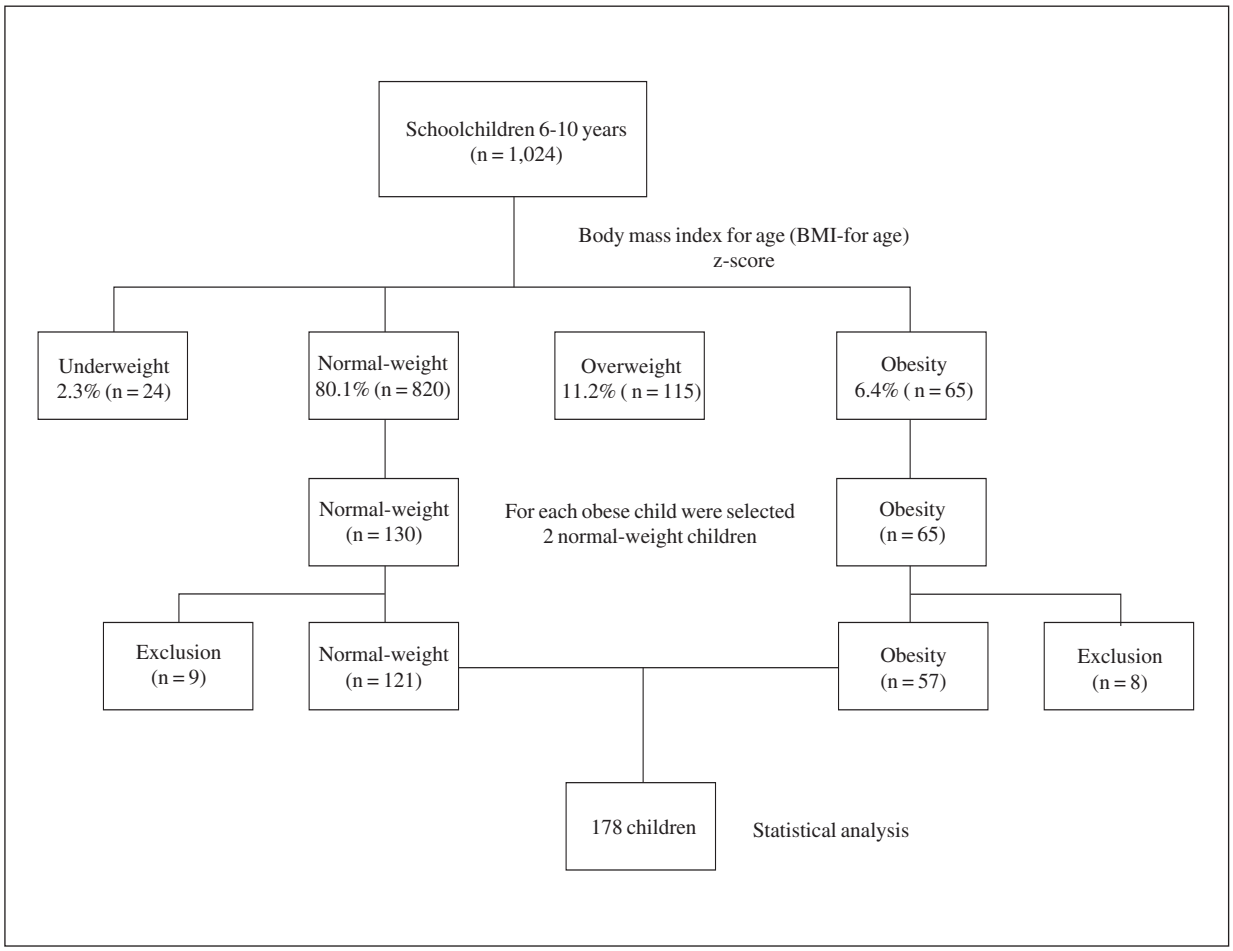

Fig. 1.—Structure of the sample selection for the study in Nova Era 2009.

We chose to use self-assessment of sexual maturation without consulting a qualified professional. However, a study by Matsudo & Matsudo has shown moderate to high concordance between the projective technique (Tanner stages) and physician assessment of sexual characteristics[34].

Finally, using BMI as a reference method for assessing child obesity at nutritional screening is also a possible limitation of this study. However, several studies have recommended this index as a good tool to predict body adiposity[35,36].

Conclusions

In conclusion, our study indicates a significant association of anthropometry, body composition, clinical and biochemical variables with adiponectin and C-reactive protein levels and insulin resistance, as assessed by HOMA-AD in obese and normal-weight children. Thus, we emphasize the importance of early identification of risk factors for cardiometabolic diseases for promoting early intervention and improved quality of life in this population.

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Common variants in genes related to lipid and energy metabolism are associated with weight loss after an intervention in overweight/obese adolescents

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Abstract

Background: **Some SNPs related to lipid and energy metabolism may be implicated not only in the development of obesity and associated comorbidities, but also in the weight loss response after a nutritional intervention.**

Objective: **In this context, the present study analyzed four SNPs located within four genes known to be associated with obesity and other obesity-related complications, and their putative role in a weight-loss intervention in overweight/obese adolescents.**

Methods: **The study population consisted of 199 overweight/obese adolescents (13-16 yr old) undergoing 10 weeks of a weight loss multidisciplinary intervention: the EVASYON programme (www.estudioevasyon.org). Adolescents were genotyped for 4 SNPs, and anthropometric measurements and biochemical markers were analyzed at the beginning and after the intervention.**

Results: **Interestingly, APOA5(rs662799) was associated with the baseline anthropometric and biochemical outcomes, whereas FTO (rs9939609) seemed to be related with the change of these values after the 10-week intervention. The other two SNPs, located in the CETP (rs1800777) and the APOA1 (rs670) genes, showed important relationships with adiposity markers. Specifically, a combined model including both SNPs turned up to explain up to 24% of BMI-SDS change after 10 weeks of the multidisciplinary intervention, which may contribute to understand the weight loss response.**

Conclusion: **Common variants in genes related to lipid and energy metabolism may influence not only biochemical outcomes but also weight loss response after a multidisciplinary intervention carried out in obese/overweight adolescents..**

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ASOCIACIÓN ENTRE VARIANTES GENÉTICAS RELACIONADAS CON EL METABOLISMO LIPÍDICO Y ENERGÉTICO Y LA PÉRDIDA DE PESO TRAS UNA INTERVENCIÓN EN ADOLESCENTES CON SOBREPESO U OBESIDAD

Resumen

Antecedentes: **Algunas variantes genéticas relacionadas con el metabolismo lipídico y energético pueden estar implicadas en la respuesta a una intervención nutricional además de estar asociadas con el desarrollo de obesidad y comorbilidades asociadas.**

Objetivo: **En este sentido, este artículo analiza cuatro polimorfismos situados en cuatro genes que han sido previamente asociados con la obesidad u otras complicaciones asociadas a la misma, así como su posible papel en la respuesta a una intervención para la pérdida de peso en adolescentes con sobrepeso u obesidad.**

Métodos: **La población en estudio está formada por 199 adolescentes con sobrepeso u obesidad (13-16 años) llevando a cabo una intervención multidisciplinar de 10 semanas para la pérdida de peso: programa EVASYON (www.estudioevasyon.org). Los adolescentes fueron genotipados para los 4 SNPs y tanto al comienzo como al final de la intervención se analizaron marcadores bioquímicos y se tomaron medidas antropométricas.**

Resultados: **Rs662799 del gen APOA5 se asoció al inicio con parámetros antropométricos y bioquímicos, mientras que el rs9939609 del gen FTO parecía estar asociado con el cambio de estas variables tras 10 semanas de intervención. Las variantes rs1800777 del gen CETP y rs670 del gen APOA1 mostraron una importante asociación con marcadores de adiposidad. Concretamente, un modelo combinado incluyendo los dos polimorfismos logró explicar hasta un 24% del cambio en el IMC-SDS tras 10 semanas de intervención.**

Conclusión: **Variantes genéticas previamente relacionadas con el metabolismo lipídico y energético, pueden repercutir no solamente en valores bioquímicos sino también en la respuesta a una intervención multidisciplinar para la pérdida de peso en adolescentes con sobrepeso u obesidad.**

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Palabras clave: *APOA1. CETP. EVASYON. FTO. APOA5.*

Introduction

Overweight and obesity during childhood and adolescence has became a growing public health problem throughout the world[1-2] to the extent that, according to the European Association for the Study of Obesity (EASO), about 16-22% of European adolescents between 14 and 17 years old are overweight or obese, with an annual increase of the prevalence of around 2% in the 1990s and 2000s[3]. These rates in childhood and adolescent obesity appear to be associated with important comorbidities in adulthood, such as type 2 diabetes, coronary artery disease or atherosclerosis, accompanied by elevated costs for public health systems[4,5]. Besides, the imbalance between an increased energy intake and a decreased energy expenditure due to inadequate dietary habits and physical activity patterns, genetic factors, as well as gene x gene and gene x environment interactions, may be also involved in obesity aetiology accounting for 40-70% of obesity phenotypes[6].

Concerning the genetic basis of obesity, several SNPs located in different genes have been found to be associated with adiposity, dietary patterns or weight loss[7,8]. In this context, several studies have shown significant relationships between adiposity, dyslipidemia, hypertension, diabetes or an increased cardiovascular risk and individual SNPs[9-18], including *APOA1, APOA5, FTO* and *CETP,* which are genes involved in the regulation of plasma lipid levels. Four SNPs that have been previously found to influence plasma lipid levels and cardiovascular disease are rs670 (*APOA1*), rs662799 (*APOA5*), rs1800777 (*CETP*) and rs9939609 (*FTO*)[19-23]. Thus, *APOA1* is a gene that encodes for Apolipoprotein A-1, the major protein component of HDL-cholesterol[24]. *APOA5* encodes for Apolipoprotein A-V, a component of several lipoprotein factors as VLDL or HDL and an important determinant of plasma triglyceride levels[25]. As for *FTO* gene, it has been widely associated with obesity[26-28]. Finally, *CETP* encodes for the plasma lipid transfer protein, a plasma protein that facilitates the transport of cholesterol esters and triglycerides between the lipoproteins[29]. However, the effects of the four SNPs after a lifestyle intervention for weight loss are in most cases still scarce. Therefore, our purpose was to evaluate the effect of these SNPs located in *FTO, APOA5, APOA1* and *CETP* genes, which have been previously associated with obesity, dyslipidemia and other obesity-related pathologies, in the metabolic response after a weight-loss intervention in overweight/obese adolescents.

Subjects and methods

The trial recruited 199 overweight or obese adolescents (39% males) undergoing a 10 week intensive lifestyle intervention, the EVASYON study (www.estudioevasyon.org), which is a lifestyle and nutritional educational weight loss program supported by a multidisciplinary team of nutritionists, physiotherapists, psychologists and paediatricians. Data from these adolescents were collected at the beginning and after 10 weeks of treatment and participants were recruited from five Spanish cities (Granada, Madrid, Pamplona, Santander and Zaragoza). The study included only 12 to 16 years old overweight or obese adolescents, according to Cole s criteria[30], which have been raised in Spain and without diagnosed disease associated with obesity or pharmacological treatment.

Written consent to participate was requested from both parents and adolescents. The study protocols were performed in accordance with the ethical standards laid down in the 1961 Declaration of Helsinki (as revised in South Korea in 2008), following the European Economic Community (EEC) Good Clinical Practice guidelines (document 111/3976/88 of July 1990) and current Spanish laws, which regulates clinical research in humans (Royal Decree 561/1993 regarding clinical trials). The study was approved by the five local ethics committees.

Multidisciplinary intervention

According to food intake questionnaires, a personalized balanced diet (30% of energy as fat, 15% as proteins and 55% as carbohydrates) and a physical activity programme was handed in to each adolescent. During the 10 week intensive program period, the adolescents attended weekly group sessions where they received nutritional and physical advice, as well as psychological support. The description of the complete EVASYON study design has been previously published elsewhere[31].

Physical Activity, Energy Intake, Metabolic and Anthropometric Data

All the adolescents were asked to fill in a series of validated questionnaires in order to determine their physical activity level and estimate their basal metabolism rates[31,32]. A semi-quantitative food-frequency questionnaire, previously validated in Spain[33], and containing 132 food items, as well as a 72-hour recall was filled in at the beginning of the follow-up. Weight and height were measured with an electronic scale (Type SECA 861, SECA, Birmingham, UK) and a telescopic height measuring instrument (Type SECA 225, SECA, Birmingham, UK) respectively. BMI was calculated as weight (in kg)/height^2 (in m^2). Then, individual BMI values were converted into standard deviation scores (SDS) using age and specific cut-points according to the Spanish children and adolescent growth references[34]. Skinfolds were measured with a skinfold calliper (Caliper Holtain; Holtain Ltd.,

Walles, UK) and waist and hip circumferences with a flexible non-stretchable measuring tape (Type SECA 200, SECA, Birmingham, UK). Pubertal developmental was determined according to Tanner stage[35]. Blood pressure was obtained using the left arm after the adolescent had rested quietly for 15 minutes using a blood pressure monitor Mod. OMRON M6 (OMROM Health Care Co., Kyoto, Japan) by following validated procedures.

Genotyping

Venous blood samples were collected at the beginning of the study. DNA was extracted from the buffy coat fraction using a commercial kit (Master PureTM; Epicentre, Madison, WI, USA) and its quality and quantity were determined with a NanoDrop ND-1000 spectrometer (NanoDrop Technologies, Wilmington, Delaware, USA). All the subjects were genotyped for 4 SNPs located within *APOA1, APOA5, FTO* and *CETP* genes (rs670, rs662799, rs1800777 and rs9939609, respectively) by using the N+S nutrigenetic test of CINFA (Olloki, Spain). Briefly, targeted regions of genomic DNA were amplified in a multiplex PCR reaction using biotinylated dCTP by using an Applied Biosystems gold plated 96-well Geneamp® PCR System 9700 (Applied Biosystems, Foster City, CA, USA). The PCR products were then hybridized onto oligonucleotide probes attached to microspheres and labeled with streptavidin-conjugated phycoerythrin (Luminex xMAP® Technology). These beads were analyzed by flow cytometry with the Luminex® 100/200TM System (Luminex Corporation, Austin, TX, USA) by following the usual protocol[36]. The presence of specific polymorphisms in the sample material was determined by correlation of the fluorescence signal intrinsic to each microsphere with the presence or absence of a corresponding phycoerythrin signal. Replicate quality control samples were included in every genotyping plate with more than 99% of concordance.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software 15.0 (SPSS INC., Chicago, IL). A χ^2 test was used to evaluate the Hardy-Weinberg equilibrium. The Kolmogorov-Smirnov test was used to determine variable distribution.

The differences in anthropometric, biochemical and energy intake variables between the SNP genotypes were tested with analysis of the covariance (ANCOVA) adjusted for confounders such as age, sex or baseline BMI-SDS (for normally distributed variables), or the Mann Whitney U test. Multivariate regression models were fitted to assess the association between the genotypes and weight loss after adjusting for confounder factors. The level of probability was set at $p < 0.05$ as statistically significant.

Results

The present study analyzed four SNPs located in *APOA1, APOA5, FTO* and *CETP* genes, previously associated with obesity, diabetes, dyslipidemia and other obesity-related pathologies. Allele frequencies of the four studied SNPs were within expected ranges for Caucasian populations and the Hardy Weinberg equilibrium was fulfilled in this population.

Anthropometric, biochemical and physical activity markers and determinants as well as dietary patterns for overweight/obese adolescents at baseline and after 10 weeks of the EVASYON programme, are shown (table I). Adiposity markers, such as weight, BMI-SDS, fat mass and waist circumference, were significantly reduced. In a similar way, the metabolic profile of the adolescents was improved after the intervention. There was a significant decrease in leptin, insulin, total cholesterol, triglycerides and C-reactive protein among other parameters. In regard to physical activity, obese adolescents not only decreased their sedentary behaviour but also improved their physical skills. Finally, after 10 weeks of intervention, the adolescents showed a significant improvement of dietary patterns decreasing total energy, total fat and SFA intake (table I).

Concerning plasma lipid levels, the rs662799 SNP of the *APOA5* gene was associated with higher levels of HDL-cholesterol at the beginning of the intervention ($B = 7.22$; $TEM = 2.80$; $p = 0.011$) but no differences were found after the intervention. Meanwhile, rs9939609 SNP of the *FTO* gene was associated with a higher decrease of HDL-cholesterol after the intervention ($B = -4.00$; $TEM = 1.39$; $p = 0.005$), as well as with a higher decrease of apolipoprotein A1 after 10 weeks of the EVASYON intervention ($B = -7.88$; $TEM = 3.10$; $p = 0.013$). On the other hand, rs670 SNP of the *APOA1* gene showed an association with apolipoprotein B levels; G allele carriers presented higher baseline apolipoprotein B plasma concentrations and, after 10 weeks of a multidisciplinary intervention, they achieved a greater decrease of the circulating levels of this apolipoprotein.

The four SNPs studied (rs670 of *APOA1* gene, rs662799 of *APOA5* gene, rs9939609 of *FTO* gene and rs1800777 of *CETP* gene), showed a strong association with adiposity indicators, both at the beginning and after 10 weeks of the EVASYON treatment (table II). In particular, SNPs in *APOA1* and *CETP* genes evidenced a significant association with weight and BMI-SDS loss after the intervention (Figure 1A and 1B). Regression analyses studying these effects are showed (table III). Concerning BMI-SDS reduction, both SNPs showed a significant effect (figs. 2A and 2B). Particularly, rs670 of *APOA1* gene seemed to

Table I
Anthropometric, biochemical, physical activity and dietary data concerning the participant adolescents (n = 199) at the beginning and after 10 weeks of intervention

	At the beginning		*After 10 weeks*		
	Mean	*TEM*	*Mean*	*TEM*	*p*
Gender (% boys)	39.2				
Age (yr)	14.5	0.08	80.2	1.1	< 0.001
Weight	83.8	1.2	80.2	1.1	< 0.001
BMI-SDS	4.5	0.2	3.8	0.1	< 0.001
Waist circunference (cm)	103.5	0.8	101.6	0.8	< 0.001
Hip circunference (cm)	90.8	2.1	88.1	2	< 0.001
Waist/Hip ratio	1.26	0.03	1.27	0.03	0.08
Waist/Height ratio	0.63	0	0.61	0	< 0.001
SBP (mm Hg)	111	1.5	106.2	1.5	<0.001
DBP (mm Hg)	74.4	0.8	70.2	0.8	< 0.001
Fat mass (kg)	37.3	0.9	32.8	0.8	<0.001
Fat mass (%)	43.7	0.6	40.1	0.5	<0.001
Σ 2 Skinfolds	57.5	0.9	51.7	0.9	< 0.001
Σ 4 Skinfolds	108.5	1.6	99.2	1.6	< 0.001
Σ 7 Skinfolds	179.7	2.2	165.2	2.4	< 0.001
Leptin (pg/ml)	5,158.6	532.3	2,999.9	304.8	< 0.001
Insulin (microU/ml)	18.6	1.9	14.2	1.1	0.005
PYY (pg/ml)	66.4	4.5	63.8	4.8	0.57
Adiponectin (pg/ml)	5,445.8	724.2	5,535.5	722.1	0.702
Glucose (mg/dL)	84.3	0.7	81.5	0.8	< 0.001
Total cholesterol (mg/dL)	155.7	2.5	143	2.5	<0.001
Tryglicerides (mg/dL)	92.9	4.1	83.3	3.9	0.002
HDL-cholesterol (mg/dL)	46.4	1	44.5	1	0.006
LDL-cholesterol (mg/dL)	90.1	2.2	82	2.2	0.009
CRP (mg/dL)	2.8	0.3	2	0.2	0.006
Sedentary activity (min/week)	543.8	6.4	521.8	6.8	0.002
Physical activity (counts)	377	13.9	408.6	13.2	0.011
Total energy (kcal)	2,188.8	68.1	1,685	56.8	< 0.001
Protein (gr)	100.9	3.6	94.7	3.3	0.047
Carbohydrates (g)	208.8	7.5	172.4	6.6	< 0.001
Lipids (g)	104.9	3.7	68	2.8	<0.001
SFA (g)	34	1.2	22.3	0.9	< 0.001
MUFA (g)	44.2	1.8	28.8	1.4	< 0.001
PUFA (g)	17	0.8	10	0.5	< 0.001

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; PYY: Peptide YY; SFA: Saturated Fatty Acids; MUFA: Monounsaturated Fatty Acids; PUFA: Polyunsaturated Fatty Acids.

explain more than a 20% of this BMI-SDS change after adjusting for age and sex. Moreover, the analysis of the combined effect of both SNPs turned out to explain more than a 24% of BMI-SDS loss after the intervention, with a decrease of 0.24 points of BMI-SDS for each minor allele present in the genotype. Similar results were obtained for weight loss. A combined regression model of *APOA1* and *CETP* was able to explain more than a 14% of weight loss after the intervention. For each minor allele present in the adolescent genotypes, they showed a decrease of -1.4 kg in body weight.

Discussion

In this study, we analyzed the contribution of four obesity-related SNPs located in the *APOA1, APOA5, FTO* and *CETP* genes to adiposity markers in a Spanish population of overweight and obese adolescents undergoing a multidisciplinary intervention programme for weight loss (EVASYON).

After three months of treatment, the adolescents achieved a significant decrease in adiposity, as well as an improvement in their physical skills and in their metabolic profile. Thus, a significant decrease in leptin, insulin, glucose and C-reactive protein levels, among other parameters, confirmed the effectiveness of the EVASYON project as an overweight/obese adolescent weight loss programme. Similar results were found in a pilot study of the EVASYON programme[37].

ApoA1 and ApoA2 are the major protein constituents of HDL-cholesterol. Concerning rs670 SNP of the *APOA1* gene, a strong association with weight and BMI-SDS loss after the 10-weeks interven-

Table II
Anthropometric data according to the SNPs rs670 (APOA1 gener) and rs1800777 (CETP gene). n = 199 obese/overweight adolescents

	APOA1 rs670			*CETP rs1800777*		
	XX (n = 102)	*XY/YY (n = 76)*	*p*	*XX (n = 172)*	*XY/YY (n = 6)*	*p*
Weight (kg)	-2.9 ± 0.3	-4.5 ± 0.3	< 0.001	-3.4 ± 0.2	-8.0 ± 2.1	< 0.001
BMI-SDS	-0.57 ± 0.04	-0.82 ± 0.05	< 0.001	-0.66 ± 0.03	-1.30 ± 0.22	0.001
Weight circumference (cm)	-1.0 ± 0.6	-3.0 ± 0.5	0.017	-1.7 ± 0.4	-5.9 ± 1.0	0.067
Waist/hip ratio	0.02 ± 0.01	0.001 ± 0.01	0.154	0.01 ± 0.01	-0.02 ± 0.01	0.279
Waist/height ratio	-0.008 ± 0.003	-0.020 ± 0.003	0.022	-0.013 ± 0.002	-0.040 ± 0.004	0.055
Body fat (Σ 7 Skinfolds)	-12.0 ± 1.7	-17.4 ± 2.1	0.044	-14.2 ± 1.4	-22.6 ± 7.5	0.227

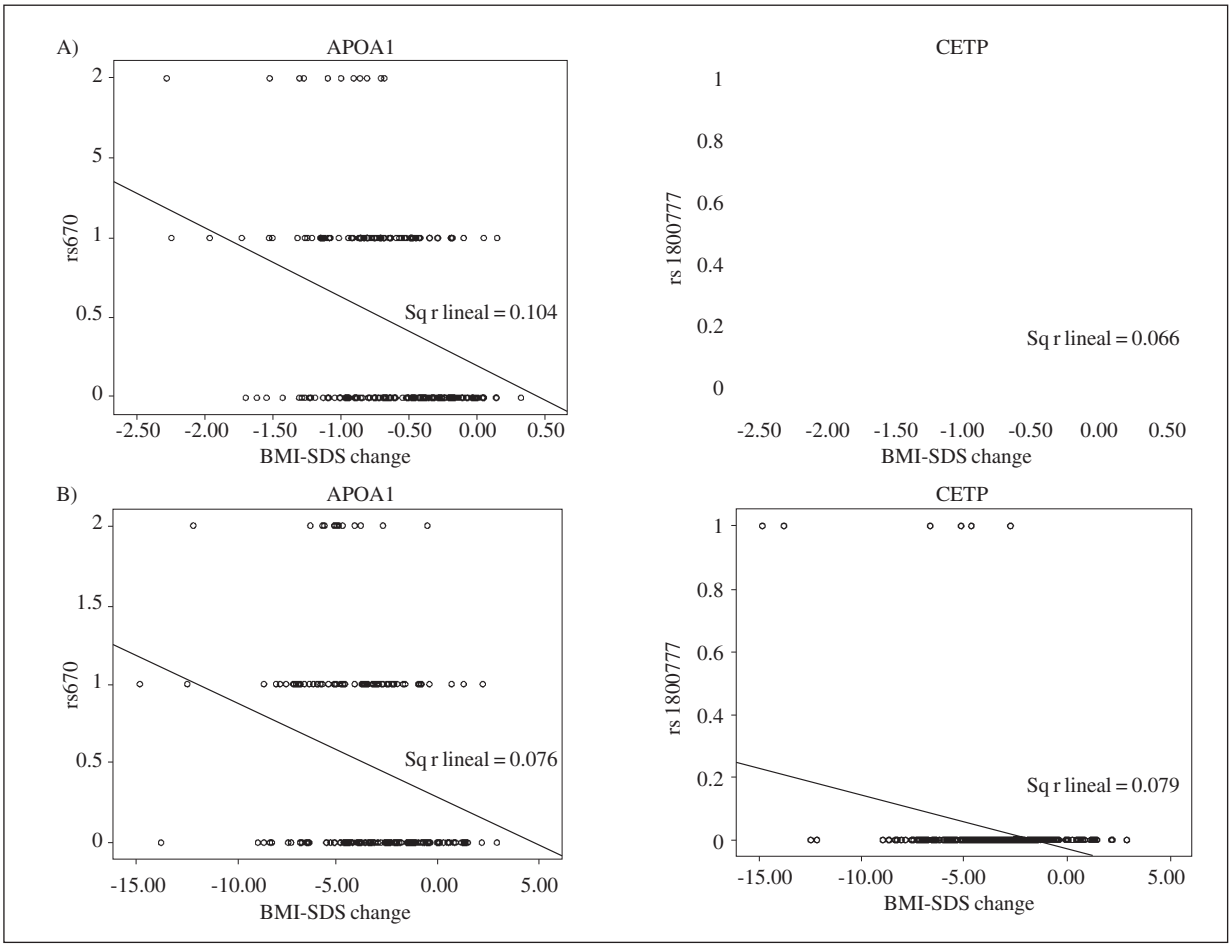

Fig. 1.—Correlations between the rs670 SNP of the APOA1 gene and the rs1800777 SNP of the CETP gene and IMC-SDS (A) and weight (B) loss.

tion was found, but there were no significant associations with plasma lipid profile before or after the intervention. In this sense, a study carried out by Xiao et al.[38] did not found a relationship between the SNP and plasma HDL-cholesterol levels or CVD in a population of controls and patients with proven CVD. On the other hand, other studies have reported an interaction between the SNP and dietary nutrients on plasma lipid levels and the metabolic syndrome. Thus, Phillips et al., found in a study of metabolic syndrome cases and controls that *APOA1* rs670 may influence metabolic syndrome, with G allele homozygotes showing an increased risk of MetS apparently explained by their increased abdominal obesity and impaired insulin sensitivity. Moreover, this association could be modulated by sex and dietary fat composition[15]. In a similar way, a recent study carried out by Rudkowska et al.[39] showed that the rs670 SNP of the *APOA1* gene inter-

Table III

Regression analyses showing the effect of two SNPs (both individually and combined): rs670 of APOA1 *and gene rs 1800777 of* CETP *gene, on weight and IMC-SDS loss after the intervention. n = 199 obese/overweight adolescents*

		IMC-SDS loss				*Weight loss*			
SNP	*Gene*	R^2	*B*	*TEM*	*p*	R^2	*B*	*TEM*	*p*
rs670	APOA1	0.213	-0.234	0.05	6.03×10^{-6}	0.116	-1.287	0.323	9.8×10^{-5}
rs1800777	CETP	0.174	-0.618	0.174	4.8×10^{-4}	0.112	-4.426	1.143	1.5×10^{-4}
	APOA1+CETP	0.241	-0.244	0.045	2.3×10^{-7}	0.147	-1.411	0.294	3.3×10^{-6}

B: effect for each minor allele present in the genotype. Linear regression analysis adjusted by age and sex.

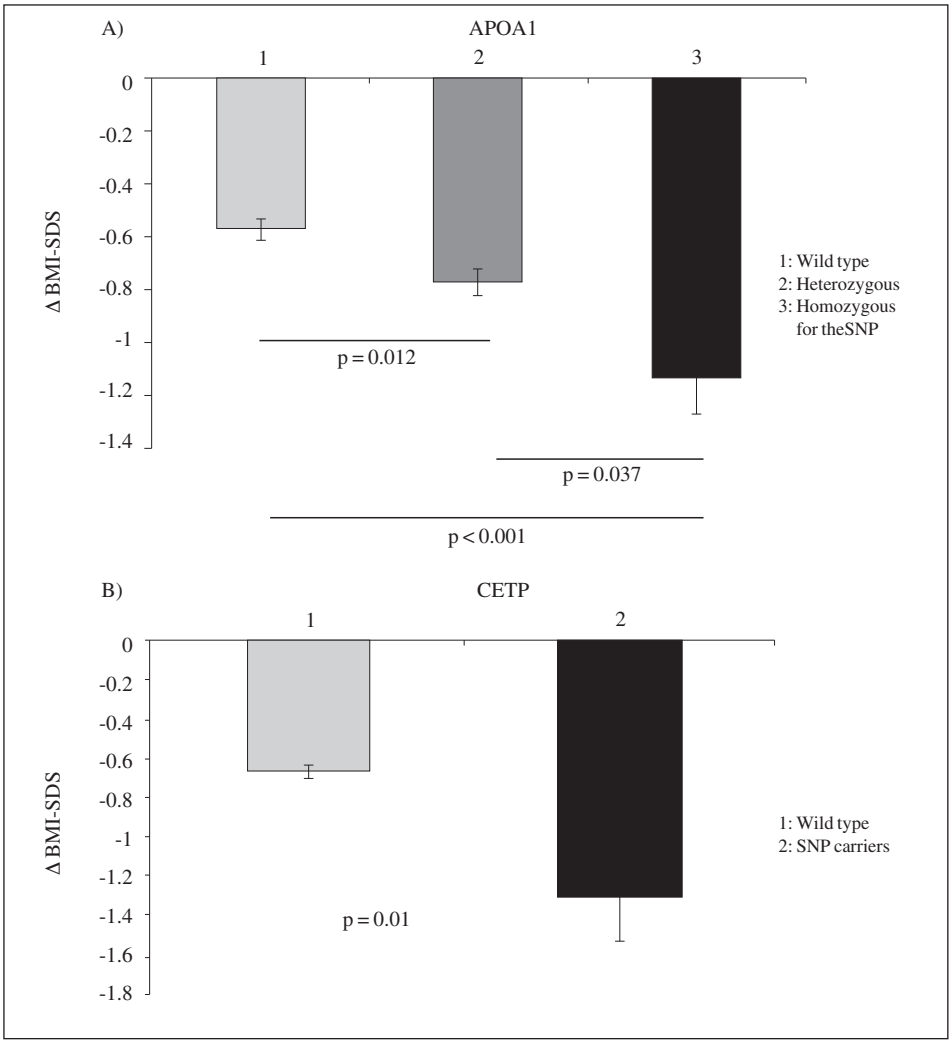

Fig. 1.—BMI-SDS change depending on rs670 SNP of APOA1 *(A) and rs1800777 SNP of* CETP *(B) genotypes.*

acted with dietary saturated fat on total cholesterol levels and with dietary total and saturated fat on LDL-cholesterol levels.

As for rs662799 SNP of *APOA5* gene, it has been largely associated with the plasma lipid profile[40-42]. In this study, this SNP has been identified as a significant predictor for plasma HDL-cholesterol concentration, with C allele carriers showing significantly higher HDL-cholesterol levels. However, these results did not in agree with works conducted in East Asian populations[41,43]. With regards to HDL-cholesterol levels after a weight loss intervention, data from literature is scarce. There are some studies analyzing the effect of the SNP on HDL-cholesterol plasma levels after fenofibrate therapy. Lai et al.[44] found that, after drug intervention, both carriers and non-carriers of the rs662799 SNP showed no significant differences in HDL-cholesterol plasma levels and similar results were described by

Feitosa et al. shortly after[45]. However, to our knowledge, no studies concerning HDL-cholesterol levels depending on this SNP have been previously conducted after a multidisciplinary weight loss intervention.

The *CETP* gene codifies for the cholesteryl ester transfer protein, which facilitates the transport of cholesteryl esters and triglycerides between the lipoproteins and, therefore, participates in plasma lipid level regulation[22]. Specifically, the rs1800777 SNP of the *CETP* gene is located within the lipid-binding region and may result in the loss of positive charge, altering binding of *CETP* to cholesteryl esters. Results concerning the analysis of this SNP are scarce. A study carried out in 2008 by Lu et al. found that, compared with the ancestral allele the rs1800777 SNP of the *CETP* gene was associated with lower plasma HDL-cholesterol levels[46]. A meta-analysis also corroborated that a dominant model of the rs1800777 SNP was accompanied by lower levels of plasma HDL-cholesterol[22]. Our results evidenced that carriers of the rs1800777 of *CETP* gene showed a strong association with adiposity indexes, both at the beginning and after 10 weeks of the EVASYON treatment, especially with weight and BMI-SDS loss after the intervention. However, to our knowledge, no studies analyzing the effects of this SNP after an intervention have been carried out to date.

Concerning the *FTO* gene, the rs9939609 SNP has been widely associated with obesity and cardiovascular disease risk[47,48], especially during childhood[49-51]. It has been demonstrated that this SNP also influences weight loss after a weight loss intervention, both in adults and children or adolescents[52]. With regards to the putative impact of rs9939609 on plasma lipid levels, our study did not shown baseline differences between the carriers and the non-carriers. On the other hand, after the 10-week intervention, A allele carriers of the SNP underwent a significant decrease of HDL-cholesterol whereas adolescents with a TT genotype presented a slightly increase in this plasma biomarker. A study carried out by Freathy et al. found that each copy of the *FTO* rs9939609 A allele was associated with lower baseline HDL cholesterol levels[53]. So far, there are no evidences in the literature on the impact that a weight loss intervention may have on HDL plasma cholesterol, in spite of the relationship between *FTO* gene and lipid metabolism. Most of the studies carried out after an intervention did not found a direct effect of rs9939609 SNP on plasma lipid levels[54,55].

One of this study's strength is the analysis of a population of adolescents. This ensures the absence of obesity-associated comorbidities or pharmacological treatments that could mask the results. Moreover, obesity treatment during adolescence should be a priority subject of study, since improvements in obesity at this stage have been demonstrated to lead to maintained changes during adulthood that could decrease the risk of developing obesity-related comorbidities, such as metabolic syndrome[56], hypertension[57] or even some types of cancer[58].

In conclusion, in this study two SNPs in the *APOA5* (rs662799) and *FTO* (rs9939609) genes were associated with HDL-cholesterol plasma levels at baseline and after the intervention, respectively. Moreover, two SNPs in the *CETP* (rs1800777) and the *APOA1* (rs670) genes showed important effects on body weight and adiposity. Specifically, a combined model including both SNPs turned up to explain up to 24% of BMI-SDS change after 10 weeks of the multidisciplinary EVASYON intervention.

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Finding new solutions in pediatric parenteral admixtures; how to improve quality and to deal with shortages

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Abstract

Introduction: **Pediatric parenteral nutrition enables normal growth even of preterm infants. Those children require, however, tailored parenteral nutrition and the creation of such can be challenging due to the risk of instability and shortages.**

Objective: **Prototypical parenteral admixtures were created using different calcium salts (organic and inorganic) and different lipid emulsions and tested for stability. 36 of parenteral admixtures containing two types of calcium salts: chloride or gluconolactobionate and different lipid emulsions (SMOFlipid® or Lipofundin MCT/LCT®) were under investigation.**

Methods: **Preliminary admixtures were prepared in two-chamber bags whereas lipid emulsions were placed separately in the second chamber. Pre-admixtures were stored for up to 21 days at +4ºC. Contents of the two chambers were combined at t = 0 or after 21 days of storage. Physical analysis of completed admixtures (visual inspection, microscopic observation, pH measurement and determination of the size distribution of oily droplets) was carried out after 21 days of the storage. Stability of lipid, commercial emulsions stored in ethylene vinyl acetate (EVA) bags for 42 days was also studied.**

Results: **Irrespectively of the time of storage of pre-admixtures and type of calcium salt and different lipid emulsions among 36 total parenteral admixtures only one showed signs of destabilization after preparation and one was unstable when stored for longer than 14 days. All other formulations were qualified to be stable during the study. All investigated commercial lipid emulsions were physically stable in EVA bags even when stored at room temperature.**

Conclusion: **The study proved that it was possible to store pre-admixture in EVA bags for 21 days at 4°C as**

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ENCONTRANDO NUEVAS SOLUCIONES EN LAS MEZCLAS PARENTERALES PEDIATRICAS; ¿CÓMO MEJORAR LA CALIDAD Y GESTIONAR EL DESABASTECIMIENTO?

Resumen

Introducción: **La nutrición parenteral pediátrica permite un crecimiento normal incluso en lactantes pretérmino. Sin embargo, estos niños requieren una nutrición parenteral a medida y la formulación de tal nutrición puede suponer un reto por el riesgo de inestabilidad y el desabastecimiento.**

Objetivo: **Se crearon mezclas parenterales prototípicas utilizando diferentes sales de calcio (orgánicas e inorgánicas) y diferentes emulsiones lipídicas probando su estabilidad. Se investigaron 36 mezclas parenterales que contenían dos tipos de sales de calcio (cloruro o gluconolactobionato) y diferentes emulsiones lipídicas (SMOFlipid® o Lipofundin MCT/LCT®).**

Métodos: **Se prepararon unas pre-mezclas en bolsas bicompartimentales mientras que las emulsiones lipídicas se colocaron de forma separada en la segunda cámara. Las pre-mezclas se almacenaron hasta 21 días a +4º C. Se combinaron los contenidos de ambas cámaras en t = 0 o después de 21 días de almacenamiento. El análisis físico de las mezclas completadas (inspección visual, observación microscópica, medición del pH y determinación de la distribución por tamaño de las gotitas lipídicas) se realizó a los 21 días de almacenamiento. También se estudió la estabilidad de las emulsiones lipídicas almacenadas en bolsas comerciales de acetato de etilen vinilo (AEV) durante 42 días.**

Resultados: **Independientemente del tiempo de almacenamiento de las pre-mezclas y el tipo de sal de calcio y de las diferentes emulsiones lipídicas de entre el total de 36 mezclas parenterales, sólo en una se vieron signos de desestabilización tras la preparación y una fue inestable cuando se almacenó más de 14 días. El resto de las formulaciones se consideraron estables durante el estudio. Todas las emulsiones lipídicas comerciales investigadas fueron estables físicamente en las bolsas de AEV, incluso cuando se almacenaron a temperatura ambiente.**

Conclusión: **El estudio mostró que es posible almacenar pre-mezclas en bolsas de AEV durante 21 días a 4° C. También se vio que el NAC (número de agregación crítica) y el CaxP (los productos de la multiplicación de**

well as that CAN (critical aggregation number) and CaxP (the products of multiplication of calcium and phosphate ions concentration) should not be used as reliable indicators of admixture physical stability. No influence of the type of calcium salts on stability of admixtures was observed.

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Key words: *Parenteral nutrition. Shortages of drugs. Pediatric parenteral mixtures. Physical stability. Two compartment bag. Calcium salts.*

las concentraciones de los iones calcio y fósforo) no deberían utilizarse como indicadores fiables de la estabilidad física de las mezclas. No se observó ninguna influencia del tipo de sal de calcio sobre la estabilidad de las mezclas.

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Palabras clave: *Nutrición parenteral. Desabastecimiento de medicamentos. Mezclas parenterales pediátricas. Estabilidad física. Bolsa bicompartimental. Sales de calcio.*

Abbreviations

CAN: Critical aggregation number.

CaxP: the products of multiplication of calcium and phosphate ions concentration.

EVA: Ethylene vinyl acetate.

Introduction

Pediatric parenteral nutrition concerns mostly premature babies with low birth weight, children with congenital malformation of digestive system, or children with insufficiently developed digestive system[1]. Parenteral intervention enables normal growth. The main recipients of parenteral nutrition therapy are preterm infants and children born before the 37th week of pregnancy. This group is frequently intolerant to enteral feeding due to anatomic and functional immaturity of the digestive tract[2].

Children and adults have different nutritional needs; therefore, compositions of admixtures must vary[3]. Parenteral intervention must be tailored: adapted to age, body weight, growth rate, metabolic parameters and co-existing diseases. Standards for prescribing and administering nutritional mixtures for children were prepared in 2005 by European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and European Society for Clinical Nutrition and Metabolism (ESPEN)[4].

Children, who require parenteral nutrition for more than three months and can be discharged may be fed parenterally at home (Home Parenteral Nutrition, HPN) to improve the quality of life and decrease health care costs. Proper parenteral admixtures and the catheter care are keys to success during such treatment. The first include the preparation of admixtures in the hospital pharmacy by the pharmacist, and allowing the improved screening for admixtures incompatibilities. The latter may be challenging as children formulas contain high concentrations of electrolytes in a low volume, which poses a higher risk of incompatibilities, such as calcium phosphate's precipitation[5]. Moreover, the concentrations of calcium and phosphate in TPN mixtures employed in neonatology often exceed the maximum values approved for use, expressed as the products of multiplication of calcium and phosphate ions concentration (CaxP < 72 mmol^2/l^2). During HPN organic salts, particularly calcium, are preferred (e.g. calcium gluconate or calcium gluconolactobionate)[6-8].

Another issue is the physicochemical behavior of oily droplets in all-in-one (AIO) admixtures. Instable lipid emulsion, i.e. formation of oily droplets larger than 5 μm, is potentially dangerous due to emboli formation[9].

Shelf life of parenteral nutrition mixtures, prepared in single-chamber bags, is limited and usually does not exceed 24 hours (including the time needed for their administration). As it is necessary for the patient to use TPN mixtures every day, collecting the mixtures from the hospital pharmacy is inconvenient for the patient's care givers, and a regular delivery expensive due to the cost of logistics. A two-chamber bag, which separates lipid emulsion from the other components, can be used to extend storage time. In this case, mixing the emulsion and the solutions, and the addition of vitamins is performed immediately before administration. It, however, reduces the patient's quality of life and increases the risk of contamination.

Problems described above become even bigger in case of drug shortage, particularly the lack of organic calcium salts or phosphate. In those cases it is extremely easy to break rule just to avoid delivery failure. Therefore the aim of the study was to determine whether it was possible to prepare physically stable pediatric admixtures after the replacement of organic calcium salts with inorganic calcium product. The other end-points were: to examine whether the change of lipid emulsion influence the physical stability and to assess the new type of ethylene vinyl acetate wrap, which was supposed to increase the quality of the PN admixture.

Materials and methods

Prototypical admixtures for the purpose of the study were prepared by pediatrics gastroenterologist of Nico-

laus Copernicus Pomeranian Trauma Center of Gdansk (Poland) using the routine approach. The main idea was to compare admixtures, in which only one ingredients changed each time. Such modifications included: replacement of organic calcium with inorganic one and replacement of Lipofundin LCT/MCT (B Braun, Melsungen, Germany) was with SMOFlipid (Fresenius Kabi, Bad Homburg, Germany).

Parenteral admixtures were prepared with a computer-controlled pump: Multicomp II (Fresenius Kabi, Uppsala, Sweden) in the parenteral nutrition department of the Hospital Pharmacy of Nicolaus Copernicus Pomeranian Trauma Center in Gdansk. Pre-admixtures were prepared in two-chamber ethylene vinyl acetate (EVA) bags (Dimix®, Diffuplast, Olgiate Olona, Italy). Lipid emulsion, Lipofundin MCT/LCT® 20% (B. Braun, Melsungen, Germany) or SMOFlipid® (Fresenius Kabi, Bad Homburg, Germany), was placed in the smaller chamber of the bag and the rest of ingredients were mixed in the other chamber: amino acid solutions – Aminoven 10% Infant® (Fresenius Kabi, Uppsala, Sweden) or Primene® 10% (Baxter, Lessines, Belgium); Glucose 40% solution (B. Braun Melsungen, Germany); Magnesium sulfate 20% solution (Polpharma, Starogard Gdanski, Poland); Potassium chloride solution 15% (WZF Polfa, Warsaw, Poland); Sodium chloride solution 10% (Polpharma, Starogard Gdanski, Poland); Calcium Pliva® 10% - solution of calcium gluconolactobionate containing 0.23 mmol Ca^{2+}/ml (Pliva Cracow, Cracow, Poland), or Calcium chloride WZF 10% – solution of calcium chloride injection containing 0.45 mmol Ca^{2+}/ml (WZF Polfa, Warsaw, Poland); Glycophos® – Sodium glycerophosphate concentrated solution (Fresenius Kabi, Uppsala, Sweden); Peditrace® – mixture of trace elements, concentrated solution (Fresenius Kabi, Uppsala, Sweden). Multi-vitamin products: Vitalipid N Infant® lipid emulsion (Fresenius Kabi, Uppsala, Sweden) and Soluvit N® lyophilisate for solution (Fresenius Kabi, Uppsala, Sweden) were added immediately after mixing of two chambers.

Twelve admixtures were manufactured using lipid emulsion Lipofundin MCT/LCT® (composition "A") and twenty-four of TPN admixtures were created using SMOFlipid® (composition "B" was formulated with organic calcium salt and composition "C" with inorganic calcium salt). Compositions of the prepared TPN admixtures, calculated critical aggregation number (CAN) and CaxP, as well as osmolality were presented in table I. Electrolytes' content was presented in table II (sodium ions originated from both Glycophos and sodium chloride, whereas chloride ions originated from the preparations of sodium chloride, potassium chloride, and calcium chloride).

After labeling, pre-admixtures were protected from light and stored in controlled temperature at 4 ± 1°C for 21 days. Each pre-admixture was prepared twice.

Pre-admixtures were transferred to room temperature approximately 4 hours prior to the analysis. Two chambers was mixed and vitamins (Soluvit N dissolved in Vitalipid N Infant) were added afterwards. This step was carried out under non-aseptic conditions to simulate home conditions, where complete (i.e. all the components mixed together) admixtures will be prepared by the caregivers.

Physical analysis of complete TPN admixtures

Procedure for the stability test was presented in Scheme I. Physical analysis of complete admixtures was carried out immediately after preparation (t = 0) and after 24 hours of storage at room temperature under dark conditions. Pre-admixtures were combined together at t = 0 or after 21 days of storage. Complete admixtures were subjected to psysicochemical stability analysis consisting of visual inspection, microscopic observation (light microscope with camera, B1 223A Motic, Wetzlar, Germany), pH measurement (pH meter, Orion 350, Beverly, USA, with combination electrode) and determination of the size distribution of oily droplets (laser diffractometer, MasterSizer E, Malvern Instruments, Malvern, UK). Laser diffractometer method allowed determination of the median diameter ($d_{0.5}$; the diameter of 50% of oily droplets lies below the value of this parameter) and the maximum diameter of 90% of oily droplets ($d_{0.9}$). Additionally, visual inspection and pH measurements of the aqueous phase of the pre-admixtures were performed.

Examination of the stability of submicron emulsions stored in Dimix® bags

The smaller chamber of a Dimix® bag was filled with 50 ml of one of the following lipid emulsions under aseptic conditions: ClinOleic®, SMOFlipid®, or Lipofundin MCT/LCT® (20% w/w of oily phase) and stored for 42 days. Two bags were prepared; one was kept in controlled temperature at 4 ± 1°C (in refrigerator), whereas the other at room temperature (21 ± 1ºC). Following this, physical analysis was performed: visual and microscopic observation, oily droplet size distribution, and pH measurements.

Results

CAN values, calculated with Multicomp Calculator program, were found to be in the range of 583-1103 mmol/l. Some of admixtures were characterized by CAN values that were higher than the commonly accepted maximal cut-offs (CAN ≤ 600 mmol/l). Admixtures 4A, 4B, and 4C possessed the highest CAN values (above 1000 mmol/l), whereas the smallest values of CAN (below 600 mmol/l) were found in samples 5A, 5B, and 5C.

Table I

Composition [ml] of TPN admixtures containing 20% parenteral emulsion Lipofundin LCT/MCT ("A") or SMOFlipid ("B", "C") and calcium gluconolactobionate 10% solution ("A" and "B") or calcium chloride 10 solution ("C")

Composition of admixture		*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*
Glucose 40%		78.7	96.9	95.7	96.5	94.2	94.7	95.4	95.6	134.3	134.1	138.1	138.2
Primene 10%		78.7	-	95.7	96.5	-	110.4	127.1	127.5	-	129.4	-	79.0
Aminoven Infant 10%		-	80.8	-	-	119.9	-	-	-	129.5	-	78.9	-
Lipofundin LCT/MCT	A	31.3	39.1	39.1	39.0	46.8	47.0	54.0	54.4	54.0	54.0	54.4	54.0
SMOFlipid	B, C	31.3	39.1	39.1	39.0	46.8	47.0	54.0	54.4	54.0	54.0	54.4	54.0
Water for injection		138.3	4.7	37.1	2.2	103.5	57.0	17.3	1.6	6.2	1.1	53.5	44.2
Glycophos		2.2	2.3	2.2	2.9	2.2	2.8	2.2	2.9	2.2	2.8	2.2	2.8
10% NaCl		6.7	6.8	3.0	2.3	6.7	15.2	6.7	6.0	6.7	11.5	12.3	11.5
15% KCl		3.1	3.2	3.2	3.2	3.1	6.3	3.2	3.2	3.2	6.3	3.2	3.2
Peditrace		3.1	3.2	3.2	3.2	3.1	3.2	3.2	3.2	3.2	3.2	3.2	3.2
20% $MgSO_4$		0.8	0.8	0.8	1.2	0.8	1.2	0.8	1.2	0.8	0.8	0.8	1.2
Calcium Pliva 10%	A, B	10.9	11.2	11.1	14.0	10.9	13.7	11.1	13.9	11.0	13.7	11.0	13.7
Calcium chloride	C	5.5	5.6	5.6	7.1	5.5	6.9	5.6	7.0	5.5	6.9	5.5	6.9
Soluvit N		4.2	3.9	3.9	3.9	3.7	3.7	3.6	3.6	3.6	3.6	3.6	3.6
Vitalipid N Infant		4.2	3.9	3.9	3.9	3.7	3.7	3.6	3.6	3.6	3.6	3.6	3.6
Total volume	A, B	358.0	252.9	295.0	265.0	384.9	355.0	325.0	313.1	355.1	360.9	361.2	355.0
	C	356.8	251.2	293.4	262.0	383.2	351.9	323.1	309.8	353.2	357.7	359.3	351.8
CAN [mmol/l]	A, B	626.4	906.5	749.5	1073	582.6	867.7	699.7	924.0	636.3	779.3	651.9	832.5
	C	640.1	927.0	768.9	1102	594.8	888.9	716.4	949.7	646.3	798.4	662.0	853.0
CIP CaxP [$mmol^2/l^2$]	A, B	43.0	92.6	64.5	133.0	37.2	70.0	53.2	94.6	44.1	67.7	42.7	70.0
	C	44.1	95.6	66.0	138.7	37.6	72.0	54.4	97.8	44.6	69.4	43.3	72.0
osmolarity [mOsm/l]	A, B	839	1404	1160	1309	978	1163	1183	1237	1369	1399	1298	1303

Table II
Content of electrolytes in TPN admixtures [mmol/l]

Component of admixture	Na^+	K^+	Mg^{2+}	Ca^{2+} TPN A, B	Ca^{2+} TPN C	Cl^- TPN A, B	Cl^- TPN C	Phosphates	SO_4^{2-}
1	44.3	17.4	3.7	7.0	7.1	49.4	63.4	6.1	3.7
2	64.2	25.4	5.3	10.2	10.4	71.4	92.2	9.1	5.3
3	32.3	21.8	4.5	8.7	8.8	39.2	56.8	7.5	4.5
4	36.7	24.3	7.5	12.2	12.5	39.1	64.1	10.9	7.5
5	41.2	16.2	3.5	6.5	6.6	46.0	59.2	5.7	3.5
6	89.0	35.7	5.6	8.9	9.0	108.9	126.9	7.9	5.6
7	48.8	19.8	4.1	7.9	8.0	55.1	71.1	6.8	4.1
8	51.3	20.5	6.4	10.2	10.4	54.3	75.1	9.3	6.4
9	44.7	18.1	3.7	7.1	7.2	50.4	64.8	6.2	3.7
10	70.0	35.1	3.7	8.7	8.9	89.6	107.4	7.8	3.7
11	70.4	17.8	3.7	7.0	7.1	76.0	94.2	6.1	3.7
12	71.2	18.1	5.6	8.9	9.0	73.5	92.8	7.9	5.6

Parenteral (PN) admixtures were characterized by high value of CaxP, i.e. 37 to 139 $mmol^2/l^2$. For admixtures 4A, 4B, and 4C the value of CaxP was twice as high as recommended (CaxP ≤ 72 $mmol^2/l^2$). Figures 1 and 2 illustrate above issues.

Visual and microscopic observations

Barely noticeable creaming was visually observed in completed admixtures after 24 hours of storage at room temperature. This occurred in all admixtures despite

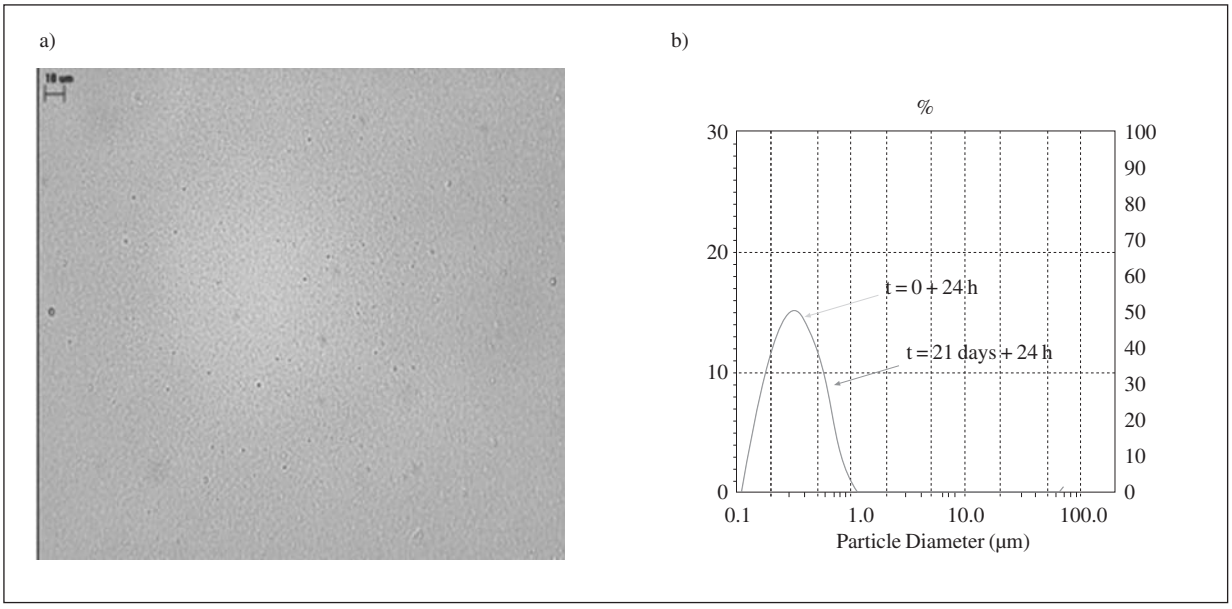


Fig. 1.—Microscopic observation at t = 0 + 24 h (a) and oily globules size analyzed at t = 0 + 24 h at t = 21 days + 24 h (b) in admixture TPN 9C.

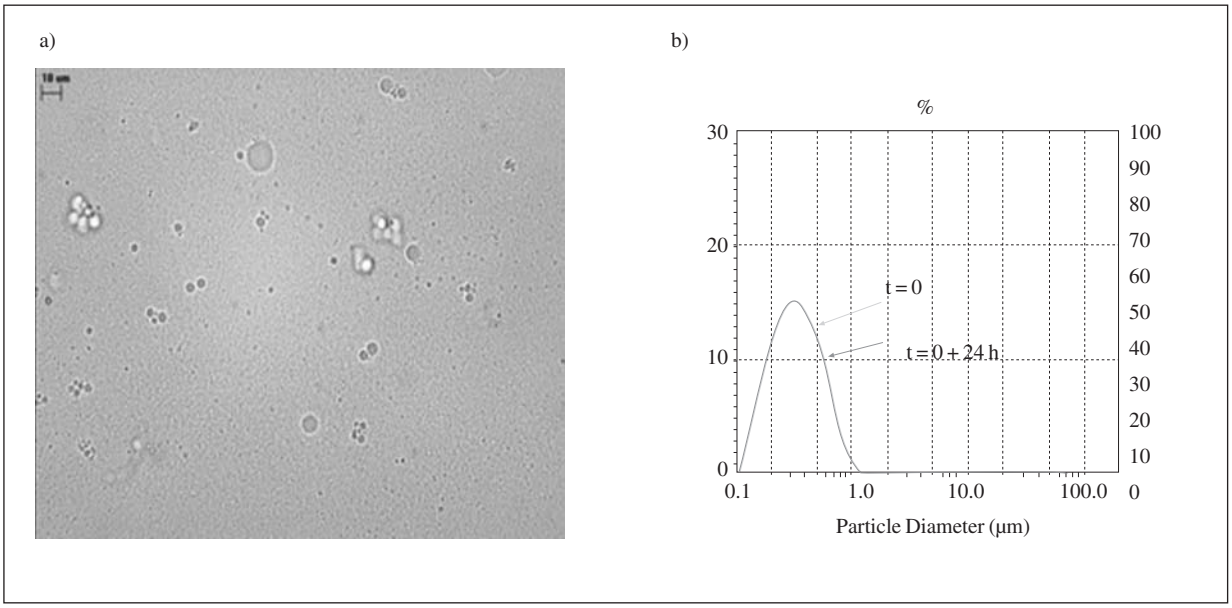


Fig. 2.—Microscopic observation of admixture TPN 1C at t = 0 + 24 h (a) and droplet size distribution at t = 0 and t = 0 + 24 h (b).

various compositions, but disappeared after short mixing.

On microscopic observation, the majority of the completed admixtures were characterized by the size of oily droplets not larger than 1 µm, considered to be safe for patients (fig. 1). Following 21 days of storage, oily droplets in TPN prepared from pre-admixture 6B had a tendency to agglomerate. However, this admixture was additionally prepared and examined after 14 days of storage at 4°C at which time no destabilization was observed. Only in one final admixture (1C), a few droplets, about 8-10 µm in size and with a tendency to agglomerate (fig. 2), were observed. As this fact was found to occur in both batches, admixture 1C was considered unstable.

Oily droplet size distribution

No oily droplets lager than 1 µm were detected in any of the admixtures (laser diffractometry method; fig. 1). The median size of oily droplets ($d_{0.5}$) in the final admixtures was determined to be 310-330 nm; 90% of oily droplets ($d_{0.9}$) were under 580-670 nm. The size of oily droplets did not change following 24-hour storage at room temperature (fig. 1). It was observed that duration of storage of pre-admixtures in two-chamber bags had no influence on droplet size distribution. (fig. 3). There were no differences between stable and unstable TPN admixtures (9C and 1C, see above) using laser diffractometry method (fig. 1 and 2).

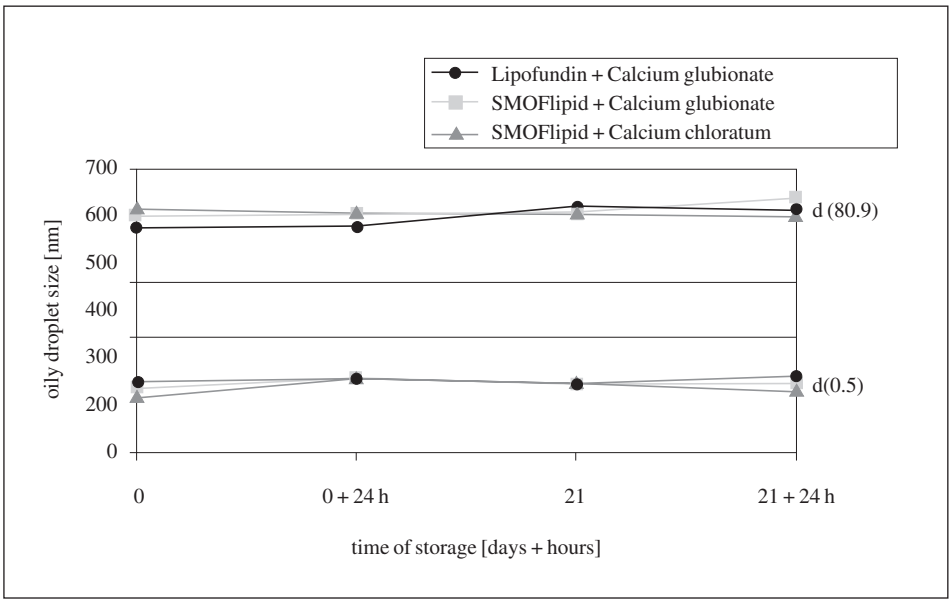


Fig. 3.—The effect of storage of TPN 1 pre-admixture for 21 days on oily deoplet size [µm].

pH measurement

The pH values of TPN admixtures were in the same narrow range as those measured before blending with lipid emulsion (5.4-6.2). These values did not change during storage (fig. 4).

Analysis of lipid emulsions in EVA bags

All lipid emulsions stored in EVA bags for 42 days at +4ºC and +21ºC were homogenous and stable. On microscopic examination, oily droplet size did not change and only a few droplets were found to be approximately 2-3 μm in size. Oily droplet size was similar for all investigated emulsions, independently of time and conditions of storage (fig. 5). The median droplet diameter ($d_{0.5}$) was in the range of 300-340 nm and the largest of oily droplets were about 540-890 nm in size. No significant changes in pH values ($p < 0.05$) of lipid emulsions stored at +4ºC and +21ºC were observed (figs. 6 and 7).

Discussion

During HPN physicians, dieticians, and nurses focus mostly on the nutritional requirements and venous

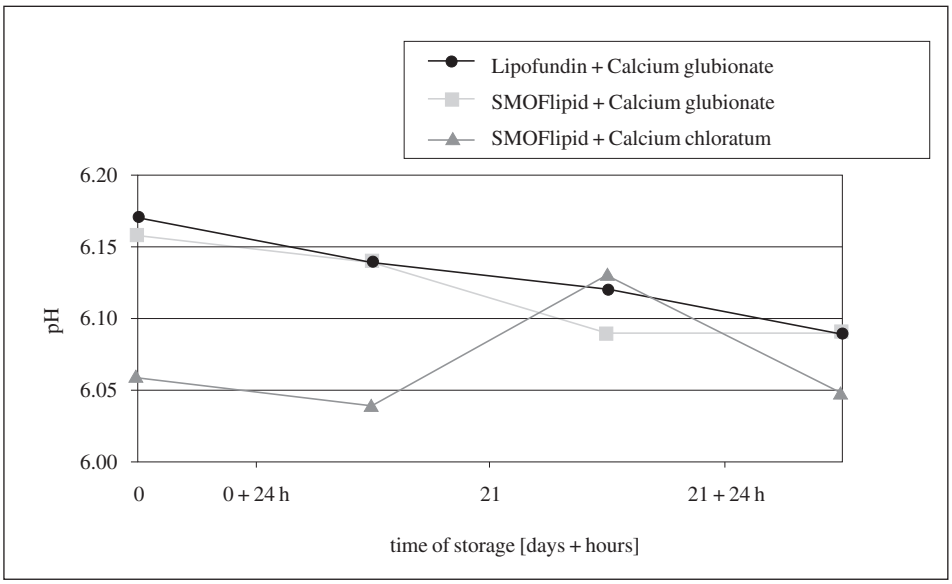


Fig. 4.—The pH values of the complete admixture (TPN 2)- the effect of various composition.

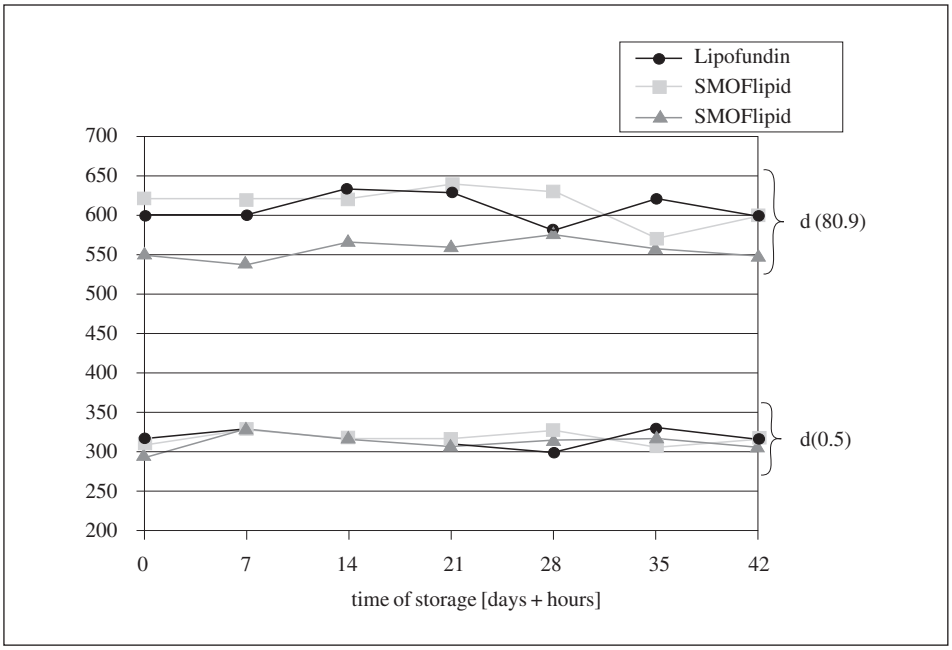


Fig. 5.—Oily droplets size distribution in lipid emulsions storage in EVA bags at room temperature during 42 days.

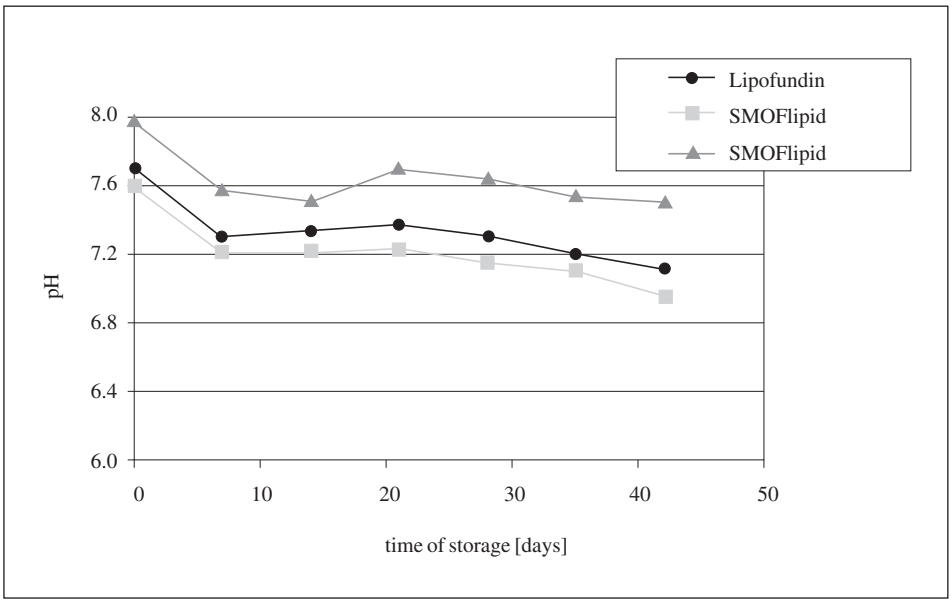


Fig. 6.—The pH values of lipid emulsions storage at 21 ± 1º C during 42 days.

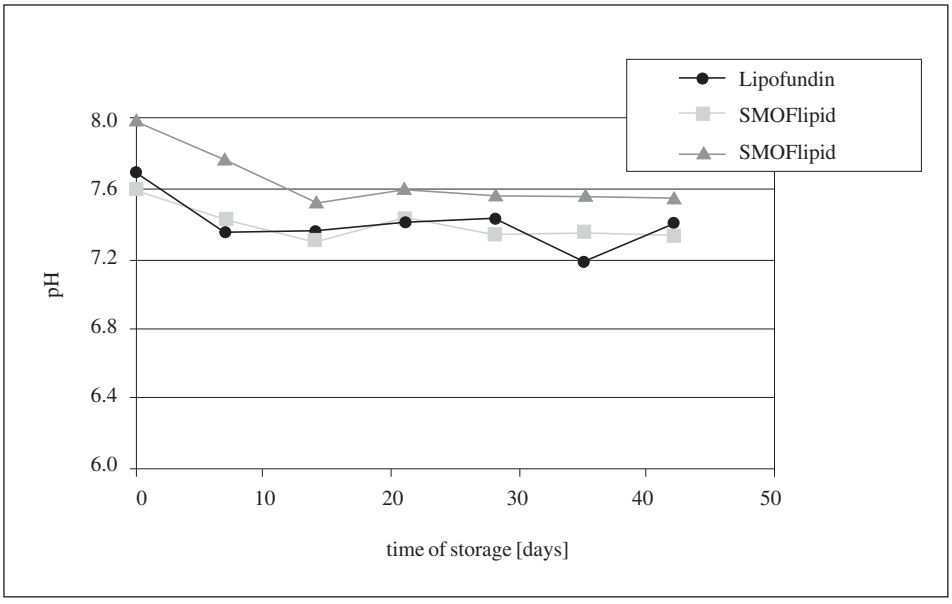


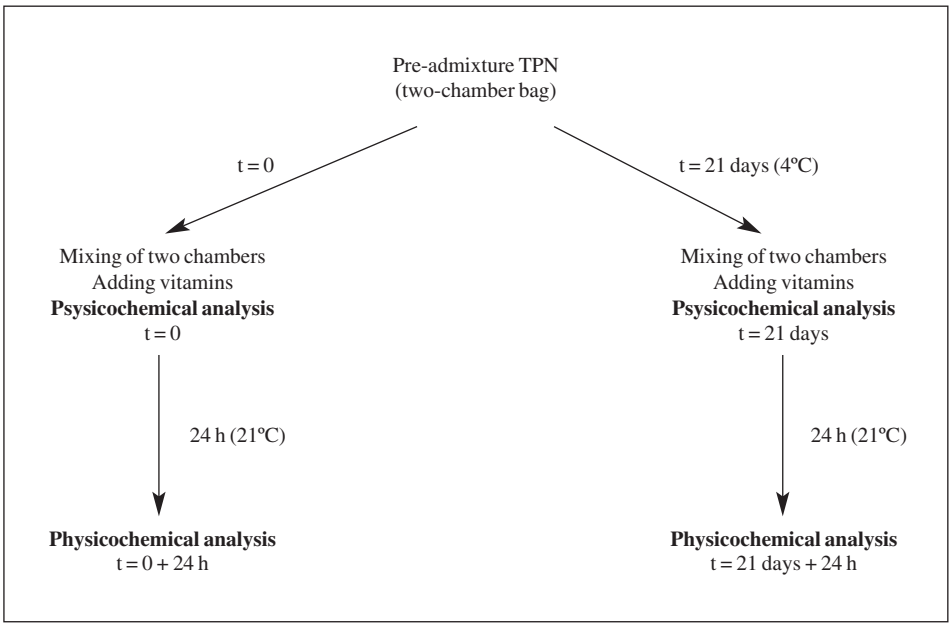
Fig. 7.—The pH values of lipid emulsions storage at 4 ± 1º C during 42 days.

access, but not the admixture itself. Hospital pharmacists, who are familiar with issues related to physical and chemical processes occurring in parenteral admixtures, should ensure patient's safety[10]. Parenteral nutrition represents a pharmaceutical challenge due to various potential incompatibilities[7].

All investigated HPN admixtures were prepared according to procedures that are routinely used at hospital pharmacies. It was interesting to notice that admixtures were characterized by nearly twice as high as physiological concentration of calcium (6.5-12.5 mmol/l Ca^{2+}) and relatively physiological concentration of magnesium ions (3.5-7.7 mmol/l Mg^{2+}). Nonstandard concentration of potassium ions (16.2-35.7 mmol/l K^{+}) resulted from the clinical needs. The values of CAN in the investigated admixtures were in the range of 583-1103 mmol/l, while CaxP was found to be between 37 and 139 $mmol^2/l^2$. Nitrogen – calorie ratio was determined to be in the range of 120-266 kcal/g N.

Barely noticeable creaming was visually observed in all completed admixtures after 24 hours of storage at room temperature; it disappeared after short mixing. Creaming was deemed to be normal and acceptable because it occurred in all admixtures despite various compositions.

The value of pH in aqueous phase of pre-admixtures and in TPN admixtures did not differ significantly and did not change during storage; therefore, all admixtures were characterized by stable pH.



Scheme 1.—Scheme of physicochemical analysis of all TPN admixtures.

On microscopic observation, all, expect one, solutions were characterized by oily droplets not larger than 1 μm in size, which are considered to be safe during intravenous administration (fig. 1). Only one completed admixture (1C) was found to be unstable due to few oily droplets, approximately 8-10 μm in size. Admixture 1C, containing calcium chloride and characterized by lower concentration of glucose, amino acids and lipids than other admixtures, was determined to be unstable on the basis of two samples. Oily droplets in admixture 6B had a tendency to agglomerate when the mixture was prepared from pre-admixtures stored for 21 days. However, no destabilization was observed in the same mixture stored for a shorter time (i.e. 14 days).

Using laser diffractometry, oily droplets larger than 1 μm in size, even in admixtures with microscopically determined large droplets or agglomerates were not observed. Laser diffractometry did not show destabilization of the completed admixtures deemed unstable (fig. 3). This result indicates that the size of oily droplets measured by laser diffractometry must always be verified by microscopic observations, especially in the case of polydispersed systems, which are submicron emulsions.

Preparing TPN admixture in a one chamber bag forces its prompt use; however, when the emulsion is separated from the other components (two-chamber bag), the duration of storage may be extended. Our study provides evidence that storing the proposed pre-admixtures in two-chamber bags for 21 days at a temperature of 4°C can be considered to be safe. Despite the high CAN (about 1000) and CaxP (90-139) values, the investigated admixtures were physically stable. This means that CAN and CaxP parameters, theoretically too high, do not limit the physical stability of TPN admixtures.

No influence of the type of calcium salts or lipid emulsion on the stability of the investigated TPN admixtures was observed. It also appeared to be safe to store lipid emulsions (Lipofundin LCT/MCT, SMOFlipid, and ClinOleic) in one of the chambers of EVA bags at +4°C as those solutions remained stable even for 42 days at a temperature of 21°C.

Conclusions

Pre-admixtures can be stored in EVA bags for 21 days at 4°C. It is possible to obtain stable TPN admixtures with high electrolyte levels. CAN and CaxP parameters may not be used as reliable indicators of admixture physical stability. No influence of the type of calcium salts on stability of admixtures was observed.

Acknowledgments

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Conflicts of Interest

The authors declare no conflict of interest.

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Original / *Síndrome metabólico*

Effect of a long-term physical exercise program and/or diet on metabolic syndrome in obese boys

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Abstract

Introduction: **There have been just a few studies examining the influence of detraining on obese boys. They conclude that any gains regress to the untrained control values during the detraining period.**

Objective: **The objective of the present study was thus to evaluate the effects of detraining (6 months) on metabolic syndrome after two types of intervention (both 31 months), one of an exercise program alone and the other of a diet-plus-exercise program, in obese boys.**

Methods: **The participants were 18 sedentary boys (8-11 years old) with a body mass index equal or greater than the 97th percentile for the age and sex (male) of the subject, without any dysfunction or metabolic problem. The participants were divided into two groups – the E group (physical exercise program) and the E+D group (physical exercise program plus a low calorie diet). Metabolic parameters were evaluated (TC, HDL, LDL, TG, glucose, insulin, Systolic Blood Pressure, and Diastolic Blood Pressure), allowing the metabolic syndrome index to be calculated.**

Results: **Changes were observed in LDL-C (effect sizes = -3.19 and -2.28) and in the LDL-C/HDL-C ratio (effect sizes = -3.02 and -1.16) in the E and E+D groups, respectively. The prevalence of metabolic syndrome and obesity was completely removed only in the E group (100% no-risk and non-obese subjects – < 90th percentile).**

Conclusions: **Detraining from a long-term exercise program (with or without diet) seems not to negatively affect the cardiovascular profile, suggesting that the program provides benefits and fosters healthy habits that can be maintained over time, preventing the development of metabolic syndrome.**

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Key words: *Obese boys. Detraining. Physical exervise. Longitudinal intervention. Metabolic syndrome.*

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EFECTOS DE UN PROGRAMA DE EJERCICIO FÍSICO Y/O DIETA A LARGO PLAZO SOBRE EL SÍNDROME METABÓLICO EN NINOS OBESOS

Resumen

Introducción: **Existen pocos estudios que examinen la influencia del desentrenamiento en niños obesos. Estos estudios concluyen que tras el desentrenamiento se regresa a los valores iniciales antes de la intervención.**

Objetivo: **El objetivo del presente estudio fue examinar los efectos del desentrenamiento (6 meses) sobre e l síndrome metabólico después de dos tipos de intervención (31 meses), una de las intervenciones consistió en un programa de ejercicio físico aislado y la otra además del ejercicio físico incluyó la dieta.**

Métodos: **Participaron 18 niños sedentarios (8-11 años) con un índice de masa corporal igual o superior al percentil 97 en función de la edad y sexo (varones) sin ninguna disfunción o problema metabólico. Los participantes fueron divididos en dos grupos: Grupo E (realizó el programa de ejercicio físico) y grupo E+D (realizó el programa de ejercicio físico más una dieta hipocalórica). Se evaluaron los parámetros metabólicos (CT, HDL-C, LDL-C, TG, glucosa, insulina y presión sistólica y diastólica) que permitieron calcular el síndrome metabólico.**

Resultados: **Se observaron cambios en el LDL-C (TE = -3.19 y -2.28) y el índice LDL-C/HDL-C (TE = -3.02 y -1.16) en el grupo E y E+D respectivamente. La prevalencia del síndrome metabólico y obesidad fue eliminada por completo en el grupo E (100% sin riesgo en niños no obesos – < percentil 90).**

Conclusiones: **El desentrenamiento tras un programa de ejercicio a largo plazo (con y sin dieta) parece no tener efectos negativos en el perfil cardiovascular, sugiriendo que el programa aporta beneficio sobre la salud (síndrome metabólico) que se mantienen en el tiempo.**

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Palabras clave: *Niños obesos. Desentrenamiento. Ejercicio físico. Intervención longitudinal. Síndrome metabólico.*

Abbreviations

BMI: Body mass index.
DBP: Diastolic Blood Pressure.
ES: Effect size.
MetS: Metabolic syndrome index.
PA: Physical activity.
SBP: Systolic Blood Pressure.

Introduction

The worldwide prevalence of childhood obesity has increased dramatically over the past three decades, and has come to be considered a pandemic of the 21st century[1]. The mechanisms responsible for the increasing prevalence of childhood obesity are not fully understood, although lifestyle changes characterized by increased caloric intake and decreased energy expenditure play a key role[2,3]. Various instruments are available to assess or estimate physical activity (PA) prior to intervention aimed at increasing it: questionnaires such as the IPAQ (International Physical Activity Questionnaire), pedometers, or accelerometers. These last have been widely used in children[4].

Governments worldwide are working to implement strategies to prevent obesity, encouraging the pursuit of healthier lifestyles[5]. Prevention, especially in young people, is universally regarded as the best method to reverse the rising global prevalence of obesity[5]. It is known that changes in lifestyle habits can reduce the risk of cardiovascular disease in adulthood[1]. In this sense, the latest Cochrane Library review suggests the need for longitudinal studies, because they would provide invaluable information on the sustainability of the beneficial effects of these interventions in overweight and obese children[5]. Many studies have examined how programs of physical exercise and/or diet plus physical exercise affect metabolic parameters in obese children. Few, however, have assessed how the subsequent detraining might influence those parameters in this obese population[6-8].

Detraining has been defined as the partial or complete loss of training-induced anatomical, physiological, and performance adaptations as a consequence of training reduction or cessation[9]. In this regard, a recent study has confirmed that there has been a marked lack of work following up the detraining after programs designed to treat pædiatric cases of obesity[8]. The few studies that exist on detraining indicate that, following short-term (3-4 months)[7,8,10] and medium-term (9 months)[6] physical exercise programs alone[8,9,11] or in combination with diet[7], there is usually a negative effect on various metabolic parameters[7,8,10]. In particular, the results show negative changes in triglycerides[6-8,10], insulin[6,10], glucose,[10] and HOMA-IR[6] following the detraining period. These studies show that, while supervised exercise can slow the progress of obesity, and improve insulin sensitivity and metabolic risk factors, once the supervised exercise has stopped, the health benefits weaken or vanish[6]. There have as yet been no studies examining the influence of long intervention programs (of at least one year) on obese boys' detraining. Long-term intervention might generate more consistent and lasting benefits[9]. Given this context, the objective of the present study was to evaluate the effects of detraining (6 months) on metabolic syndrome after an intervention (31 months –including holiday period) of an exercise program and of a diet-plus-exercise program in obese boys.

Material and methods

Study design

The study was of a quasi-experimental design, with the intervention being conducted from november 2007 to june 2011.

Subjects

A total of 105 boys were invited to participate through the collaboration of various schools in the town of Cáceres (Spain). The inclusion criteria were: (i) a body mass index (BMI) equal to or greater than the 97th percentile for the age and sex (male) of the subject, and (ii) age between 8 and 11 years as defined by Spanish population curves[11]. Subjects were excluded if they were: (i) regularly practising physical activity (PA), or following an exercise program or some other therapy (n = 65); (ii) involved in any weight control program (n = 18); (iii) were taking any medication (n = 8); (iv) had any type of dysfunction limiting their PA (n = 2); other reasons (metabolic problems, unable attend the exercise program, etc.) (n = 24). The final sample consisted of 18 Caucasian boys (10.7±0.9 years). They were divided into two groups the exercise group (E group) who followed a multi-sports exercise program (n = 8, 10.9 ± 1.0 years), and the physical exercise program plus a low calorie diet (E+D group) who followed a combination of two programs –the exercise program and a low calorie diet (n = 10, 10.5 ± 0.85 years). Several subjects ate at their school's refectory (were included in the E group), making it impossible to randomly assign membership to one or the other group. All the children's parents completed a prior informed consent form. The subjects were referred to the Servicio de Pediatría del Hospital San Pedro de Alcántara of Cáceres (Spain) for evaluation. The study was approved by the Bioethics and Biosafety Committee of the University of Extremadura (Spain) and respected the principles of the Declaration of Helsinki.

Interventions

Exercise program

The exercise program was based in a multi-sports hall, supervised by two MSc's in Sports Sciences (AGH & AMD), and under the overall supervision of two PhD's in Sports Sciences (JMS & YE). The program design was based on previous studies[6,7] and on the more than 15 years experience in implementing this type of health-related exercise program of two of the authors (JMS & YE). The program was of three weekly 90-min sessions. It comprised a warm-up (15-20 min), a main part consisting of pre-sports and multi-sports games with a moderate to vigorous intensity aerobic component (60-65 min), and a cool-down (5-10 min). A progression was established to steadily ramp the subjects up to 60-65 minutes of moderate to vigorous intensity (table I). The intensity of the session was monitored by accelerometry to ensure that all the subjects performed the activities with the same intensity. A Caltrac accelerometer (Hemokinetics, Madison, WI, USA) was used to this end, programmed to function as a PA monitor[12]. This uniaxial accelerometer contains a piezoelectric bender element which assesses the intensity of movement in the vertical plane. Its validity has been demonstrated as a method for estimating energy expenditure in children[13], and it has been used in other studies[12,14]. Although it does not record such activities as rowing or swimming, no activity of this type was used either in the exercise program or in the subjects' daily PA for the duration of the study.

Compliance was assessed as percentage of exercise sessions attended, and was found to be good, with the children attending more than 78% (81% and 77% in E and E+D group, respectively) of the total exercise sessions (230 sessions). Quantifying the intensities of 13 of the sessions/year selected at random showed no significant differences between the E and the E+D groups in any session, with a mean of 79 and 81 motion counts per session. In the measurement sessions, each child wore an accelerometer. The values taken were the mean of the exercise performed by the group. Not all the sessions were quantified since the programming and placement of the accelerometers meant taking time away from the physical exercise program. The use of accelerometers allows one to objectively quantify the subjects' PA, ensuring that the intensity was similar in the two groups. In developing treatment strategies for obesity, one requires quantitative information on PA to provide more effective goals[15].

Table I
Main exercise intervention program

Time (months)	*Exercise intensity**	*Exercise duration (min)*
0-6	Moderate	60-65
6-12	Moderate	40
	Moderate to Vigorous	20-25
12-18	Moderate	30
	Moderate to Vigorous	30-35
18-24	Moderate	15
	Moderate to Vigorous	45-50
24-31	Moderate to Vigorous	60-65

* All exercise training sessions started with 15-20 minutes warm-up exercises and ended with 5-10 minutes cool-down exercises.

Diet program

The low-calorie diet consisted of five balanced meals spread throughout the day, with an energy intake of 1,500 kcal/day. It was designed by two endocrinologists (JA & PB) of the Pædiatric Service of the San Pedro de Alcántara Hospital in Cáceres (Spain). In this sense, there have been studies that recommend diets of between 1,500 and 1,800 kcal/day in obese children who are still growing, since in this way their growth and development are not compromised. Thus the diet prescribed was of 1,500 kcal/day, similar to that of other studies[16]. The diet consisted of 57% carbohydrates, 17% proteins, and 26% fats. Foods were selected according to the subject's dietary habits. A series of general recommendations were established focused on basic healthy lifestyle eating: consume ≥ 5 servings of fruits and vegetables every day; minimize sugar-sweetened beverages such as soft drinks, sports drinks, and sugar-added fruit juices; have more meals prepared at home rather than purchasing take-away restaurant food; etc. Regular meetings were held with the children's parents for the control and monitoring of the diet.

Measurements

Each subject was evaluated for the following parameters: eating habits, daily PA, pubertal status, and metabolic parameters. The evaluations were made at the start (baseline), and at 31 (3rd-year) and 37 (detraining) months into the program.

Eating habits

Nutrition was assessed with a self-reported 3-day food record (2 weekdays and 1 weekend day in succession – Thursday, Friday, and Saturday) filled in by the parents. The weight of the food was estimated from the parents' records. A computerized database NutrIber was used to calculate the daily intake[17]. Thus the program recorded the average of the three days (kcal/day).

Daily physical activity

Daily PA was measured before the intervention, during the follow-up, and in detraining with a validated

uniaxial accelerometer (Caltrac) covering a 3-day period (thursday, friday, and saturday), except during bathing and swimming. All participants were instructed to record the amount of time spent cycling or swimming during the evaluation period. At the beginning and the end of the day, the subjects recorded the number of "motion counts" of the accelerometer, following previously published protocols[12]. The final Caltrac score was recorded, as also was the average of the three days (motion counts per day). Figure 1 shows the evolution of the physical activity carried out over the three years and the detraining period.

Pubertal status and kinanthropometry

Pubertal stage was evaluated by a trained pædiatrician according to pubic hair development using the Tanner classification criteria[18]. This evaluation was applied to ensure that changes throughout the exercise program were not due to differences in the evolution of pubertal status, which otherwise could influence the results. The kinanthropometric measurements followed the International Standards for Anthropometric Assessment (ISAK) protocol[19]: body height, body weight, and waist circumference. Height and weight were measured using standard procedures. BMI was calculated as weight divided by height squared (kg/m^2), and the obese prevalence were determined[11]. Waist circumference was measured three times with a flexible tape at the midpoint between the last rib and the iliac crest at the end of a normal expiration. Standard equipment was used: a scale-mounted stadiometer (Seca, Berlin, Germany), a weight scale (Seca, Berlin, Germany), and a non-extensible measuring tape (Holtain, Crymych, Great Britain).

Metabolic parameters

A venous blood sample was collected after at least 10 h overnight fasting. Aliquots of 5 mL were then assayed for the concentrations of plasma total cholesterol (Chod-Pad assay, automatic analyser), HDL (HDL-C plus assay, automatic analyser), triglyceridæmia (Chod-Pad assay, automatic analyser), blood glucose (glucose HK assay, automatic analyser), and insulinæmia (human insulin RIA kit, Linco Research, Missouri, USA). The brachial resting BP was measured 3 times at 2-min intervals after 10 min of rest in supine position with the back supported, using a validated automated device (OMRON RX, Matsusaka, Japan). The homeostasis model assessment of insulin resistance (HOMA-IR) was used to measure the changes in insulin sensitivity among the subjects, and was calculated using the following formula[20]: fasting plasma insulin (μU/mL) × fasting plasma glucose (in mg/dL) ÷ 22.5 × 18.182. The following atherogenic indices were also calculated: LDL/HDL ratio and TC/HDL ratio. The mean arterial pressure was then calculated using the following formula: DBP + (0.333 × (SBP-DBP)).

Metabolic Syndrome Index

The Metabolic Syndrome (MetS) index was calculated as the sum of the age-sex standardized scores of waist circumference, TG-to-HDL-C ratio, mean arterial pressure, and fasting insulin. The validity of this MetS index has been previously tested using confirmatory factor analysis[21]. Metabolic syndrome was considered to be present when a boy had a MetS index above 4.2.

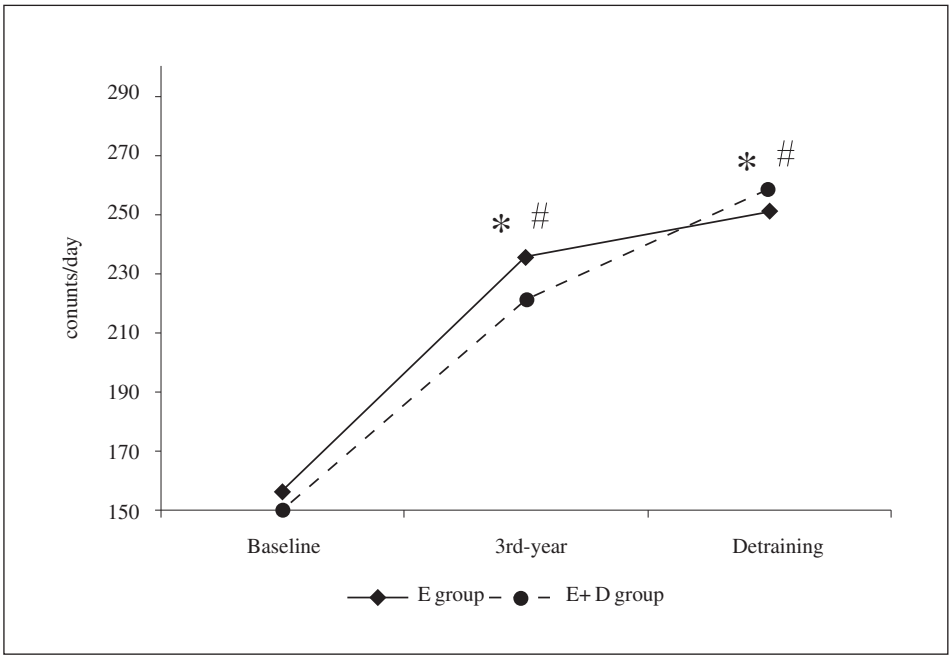

*Fig. 1.—Changes in daily PA at the baseline, third year, and detraining evaluations in obese boys; *p < 0.05 in the E group; #p < 0.05 in the E+D group.*

Detraining

At the end of the 3-year intervention programs, the participants were encouraged to join sports activities independently. Thus, 72% of the E group subjects and 75% of the E+D group subjects performed regular physical exercise during detraining, thereby increasing their daily PA compared to the baseline. Following detraining, the subjects were invited back to undertake a re-evaluation of their metabolic parameters. The same methods described previously were used in the re-evaluation.

Statistics

All the variables satisfied the tests of homoskedasticity (Levene test) and normality (Kolmogorov-Smirnov test) of their distributions. We nonetheless used a non-parametric test as is recommended in cases of small samples[22]. The basic descriptive statistics (means and standard deviations) were calculated. The Kruskal-Wallis test was applied to reveal overall inter-group differences (between the E and E+D groups), and measurements showing significant differences were further analysed for differences between individual groups by the Mann-Whitney U test (baseline *vs* detraining, and 3rd year *vs* detraining). Cohen's categories were used for the magnitudes of the effect size (ES): small if $0 \leq |d| \leq 0.2$; medium if $0.2 < |d| \leq 0.5$; and large if $|d| > 0.5$[23]. Metabolic syndrome and obese prevalence were compared using Pearson's χ^2. The level of significance for all statistical tests was set at $p \leq 0.05$. All calculations were performed using SPSS (version 16.0).

Results

The variables satisfied the tests of normality (Kolmogorov-Smirnov: $0.351 \geq z \leq 1.142$, $p > 0.05$) and homoscedasticity (Levene: $0.008 \geq F \leq 3.784$, $p > 0.05$). Also, there were no inter-group differences in eating habits, daily PA, ponderal status, or metabolic parameters at the start of the program. Table II lists the characteristics of the groups.

Intra-group differences

Table III shows the changes and treatment effects at the different evaluations (baseline [a], 3rd-year [b], and detraining [c]) in the kinanthropometric and metabolic parameters. Changes were observed neither in daily PA nor in pubertal status until the detraining (table II). This indicates that the changes brought about by the intervention cannot be attributed to these variables. However, there were changes in obese prevalence and both groups in detraining ($p < 0.05$) (fig. 2a). For the E group, there were differences between different moments of evaluation in TC (baseline *vs* detraining, $p = 0.014$, ES = -3.75; b>c, $p = 0.025$, ES = -1.40), LDL-C (baseline *vs* detraining, $p = 0.014$, ES = -3.19), LDL-C/HDL-C ratio (baseline *vs* detraining, $p = 0.014$, ES = -3.02), the TC/HDL-C ratio (baseline *vs* detraining, $p = 0.014$; ES = -0.46), and glycæmia (3rd-year *vs* detraining, $p = 0.024$, ES = 3.44). For the E+D group, there were differences between evaluations in LDL-C (baseline *vs* detraining, $p = 0.004$, ES = -2.28), the LDL-C/HDL-C ratio (baseline *vs* detraining, $p = 0.017$, ES = 1.62), insulinæmia (baseline *vs* detraining, $p = 0.034$, ES = 1.10), and HOMA-IR (baseline *vs* detraining, $p = 0.047$, ES = 1.03).

With respect to obesity, in the E group its prevalence was reduced to 0% (all boys below 90th percentile). In the E+D group, 20% of boys did not cease to be obese (fig. 2a). For its parts, regarding to metabolic syndrome, in the E group its prevalence was reduced to an index below the threshold established as representing metabolic risk in 100% of the subjects ($p = 0.001$). In the E+D group, the equivalent proportion with reduced prevalence was 50% of the subjects ($p > 0.05$) (fig. 2b).

Inter-group differences

Table IV shows the inter-group differences in metabolic parameters. There were no differences between the two groups ($p > 0.05$).

Discussion

The present study analysed the effects of detraining (six months) from a longitudinal intervention program

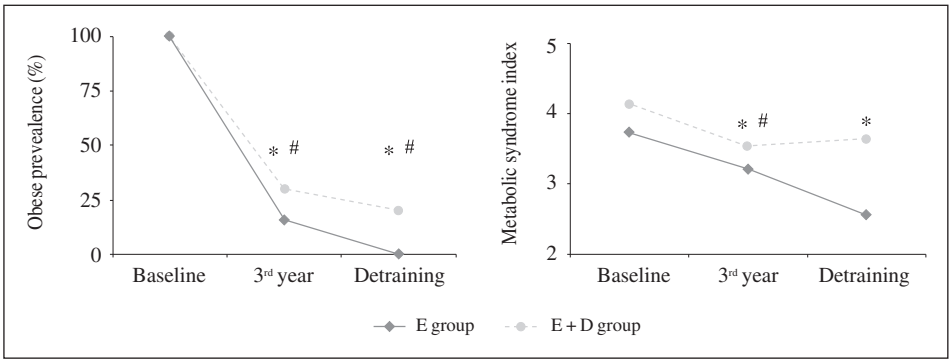

*Fig. 2.—Changes in the Metabolic Syndrome Index (a) and ponderal status (b) at the baseline, third year, and detraining evaluations in obese boys. Prevalence of metabolic syndrome and obesity: *p < 0.05 in the E group; #p < 0.05 in the E + D group.*

Table II
Eating habits, daily PA, pubertal status, kinanthropometric, ponderal status, and metabolic syndrome index at baseline, third year, and detraining evaluations in obese boys

	Baseline			*Third year*			*Detraining period*		
Variables	*E group Mean ± SD (n = 8)*	*E+D group Mean ± SD (n = 10)*	*Intergroup differences p*	*E group Mean ± SD (n = 8)*	*E+D group Mean ± SD (n = 10)*	*Intergoup differences p*	*E groups Mean ± SD (n = 8)*	*E+D group Mean ± SD (n = 10)*	*Intergroup differences p*
Eating habits									
Energy intake (kcal/day)	1952.4 ± 202.8	1928.6 ± 257.4	0.673	1752.4 ± 202.8	1528.6 ± 227.1	0.077	1833.4 ± 302.8	1928.6 ± 257.4	0.332
Daily PA									
3-day physical activity (counts/day)	156.2 ± 36.7	149.9 ± 36.3	0.914	235.3 ± 45.1	221.0 ± 67.1	0.427	250.9 ± 39.1	257.9 ± 45.2	0.923
Pubertal status									
Tanner stage (pubic hair)	1.62 ± 0.52	1.80 ± 0.63	0.937	3.00 ± 0.21	2.57 ± 0.46	0.635	3.33 ± 0.22	3.50 ± 0.14	0.783
Kinanthropometric									
Height (m)	1.49 ± 0.07	1.47 ± 0.09	0.235	1.62 ± 0.07	1.60 ± 0.13	0.653	1.66 ± 0.08	1.63 ± 0.12	0.493
Weight (kg)	62.4 ± 11.1	60.5 ± 11.8	0.815	76.6 ± 14.0	71.9 ± 18.4	0.598	76.8 ± 16.0	75.5 ± 21.0	0.903
Waist circumference (cm)	94.0 ± 9.38	92.0 ± 8.06	0.538	88.4 ± 8.45	87.5 ± 11.9	0.874	90.5 ± 16.6	94.3 ± 12.5	0.687
Ponderal status									
Obese (%) #*	100	100	1.000	15.5	30.0	0.768	0.0	20.0	0.648
Metabolic Syndrome Index									
At risk (%)*	62.5	50.0	0.894	0.0	25.0	0.231	0.0	43.0	0.052

* chi-squared test; # ≥ 97th percentile.

Table III
Mean and standard deviation of metabolic parameters at the baseline, third year, and detraining evaluations in obese boys

		Intervention time		*Detraining time*			*Differences with detraining evaluations*			
		Baseline (a)	*3-year (b)*	*6 months (c)*	*Kruskal-Wallis*		*a vs c*		*b vs c*	
	Group	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*H*	*p*				
TC (mg/dl)	E	171.9 ± 16.7	150.4 ± 23.2	127.3 ± 2.08	9.509	0.009	**0.014**	-3.75	**0.025**	-1.40
	E+D	161.7 ± 24.5	153.1 ± 24.3	142.8 ± 23.6	2.826	0.243	0.143	-0.79	0.283	-0.43
HDL-C (mg/dl)	E	53.2 ± 6.84	55.8 ± 6.91	54.7 ± 7.23	0.547	0.761	0.759	0.21	0.365	-0.16
	E+D	44.2 ± 11.6	53.6 ± 20.2	55.8 ± 21.8	1.257	0.533	0.416	0.66	0.775	0.10
LDL-C (mg/dl)	E	106.1 ± 17.8	82.6 ± 17.7	59.3 ± 10.7	8.459	0.015	**0.014**	-3.19	0.101	-1.59
	E+D	101.3 ± 16.4	81.0 ± 18.2	67.8 ± 12.8	11.742	0.003	**0.004**	-2.28	0.100	-0.84
TG (mg/dl)	E	62.9 ± 30.9	59.6 ± 16.1	67.0 ± 34.8	0.041	0.980	0.683	0.12	0.881	0.27
	E+D	81.1 ± 57.2	92.4 ± 50.6	95.5 ± 78.3	0.527	0.768	0.914	0.21	0.721	0.05
LDL-C/HDL-C	E	2.00 ± 0.29	1.48 ± 0.23	1.11 ± 0.30	11.411	0.003	**0.014**	-3.02	0.101	-1.38
	E+D	2.42 ± 0.66	1.73 ± 0.82	1.38 ± 0.62	6.835	0.033	**0.017**	-1.62	0.352	-0.48
TC/HDL-C	E	3.25 ± 0.28	2.69 ± 0.17	2.36 ± 0.33	10.953	0.004	**0.014**	-0.46	0.297	-1.26
	E+D	3.83 ± 0.97	3.16 ± 1.17	2.86 ± 1.12	4.595	0.101	0.065	-0.93	0.391	-0.26
Insulin (μU/ml)	E	12.7 ± 8.51	13.8 ± 3.70	13.6 ± 4.20	1.926	0.382	0.307	0.28	0.655	0.20
	E+D	9.73 ± 2.41	17.8 ± 6.76	19.9 ± 12.9	7.318	0.026	**0.034**	1.10	1.000	0.20
Glucose (mmol/l)	E	91.4 ± 5.95	78.8 ± 3.35	88.7 ± 2.31	10.057	0.007	0.469	-0.60	**0.024**	3.44
	E+D	87.6 ± 5.50	88.4 ± 8.06	89.7 ± 5.46	0.795	0.672	0.435	0.38	0.424	0.19
HOMA-IR	E	2.90 ± 2.17	2.68 ± 0.78	3.17 ± 0.97	1.434	0.488	0.307	0.16	0.456	0.56
	E+D	2.08 ± 0.57	3.91 ± 1.64	4.51 ± 3.28	5.969	0.050	**0.047**	1.03	1.000	0.23
SBP (mm Hg)	E	110.0 ± 7.86	110.5 ± 10.9	110.7 ± 3.05	0.054	0.973	0.838	0.11	1.000	0.02
	E+D	117.2 ± 14.4	113.0 ± 9.63	113.5 ± 10.0	0.257	0.879	0.786	-0.29	0.838	0.05
DBP (mm Hg)	E	64.1 ± 6.45	63.5 ± 6.66	63.3 ± 4.93	0.053	0.974	0.836	-0.13	0.858	-0.03
	E+D	67.9 ± 8.48	60.1 ± 4.88	67.0 ± 3.26	4.543	0.103	0.828	-0.13	0.836	0.59

Table IV
Differences between groups for the changes in metabolic parameters

	E *Mean ± SD*	*E+D* *Mean ± SD*	*Mann-Whitney U*		
			U	*p*	*ES*
ΔTC (mg/dl)					
Baseline - detraining	-46.0 ± 17.1	-22.3 ± 13.3	2.00	0.058	-1.57
Year 3 - detraining	-11.3 ± 7.57	-11.5 ± 9.63	8.00	0.796	0.02
ΔHDL-C (mg/dl)					
Baseline - detraining	3.00 ± 7.21	10.0 ± 11.6	5.50	0.361	-0.71
Year 3 - detraining	2.33 ± 6.81	2.33 ± 4.63	9.00	1.000	0.00
ΔLDL-C (mg/dl)					
Baseline - detraining	-47.3 ± 15.6	-35.8 ± 12.6	5.50	0.361	-0.82
Year 3 - detraining	-14.7 ± 4.51	-13.8 ± 11.7	7.50	0.697	-0.10
ΔTG (mg/dl)					
Baseline - detraining	-8.00 ± 16.8	16.8 ± 29.9	5.00	0.302	-0.99
Year 3 - detraining	6.00 ± 23.8	-0.17 ± 35.8	8.00	0.796	0.20
ΔLDL-C/HDL-C					
Baseline - detraining	-0.95 ± 0.25	-1.02 ± 0.39	7.50	0.697	0.21
Year 3 - detraining	-0.31 ± 0.17	-0.39 ± 0.33	9.00	1.000	0.29
ΔTC/HDL					
Baseline - detraining	-0.99 ± 0.31	-0.92 ± 0.47	6.00	0.439	-0.17
Year 3 - detraining	-0.30 ± 0.29	-0.38 ± 0.33	9.00	1.000	0.26
ΔInsulin (μU/ml)					
Baseline - detraining	3.81 ± 5.55	6.08 ± 5.41	5.00	0.456	-0.41
Year 3 - detraining	-0.57 ± 1.92	2.41 ± 7.01	7.00	0.606	-0.55
ΔGlucose (mmol/l)					
Baseline - detraining	-4.00 ± 3.60	5.17 ± 4.49	2.00	0.060	-2.22
Year 3 - detraining	8.67 ± 2.52	4.00 ± 3.03	1.50	0.051	1.66
ΔHOMA-IR					
Baseline - detraining	0.71 ± 1.34	1.44 ± 1.30	5.00	0.456	-0.82
Year 3 - detraining	0.79 ± 1.87	0.71 ± 1.34	8.00	0.796	0.05
ΔSBP					
Baseline - detraining	-0.33 ± 6.81	-1.23 ± 4.60	7.50	0.697	0.15
Year 3 - detraining	-0.11 ± 5.36	-0.23 ± 5.60	8.00	0.796	0.02
ΔDBP					
Baseline - detraining	-0.21 ± 5.81	-0.23 ± 5.60	9.00	1.000	0.00
Year 3 - detraining	-0.10 ± 5.36	0.43 ± 6.23	8.00	0.796	-0,09

based on exercise and/or diet on metabolic parameters in obese boys. To the best of our knowledge, the present work is the first of this type to study the detraining that follows a longitudinal intervention program in obese boys. The results indicated that the changes achieved in the metabolic parameters after both longitudinal interventions were maintained following the detraining, and even improved, especially in the lipid profile. Similarly, there was a reduction in the prevalence of obese and metabolic syndrome in the subjects after the intervention period, and this also was maintained after detraining in the E group. The results thus suggest that long-term exercise (with or without diet) generates lasting, healthy habits that might prevent and alleviate metabolic syndrome. However, due to the number of subjects (n = 18), the present study it can be considered only a preliminary investigation.

Intra-group differences

In the lipid profile of the obese subjects, various indicators improved after detraining in both interventions. There stand out the reductions relative to the baseline in LDL-C in the E group (ES = -3.19) and in the E+D group (ES = -2.28), and in the LDL-C/HDL-C ratio in the E group (ES = -3.02) and in the E+D group (ES = -1.62). This shows the importance of aerobic exercise[24] and combined aerobic-plus-diet[25] programs in generating benefits in LDL-C in an obese pædiatric population. In this sense, a study by Shalitin et al.[7] confirmed that even short-term exercise and exercise-plus-diet programs led to decreases in LDL-C levels that were preserved at the end of 1 year, despite weight gain. The indication is thus that both short- and long-term exercise interventions may provide benefits in the prevention of part of obesity-related morbidity. The only parameter that was reduced from the three-year period to detraining was TC, particularly marked in the E group (ES = -1.40). Contrary to these findings, other studies have reported increases in TG after physical exercise and/or diet programs (detraining) with TC remaining unchanged (3-10 months)[6,7]. The levels of the other lipid parameters remained close to the initial values, especially in the case of the combined program of diet plus physical exercise, as has also been reported in other studies in the literature[7]. These results demonstrate that short/medium-term interventions are insufficiently effective at maintaining beneficial effects in the long term (after termination of the programs). Therefore, intervention programs for obese boys probably require either ongoing support or longer durations for the benefits to be maintained over time. Such an approach would preserve the beneficial effect of the program and prevent the morbidity associated with obesity by fostering the generation of healthy habits in later life.

Regarding the insulin resistance markers, the detraining appeared to have a negative influence on these in both interventions. Thus, there was a significant increase in glucose levels from the three-year period to detraining with a large ES (ES = 3.44). Confirming this result, another study observed an increase in this parameter after three months detraining (ES = 0.23), and especially emphasized the importance of exercise in controlling this parameter[6]. Similarly, after the combined (E+D group) intervention there was an increase in insulin in the detraining (ES = 1.10), and consequently also in HOMA-IR (ES = 1.03). This could reflect the importance of diet in the control of these parameters, as indicated by the results of previous studies[7].

Finally, with respect to the metabolic syndrome, in the E group the prevalence in obese children decreased ($\chi^2 = 6.571$, $p < 0.001$). In this same line, another study has documented dramatic reductions in the prevalence of metabolic syndrome in obese children in an 8-week period of exercise training targeted at the fat (max) zone[26]. There have been no other studies that analyse detraining and metabolic syndrome, and the present study has shown that, after detraining, no subject surpassed the index established as representing metabolic risk (≥ 4.2)[21]. It therefore seems that physical exercise is consolidated as a key factor in the prevention of cardiovascular disease risk in obese children, and that this is so even after controlled termination of the program[27,28]. However, it is likely that boys included in the study were those with a high level of motivation, so they might continue following the program (exercise and diet) after finishing the intervention.

Inter-group differences

No differences were observed in any of the parameters evaluated after the detraining period, suggesting that the two interventions generate similar long-term changes in these parameters. These results appear to indicate that the long-term benefits of the two interventions are equivalent, as also they were during the detraining. Thus, it would seem that in the long term there is no requirement for any comprehensive medical control (dietician and/or endocrinologist) of the obese subject's diet, although healthy habits together with moderate-vigorous physical exercise could generate benefits in this regard.

Conclusions

In conclusion, the detraining from a long-term program of physical exercise alone or in combination with a low calorie diet seemed to have no negative effects on metabolic parameters (parameters not worsen), thus helping resolve metabolic syndrome or prevent its emergence. Indeed, the subjects in the E group classified with metabolic syndrome ceased to be so after the physical exercise program, and this status

was maintained after detraining. These results suggest that long-term programs of this kind promote benefits and healthy habits in obese boys that are maintained over time. In particular, such non-invasive intervention could be applied for a variety of motives, for instance, when subject are unwilling or unable to undergo clinical treatment or intervention. The results also highlight the importance of exercise itself in maintaining the benefits that have been obtained in the metabolic parameters of obese boys.

Limitations

A number of limitations of this study need to be borne in mind. First, there was a lack of initial randomization of the groups. Nonetheless, the homogeneity of the groups was supported by the absence of initial differences in any of the variables (table I). Second, while the absence of a no-intervention control group was clearly far from ideal, it was unavoidable since it proved impossible to find a group of obese children who were not partaking in any type of intervention to improve their condition. Third, the number of subjects in the study was small (n = 18), although the study's longitudinal character could make this limitation of only relative importance. And fourth, we did not record the type of activity or sport performed by each subject during the course of detraining. Such information could have been useful in interpreting the results.

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Nutrición Hospitalaria

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Original / *Nutrición enteral*

Evaluación organoléptica de suplementos de nutrición enteral

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Resumen

Introducción y objetivos: **La nutrición enteral (NE) está indicada en pacientes que, aunque no pueden consumir suficientes cantidades de alimentos, mantienen una función del aparato digestivo suficiente para recibir, digerir y absorber nutrientes.**

Los Suplementos Orales Nutricionales (SON) son fórmulas nutricionalmente completas o incompletas (en función de que aporten o no todos los nutrientes necesarios para servir como única fuente de nutrientes), que completan una dieta oral insuficiente.

Con este estudio se pretende valorar las características organolépticas de suplementos nutricionales orales hiperproteicos, normoproteicos y enriquecidos con fibra.

Material y métodos: **Cata de SON, llevada a cabo en el Servicio de Endocrinología y Nutrición del Consorcio Hospital General Universitario de Valencia desde octubre de 2012 a febrero de 2013.**

Se evaluaron 137 SON en total, de los cuales 47 eran hiperproteicos, 46 normoproteicos y 44 con fibra.

Resultados: **De los SON evaluados, en el grupo de los hiperproteicos obtuvieron los 3 siguientes las mejores puntuaciones: Fresenius Prot Energy Drink® (21,27, sabor vainilla), Nut Avant Estándar® (20,3, sabor fresa) y Resource Protein® (20,01, sabor chocolate)**

En el grupo de los SON normoproteicos los 3 mejor valorados fueron: Ensure Plus® (22,3, sabor plátano), Ensure Plus® (21,9, sabor melocotón) y Fresubin Energy Drink® (21, sabor fresa)

En el grupo de los SON enriquecidos con fibra los 3 más apreciados fueron: Fresubin 2 Kcal Fibre Drink® (23,78, sabor vainilla), Ensure Plus TwoCal® (22,9, sabor plátano) y Fortimel Compact® (21,5, sabor fresa)

Conclusiones: **El estudio puede orientar a los profesionales sanitarios sobre los SON que pueden resultar más aceptados por el paciente, de manera que los SON cumplan su objetivo y restauren o mejoren el estado nutricional, pues la intervención con SON es segura y costo-efectiva, ya que mejora tanto la funcionalidad como la calidad de vida.**

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Palabras clave: *Suplementos orales nutricionales. Desnutrición.*

SENSORY EVALUATION OF ENTERAL NUTRITIONAL SUPPLEMENTS

Abstract

Introduction and objectives: **Enteral nutrition (EN) is indicated in patients who, although they may not eat enough food, maintain a sufficient function to receive, digest and absorb nutrients digestive system.**

Oral Nutritional Supplements (SON) are nutritionally complete or incomplete formulas (depending on whether or not provide all the nutrients needed to serve as the sole source of nutrients), which supplement inadequate oral diet.

This study aims to evaluate the organoleptic characteristics of hyperproteic, normoproteic and fiber-enriched oral SON.

Material and methods: **SON test, carried out at the Department of Endocrinology and Nutrition Consortium Hospital General Universitario de Valencia from October 2012 to February 2013.**

137 SON were evaluated in total, of which 47 were hyperproteic, 46 normoproteic and 44 enriched in fiber.

Results: **Of the SON evaluated in the group of hyperproteic the following 3 SON obtained the best scores: Fresenius Prot Energy Drink® (21,27, vanilla flavor), Avant Standard Nut® (20.3 , strawberry flavor) and Resource® Protein (20.01, chocolate flavor)**

In the group of normoproteic SON the 3 best rated were: Ensure Plus® (22.3, banana flavor), Ensure Plus® (21.9, peach flavor) and Fresubin Energy Drink® (21, strawberry flavor)

In the group of fiber-enriched the 3 SON most appreciated were: 2 Kcal Fresubin Fibre Drink® (23.78, vanilla flavor), Ensure Plus® TwoCal (22.9, banana flavor) and Fortimel Compact® (21.5, strawberry flavor)

Conclusions: **The study aims to guide clinicians on what SON may be more acceptable to the patient, so that the SON serve their purpose and restore or improve nutritional status, as the SON intervention is safe and cost - effective, since they improve both the functionality and quality of life.**

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Key words: *Oral nutritional supplement. Malnutrition.*

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Abreviaturas

SON: Suplementos Orales Nutricionales.
PREDyCES: Prevalencia de la Desnutrición Hospitalaria y Costes asociados en España.
NE: Nutrición enteral.

Introducción

El estudio de la desnutrición hospitalaria es fundamental debido a los efectos deletéreos que ésta tiene sobre los órganos y estructuras que permiten el correcto funcionamiento de los aparatos y sistemas endocrinometabólico, inmunitario, gastrointestinal, renal, cardiorrespiratorio, etc. Todo ello se traduce en una mayor morbimortalidad, menos respuesta a los tratamientos, mayor estancia hospitalaria, mayor número de complicaciones infecciosas, retraso en los procesos de cicatrización de heridas y mayor costes socio-económicos[1-3].

En el adulto se han referido numerosos datos acerca de la prevalencia de la malnutrición en el medio hospitalario, llegando a alcanzar entre el 30 y el 50% de los pacientes ingresados. En nuestro país, el estudio PREDyCES® (Prevalencia de la Desnutrición Hospitalaria y Costes asociados en España) mostró que el 23% de los pacientes hospitalizados se encontraban en situación de riesgo nutricional[4,5,6].

Se entiende por Nutrición Enteral (NE) la administración de nutrientes químicamente definidos y parcial o totalmente metabolizados a través del tubo digestivo, por boca o por sonda, para conseguir una nutrición adecuada[7].

Los Suplementos Orales Nutricionales (SON) son fórmulas nutricionalmente completas o incompletas (en función de que aporten o no todos los nutrientes necesarios para servir como única fuente de nutrientes), que completan una dieta oral insuficiente[8].

La indicación debe hacerse con una información exacta sobre la ingesta voluntaria de alimentos por vía oral, el estado nutricional del paciente, y la capacidad funcional del mismo. Por tanto, se deben utilizar si el paciente presenta una ingesta oral insuficiente habiendo recibido consejos dietéticos y/o tiene, alteraciones en la deglución, capacidad de absorción alterada, o circunstancias sociales que hacen difícil una modificación dietética.

Por tanto, los objetivos que hay que plantear a la hora de prescribir los suplementos orales son aumentar la ingesta total de nutrientes, mantener y/o recuperar el estado nutricional, la capacidad funcional y/o la calidad de vida y reducir la morbimortalidad.

La elección de un suplemento nutricional debe de basarse en la composición del mismo, en sus características físicas (sabor, olor, textura…) y en la enfermedad de base. Asimismo debe ajustarse en la medida de lo posible a los gustos del paciente. Existen diferentes tipos de fórmulas, algunas diseñadas con nutrientes específicos para determinadas enfermedades, trastornos o afecciones (úlceras por presión, estreñimiento, diarrea, etc.) y otras que van destinadas a pacientes sin necesidades específicas. Ambas, además, se clasifican según predomine uno u otro nutriente.

No son muchos los estudios que se realizan relacionados con los SON, pero sí es cierto que mejoran la calidad de vida de los pacientes tanto hospitalizados como institucionalizados. Se sabe que el envejecimiento se asocia a cambios en la composición corporal de un sujeto que van a influir directamente sobre su estado nutricional, tales como el aumento y la redistribución de la masa grasa, la disminución de la masa magra y la pérdida de contenido mineral óseo. Asimismo, se producen pérdidas sensoriales que repercuten en la pérdida del placer de comer, en la elección de los alimentos y, por tanto, en su estado nutricional. Si a este hecho, se une la xerostomía, muy común entre las personas mayores al igual que la disfagia, y que se produzca una alteración en la regulación del sistema inmunitario que implica un mayor riesgo de desarrollar enfermedades infecciosas e inflamatorias, estamos contribuyendo al desarrollo de un estado de desnutrición grave[8-10]. Todo ello trae como consecuencia el aumento de las comorbilidades, agravamiento de enfermedades subyacentes y un incremento de la morbi-mortalidad. Además, las visitas hospitalarias son más frecuentes y las estancias más prolongadas, lo que conlleva un mayor gasto sanitario. Un ejemplo de ello lo muestra el estudio del gasto sanitario total para tratar la desnutrición en Reino Unido que es de 8.970 millones de euros frente a los 2.100 por el resto de enfermedades, de manera que el coste anual de la desnutrición representa el doble del coste que el tratamiento de la obesidad[11]. Otro ejemplo lo muestra un estudio llevado a cabo en dos hospitales públicos de Portugal, en el que se concluye que el disgnóstico de desnutrición incrementa los costes de hospitalización en un 20%[12].

En España, más de la mitad de los ancianos hospitalizados padecen desnutrición o riesgo de sufrirla y sólo el 16% de éstos reciben tratamiento nutricional[13]. Es por ello por lo que, cada vez más, los laboratorios especializados en productos nutricionales preparan y mejoran la composición de los suplementos. Son completos, específicos y perfectos para cubrir las necesidades dietéticas de los pacientes que lo requieran. Pero, para cumplir su función, tienen que ser ingeridos por las personas y para eso tienen que tener buenas características organolépticas, matiz importantísimo que a veces no se tiene muy en cuenta en la fabricación de estos productos. Revisando referencias bibliográficas al respecto, no se han encontrado estudios relacionados con las características organolépticas de los SON, y es por este motivo por el que se vió la necesidad de llevar a cabo este estudio.

Objetivo

Valorar las características organolépticas de suplementos nutricionales orales hiperproteicos y normo-

proteicos, hiper y normocalóricos, y enriquecidos con fibra.

Metodología

Se llevó a cabo una cata de SON en el Servicio de Endocrinología y Nutrición del Consorcio Hospital General Universitario de Valencia desde octubre de 2012 a febrero de 2013. Se evaluaron vademecums de SON de 8 laboratorios diferentes: Vegenat®, Nutricia®, Persan®, Gcn®, Fresenius Kabi®, Nestlé®, Wallax® y Abbott®. Se clasificaron 137 SON en hiperproteicos (contenido proteico ≥18%), normoproteicos (contenido proteico <18%) y enriquecidos con fibra (aporte de fibra ≥ 4 g de fibra/100 ml). A su vez, en los tres casos, los SON se subdividieron en hipercalóricos cuando el aporte calórico es >1 kcal/mL, y normocalóricos cuando el aporte calórico es ≤1 kcal/mL. De esta manera se analizaron las características organolépticas de 47 SON hiperproteico (39 hipercalóricos y 8 normocalóricos); 46 SON normoproteicos (36 hipercalóricos y 10 normocalóricos); y 44 SON enriquecidos con fibra, de los cuales 19 son hiperproteicos (13 hipercalóricos y 6 normocalóricos) y 25 son normoproteicos (16 hipercalóricos y 9 normocalóricos). En este último caso se evaluaron 44 aunque se habían tenido en cuenta 47 en principio pero hubo tres SON que no se consiguieron para la realización de las catas. Todos los SON analizados se recogen en el Anexo I y todos ellos se caracterizan por estar financiados por la Seguridad Social y pautados vía oral.

Una vez se obtuvo la distribución definitiva según los criterios anteriores, se organizaron 9 catas, 3 para SON hiperproteicos siendo 7 los sabores estudiados (vainilla, albaricoque, chocolate, frutas del bosque, plátano, fresa y capuccino/café), 3 para SON normoproteicos siendo 16 los sabores (vainilla, vainilla-limón, manzana, plátano, champiñón, fresa, frutas del bosque, frambuesa, melocotón, naranja, naranja-melocotón, albaricoque, chocolate, café, caramelo y neutro) y, por último, 3 para SON enriquecidos con fibra siendo 9 los sabores (vainilla, chocolate, café, caramelo, leche merengada, fresa, naranja, plátano y frambuesa). Por tanto, teniendo en cuenta todo lo detallado previamente, las catas quedaron programadas de la siguiente manera: las 3 catas de los 47 SON hiperproteicos, 16 en la primera, 15 en la segunda y 16 en la tercera; las 3 catas de los 46 SON normoproteicos, 16 en la primera, 14 en la segunda y 16 en la tercera; y las 3 catas de los 44 SON enriquecidos con fibra, 16 en la primera, 15 en la segunda y 13 en la tercera. En la tabla I se detallan el número de SON de los cuatro sabores mayoritarios evaluados según la clasificación principal.

La persona responsable de las catas planificó las mismas por sabores y en función de la disponibilidad de los SON. Dada la mayor cantidad en SON sabor vainilla, chocolate y fresa, estos tres sabores fueron los primeros en ser evaluados en cada una de las 3 catas de cada uno de los grupos y el resto de SON se distribuyeron aleatoriamente a lo largo de la cata. De esta manera, las 3 catas de los 47 SON hiperproteicos quedaron organizadas en 16 (14 sabor vainilla y 2 sabor albaricoque), 15 (10 sabor chocolate, 1 sabor frutas del bosque y 4 sabor plátano) y 16 (8 sabor fresa y 8 sabor capuccino/café). Las 3 catas de los 46 SON normoproteicos quedaron en 16 (10 sabor vainilla, 1 sabor vainilla-limón, 1 sabor manzana, 1 sabor champiñón y 3 sabor plátano), 14 (6 sabor fresa, 1 sabor frutas del bosque, 1 sabor frambuesa, 3 sabor melocotón, 1 sabor naranja, 1 sabor naranja-melocotón y 1 sabor albaricoque) y 16 (6 sabor chocolate, 5 sabor café, 2 sabor caramelo y 3 sabor neutro). Por último, las 3 catas de los 44 SON enriquecidos con fibra quedaron en 16 sabor vainilla, 15 (8 sabor chocolate, 4 sabor café, 1 sabor caramelo, 2 sabor leche merengada) y 13 (8 sabor fresa, 1 sabor naranja, 3 sabor plátano y 1 sabor frambuesa). En este último caso, como se ha explicado anteriormente, hubo 3 SON (1 sabor café, 1 sabor melocotón y 1 sabor frutas del bosque) que no se pudieron conseguir.

En cada una de las 9 catas participaron 10 personas entre profesionales sanitarios y estudiantes (endocrinólogos, farmacéuticas, dietistas-nutricionistas y estudiantes de medicina y de nutrición humana y dietética), además del responsable de la organización de la cata que también era profesional sanitario. Los participantes fueron siempre los mismos en las 9 catas para evitar que, el hecho de que fueran diferentes, pudiera influenciar en los resultados. Para poder llevarlas a cabo se emplearon vasos transparentes numerados, cada uno asociado a un SON, y sólo era conocedor la persona encargada de la preparación y organización de las catas, que para ello utilizaba un despacho anexo. En otro despacho se situaron los participantes de las catas, de manera que ambos despachos estaban totalmente separados y los participantes no podían saber qué SON estaban analizando. Las catas no se realizaban en ayunas, tratando de evitar que el apetito falseara por exceso la puntuación de los SON valorados en primer lugar, cuya distribución era aleatoria, y siempre a la misma hora, 08:15 h de la mañana. Las sesiones de cata tenían una duración máxima de 45 minutos. Para evitar el sesgo por agotamiento de las papilas gustativas los participantes se enjuagaban la boca con agua a temperatura ambiente entre cada producto para minimizar el riesgo de que la anterior valoración influyera sobre el nuevo producto a catar. Se evaluaron una media de 15 SON por cata.

La valoración de los características organolépticas de los SON se divide en tres fases: fase visual (color), fase olfato-gustativa (olor, sabor y gusto residual) y fase textural (textura y densidad), otorgándole a cada característica sensorial una puntuación de 1 a 5. En cuanto a la primera fase, se valora que el color se corresponda con el sabor del suplemento que se toma, siendo 1 cuando no hay correlación y 5 cuando hay máxima correlación. En cuanto a la segunda fase, la detección de olor no acorde con el sabor esperado se valora

Anexo I

	Hiperprotéicos (n = 47)		*Normoprotéicos (n = 46)*		*Enriquecidos con fibra (n = 44)*			
					Hiperprotéicos (n = 19)		*Normoprotéicos (n = 9)*	
	Hipercalóricos (n = 39)	*Normocalóricos (n = 8)*	*Hipercalóricos (n = 36)*	*Normocalóricos (n = 10)*	*Hipercalóricos (n = 13)*	*Normocalóricos (n = 6)*	*Hipercalóricos (n = 16)*	*Normocalóricos (n = 9)*
VEGENAT ®	Supressi® (2)	Vegestart Complet® (3)	Supressi NP® (2)	T-DIET Plus Standard® (2) T-DIET plus high protein® (2)	T-DIET plus energy® (2)	–		
NUTRICIA ®	Fortimel extra® (4)	–	Fortimel Energy® (6) Fortimel Yog® (2)	–	T-DIET 20/2® (3) Fortimel Compact® (2)	Fortimel Complete® (4)	Fortimel energy multifibre® (5)	–
PERSAN ®	Nut Avant Plus® (5) Nut Avant HP® (5) Nut Avant Estándar® (5)	– -	– -	–	–	–	–	NutAvant Fibra® (5)
GCN ®	–	–	B1 Plus® (2)	–	–	–	–	Bi1Fibra® (2)
FRESENIUS KABI ®	Fresenius 2 Kcal Drink® (2) Fresenius Prot Energy Drink® (4)	–	Fresenius Energy Drink® (4)	Fresubin original Drink® (2)	Fresubin 2 Kcal fibre DRINK® (2)	–	Fresubin energy fibre DRINK® (3)	–
NESTLÉ ®	Resource 2.0® (2) Resource HP/HC® (3) Renutryl® (3)	Resource protein® (5)	Resource energy® (5) Resource 2.0 Shot® (2)	–	Resource 2.0 fibre® (1) Resource Senior Active® (3)	Resource protein fibra® (2)	–	–
WALLAX ®	Nuttenex hiperproteico®(1)	–	–	-Nuttenex® (6)	–	–	–	Fibtenex® (2)
ABBOTT ®	Ensure plus Advance® (3)	–	Ensure plus® (9) Ensure plus fresh® (1) Ensure Plus Savoury® (1) Ensure Plus Live® (2)	–	–	–	Ensure Plus Fiber® (3) Ensure Plus TwoCal® (3)	–

Tabla I
Clasificación del número de SON de los cuatro sabores principales evaluados

SON/Sabores	*Chocolate*	*Vainilla*	*Fresa*	*Café*	*TOTALES*
Hiperproteicos n = 47	10	14	8	8	40
Normoproteicos n = 46	6	10	6	5	27
Con fibra n = 44	8	16	8	4	36
TOTALES n = 137	24	40	22	17	103

negativamente, al igual que la presencia de gusto residual (regusto que se queda después de haber ingerido el producto); sin embargo en el caso del sabor, cuánto más se perciba el sabor esperado, mayor puntuación se le otorga lo cual depende de la palatabilidad de cada persona. Por último, en cuanto a la tercera fase, la textura suave y la baja densidad que presente un suplemento nutricional son valoradas positivamente. También se obtuvo la puntuación del total de características organolépticas para cada suplemento de tal manera que, la máxima puntuación que se le puede otorgar, es de 30.

Resultados

Teniendo en cuenta la gran variedad de SON analizados y la diversidad de sabores de los mismos sólo se van a mostrar los resultados referentes a los cuatro sabores mayoritarios atendiendo a la clasificación principal: chocolate, vainilla, fresa y café. Se destacarán, así mismo, otros sabores no mayoritarios pero que han obtenido una alta calificación. Por otra parte, teniendo en cuenta el tipo de estudio y la colaboración desinteresada de las casas comerciales que colaboraron prestando sus productos, no se especificarán aquellos SON que han obtenido las peores puntuaciones en las diferentes catas.

SON hiperproteicos

Los tres SON hiperproteicos que obtuvieron las puntuaciones totales más altas de cada uno de los cuatro sabores mayoritarios se pueden observar en la tabla II, desglosadas sus características organolépticas.

Tabla II
Características organolépticas de los tres SON hiperprotéicos de mayor puntuación de los cuatro sabores mayoritarios

SON hiperprotéicos/ Características organolépticas		*Color*	*Olor*	*Sabor*	*Gusto residual*	*Textura*	*Densidad*	*Total*
CHOCOLATE (n = 10)								
1º	Resource Protein®	3,73	2,82	3,09	3,18	3,64	3,55	20,01
2º	Resource HP/HC®	3,64	3,09	3,36	2,64	3,36	2,64	18,73
3º	Nut Avant Estándar®	3,209	2,91	2,82	2,45	3,27	3,55	18,09
VAINILLA (n = 14)								
1º	Fresenius Prot Energy Drink®	3,64	3,36	3,36	2,91	4,18	3,82	21,27
2º	Nuttenex Hiperproteico®	3,73	3,27	2,64	2,82	3,91	3,55	19,92
3º	Resource Protein®	3,64	3,45	3	2,82	3,55	3,45	19,91
FRESA (n = 8)								
1º	Nut Avant Estándar®	3,3	3,2	3,1	3	3,9	3,8	20,3
2º	Nut Avant HP®	3,3	3	2,8	3,3	3,9	3,9	20,2
3º	Renutryl®	2,7	3,8	3,5	3,4	3,1	2,6	19,1
CAFÉ (n = 8)								
1º	Fortimel Extra®	2,9	3,3	2,8	2,6	3,2	3,3	18,1
2º	Resource Protein®	2,6	3,4	2,3	2,2	2,9	3	16,4
3º	Nut Avant HP®	2	2,7	2	1,9	3,1	3,7	15,4

Aunque en la tabla II se muestran los tres mejor puntuados de los cuatro sabores principales, es interesante destacar que, en el sabor albaricoque (n = 2), el mejor puntuado fue Resource 2.0® con 19,45 puntos, el SON de sabor frutas del bosque (n = 1) Fresubin 2 Kcal Drink® tuvo 19,36 puntos y en el sabor plátano (n = 4), la mejor puntuación fue Nut Avant Plus® con 18,01 puntos. En los tres casos son valores muy próximos a los obtenidos con los cuatros sabores principales desglosados en la tabla anterior.

SON normoproteicos

Los tres SON normoproteicos que obtuvieron las puntuaciones totales más altas de cada uno de los cuatro sabores mayoritarios se pueden observar en la tabla III, desglosadas sus características organolépticas.

Es importante mencionar que, a pesar de que en la tabla III se recogen las puntuaciones totales de los cuatro sabores principales, la mayor puntuación total en los SON normoproteicos se obtuvo en el sabor plátano (n = 3) con 22,3 puntos en el caso de Ensure Plus®, seguido del sabor melocotón (n = 3) con 21,9 puntos de nuevo en el caso de Ensure Plus®. Destacar que la máxima puntuación en el sabor chocolate que es de 20,50 en Resource Energy® coincide con la máxima puntuación obtenida en el sabor caramelo (n = 2) que es de 20,57 en Fortimel Energy®.

SON enriquecidos con fibra

Los tres SON enriquecidos con fibra que obtuvieron las puntuaciones totales más altas de cada uno de los cuatro sabores mayoritarios se pueden observar en la tabla IV, desglosadas sus características organolépticas.

De igual modo que en los casos anteriores, aunque en la tabla IV se representan las puntuaciones totales de los cuatro sabores principales, cabe destacar que, después de la puntuación de 23,78 para el caso del sabor vainilla Fresubin 2 kcal Fibre Drink®, le sigue la puntuación de 22,9 para el sabor plátano que se da en el caso de Ensure Plus TwoCal®.

La figura 1 muestra las puntuaciones totales más altas obtenidas con cada uno de los cuatro sabores principales en los tres tipos de SON.

Discusión

La valoración de las características organolépticas de los SON en este trabajo es un estudio que complementa la gran cantidad de evidencias científicas que demuestran que los SON mejoran el estado nutricional y previenen la aparición de malnutrición en pacientes que no llegan a cubrir sus necesidades nutricionales con la dieta convencional, además de reducir la aparición de complicaciones así como favorecer la reducción de la estancia hospitalaria y de la mortalidad[14].

Tabla III
Características organolépticas de los tres SON normoprotéicos de mayor puntuación de los cuatro sabores mayoritarios

SON normoprotéicos/ Características organolépticas	*Color*	*Olor*	*Sabor*	*Gusto residual*	*Textura*	*Densidad*	*Total*
CHOCOLATE (n = 6)							
1º Resource Energy®	4,2	3,8	3,3	2,2	3,5	3,5	20,5
2º Ensure Plus®	3,8	3,4	2,7	2,5	3,6	3,4	19,4
3º Fresubin Energy Drink®	2,7	3,1	3,6	3	3,1	3,4	18,9
VAINILLA (n = 10)							
1º Ensure Plus®	2,9	3	2,9	2,7	3	2,9	17,4
2º Fresubin Energy Drink®	1,7	2,6	3,2	2,8	3,4	3,3	17
3º Resource 2.0 Shot®	3,1	2,6	3	2,8	2,7	2,3	16,5
FRESA (n = 6)							
1º Fresubin Energy Drink®	3,2	3,6	3,8	3,5	3,3	3,6	21
2º Nuttenex®	3,4	3,1	2,7	2	3	3,5	17,7
3º Resource Energy®	2,4	2,7	2	2,1	2,6	2,8	14,6
Fortimel Energy®	2,3	2,5	2,2	2	2,7	2,9	
CAFÉ (n = 5)							
1º Resource Energy®	3,7	3,7	3,2	2,4	3,1	3,3	19,4
2º Fresubin Energy Drink®	2,4	3,3	2,8	2,7	3,2	3,3	17,7
3º Ensure Plus®	3,2	2,6	2,1	1,4	3	2,9	15,2

Tabla IV
Características organolépticas de los tres SON enriquecidos con fibra de mayor puntuación de los cuatro sabores mayoritarios

SON enriquecidos con fibra/ Características organolépticas		*Color*	*Olor*	*Sabor*	*Gusto residual*	*Textura*	*Densidad*	*Total*
				CHOCOLATE (n = 8)				
1º	T-DIET Plus High Protein®	3	3,55	3,45	3	3,82	3,64	20,46
2º	Fresubin Energy Fibre Drink®	3,56	3,18	2,73	2,09	3,27	3,18	18,01
3º	Fortimel Compact®	2,91	3	2,82	2,82	3,18	2,73	17,46
				VAINILLA (n = 16)				
1º	Fresubin 2 Kcal Fibre Drink®	4	3,67	4	3,89	3,89	4,33	23,78
2º	Fresubin Energy Fibre Drink®	3,56	3,33	3,33	3	4	4,11	21,33
3º	Ensure Plus TwoCal®	3,89	3,78	3,89	3,56	3,44	2,56	21,12
				FRESA (n = 8)				
1º	Fortimel Compact®	3,2	3,5	4	3,1	4	3,7	21,5
2º	Ensure Plus TwoCal®	4,3	3,6	3,3	3,2	3,2	3,3	20,9
3º	Nut Avant Fibra®	4,1	3,8	2,6	2,2	3,3	3,1	19,1
				CAFÉ (n = 4)				
1º	Fortimel Complete®	2,73	3,18	2,64	2,55	3,09	3,09	17,28
2º	T-DIET 20/2®	3,55	3,73	2,27	2,45	1,73	1,27	15
3º	Nut Avant Fibra®	2,27	1,91	1,64	1,73	2,45	2,36	12,36

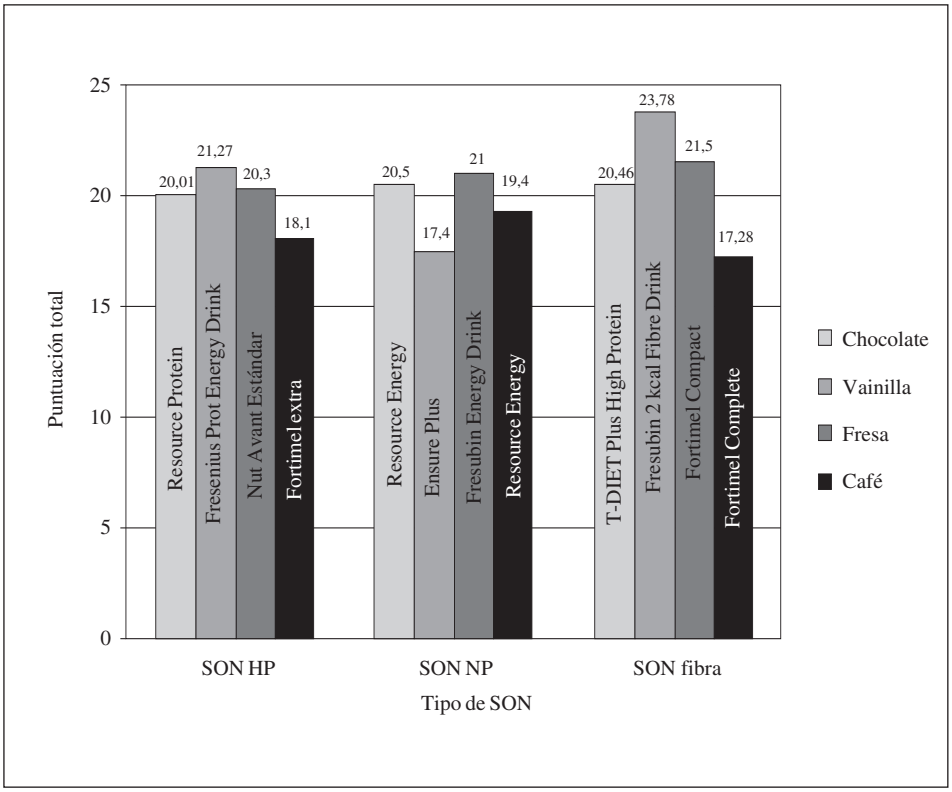

Fig. 1.—Puntuaciones totales más altas de los cuatro sabores principales para cada tipo de SON.

Aunque sólo se han mostrado los resultados totales y por características organolépticas referentes a los tres mejores valorados de los cuatro sabores principales, no en todos estos casos se alcanzaron las puntuaciones totales más altas en cada una de las categorías. De los SON hiperproteicos evaluados, las tres mejores puntuaciones fueron: Fresenius Prot Energy Drink® (21,27, sabor vainilla), Nut Avant Estándar® (20,3, sabor fresa) y Resource Protein® (20,01, sabor chocolate). En el caso de los SON normoproteicos, los tres mejor valorados fueron: Ensure Plus® (22,3, sabor plátano), Ensure Plus® (21,9, sabor melocotón) y Fresubin Energy Drink® (21, sabor fresa). Por último, en el grupo de los SON enriquecidos con fibra los tres más apreciados fueron: Fresubin 2 kcal Fibre Drink® (23,78, sabor vainilla), Ensure Plus TwoCal® (22,9, sabor plátano) y Fortimel Compact® (21,5, sabor fresa).

Se ha dado especial importancia a las características organolépticas de los SON para poder extrapolar a la mayor ó menor aceptación de los mismos por parte de los pacientes. No hay que olvidar que no se ha tenido en cuenta la composición de los suplementos que, evidentemente, influye en la palatabilidad y, en última instancia, en la valoración de los caracteres organolépticos evaluados. En ocasiones se utilizan muchos azúcares simples o grasas saturadas para dar buena palatabilidad, pero se dejan de lado algunas vitaminas importantes o ácidos grasos con funciones importantísimas, como el EPA o el DHA (ácido eicosapentaenoico y ácido docosahexaenoico), ácidos grasos -3 con importantes propiedades antiinflamatorias y citoprotectoras pero que pueden otorgar un sabor y olor desagradables al suplemento. Algunas vitaminas tampoco forman parte de ciertos suplementos, como la B_{12} o la B_9, importantes en la formación de glóbulos rojos y prevención de anemia. Y como minerales importantísimos, principalmente para el anciano frágil, son el calcio y el hierro con función a nivel óseo y sanguíneo, y que son imprescindibles para algunos laboratorios en su formulación.

Limitaciones y propuestas

Una de las limitaciones con la que nos hemos encontrado a la hora de realizar estas catas y que es importante mencionar es que las catas se llevaron a cabo con profesionales sanitarios y estudiantes sanos y no en pacientes, por lo que hay que tener en cuenta este hecho dado que éstos pueden presentar alterados los órganos de los sentidos (vista, olfato y gusto), ya que los resultados seguramente serían diferentes. Ejemplo de ello serían los pacientes oncológicos que presentan alteraciones en el gusto y el olfato, como efecto secundario al tratamiento de radio o quimioterapia que reciben. Como consecuencia, los sabores pueden estar disminuidos, potenciados o bien alterados, incluso es frecuente presenciar en estos casos un regusto metálico y/o amargo en ciertos alimentos. Otro caso serían los pacientes ancianos, en los que el propio envejecimiento produce una disminución de la agudeza visual así como de la sensibilidad gustativa (hipogeusia) y pérdidas importantes en el olfato (hiposmia). Es por todo lo citado anteriormente que sería interesante desarrollar este estudio en un futuro con pacientes que presenten diversos tipos de patologías que estén relacionadas también con déficits en los órganos de los sentidos, ya que al fin y al cabo es el destinatario final de estos suplementos[8,15].

Otra de las limitaciones encontradas es que se evaluaban una media de 15 SON por cata. A pesar de que las catas no se realizaban en ayunas y que para evitar la interferencia en la valoración organoléptica por el agotamiento de las papilas gustativas se disponía de agua, hay que tener en cuenta el posible sesgo de agotamiento durante las catas. Por ello, podría ser conveniente en un estudio futuro, la planificación de catas con un menor número de SON.

Conclusiones

Habiendo realizado una revisión bibliográfica y no obteniendo resultados relacionados con el estudio de las características organolépticas en SON, podemos concluir que este trabajo es pionero en este campo. Es por ello que, a pesar de las limitaciones encontradas y las posibles propuestas de mejora en estudios posteriores que podrían llevarse a cabo, se sabe que los SON constituyen una intervención terapéutica segura y coste-efectiva que mejoran tanto la funcionalidad del paciente como su calidad de vida. Adicionalmente, también sabemos por el estudio PREDyCES® que la desnutrición hospitalaria es un proceso altamente prevalente asociado al aumento de la morbilidad y mortalidad así como a elevados costes sanitarios[16,17]. La importancia de este trabajo radica en que la valoración de las características organolépticas de los suplementos puede determinar la mayor o menor aceptación de éstos por parte de los pacientes así como su adherencia al tratamiento y como consecuencia, reducir el riesgo de desnutrición[18].

Conflicto de intereses

Los autores declaran no tener conflicto de intereses ni vinculación con ninguno de los laboratorios que suministraron productos para la realización de este estudio.

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Original / *Alimentos funcionales*

Actividad antiinflamatoria de un extracto polifenólico de hueso de olivas en la línea celular de monocitos humanos THP1-XBLUE-CD14

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Resumen

El objetivo de este trabajo es evaluar la actividad antiinflamatoria de un extracto de naturaleza polifenólica de huesos de oliva.

Material y métodos: **Se incubó la línea celular THP1-XBlue-CD14 (invivogen), 80.000 células/pocillo, provocando inflamación (activación de NF-kb) mediante 0.1 µg/ml LPS (lipopolisacárido de E. coli) durante 24 horas. Se evaluó la presencia del extracto (10 y 50 mg/l, concentraciones bioseguras) durante 2 horas a 37 ºC, previa (efecto preventivo) y posterior a la activación proinflamatoria (efecto terapéutico) y se cuantificó colorimétricamente la actividad de fosfatasa alcalina, que se expresa bajo el control del promotor del factor transcripcional de NF-kb. Se evalúa el % actividad de NF-kb en efecto preventivo y terapéutico respecto a cultivos control de células con LPS y sin extracto añadido, que se consideran 100% de NF-kb.**

Resultados: **La capacidad antiinflamatoria preventiva del extracto a 50 mg/l es del 25,5% (IC 95% 16,8-34,2) y el efecto terapéutico del 34,9% (IC 95% 25,3-44,4) para la misma concentración, no presentando actividad significativa a 10 mg/l.**

Conclusión: **Se muestra una actividad de los polifenoles extraídos de los huesos de aceitunas, tanto preventivo de la inflamación como terapéutico de eliminación de la inflamación a través de la inhibición del factor NF-kB previamente activado por LPS a concentraciones de 50 mg/l de polifenoles que previamente se han mostrado seguras.**

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Palabras clave: *Polifenoles. Actividad antiinflamatoria. Extracto de huesos de oliva. Factor NF-kb. Lipopolisacárido de E. coli.*

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ANTI-INFLAMMATORY ACTIVITY OF OLIVE SEED POLYPHENOLIC EXTRACT IN THE THP1-XBLUE-CD14 HUMAN MONOCYTES CELL LINE

Abstract

The aim of this study was to assess the anti-inflammatory activity of a polyphenolic extract from olive pits.

Material and methods: **The THP1-XBlue-CD14 (invivogen) cellular line, 80,000 cells/well, was incubated and inflammation (activation of NF-kb) was produced with 0.1 mg/mL of LPS (lipopolysaccharide from E. coli) for 24 hours. We assessed the presence of the extract (10 and 50 mg/L, biologically safe concentrations) for 2 hours at 37º C, before (preventive effect) and after (therapeutic effect) the proinflammatory activation, and the activity of alkaline phosphatase, which is expressed under the control of the NF-kb transcriptional factor, was quantified by colorimetry. The percentage of activity of NF-kb as preventive effect and therapeutic effect was assessed by comparing it to control cultures of cells with LPS and without extract, which are considered 100% of NF-kb.**

Results: **The preventive anti-inflammatory capacity of the extract at 50 mg/L was 25.5% (95% CI: 16.8-34.2) and the therapeutic effect 34.9% (95% CI: 25.3-44.4) for the same concentration, without any significant activity at 10 mg/L.**

Conclusion: **An activity of polyphenols extracted from olive pits is shown, both in preventing inflammation and therapeutically eliminating inflammation through inhibition of NF-kB factor previously activated by LPS at concentrations of 50 mg/L of polyphenols, which previously haven been shown to be safe.**

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Key words: *Polyphenols. Anti-inflammatory activity. Extract from olive pits. NF-kb factor. Lipopolysaccharides from E. coli.*

Introducción

Existe un creciente interés por sustancias con capacidad neuroprotectora, proponiéndose en la bibliografía distintos mecanismos de acción para explicar dicha capacidad, entre las que se pueden citar la acción antiinflamatoria, la modulación de vías de señalización intracelular, la modulación de la expresión de proteínas, la inhibición de las vías apoptóticas o la acción antioxidante[1].

Se está produciendo también una tendencia hacia el consumo de alimentos funcionales, con el consiguiente desarrollo de alimentos innovadores capaces de influir sobre la salud[2,3]. En este sentido, en los últimos años se han lanzado numerosos productos al mercado con un menor contenido en grasa total o en grasas perjudiciales, un enriquecimiento en compuestos que contribuyen a mejorar la salud cardiovascular (fitoesteroles, DHA, ácidos grasos poliinsaturados, etc.) o bien productos dietéticos con alto contenido en fibras con efecto saciante que permitan una disminución de la ingesta y un control del apetito.

Entre los compuestos bioactivos, es patente que los antioxidantes pueden anular los efectos perjudiciales de los radicales libres en las células[4] y que las poblaciones que siguen una dieta de frutas y vegetales ricos en polifenoles y antocianinas tienen menor riesgo de contraer cáncer, enfermedades cardíacas y algunas enfermedades neurológicas[5]. Sugiriéndose que los compuestos antioxidantes pueden prevenir la degeneración macular[6], inmunidad suprimida debido a una nutrición pobre[7], y neurodegeneración, que son causados por el estrés oxidativo[8]. Sin embargo, a pesar del papel claro del estrés oxidativo en las enfermedades cardiovasculares, el uso de vitaminas antioxidantes no han mostrado ninguna reducción clara en el progreso o riesgo de contraer enfermedades cardíacas[9], sugiriéndose que la combinación con otras sustancias en las frutas y vegetales (posiblemente los flavonoides) puedan explicar la mejor salud cardiovascular de quienes consumen más frutas y vegetales[10].

La producción de antioxidantes naturales y los antioxidantes que se obtienen con la alimentación, no es suficiente para la mayoría de las personas, por esa razón muchas compañías alimentarias y de nutracéuticos venden formulaciones de antioxidantes como suplementos dietéticos y estos son ampliamente consumidos en los países industrializados[11]. Estos suplementos pueden incluir químicos específicos antioxidantes, como el resveratrol (de las semillas de uva), hidroxitirosol procedente de la oliva, combinaciones de antioxidantes, como el "ACES" productos que contienen beta-caroteno (provitamina A), vitamina C, vitamina E y Selenio, o hierbas especiales que contienen antioxidantes, como el té verde y el jiaogulan. Aunque algunos de los niveles de vitaminas antioxidantes y minerales en la dieta son necesarios para la buena salud, hay considerables dudas sobre si los suplementos antioxidantes son beneficiosos y, en caso afirmativo, que antioxidantes lo son y en qué cantidades[5,12-14].

Las materias primas del olivo han motivado investigaciones en los últimos años relacionadas con la recuperación de antioxidantes de los residuos. Una parte de ellas se centran en la obtención de efluentes acuosos del proceso de obtención del aceite de oliva[15]. En otros casos, la recuperación de sustancias de interés se centra en otros tipos de matrices como residuos sólidos[16], pulpa[17], hojas[18] o madera de olivo[19]. En general el componente mayoritario de los extractos de hoja de olivo es la oleuropeina, también son abundantes las referencias relacionadas con el hidroxitirosol[20] que se considera el principal compuesto derivado de la oleuropeína con incluso una capacidad antioxidante superior[15], si bien la actividad general de los extractos parecen apoyarse en efectos sinérgicos entre las sustancias que lo componen.

El objetivo de este trabajo ha sido evaluar el potencial efecto antiinflamatorio, más que de un polifenol concreto, de la mezcla de polifenoles extraídos de los huesos de olivas, utilizando para ello el efecto inflamatorio de los liposacáridos de E. coli sobre un cultivo de monocitos humanos.

Material y métodos

El estudio de la actividad antiinflamatoria de los extractos de huesos de olivas se ha realizado utilizando como biomarcador el factor transcripcional NF-kb, que se activa en caso de daño celular y transduce la señal provocando cambios a nivel celular y molecular[21]. Así pues, se ha procedido a reproducir el proceso inflamatorio (activación de NF-kb) y se ha evaluado si la presencia de los extractos revierten el proceso inflamatorio. Para ello, se ha empleado la línea celular THP1-XBlue-CD14 (invivogen), derivada de monocitos humanos, en la que la enzima fosfatasa alcalina se expresa bajo el control del promotor del factor transcripcional de NF-kb. La actividad de la fosfatasa alcalina puede medirse mediante una reacción enzimática con técnicas colorimétricas de modo que una mayor actividad de fosfatasa alcalina se relaciona directamente con mayor cantidad de NF-kb y por tanto menor efecto anti-inflamatorio.

Para la realización del ensayo, se siembran las células en placas multipocillo de 96 pocillos a una concentración de 80.000 células por pocillo y se incuban con distintas concentraciones de polifenoles totales del extracto del huesos de oliva durante 2 horas a 37ºC y 5% de CO_2. Posteriormente se añade un activador de NF-kb, LPS 0.1 mg/ml (lipopolisacárido de *E.coli*) que induce estrés celular, y se deja incubar durante 24 horas. Tras el período de incubación se analiza la actividad de NF-kb. Paralelamente, el estudio también se ha realizado induciendo primero la inflamación con LPS (incubación 2 horas) y posteriormente añadiendo el extracto, para observar si es capaz de revertir el efecto. Se realizaron de cada procedimiento dos ensayos independientes y con tres replicas por ensayo. Las concentraciones de polifenoles totales

del extracto de huesos de olivas (mayoritariamente hidroxitirosol y oleuropeina) se ha utilizado a concentraciones de 10 y 50 mg/l, viables según estudios previos[22] y muy por debajo de la LD50 de 800 mg/l de extracto.

La actividad de NF-kb se mide indirectamente mediante un ensayo colorimétrico con el reactivo quanti-Blue (invitrogen). El reactivo quanti-Blue contiene el sustrato fosforilado que hidroliza la fosfatasa alcalina, la actividad de la fosfatasa libera un compuesto cromogénico que puede analizarse midiendo la absorbancia a 655 nm. Como la expresión de la fosfatasa alcalina está dirigida por el promotor de NF-kb, los resultados de actividad de NF-kb son directamente proporcionales a la actividad de la fosfatasa alcalina, y la actividad de la fosfatasa es proporcional a la absorbancia. De modo que a mayor actividad de NF-kb mayor absorbancia. La expresión de resultados de actividad de NFkb se realiza respecto a las células control positivo (tratadas con LPS) haciendo uso de la siguiente fórmula:

$$\% \text{ Actividad de NFkb} = (\text{Abs}_{655\,nm} \text{ muestra} / \text{Abs}_{655\,nm} \text{ control LPS}) \times 100$$

Resultados

A partir del estudio previo de citotoxicidad[22] con el extracto de olivo y el rango de concentración no tóxica se evaluó la respuesta del biomarcador factor transcripcional NFkb, relacionando una disminución de la actividad de NFkb con una potencial actividad antiinflamatoria. Para ello se ha empleado la línea celular THP1-Xblue-CD14. El diseño experimental se realizó considerando dos opciones: efecto preventivo, incubación con los extractos primero, y posteriormente la inducción de la estimulación del biomarcador (NFkb) con el tratamiento con LPS. Y la otra opción, efecto terapéutico, estimulación primero del biomarcador (NFkb) e incubación con los extractos después. Paralelamente a la evaluación del efecto sobre la actividad de NFkb se analizó la viabilidad celular para comprobar el estado de las células después del tratamiento con los extractos, siendo en todos los casos viables. Los porcentajes de actividad de NFKb están expresados en la tabla I.

Tabla I
Actividad inflamatoria provocada por LPS de E. coli, cuantificada mediante NFKb, en monocitos humanos y efectos preventivo y terapáutico de 10 y 50 mg/l de polifenoles del extracto de huesos de aceitunas. Se considera 100% de actividad inflamatoria en ausencia de extracto

Media ± SD (IC 95%)	*% NFKb Efecto preventivo*	*% NFKb Efecto terapéutico*
Cels + LPS	100,0 ± 8,0 (91,6-108,4)	
+ 10 mg/l extracto	109,4 ± 23,6 (84,6-134,2)	91,0 ± 1,6 (89,3-92,7)*
+ 50 mg/l extracto	74,5 ± 8,3 (65,8-83,2)**	65,1 ± 9,1 (55,6-74,7)**

* $p < 0,05$; ** $p < 0,001$.

Las células tratadas con LPS se considera que activan a NFkb al 100% y respecto a este valor se expresa la actividad de NFkb de los cultivos con extracto en efecto preventivo y terapéutico.

La capacidad antiinflamatoria del extracto se determinó a partir del efecto evaluado sobre la actividad de NFKb considerando la disminución de la actividad de NFkb como potencial actividad antiinflamatoria. Así pues, el poder antiinflamatorio se estableció de forma relativa teniendo como referencia de no actividad antiinflamatoria el tratamiento con LPS. Los resultados se muestran gráficamente en la figura 1, destacando

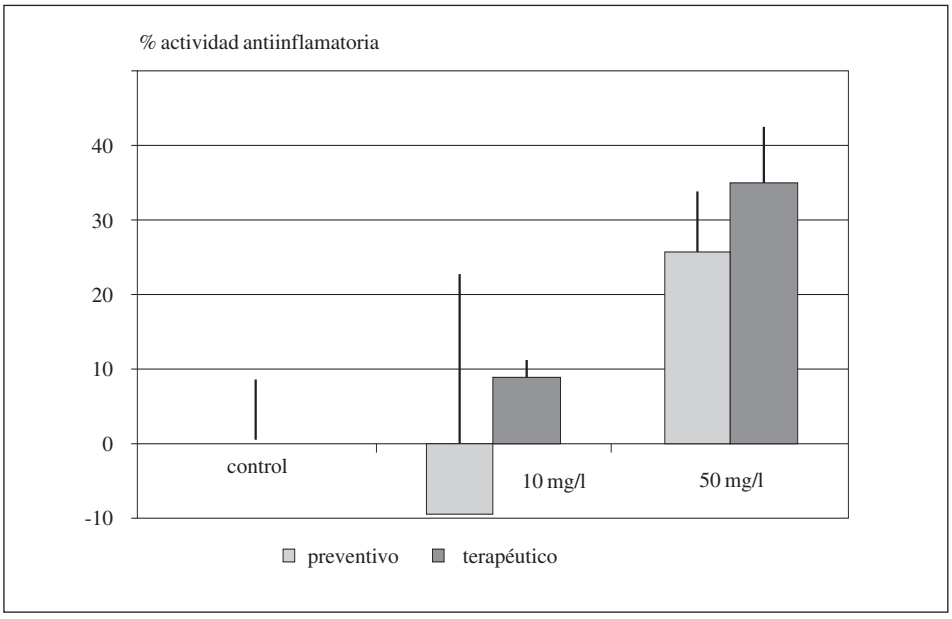

Fig. 1.—Porcentaje de actividad antiinflamatoria preventiva y terapéutica de extracto de polifenoles de huesos de olivas a 10 y 50 mg/l sobre la inflamación producida por 0,1 µg/ml de lipopolisacárido de E. coli en monocitos humanos.

una reducción preventiva de la actividad inflamatoria mediante la adición de 50 mg/l de extracto en un 25,5% (IC 95% 9,2-41,8), no presentando esta actividad a la concentración menor de 10 mg/l. En el efecto terapéutico se obtuvieron resultados positivos de poder antiinflamatorio sobre la inflamación provocada previamente y en concreto del 34,9% (IC 95% 17,8-52,0) de disminución con 50 mg/l del extracto.

La comparación entre las dos experiencias, simulación efecto preventivo y terapéutico, muestra la misma tendencia en los extractos analizados, presentando capacidad antiinflamatoria significativa a la concentración de 50 mg/l.

Discusión

El efecto de la alimentación en la salud se atribuye a la presencia de ciertos compuestos que ejercen una acción beneficiosa, los compuestos bioactivos. Dada la importancia de los compuestos bioactivos en los sectores de la alimentación y farmacéutico, actualmente existe un gran interés en la identificación de nuevos compuestos bioactivos y/o en la identificación de nuevas propiedades de los mismos, siendo este el marco de actuación en el presente trabajo.

La evaluación in vitro e in vivo de compuestos bioactivos se basa en modelos experimentales que reproducen el proceso biológico de interés, mediante sistemas sensibles a factores externos y cuyas posibles fluctuaciones sean medibles. La herramienta esencial para el diagnóstico de la bioactividad es la selección del biomarcador adecuado. En el presente estudio, se ha utilizado como biomarcador del proceso inflamatorio el producido por el lipopolisacárido de E. coli (LPS) sobre la línea celular THP1-XBlue-CD14[21] y el efecto preventivo y terapéutico que pueden ejercer los polifenoles extraídos de los huesos de aceitunas, encontrándose un efecto antiinflamatorio, tanto preventivo como terapéutico a una concentración de 50 mg/l de polifenoles. Estas células constituyen un modelo homogéneo, altamente reproducible y con una alta supervivencia de células, frente al empleo de cultivos primarios de neuronas de ratón de distintas regiones del sistema nervioso, que presentan una muy baja tasa de supervivencia en cultivo[23,24].

Los polifenoles contenidos en los extractos procedentes del olivo presentan propiedades antioxidantes que hacen que sean candidatos para la investigación de enfermedades neurodegenerativas[25]. Además tienen otras actividades biológicas que le confieren importancia dentro de la "Dieta mediterránea"[26]. Se ha demostrado, además de otros efectos beneficiosos, el poder protector de la ingesta de flavonoides, compuestas fenólicos contenidos en vinos, vegetales y frutas frente a la demencia[27]. También se ha encontrado evidencia de actividad anticancerígena de los polifenoles extraídos del aceite de oliva[28], mediante la utilización de células de leucemia promielocítica humana, en las que se observa inhibición de su crecimiento con polifenoles del aceite de oliva virgen.

Otros autores encuentran efectos positivos también[29] en el uso de polifenoles procedentes de las aguas del procesado de aceituna en la línea celular PC12, así, sometiendo a dichas células a estrés oxidativo y midiendo la citotoxicidad, se observa una citoprotección de las células cerebrales con los extractos. Y algunos autores encuentran que los extractos de los residuos del olivo presentan actividad antioxidante[16], mediante ensayos ORAC y DPPH en células umbilicales endoteliales humanas.

Otros compuestos naturales tienen efectos antiinflamatorios como algunos ácidos grasos como el eicosapentanoico, docosahexanoico, linoleico conjugado y ácidos grasos monoinsaturados, mediante diferentes mecanismos de actuación[30].

Conclusión: en el presente estudio se muestra una actividad antiinflamatoria de los polifenoles extraídos de los huesos de aceitunas, tanto en su aspecto de prevención de la inflamación, como en su efecto terapéutico de eliminación de la inflamación ya instaurada a concentraciones de 50 mg/l de polifenoles totales que previamente se han mostrado seguras.

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Original / *Vitaminas*

Fat-soluble vitamin deficiencies after bariatric surgery could be misleading if they are not appropriately adjusted

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Abstract

Objective: **To evaluate the differences in frequency of fat-soluble vitamin deficiencies if we adjust their levels by its main carriers in plasma in patients undergoing Biliopancreatic diversion (BPD) and Roux-en-Y gastric bypass (RYGB).**

Research Methods & Procedures: **We recruited 178 patients who underwent RYGB (n = 116 patients) and BPD (n = 62 patients) in a single centre. Basal data information and one-year after surgery included: anthropometric measurements, fat-soluble vitamins A, E and D, retinol binding protein (RBP) and total cholesterol as carriers of vitamin A and E respectively. Continuous data were compared using T-Student and proportions using chi-square test.**

Results: **There was a vitamin D deficiency of 96% of all patients, 10% vitamin A deficiency and 1.2% vitamin E deficiency prior to surgery. One year after surgery, 33% of patients were vitamin A deficient but the frequency reduced to 19% when we adjusted by RBP. We found a vitamin E deficiency frequency of 0% in RYGB and 4.8% in DBP one year after surgery. However, when we adjusted the serum levels to total cholesterol, we found an increased frequency of 8.7% in RYGB group for vitamin E deficiency and 21.4% in DBP (p = 0.04).**

Conclusion: **We have found a different frequency of deficit for fat-soluble vitamin both in BPD and RYGB once we have adjusted for its main carriers. This is clinically relevant to prevent from overexposure and toxicity. We suggest that carrier molecules should be routinely requested when we assess fat-soluble vitamin status in patients who undergo malabsorptive procedures.**

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Key words: *Bariatric Surgery. Vitamin. Fat soluble. BPD. Gastric bypass Roux.*

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LAS DEFICIENCIAS DE VITAMINAS LIPOSOLUBLES TRAS LA CIRUGÍA BARIÁTRICA PUEDEN SER PERJUDICIALES SI NO SE AJUSTAN ADECUDADAMENTE

Resumen

Objetivo: **Evaluar las diferencias en la frecuencia de las deficiencias de vitaminas liposolubles si ajustamos sus concentraciones mediante sus principales transportadores plasmáticos en pacientes sometidos a derivación biliopancreática (DBP) y derivación gástrica en Y de Roux (DGYR).**

Métodos de investigación y procedimientos: **Reclutamos a 178 pacientes sometidos a DGYR (n = 116 pacientes) y DBP (n = 62 pacientes) en un único centro. Los datos de información basal y al año de la cirugía incluyeron: mediciones antropométricas, vitaminas liposolubles A, E y D, proteína de unión al retinol (PUR) y el colesterol total como transportadores de las vitaminas A y E, respectivamente. Los datos continuos se compararon utilizando la t de Student y para las proporciones el test chi cuadrado.**

Resultados: **Hubo una deficiencia de vitamina D en el 96% de todos los pacientes, de vitamina A en el 10% y de vitamina E en el 1,2% antes de la cirugía. Un año después de la cirugía, el 33% de los pacientes tenía deficiencia de vitamina A pero la frecuencia se redujo al 19% cuando ajustamos para la PUR. Encontramos una frecuencia de deficiencia de vitamina E en el 0% de los pacientes con DGYR y en el 4,8% de aquellos con DBP un año después de la cirugía. Sin embargo, cuando ajustamos las concentraciones séricas de colesterol total, encontramos un aumento de la frecuencia de hasta el 8,7% de deficiencia de vitamina E en el grupo con DGYR y del 21,4% en el grupo con DBP (p = 0,04).**

Conclusión: **Encontramos una frecuencia diferente de déficit de vitaminas liposolubles tanto en DBP como en DGYR una vez que ajustamos para sus principales transportadores. Esto es clínicamente relevante para evitar la sobreexposición y la toxicidad. Sugerimos que se deberían solicitar de forma rutinaria las moléculas transportadoras a la hora de evaluar el estado de vitaminas liposolubles en pacientes sometidos a procedimientos que entrañan malabsorción.**

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Palabras clave: *Cirugía bariátrica. Vitamina. Liposoluble. Derivación biliopancreática. Derivación gástrica en Y de Roux.*

Introduction

Obesity and morbid obesity represent a growing worldwide serious health problem. It affects a significant percentage of young and adult population and is associated to chronic comorbidity[1].

Bariatric surgery is a procedure commonly used in the management of obesity with BMI greater than 40 or 35 kg/m^2 with comorbidities. It has been found to be the only effective long-term treatment for morbid obesity[2]. Multiple studies have shown weight loss and resolution or improvement of comorbidities after bariatric surgery.

Although the benefits have been proved in clinical trials, they are not exempt from several, mineral and vitamin deficiencies, mainly in intestinal bypasses procedures as biliopancreatic diversion and gastric bypass compared to restrictive techniques[3].

Several factors contribute to produce metabolic deficiencies, like reduced caloric intake, gastric volume reduction, gastrointestinal tract bypass and malabsorption, poor food tolerability and lack of compliance with oral supplementation. It also has been found that morbid obese population present with vitamin and mineral deficiencies even before surgery in a significant proportion. An explanation would be the lack of intake of enriched food in proteins, vitamins, minerals and fiber, and the abuse of high caloric density meals with poor nutritional value[4].

Fat-soluble vitamin deficiencies can lead to several disorders with different severity. Some of them are well known and highly prevalent, like vitamin D deficiency[5]. Other fat-soluble vitamin deficiencies vary in a range of dysfunction and severity, like vitamin A or E deficiency. Despite the lack of knowledge about the clinical implication of vitamin A deficiency after bariatric surgery, reports of cases have shown the occurrence of severe ophthalmic complications as corneal xerosis or night blindness, and dermopathy[6]. In addition the pathophysiology of vitamin E deficiency and its clinical implications are less known.

Objective

Although there are several publications on this topic, there is controversy about the different prevalence reported in literature about fat-soluble vitamin deficiencies in bariatric surgery and the best method for diagnosis and monitor treatment. Our hypothesis intends to illustrate that frequency of fat soluble vitamin deficiencies can vary if we adjust their levels to its carrier proteins.

Material and methods

Participants

We recruited retrospectively 178 patients who underwent Roux-en-Y gastric bypass (RYGB) (n = 116 patients; 65.1%) and biliopancreatic diversion (BPD) (n = 62 patients; 34.9%) in a single center, between january 2009 and march 2011.

Clinical and biochemical data were obtained from medical charts before surgery and one-year follow-up. All patients signed a written informed consent prior to surgery in which it was specified that clinical and analytical data collected before the bariatric procedure and during follow-up could be potentially used in an anonymous way for investigation and publication. This study was approved by the Ethics Committee of the Hospital Clinico San Carlos and was in compliance with the Helsinki Declaration.

Bariatric procedures

Eligibility for RYGB or DBP procedures varied according to the patients' clinical characteristics and comorbidities, evaluated by the coordinated team of endocrinologist and bariatric surgeon. All surgeries were performed laparoscopically in a single center. RYGP consisted of the creation of a small vertical gastric pouch of approximately 15-20 ml, a 150-200 cm Roux limb and a 50-100 cm biliopancreatic limb. BPD included two types of procedures: a classic duodenal switch (14 cases) and a single-anastomosis duodeno-ileal bypass with sleeve gastrectomy or SADI-S (48 patients). In the classic duodenal switch, a sleeve gastric resection was followed by a douodeno-ileal bypass with a 250 cm alimentary limb and a 75-100 cm common channel. SADI-S was performed as described previously[7]; it consisted of a one-loop duodenal switch in which after the sleeve gastrectomy (performed over a 54 Fr [18mm] bougie) and the duodenal division, the proximal duodenal stump was end-to-side anastomosed to the ileum at 250 cm form the ileocecal valve, thus creating a long biliopancreatic channel and a 250 cm common + alimentary limb. Because SADI-S is a simplified duodenal switch which has proved to behave in the same way as the classic duodenal switch, both techniques were considered under the BPD group for statistical analyses.

Examinations

Basal data information and one-year after surgery included: anthropometric measurements (height, weight, body mass index [BMI], calculated as weight (kg)/height (m^2), percentage weight loss [%WL]), fat-soluble vitamins A, E and D, and retinol binding protein (RBP) and total cholesterol as carriers of vitamin A and E, respectively. An absolute concentrations of fat-soluble vitamins as well the ratio vitamin A/RBP and vitamin E to total cholesterol were registered. The specific level for each deficiency were established at vitamin A < 0.30 mg/L, vitamin A/RBP < 0.65 mg/mg, vitamin E < 5.0 mg/L, vitamin E/cholesterol < 5.0 mg/g and 25(OH) vitamin D < 30 ng/mL.

Biochemical methods

Blood samples were collected after overnight fasting. After centrifugation serum was separated immediately, protected from light and frozen to -80ºC until analysis. Vitamin A and E measurements were performed with the use Liquid Chromatography of Chromsystems Diagnostics® (Munich, Germany) in a Shidmazu HPLC whit UV detection at 325 nm and 295 nm. The calibration standard is traceable to NIST 968e reference material. The interassay coefficient of variation was 6.4% and 7.17% for levels of 0.38 and 0.75 mg/L of Vitamin A, and for levels of 7.57 and 18.55 mg/L of Vitamin E was 5.3% and 5.4% respectively. The quality of the method is evaluated by UKNEQAS (United Kingdom National External Quality Assessment Scheme).

Total 25(OH) vitamin D was measured by a competitive direct Immunoassay through quimioluminiscency in a Liason analyzer (DiasSorin®, Saluggia, Italy). The method uses magnetic particles covered with a specific antibody anti-25(OH) vitamin D (solid phase) and conjugated 25(OH)vitamin D with an isoluminol derivate. The method has a functional sensitivity below 4 ng/mL, analytic range to 150 ng/mL, and the interassay coefficient of variation was 10.7% and 9.9% for levels of 17.43 and 112 ng/mL of 25(OH) vitamin D respectively. The quality of the method is evaluated by DEQAS (Vitamin D External Quality Assesment Scheme).

Total Cholesterol was measured in Olympus AU 5400® (Beckman Coulter Diagnostics. Brea, California, USA)with a cholesterol-oxidase method. The calibrator is traceable to NIST SRM 909b. The analytical range is 20-700 mg/dl and the quality of the method is evaluated by External Quality Program of SEQC (Sociedad Española de Química Clínica).

Retinol Binding protein is measured for Nephelometry in a BN Prospec (Siemens Diagnostic. Munich Germany).The analytical range is 1-20 mg/dl.

Statistical analysis

Descriptive results were expressed as mean ± standard deviation for continuous variables. Categorical variables were summarized as percentages and interquartile range (IQR).

The main outcomes was to evaluate the differences in the proportion for each fat-soluble vitamin deficiency between both groups of surgery (RYGP and BPD), at one year after surgery. Statistically significance differences for the main outcomes were determined in lineal regression models, with each vitamin concentration as the dependent variable and the type of surgery (RYGP or BPD), age, gender, weight, BMI one year after surgery and weight's percentage lost as independent variables. Continuous data were compared between groups using T-Student and proportions using chi-square test. The p values were two-sided and statistical significance was considered when $p < 0.05$. All statistical analyses were performed using the Statistical Package for Social Sciences, version 15.0 ((IBM SPSS Statistics Inc., Chicago, IL, USA).).

Results

Basal characteristics

Among the 178 patients evaluated, 48 (27%) were male and 130 (73%) were female with a mean age of 47 (11.8), ranging from 18 to 69 years old. The BMI before surgery ranged between 30.6 to 71.7 kg/m^2, with a mean of 44 (6) kg/m^2.

Patients were similar in age and BMI at baseline, with a higher proportion of female patients in gastric bypass group (RYGP) compared to biliopancreatic diversion (BPD) ($p < 0.001$) (table I).

Weight lost

Those patients in the group for the biliopancreatic diversion experienced a greater % WL than those in the bypass surgery group (37.2% *vs* 33.4%, $p = 0.012$) one year after surgery (table I).

Vitamin concentrations

Before surgery, the median concentration for 25(OH) vitamin D was 17.2 (IQR: 13.8-24.3) ng/ml. 98.2% of all patients had a 25(OH) vitamin D less than

Table I
Basal characteristics and weight changes after the bariatric procedures

Characteristics	*Roux-en-Y gastric bypass*	*Biliopancreatic diversion*	*P value*
Age (years)	45.28 ± 20.2	47.7 ± 13	.20
Women (%)	81.9	56.5	.001
BMI before surgery (kg/m^2)	43.7 ± 5.3	44.5 ± 7.3	.41
BMI 1 year after surgery (kg/m^2)	29 ± 4.6	28 ± 5.7	.28
Percentage weight loss	33.4 ± 8	37.2 ± 10	.012

BMI: body mass index.
Data presented as percentages or median ± standard deviation.

30 ng/ml considered as insufficient. One year after surgery, all patients in both groups needed supplementation with 25OH-vitamin D (oral calcifediol 16.000 U periodically as needed) for insufficient vitamin D levels.

Before surgery 10% of patients presented with vitamin A deficiency (absolute or adjusted ratio levels), whereas vitamin E deficiency was almost imperceptible affecting only 1.2% of patients.

In relation to vitamin A concentration, we observed a considerable frequency for vitamin A deficiency one year after surgery when we measured the absolute serum levels of Vitamin A (< 0.30 mg/l); with a frequency of 27,5% in RYGB group and 38,1% in DBP group (p = 0.14). When vitamin A levels were adjusted to RBP (vitamin A/RBP < 0.65 mg/mg) the frequency diminishes to 17.4% in RYGP and 21.4% in DBP (*p = 0.58*).

Only two patients (1 in each group) presented with severe deficit for vitamin A/RBP one year after surgery, considered as less than 0.55 mg/mg. Most patients with deficiency had serum levels considered as mild (> 0.60 mg/mg).

We also found a vitamin E deficiency (< 5.0 mg/l) frequency of 0% in RYGB and 4.8% in DBP one year after surgery (*p = 0.06*). However, when we adjusted the serum levels to total cholesterol (vitamin E/cholesterol < 5.0 mg/g), we found an increased frequency of 8.7% in RYGP group for vitamin E deficiency and 21.4% in DBP (*p* = 0.059). We have found statistically significance differences in vitamin E deficiency before and after adjustment for total cholesterol in RYGB (*p = 0.04*) and in DBP (*p = 0.04*) (fig. 1).

Only 1 patient in DBP presented with serum level for vitamin E/Chol considered as severe (< 4.0 mg/g), being most of them (86.6%) considered as mild (4.5-4.9 mg/g).

Discussion

Although bariatric surgery is a highly effective procedure for the treatment of obesity and morbid obesity, it may be associated with some nutritional and metabolic deficits. Among them, fat soluble vitamins deficiencies are prevalent due to inadequate intake and/or malabsorption and alteration of its normal metabolism. Once, the deficit was established, it is mandatory to supplement and replace it in a safe and effective way. Vitamin A, E and D are not exempt from side effects and toxicity if they are not properly indicated and monitored along the follow up.

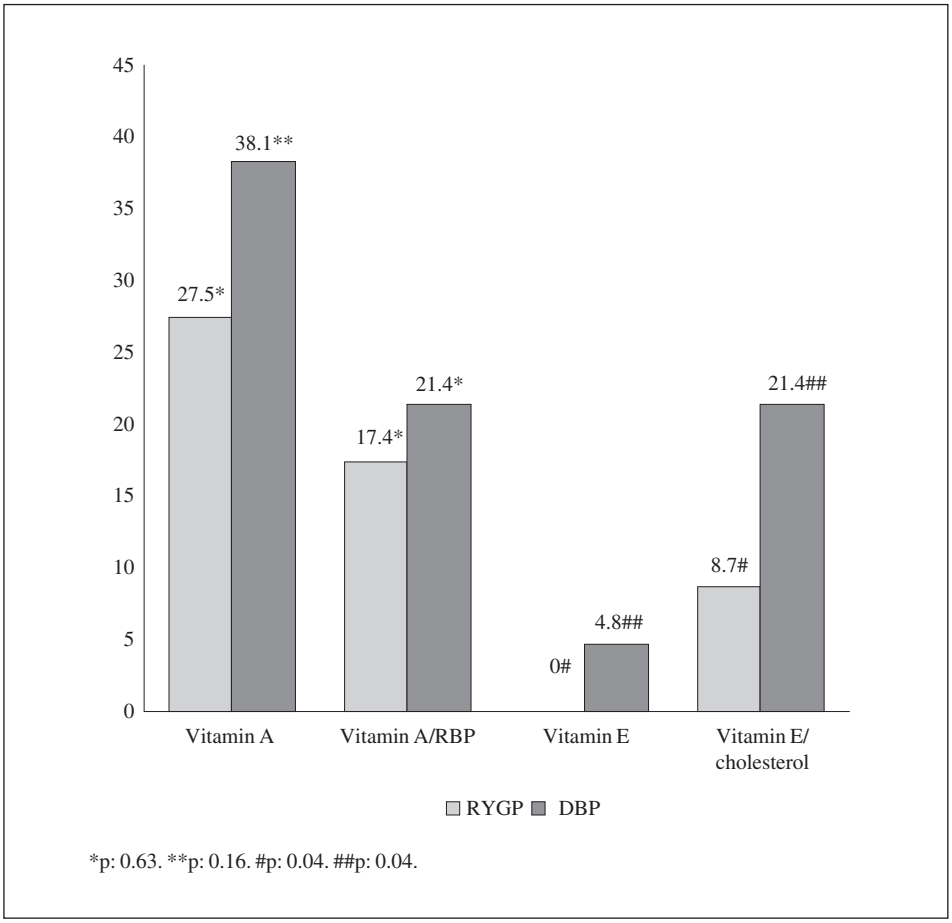

Fig. 1.—Percentage for fat-soluble vitamin deficiency one year after surgery (%) both absolute and adjusted by main molecule carrier.

Eventually, restrictive procedures could associate fat soluble vitamin deficiencies due to decreased oral intake, avoidance of certain meals as a result of digestive intolerance and protein carrier deficits; although the literature doesn't support this firmly[8]. We have evaluated those patients at higher risk for fat-soluble vitamin deficiency, such as those that occur in patients who underwent RYGB and DBP.

Several factors contribute for fat-soluble vitamin deficiency risk. Poor nutritional status before surgery, aggravated by diminished oral intake contribute to preoperative deficit. After surgery, the decreased intake due to reduced stomach poach and malabsorptive intestinal bypass or diversions, are the main mechanisms for fat soluble vitamin deficiency.

The prevalence of (25OH) vitamin D deficiency in general population is proven to be high ranging from 4 to 39% in Europe, with a lower limit level between 25-30 ng/ml in different studies[9]. Obese population is at high risk for 25(OH) vitamin D deficiency due to reduced bioavailability as it is placed in adipose tissue[10]. There is a double vitamin D origin: a significant proportion is produced in skin from cholesterol and ultraviolet radiation, and a smaller proportion comes from fish, eggs, dairy products, cereals, oils and meat. In Spain, 81.6% presented vitamin D intake under dietary references[11].

In our series, there is a high frequency (99.2%) for (25OH) vitamin D deficiency prior to surgery and a need for oral supplementation due to levels under 30 ng/ml in all patients after surgery. This is consistent with other results previously reported, as published by Ducloux et al in France and Moizé et al in Spain, who found a high prevalence for vitamin D deficiency of 96% and 94% before bariatric surgery, respectively[10,12].

We have found a result of 10% of patients presenting a vitamin A deficiency prior to surgery both absolute and corrected for RBP, similar to other series[4]. This represents an adequate nutritional status prior to surgery and the most likely cause of this deficiency would be a decreased intake in vitamin A. Prior to surgery, in the absence for protein malnourishment with adequate RBP and prealbumin levels, absolute vitamin A levels may be equally valid.

In contrast, an important frequency for vitamin A deficiency one year after surgery was detected. Since malabsorptive procedures began to be performed, both patient series and clinic cases have been published for vitamin A deficiency[13]. However, according to medical literature, the range for this deficiency is very wide. Clinical signs and symptoms for severe vitamin A deficiency such as night blindness, xeroftalmia and hyperkeratosis are infrequent in this population[14].

In our sample, 33% of patients had vitamin A deficiency, when taking into account the absolute vitamin A levels, whereas if they are adjusted to RBP, the percentage of deficiency is reduced to 19% of subjects. After surgery, any disturbance that could associate protein malnourishment (intercurrent disease such infection, extended fasting or chronic diarrhea) can present with short half-life protein deficiencies; like RBP or prealbumin. Therefore, we should confirm vitamin A deficiency once we have adjusted for RBP[15], so we avoid overtreatment and risk of toxicity.

According to these findings, 36.7% of patients in RYGB group and 43.8% in DBP would have been incorrectly diagnosed with vitamin A deficiency if we only consider absolute levels of vitamin A. This represents an important overestimation with clinical relevance, as it implies potential treatment with high doses of vitamin A supplementation. When chronically administered, toxicity can associate ataxia, alopecia, hyperlipidemia, hepatotoxicity, bone and muscle pain, teratogenia during the first trimester of pregnancy, visual impairment or increased bone fractures due to osteoporosis among others[16].

Some prior publications have assessed the relationship between obesity and vitamin A deficiency, both pre and postoperatively[17,18]. Pereira et al. reported a prevalence of 14% for vitamin A deficiency preoperative in a cohort of morbid obese patients and 52% three months after gastric bypass, measuring retinol in serum while patients were being supplied with 5,000 IU of retinol acetate. In patients who underwent RYGB in our series, the frequency for vitamin A deficiency was substantially lower (17.4%) one year after surgery, once we have corrected for its main carrier protein (RBP). Slater et al. also found a high prevalence for vitamin A deficiency after DBP; in fact, 69% of patients had low vitamin A levels. In contrast with these results, we have found a frequency for vitamin A deficiency in DBP of 38%, which reduces to 21% once we have adjusted for RBP. The lack of adjustment for vitamin A carrier protein could be one of the main reasons for the discrepancies between results in literature.

Finally, we have observed a significant frequency for vitamin E deficiency once adjusted by total cholesterol. Vitamin E status after bariatric surgery is less known, although the clinical manifestations of this deficit are uncommon. The data published before range between 4-10% in different series[19,20]. In fact, a significant increment of this deficiency both in RYGB and DBP took place after cholesterol adjustment. This has clinical impact, as many patients are on treatment for hypercholesterolemia and others have low cholesterol levels due to malabsorption and decreased oral intake. Therefore vitamin E levels could be underestimated incorrectly. The clinical impact of vitamin E deficiency in these patients is unknown and there are not general recommendations for oral supplementation. Most patients in our series had mild deficiency which is easily supplemented with a daily dose between 200-400 mg of alpha-tocopherol.

Conclusion

Our data suggest that when vitamin A and E are evaluated, they must be adjusted by their carrier molecules

to avoid incorrect interpretations, and thereby to prevent from overexposure and toxicity. We suggest that carrier molecules should be routinely requested to assess fat-soluble vitamin status in patients who undergo malabsorptive procedures.

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High prevalence of vitamin D insufficiency among elite Spanish athletes; the importance of outdoor training adaptation

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Abstract

Introduction: **The discovery of vitamin D muscle receptors in the last few years suggested a significant role in muscle tissue, pointing out athletes as a special group. Specific data are scarce.**

Aim: **The main aim of the current paper was to provide, for the first time, comparable data about vitamin D status in elite Spanish athletes by sport, age, season and training environment.**

Methods: **Four hundred and eight elite athletes with a mean age of 22.8 ± 8.4 years were recruited from the High-performance sport centre in Barcelona for this cross-sectional study. Athletes from 34 different sports modalities were analysed. Data were available for vitamin D status, training environment, seasonality and number of medical visits. All data were analysed using SPSS version 18.0.**

Results: **Mean 25(OH)D of all athletes was 56.7 ± 23.4 nmol/L. Approximately 82% of the athletes were below the optimal levels, (< 75nmol/l), 45% had moderate deficient levels (< 50 nmol/L) and 6% had severe deficiency (< 27.5 nmol/L). We have observed a steady increase in 25(OH)D concentrations with increasing age ($p < 0.01$) Highest levels were observed in those subjects training outdoors compared with those training indoor ($p<0.01$). Differences between sport modalities were observed. Even during summer, 87% of the athletes had insufficient 25(OH)D concentrations.**

Conclusion: **There is a high prevalence of vitamin D insufficiency among elite Spanish athletes. Outdoor training could ensure vitamin D sufficiency and differences between sports modalities should be taken into account for future research. The results contribute to identify the need of optimizing vitamin D status across athletes.**

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Key words: *25(OH)D concentrations. Elite ahtletes. Sun exposure. Sports modalities. Training.*

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ALTA PREVALENCIA DE INSUFICIENCIA DE VITAMINA D ENTRE DEPORTISTAS DE ÉLITE ESPAÑOLES; LA IMPORTANCIA DE LA ADAPTACIÓN DEL ENTRENAMIENTO AL AIRE LIBRE

Resumen

Introducción: **En los últimos años, el descubrimiento de receptores musculares para la vitamina D sugiere un papel significativo de esta vitamina en el tejido muscular, adquiriendo una relevancia especial en deportistas. No existen apenas datos disponibles acerca de las concentraciones de vitamina D en deportistas de élite Españoles.**

Objetivo: **El objetivo del presente trabajo ha sido analizar y proporcionar datos comparables sobre el estado de vitamina D de atletas de élite españoles y la influencia de factores como la edad, la estación del año o el lugar de entrenamiento.**

Métodos: **Cuatrocientos ocho atletas de élite pertenecientes al centro de alto rendimiento de San Cugat del Vallés, en Barcelona, fueron seleccionados con toma de datos transversal. La edad media fue de 22,8 ± 8,4 años con un total de 34 modalidades deportivas diferentes. Entre las variables analizadas se obtuvieron las concentraciones plasmáticas de vitamina D, el número de visitas médicas anuales, la toma de suplementos, la estación del año y el lugar de entrenamiento. La estadística se realizó con el programa SPSS versión 19.0.**

Resultados: **La concentración media de 25(OH)D de la muestra total fue de 56.7 ± 23.4 nmol/L. Aproximadamente el 82% de los atletas obtuvieron concentraciones sanguíneas por debajo de los niveles óptimos (< 75nmol/L). Dentro de estos, el 45% presentó deficiencia moderada (< 50 nmol/L) mientras que un 6% deficiencia severa (< 27,5 nmol/L). Se observó un aumento lineal de las concentraciones de 25(OH)D con la edad ($p < 0,01$) y concentraciones más altas en las modalidades deportivas con entrenamiento al aire libre (tenis, natación piscina descubierta…) en comparación con los que entrenan bajo techo (natación piscina cubierta, balonmano..) ($p < 0,01$). Incluso durante los meses de verano, el 87% de los atletas obtuvieron concentraciones insuficientes de vitamina D en su mayoría los que entrenan en interior. Señalaron no tomar suplementos vitamínicos.**

Conclusiones: **Existe una alta prevalencia de insuficiencia de vitamina D entre los deportistas de élite españoles. El entrenamiento al aire libre podría garantizar la suficiencia de vitamina D y las diferencias encontradas entre las distintas modalidades deportivas se deben tener en cuenta para futuras investigaciones. Los resultados contribuyen a identificar la necesidad de optimizar los niveles de vitamina D en deportistas de élite.**

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Palabras clave: *Concentraciones de 25(OH)D. Deportistas de élite. Exposición solar. Modalidades deportivas. Entrenamiento.*

Introduction

Vitamin D is essential for a vast number of physiologic processes, such as an active role in immune function, protein synthesis, inflammatory response or cellular growth, and thus adequate concentrations are necessary for advantageous optimal health[1,2]. With over 80% of the general worldwide population considered vitamin D insufficient (< 75 nmol/L)[3-5], it is likely that many athletes fall into the same category. Although no evidence exists that athletes have a higher daily requirement than the general population[6], the discovery of vitamin D muscle receptors in the last few years suggested a significant role for vitamin D in muscle tissue. In fact, it has been identified as a regulator of skeletal muscle[1,7,8], pointing out athletes as a possible risk group. Vitamin D has been proposed to be, together with testosterone, the other steroid hormone that is important for muscle function and strength, and could play an important role on enhancing athletic performance[7,9-12]. A recent European study suggested that cardiorespiratory fitness and muscular strength is positively associated with 25(OH)D concentrations in male and female adolescents, respectively[13]. In addition, the first symptom of vitamin D deficiency is muscle weakness, hypotonia, prolonged time to peak muscle contraction, as well as prolonged time to muscle relaxation[14], which can severely affect the athlete population.

Vitamin D storage and concentrations in this population group could be compromised, and its deficiency may have an impact on decreased physical performance and health with higher predisposition to stress fractures[15].

In the last decade, researchers have examined 25(OH)D levels among various groups of athletes, ranging from gymnasts and runners to jockeys. And although some findings have suggested that vitamin D levels in athletes are comparable to those of the general population, results have found that vitamin D status is variable and is mainly dependent on type of sport, outdoor-indoor training time (during peak sunlight and season), skin color, and geographic location[15], which makes it necessary to study athletes independently by regions.

Even if Spain is a Mediterranean country, located at the south of Europe at 40º N, and caucasian skin color, some previous studies have already reported low vitamin D status among Spanish adolescents and elderly population[16,17], but little is known about vitamin D status among elite Spanish athletes.

Objectives

Therefore, the main aim of the current paper was to provide, for the first time, comparable data about vitamin D status in elite Spanish athletes of 35 different sport modalities. One of the main objectives was to describe vitamin D status in elite Spanish athletes and to analyze vitamin serum concentrations by sex, sport, season and training outdoor or indoor.

The results could contribute to identify the need of optimizing vitamin D status across athletes.

Methods

Four hundred and eight elite athletes with a mean age of 22.8 ± 8.4 years were recruited from the High-performance centre in Sant Cugat del Vallés, Barcelona, using elite athletes as primary sampling units and sports as secondary sampling units for this Cross-sectional study (CSS). Criteria for athletes' selection included active sport competition activity and no health problem declared. In total, 408 athletes from 34 different sports modalities were analysed. Data were available for aerobics, athletics, car racing, handball, basketball, boxing, combat, cycling, alpine ski, football, gymnastics, golf, weightlifting, pentathlon, skeleton, taekwondo, triathlon, volleyball, yachting, kayak, field hockey, shot, motorcycling, swimming, synchronized swimming, tennis, table tennis, rolling skate, waterpolo, fencing, diving board jump and also the referees of the National Basketball league (ACB). The data were obtained within the rutine medical assessment the elite athletes must pass periodically at the High Performance Center. They all sign an informed consent in order the data obtained can be used for research anonymously.

Subjects were classified according to outdoor or indoor training as shown in table II in the results part.

Specimen collection and biochemical analyses

Fasting blood samples were collected by venipuncture between eight and nine o'clock in the morning. For the measurement of vitamin D, blood was collected in EDTA tubes, immediately placed on ice, and centrifuged within 30 min (3,500 rpm for 15 min). The supernatant fluid was transported at a stable temperature of 4-7°C to the central laboratory in Barcelona, and stored there at -80°C until assayed.

Vitamin D status

Plasma 25(OH)D was analysed by Immunoassay quimioluminiscent in a Roche Elecsys Analizer 170[18] in Barcelona. The sensitivity of this method is 4.01 ng/mL 25(OH)D. The CV for the method was 8.5%.

Seasonality

The variable "blood extraction date" was used to compute seasonality defined as following and similar

to previous studies[13,19,20]: Winter (1; January through March), Spring (2; April through June), summer (3; July through September) and Autumn (4; October through December).

Statistical analysis

Descriptive statistics were performed and values are shown as mean and standard deviation. Frequency statistics for categorical variables are shown as valid percentage. For this study, vitamin D status was classified into four groups (vitamin D sufficiency/optimal levels >75 nmol/l; insufficiency 50-75 nmol/l; deficiency 27.5-49.99 nmol/l and severe deficiency <27·5 nmol/l) following international guidelines[21]. The differences between sex, vitamin D status groups, sports, training environment groups and seasonality were analysed using one-way ANOVA. All data were analysed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

Table I shows descriptive characteristics of the study sample stratified by 25(OH)D concentration. Prevalence rates of vitamin D status according to the aforementioned sufficient–insufficient classification are shown. Mean 25(OH)D of all athletes at baseline was 56.7 ± 23.5 nmol/L. Considering the cut-off set for adults at 75nmol/l, approximately 82% of the athletes were below the optimal levels, for both males and females. Approximately, 45% had moderate deficient levels (< 50 nmol/L) and 6% had severe deficiency (< 27.5 nmol/L). As no significant differences have been observed between sexes, the sample has been analyzed as a whole. None of the subjects reported any vitamin D supplement intake. The number of annual medical visits did not show any significant influence on vitamin D groups.

Analyzing vitamin D status by age, we have observed a steady increase in 25(OH)D concentrations with increasing age, with significant differences between the younger group (Q1) and the third quartile group (Q3) (48.5 ± 18.7 nmol/L and 61.8 ± 27.0 nmol/L), respectively; ($p < 0.01$) (fig. 1).

Differences in 25(OH)D concentrations were observed by training environment. Our results show that the highest levels were observed in those subjects training outdoor compared with those training indoor for the whole sample ($p < 0.01$). Those differences have been also observed within the vitamin D groups. Although not significant, within the vitamin D sufficient group, those subjects training outside got higher 25(OH)D concentrations compared with those training inside. Same results were obtained for the insufficient group with higher vitamin D levels for those training outdoor (table I).

Table II shows vitamin D concentrations splitted by sport modality according to training environment (indoor-outdoor). Differences between sports were observed. Highest mean 25(OH)D concentrations were obtained in synchronized swimmers, tennis players, swimmers, rolling skaters, field hockey players, athletics and waterpolo players, most of them with outdoor training. While lower 25(OH)D concentrations were obtained in handball players, boxers, fencers, alpine skiers, gymnast, table tennis players and diving board jump, all training indoor.

Figure 2 presents differences in 25(OH)D concentrations by season according to blood extraction date and environment. Surprisingly, the mean highest levels of the global sample were observed in winter. Further analysis indicates that most of the athletes measured in wintertime were outdoors trainers. Even during summer, 87% of the

Table I
Descriptive characteristics of Spanish elite athletes splitted by vitamin D sufficiency or insufficiency (nnom/l)

	(75 nmol/l) Total = 408 Mean ± SD	*Vitamin D Insufficiency (≥ 75 nmol/l n = 334 Mean ± SD*	*Vitamin D Sufficiency n = 73 Mean ± SD*
25(OH)D concentrations (nmol/L)	56.7 ± 23.5	48.5 ± 13.6	93.7 ± 22.9
Males n = 238	56.7 ± 22.7		
Females n = 170	56.7 ± 24.5		
Severe deficiency/deficiency/ insufficiency/sufficiency	5.6/38.7/37.7/17.9	72.1%	17.9%
Age (years)	22.8 ± 8.4	23.1 ± 8.9	21.8 ± 6.0
Blood extraction season % (winter/spring/summer/autumn)	8.4/19.8/42.8/29.0	6.9/19.5/45.5/28.1	15.1/21.9/30.1/32.9
Training session environment % (indoor/outdoor)	39.9/60.1	44.4/55.6	20.8/79.2
Training session indoor	49.3 ± 18.6	45.1 ± 13.4	87.5 ± 15.1
Training session outdoor	62.4 ± 25.9	51.2 ± 13.9	95.8 ± 24.7
Number of medical visits per year	4.1 ± 5.2	4.1 ± 5.7	3.9 ± 2.6

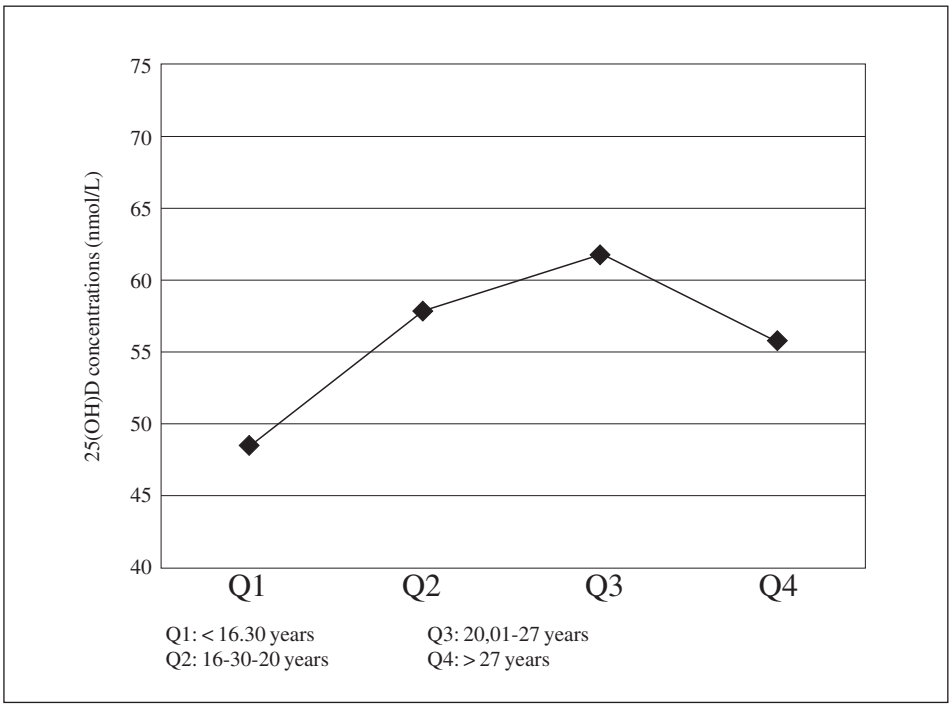

Fig. 1.—Differences in 25(OH)D concentrations (nnom/L) by age quartiles.

athletes were vitamin D insufficient. Lower values of 25(OH)D concentrations were observed for those training indoor compared with those training outdoor during all seasons (all $p < 0.05$ except winter time).

Discussion

Although extensive data exist in documenting vitamin D concentrations of the general population[22,23], limited comparable information is available, specifically for the athletic population. Those existing studies have mainly focused on one sport modality with a reduce number of subjects[24]. Vitamin D status is variable and dependent on several determinants like type of sport, outdoor-indoor training time (during peak sunlight and season), skin color, and geographic location[15]. It makes necessary to study results by regions and sports modalities.

To the best of our knowledge, the data obtained in this study are the first aiming at establishing descriptive 25(OH)D status in occidental elite athletes of different sport disciplines, taking also into account seasonal and training variations.

Results of our study indicated that approximately 82% of the athletes were below the optimal levels (< 75 nmol/L). Approximately 45% were below < 50 nmol/l which is the optimal level for maintaining bone health in adults according to the report of the Institute of Medicine launched in 2011[23]. A general hypovitaminosis problem ranging from 13 to 72% has already been postulated in studies performed in young people in several European countries[3,25-27], USA and Canada[28,29]. Studies in athletes are also in line with our deficiency prevalence[30-33]. Morton et al (2012) concluded that vitamin D concentrations for 65% of their athletes were insufficient (< 50 nmol·L(-1)) in winter[31]. Similar results were obtained by Constantini et al (2010), that reported vitamin D insufficiency in 73% of the measured athletes.

Complications from vitamin D insufficiency are often late-onset rather than immediate, given that the majority of subjects with vitamin D insufficiency are completely asymptomatic, and this fact complicates diagnosis[12]. But in athletes, the impact on decreasing physical performance due to muscle weakness could be more evident. An adequate vitamin D level together with the stimulus of weight-bearing exercise should be required in athletes, especially during adolescence for bone formation and cell growth[16,34]. Despite of optimal 25(OH)D levels are no exception to the controversy, superior benefits are observed at even greater levels, due to only at 25(OH)D levels >100 nmol/L, does vitamin D begin to be stored in the muscle and fat for future use[35]. As fat is required for vitamin D storage, the low subcutaneous fat levels that some athletes have could also compromise their vitamin D status. Although research has found that athletes generally do not meet the dietary reference intake for vitamin D, inadequate endogenous synthesis is the most probable reason for insufficient status[15]. Some sports could be at higher risk. Our results showed that rhythmic gymnasts, long distance runners, skeleton or cyclers got the lowest vitamin D concentrations (lower than 52 nmol/L).

As expected, differences in vitamin D concentrations were found in athletes participating in indoor activities compared with those involved in outdoor

Table II
25(OH)D concentrations (nmol/L) according to sport modality and indoor/outdoor training

	Total			*Indoor*			*Outdoor*		
Sport modality	*N*	*Mean*	*SD*	*N*	*Mean*	*SD*	*N*	*Mean*	*SD*
ACB REFEREES	32	51.1	12.4	32	51.1	12.4	–	–	–
AEROBIC	2	44.7	12.2	2	44.7	12.2	–	–	–
ALPINE SKI	3	33.0	8.0	3	33.0	8.0	–	–	–
ARTISTIC GYMNASTICS	17	44.2	15.6	17	44.2	15.6	–	–	–
ATHLETICS	48	60.1	27.7	1	41.4	–	47	60.5	27.8
BASKETBALL	2	74.0	0.5	2	74.0	0.5	–	–	–
BOXING	8	45.5	15.3	8	45.5	15.3	–	–	–
CAR RACING	2	40.2	7.0	–	–	–	2	40.2	7.0
CYCLING	20	52.2	18.3	–	–	–	20	52.2	18.3
DIVING BOARD JUMP	13	41.3	12.5	13	41.3	12.5	–	–	–
FENCING	6	43.9	8.2	6	43.9	8.2	–	–	–
FIELD HOCKEY	12	61.3	11.7	–	–	–	12	61.3	11.7
FIGHTING	16	50.0	14.7	16	50.0	14.7	–	–	–
FOOTBALL	5	61.1	27.5	–	–	–	5	61.1	27.5
GOLF	9	61.7	15.5	–	–	–	9	61.7	15.5
HANDBALL	12	42.0	15.8	12	42.0	15.8	–	–	–
KAYAK	8	40.1	6.3	–	–	–	8	40.1	6.3
MOTORCYCLING	6	60.6	31.0	–	–	–	6	60.6	31.0
PENTATHLON	6	60.4	16.9	–	–	–	6	60.4	16.9
RHYTHMIC GYMNASTICS	7	45.3	8.3	7	45.3	8.3	–	–	–
ROLLER HOCKEY	1	55.2	.	1	55.2	.	–	–	–
ROLLING SKATE	4	62.9	17.9	–	–	–	4	62.9	17.9
SHOOTING	2	61.3	13.2	2	61.3	13.2			
SKELETON	1	34.7	.	–	–	–	1	34.7	–
SWIMMING	58	69.2	21.9	2	64.5	13.4	56	69.4	22.2
SYNCHRONIZED SWIMMING	11	88.5	35.2	–	–	–	11	88.5	35.2
TABLE TENNIS	11	33.6	11.4	11	33.6	11.4	–	–	–
TAEKWONDO	21	55.3	21.9	21	55.3	21.9	–	–	–
TENNIS	5	98.4	61.2	–	–	–	5	98.4	61.2
TRIATHLON	3	50.4	8.2	–	–	–	3	50.4	8.2
VOLLEYBALL	14	57.4	19.3	13	56.1	19.3	1	75.0	–
WATERPOLO	37	60.7	23.0	11	73.9	23.4	26	55.1	20.9
WEIGHTLIFTING	2	53.1	1.4	2	53.1	1.4	–	–	–
YACHTING	4	49.2	27.1	–	–	–	4	49.2	27.1
TOTAL	408	56.7	23.5	150	49.3	18.6	226	62.4	25.9

activities. Our results indicated that the highest mean of 25(OH)D concentrations were obtained for those training outdoors. Interestingly, synchronized swimmers who trained outdoor during the whole day, obtained higher 25(OH)D concentrations than swimmers training outdoor but early in the morning or late in the evening. Data are in line with other studies[36,37]. Lovell et al. reported that the majority (83%) of female Australian indoor athletes were at vitamin D insufficiency[38]. In the study of Constantini et al (2010), a higher prevalence of vitamin D insufficiency was observed among dancers (94%), basketball players (94%), and Taekwondo fighters (67%), but they also obtained higher vitamin D deficiency prevalence among indoor training athletes comparing with those training outdoor (80% vs 48%; $P < 0.01$)[32].

Seasonal differences were also found regarding 25(OH)D concentrations, confirming the results of other studies across Europe[27,39-41]. Casual exposure to sunlight is thought to provide most of the vitamin D requirements of the human population[39]. Many outdoor athletes avoid peak sunlight hours during summer time, opting to practice early in the morning or late at night, which greatly reduces UVB exposure[42], putting them at considerable risk of vitamin D insufficiency even in the sunny months. Galán et al (2012) proposed 25(OH)D concentrations of > 122.7 nmol/L in autumn in order to have adequate levels in spring. In our study, none of the analysed athletes achieved these concentrations, independently of the season. Our results reveal lower vitamin D values during summer time than in wintertime. But most of the athletes measured in winter time were outdoors trainers and probably do not avoid this peak sunlight for training as in summer time. These higher concentrations could be also due to a low number of subjects measured at wintertime and to seasonal influences in winter blood extraction that was performed from January to March.

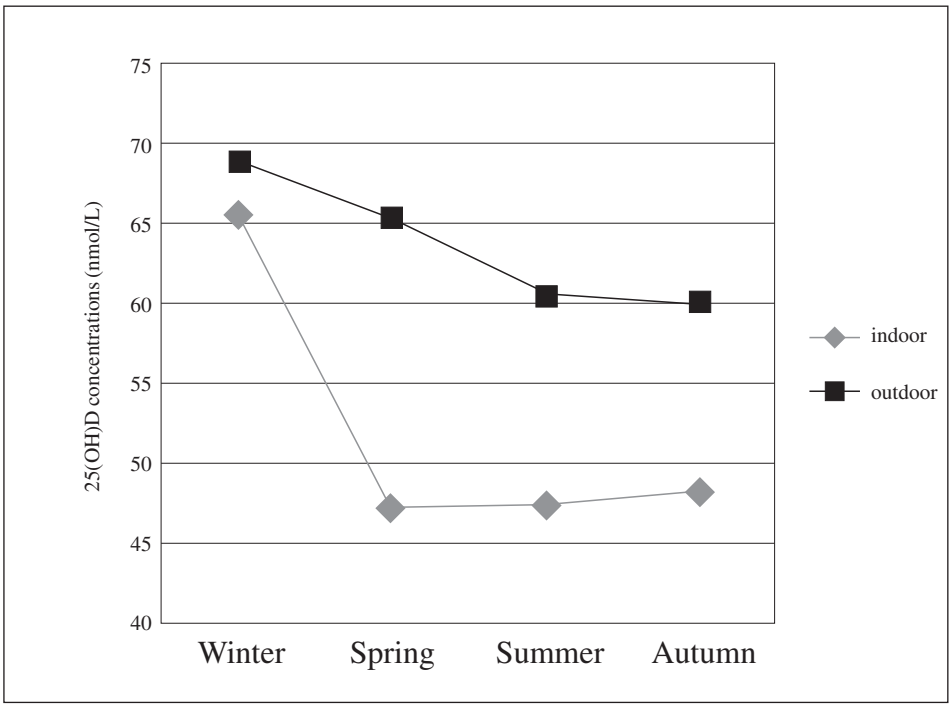

Fig. 2.—Differences in 25(OH)D concentrations (nnom/L) by season and training enrivonment.

Although we have to keep in mind that the results of vitamin D concentrations are variable according to different parameters, geographical location (latitude) or gender do, it does not appear to be the case in our results nor to be the major risk factors for vitamin D insufficiency in athletes. As stated above, lack of sun exposure appears to be the main risk factor, putting, indoor athletes and those who avoid peak daylight hours, regardless of latitudinal location, at the greatest risk for vitamin D insufficiency[37,42].

Ultraviolet light irradiation has been proposed for improving athletic performance and decreasing chronic sports related pain[35]. German Olympic officials considered these effects significant enough for UVB radiation to be considered an ergogenic aid[35], not forbidden and not blamed as doping.

Synthesis of vitamin D from the sun is also dictated by age[42]. And when analyzing vitamin D status by age, a steady increase in 25(OH)D concentrations with increasing age is observed, but those at younger ages have also higher rates of indoor training (data not shown). Our data agree with other published data[3]. It is important to emphasize these lower vitamin D concentrations found in younger athletes. Optimal vitamin D levels are essential at early ages for an adequate growth and development. Normally, active children and adolescents practice their sports activities after school, when sunset is coming or in an indoor environment, with negative consequences for their vitamin D status.

Although dietary intake of our subjects has not been included in this study, there is consistency in the literature regarding inadequate vitamin D intake among athletes. Moreover, due to low levels of vitamin D found and that none of the athletes reported vitamin D supplementation, supplementation could be considered, especially in those training indoor and at older ages. This is in accordance with emerging evidence emphasizing the need of vitamin D supplementation in high-risk groups especially during lack of sun exposure months[43]. Unfortunately, there are limited experimental studies available and even fewer that demonstrate a performance enhancement from vitamin D supplementation. In favour, Magee et al (2013) reported that all doses of supplementation significantly increased 25(OH)D concentrations in Irish athletes, and corrected any insufficiencies/deficiencies in their subset of athletes[44]. It has been also suggested that vitamin D supplementation in individuals with low vitamin D status may improve muscle strength and have beneficial effects on muscular performance and injury occurrence in athletes[45-47]. This is believed to be due to an increase in the size and amount of type II (fast twitch) muscle fibers associated with vitamin D supplementation[33]. It should be noted that type II fibers are predominant in power and anaerobic activities, and are recruited first to prevent falls, associated with muscle strength[48,49]. Close et al. suggested that skeletal muscle may require higher serum concentrations for a response, compared to other tissues[33].

Investigators have recently become interested in examining this possible link between vitamin D and the prevention of stress fractures in athletic individuals. Our data about the annual medical visits indicated that there were no differences according to vitamin D concentrations. We have not found well-controlled studies examining an association between medical visits regarding to stress fractures and serum 25(OH)D levels in a strictly athletic population, but some data in

the military environment have been found. Following these studies and in agreement with our findings, Valimäki et al.[50] observed no difference in 25(OH)D levels among male recruits who developed a stress fracture during training compared with those who did not.

There is, however, an ongoing debate on the influence of vitamin D supplementation or fortified foods in young-healthy people[43]. But most experts agree that the combination between high intake of vitamin D, through dietary sources and ultraviolet B (UVB) exposure is necessary to obtain optimal serum vitamin D levels[51].

There are some limitations in our study. Unfortunately, due to the difficulties on assessing elite athletes and test them, few variables are available regarding vitamin D, and we cannot be certain that other unmeasured confounders have not influenced our observations.

Despite the aforementioned limitation, the study use of a large number of elite athletes from 32 different sports modalities, which provide a deeper understanding of the vitamin D status in athletes, which is an additional strength of our work. The majority of the studies only assess one sport modality and with small sample.

Conclusion

Considering the cut-off set adults at 75nmol/l, approximately 82% of the athletes were below the optimal levels, for both males and females. This study highlights a high prevalence of vitamin D insufficiency among elite Spanish athletes and demonstrats that outdoor training is an appropriate way to increase vitamin D concentrations in athletes, mostly during winter and early spring.

The current data supports previous findings that athletes living even at Mediterranean countries exhibit inadequate vitamin D concentrations, but differences among sports modalities have been observed, and should be taken into account for future research. Those athletes practicing sports modalities which favour lower body fat storages that could have an impact on vitamin D concentrations should be deeper analyzed.

Given the recent findings, it is recommended that sports dietitians and physicians routinely assess vitamin D status and make clear recommendations in order to help athletes achieve an optimal serum 25(OH)D concentration.

The results of the study could contribute to identify the need of optimizing vitamin D status across athletes. But further research is needed to determine the effect of vitamin D status on training, injury, and performance in elite athletes and their future health.

Competing interest

None of the authors had any conflict of interests.

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Contributorship statement

FD, LT,DD planned the study, recruited athletes and data collection; JV, MGG performed the statistical analysis; JV and MGG participated in the data interpretation. JV, MGG, FD participated in the literature search. JV wrote the paper. All authors read and approved the final manuscript.

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Evaluación de una intervención nutricional en personas mayores: el proyecto Edumay

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Resumen

Introducción: **La adhesión a un patrón de Dieta Mediterránea está asociado a una reducción de la morbi-mortalidad, y a una mejora de la calidad de vida.**

Objetivos: **Evaluar una intervención nutricional en personas mayores independientes a través de un programa de educación que favorezca el conocimiento de los alimentos y la confección de dietas adecuadas, promocionando un patrón de dieta saludable.**

Métodos: **Estudio cuasi-experimental realizado en un colectivo de personas mayores que residen en apartamentos tutelados del Ayuntamiento de Pamplona (n = 41). La intervención consistió en seis sesiones de educación grupal y una entrevista motivacional individual en un periodo de tres meses. Se evaluó la adhesión a la Dieta Mediterránea a través de un cuestionario de 14 puntos previamente validado.**

Resultados: **El 80,5% de los participantes fueron mujeres, con una mediana de edad de 79 años, en gran proporción viudas (48,8%) y con estudios primarios (58,5%). Tras la intervención nutricional el porcentaje de participantes que consumió dos o más raciones de verduras u hortalizas aumentó significativamente con respecto al grupo control (p = 0,042). De forma similar en comparación con el grupo control hubo un mayor incremento en el porcentaje de individuos que consumían 3 raciones de legumbres a la semana (p = 0,042), 3 o más veces por semana frutos secos (p = 0,003) y que tomaban preferentemente carne de pollo, pavo o conejo en vez de ternera, cerdo, hamburguesas o salchichas (p = 0,011).**

Discusión: **Una intervención basada en educación nutricional individual y grupal consiguió una mejora significativa en diversos parámetros de adhesión a un patrón de Dieta Mediterránea.**

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Palabras clave: *Envejecimeinto. Educación nutricional. Dieta mediterránea. Viviendas tuteladas.*

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EVALUATION OF A NUTRITIONAL INTERVENTION AMONG ELDERLY PEOPLE: THE EDUMAY PROJECT

Abstract

Background: **The adherence to a Mediterranean Dietary Pattern is associated with a morbi-mortality reduction, and with a better quality of life.**

Objectives: **To evaluate a nutritional intervention among independent elderly people enrolled in an educational program to increase the knowledge of the food and daily diets, promoting a healthy dietary pattern.**

Methods: **Quasi-experimental design conducted in elderly participants who lived in foster home apartments owned by the City Council of Pamplona (n = 41). The intervention was based on six group sessions and an individual motivational session in a period of three months. Adherence to Mediterranean diet was evaluated through a 14-point scale previously validated.**

Results: **Eighty point five per cent of participants were women, with a median age of 79 years, the majority of them widowed (48.8%) and with primary education (58.5%). After the nutritional intervention the percentage of participants who consumed two or more servings of vegetables increased significantly versus the control group (p = 0.042). Similarly, in comparison with the control group, there was an increase in the percentage of participants who consumed three servings per week of legumes (p = 0.042), three or more servings per week of nuts (p = 0.003), and those who consumed preferably meat from chicken, turkey, or rabbit instead of veal, pork, hamburgers, or sausages (p = 0.011).**

Discussion: **An intervention based on individual and group sessions improved significantly several parameters of a Mediterranean dietary pattern.**

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Key words: *Elderly. Nutritional education. Mediterranean diet. Foster homes.*

Introducion

Actualmente en España cumplen 65 años más de 300.000 personas cada año, tres veces más que a mediados del siglo pasado, y esta cifra sigue aumentando casi exponencialmente. Según datos del Instituto Nacional de Estadística de 2011, el 17% de la población española (casi 8 millones de personas) tiene más de 65 años[1].

En este contexto, el Plan de Acción Internacional de Madrid sobre el envejecimiento, fruto de la última Asamblea Mundial sobre este tema auspiciada por las Naciones Unidas considera como ámbitos prioritarios en la vejez el fomento de la salud y el bienestar y la creación de entornos propicios y favorables[2]. Una de las estrategias más eficientes para promover la salud en las personas mayores es la educación nutricional[3] ya que, con frecuencia, las personas mayores, por diversas razones, se encuentran en situación de riesgo nutricional, sin saberlo[4].

Las conductas respecto a la Educación Nutricional se identifican a través de las necesidades, las percepciones, las motivaciones y los deseos del grupo objetivo. Así, aunque las personas mayores tienen unos hábitos muy arraigados, también están más motivados para aprender y adoptar conductas y prácticas que contribuyan al mantenimiento de un buen estado de salud, ya que desean mantener su independencia. Existen diversos estudios que demuestran que la Educación Nutricional es eficaz en este tipo de población[5,6].

El estudio PREDIMED, un ensayo aleatorizado multicéntrico, desarrollado en España, ha demostrado que una Dieta Mediterránea suplementada con aceite de oliva virgen o frutos secos disminuye el riesgo de enfermedad cardiovascular[7]. De modo que parece evidente la relación entre los buenos hábitos alimentarios y la salud, así como la necesidad de una educación nutricional en la última etapa de la vida.

Un patrón de Dieta Mediterránea se caracteriza por el uso de aceite de oliva (sobre todo virgen) como principal fuente de grasa, un elevado consumo de frutas (postre habitual), verduras, hortalizas, legumbres, pescados y cereales no refinados, bajo consumo de cárnicos (principalmente reducido en carnes rojas) y lácteos, y un consumo de vino tinto en las comidas[8]. Esta dieta es reconocida en el ámbito internacional como modelo de dieta saludable, por sus efectos en la prevención y tratamiento de enfermedades crónicas (enfermedades cardiovasculares, obesidad, osteoporosis, diabetes y cáncer)[9-11], patologías que constituyen las principales causas de muerte en el mundo desarrollado. Además, se ha observado que haciendo una planificación previa adecuada este patrón dietético se puede ajustar a la situación económica de la población anciana[12]. También es cierto que los patrones alimentarios y los consumos de energía y nutrientes han cambiado notablemente en los últimos 40 años en España, habiendo algunas diferencias en la actualidad con la dieta Mediterránea tradicional y saludable[13].

Por todo lo anteriormente expuesto se precisan estudios que evalúen con evidencias científicas los efectos de la implantación de un programa de Educación Nutricional basado en la promoción de una dieta Mediterránea tradicional en las personas mayores.

Objetivo

Evaluación de la efectividad de un programa de Educación Nutricional dirigido a las personas mayores residentes en los Apartamentos Tutelados del Ayuntamiento de Pamplona, con el fin de mejorar sus conocimientos y habilidades para la confección de dietas adecuadas, promocionando un patrón de Dieta Mediterránea como ejemplo de patrón dietético saludable. El proyecto se denomina EDUMAY (EDUcación en las personas MAYores).

Métodos

La población de estudio fueron los residentes de los Apartamentos Tutelados (AT) del Área de Bienestar Social del Ayuntamiento de Pamplona (Navarra).

Los Apartamentos Tutelados son Unidades de convivencia supervisadas y apoyadas en la prestación de servicio para personas mayores de 65 años. Estos alojamientos alternativos están destinados a personas autónomas y con graves problemas de alojamiento. Se facilita el acceso a los AT, preferentemente, a las personas mayores que residan en el barrio en el que está ubicado cada AT.

En el momento que se inició el estudio, el Ayuntamiento de Pamplona contaba con 3 edificios, con un total de 110 apartamentos localizados en tres barrios distintos: Edificio Txoko Berri, situado en el barrio de San Juan, en el que vivían 29 personas; Edificio Arga, en el barrio de la Rochapea, en el que vivían 29 personas; y el Edificio Iturrama, situado en el barrio del mismo nombre y con 29 residentes.

Se realizó un estudio cuasi-experimental, con una intervención de Educación Nutricional en los residentes del edificio Txoko Berri. Los conocimientos y actitudes tras la implantación del programa se compararon con los de los residentes de los Apartamentos Arga e Iturrama (grupo control) que no participaron en el programa.

Reclutamiento de participantes

Se inició con una charla informativa a la que se animó a asistir a la totalidad de los residentes de los apartamentos. Se les propuso participar en el proyecto, explicándoles el objetivo y la importancia de su participación, así como la necesidad de un consentimiento informado. El protocolo de estudio fue aprobado por el comité de ética de la investigación clínica de la Universidad de Navarra.

Criterios de inclusión

El único criterio de inclusión fue el deseo de participar de forma voluntaria en el programa de educación nutricional, para lo que debían firmar el impreso de consentimiento informado

Estado de situación inicial.
Evaluación basal de los participantes

Se realizó una primera entrevista semi-estructurada personal, con el fin de conocer los datos sociodemográficos de las personas mayores así como su grado de adhesión a la Dieta Mediterránea mediante un cuestionario de 14 puntos previamente validado y utilizado con éxito en estudios previos[14]. En todos los casos dicho cuestionario fue administrado por el mismo investigador.

Programa de Educación Nutricional

Se realizaron un total de seis sesiones de educación grupal de 50 minutos de duración con grupos de 8 a 10 personas. Los contenidos impartidos fueron los siguientes:

1. Importancia de la alimentación
2. Los grupos de alimentos
3. La planificación de menús
4. Recomendaciones dietéticas en problemas de salud frecuentes: estreñimiento, incontinencia urinaria y osteoporosis.
5. Patologías relacionadas con la alimentación: enfermedades cardiovasculares, hipertensión arterial, colesterol elevado, diabetes Mellitus y obesidad.

La estructura de las sesiones seguía el siguiente esquema:

1. Introducción.
2. Exposición de 30 minutos por parte del profesional sanitario, abordando distintos aspectos del patrón alimentario mediterráneo, y posterior turno de preguntas que permitiera aclarar dudas derivadas del seguimiento de la Dieta Mediterránea.
3. Juegos de memoria sobre el tema trabajado.

Al finalizar la charla, se entregaron trípticos informativos sobre los contenidos impartidos en cada sesión para que los participantes pudiesen leerlo en casa.

También se realizó una entrevista de motivación individual a todos los participantes con el fin de resolver problemas específicos e individualizar los contenidos de las sesiones grupales realizadas en función de las patologías concretas que cada anciano padecía.

Los consejos que se dieron a los residentes del grupo de intervención nutricional respecto a la Dieta Mediterránea fueron los siguientes:

- Utilizar aceite de oliva generosamente en la cocina y en la mesa como única grasa culinaria (para cocinar y aliñar).
- Condimentar con tomate, ajo, cebolla y hierbas aromáticas.
- Usar sofritos.
- Consumir a diario: frutas, verduras, hortalizas y legumbres, hasta alcanzar un total de 5 raciones al día de alimentos vegetales . Además, si el anciano era consumidor regular de vino, se recomendaba ingerir un vaso al día (150 cc los hombres y 100 cc las mujeres,), acompañando las comidas.
- Consumir de manera ilimitada frutos secos (crudos y sin sal), huevos, pescado (recomendado para el consumo diario), marisco, carnes blancas, queso fresco y cereales.
- Consumir con moderación (< 3 veces por semana): jamón tradicional, carnes rojas (después de retirar toda la grasa visible), chocolate (sólo chocolate negro con más del 50% de cacao) y quesos duros.
- Evitar los siguientes alimentos: mantequilla, nata y margarina; embutidos y patés; pato; repostería comercial (no casera); postres comerciales (flanes, natillas); patatas fritas de bolsa; y bebidas y refrescos edulcorados y productos precocinados.

Efectividad del programa de Educación Nutricional

Tras la intervención de Educación Nutricional que duró tres meses, se repitieron las entrevistas, con el fin de valorar de nuevo el grado de adhesión a la Dieta Mediterránea. Se calcularon las diferencias encontradas respecto a su nivel basal y se evaluaron las diferencias en los cambios encontrados en los participantes del programa de Educación Nutricional tras participar en el programa con respecto al grupo control.

Finalmente los participantes del estudio completaron un cuestionario de satisfacción global con el programa, dándoles oportunidad a valorar los contenidos impartidos, el profesorado, la metodología didáctica empleada así como la organización y su grado de satisfacción general.

Análisis estadístico

La información contenida en los cuestionarios cumplimentados se recogió en una base de datos para su posterior análisis de los datos.

Las variables continuas se expresaron como medianas (percentil 25, percentil 75), ya que no seguían una distribución normal, según el test de Kolmogorov-Smirnov y se compararon con el test U de Mann Whit-

ney con el fin de evaluar las diferencias entre el grupo de intervención (Educación Nutricional) y el grupo control. Las variables categóricas se expresaron como proporciones y la comparación entre grupos se realizó con el test de la Chi cuadrado de Pearson y el test exacto de Fisher.

Las comparaciones pre-post intervención se realizaron mediante el test de McNemar para datos emparejados en la comparación de variables cualitativas y el test de Wilcoxon para muestras emparejadas para las variables continuas.

Fue considerada como variable dependiente principal del estudio la diferencia entre el grupo de intervención y el grupo control en la mejoría de la puntuación a la adhesión del índice de 14 puntos del patrón de Dieta Mediterránea.

Todos los valores p presentados fueron a doble cola, una $p < 0,05$ será considerada como estadísticamente significativa. Se realizarán los análisis con el programa estadístico SPSS v. 15.0 (SPSS Inc., Chicago, IL, USA).

Resultados

La muestra final fue de 41 participantes (13 en el grupo de Educación Nutricional y 28 en el grupo control), después de excluir a 9 personas interesadas inicialmente pero que no acudieron a las entrevistas y/o charlas educativas acordadas.

Su mediana de edad fue de 79,2 años (71,4; 83,1). El 80,5% eran mujeres. Casi la mitad de los participantes (48,8%) estaba viudo. Además, el 58,5 % de los participantes había cursado estudios primarios, el 26,8% no había finalizado dichos estudios y ninguno de ellos tenía estudios superiores (tabla I).

Al comienzo del estudio, todos los participantes del programa de Educación Nutricional y el 85,7% de los del grupo control autodeclararon que su alimentación era correcta, no llegando a ser estas diferencias estadísticamente significativas (p = 0,288). (datos no mostrados).

De los 41 participantes, 37 respondieron al cuestionario de adhesión a la Dieta Mediterránea, mientras que los 4 restantes afirmaron recibir la comida desde el servicio de comedor y no quisieron contestar**.** Al inicio del programa, el 84% de los participantes consumía aceite de oliva. Asimismo, más del 80%, evitaba el consumo diario de grasas (carnes rojas, hamburguesas, embutidos, margarina, mantequilla o nata) y de bebidas azucaradas y/o carbonatadas, mientras que sólo un 8,1% de los participantes consumía tres raciones de legumbres a la semana.

Por otro lado, los participantes del grupo control consumían más aceite de oliva (p = 0,008) y más verduras y hortalizas (p = 0,040) que el grupo que fue asignado a Educación Nutricional. En el resto de ítems no hubo diferencias estadísticamente significativas.

Respecto al grado de adhesión a la Dieta Mediterránea de los participantes, la puntuación obtenida por aquellos asignados al grupo control e intervención fue de 8,75 (DE: 1,62) y 7,38 (DE: 1,56) respectivamente, de los 14 puntos totales que se podía obtener en total.

Tabla I
Características sociodemográficas de los participantes

	Grupo Educación Nutricional n = 13	*Grupo control n = 28*	*Valor p*
Sexo [n, (%)]			0,650[a]
Hombres	2 (15,38)	6 (21,43)	
Mujeres	11 (84,62)	22 (78,57)	
Edad (años) [mediana (C1;C3)]	79,26 (70,87;83,28)	77,35 (71,63;82,94)	0,978[b]
Estado civil [n, (%)]			1,000[c]
Soltero	3 (23,1)	5 (17,9)	
Casado	2 (15,4)	4 (14,3)	
Viudo	6 (46,2)	14 (50,0)	
Separado o divorciado	2 (15,4)	5 (17,9)	
Nivel de estudios [n, (%)]			1,000[c]
Analfabeto	0 (0,0)	2 (7,1)	
Sin acabar primaria	4 (30,8)	7 (25,0)	
Primaria o graduado escolar	8 (61,5)	16 (57,1)	
Formación Profesional ó Bachillerato Unificado Polivalente	1 (7,7)	3 (10,7)	
Estudios universitarios	0 (0,0)	0 (0,0)	

[a]Chi-cuadrado de Pearson.
[b]U de Mann-Whitney.
[c]Test Exacto de Fisher.
C1: Cuartil 1.
C3: Cuartil 3.

Tres meses después de haber participado en el programa educativo la puntuación media para el grupo de intervención fue de 9,38 (DE: 2,18), justo dos puntos por encima de la puntuación inicial. Estas diferencias antes y después de la intervención fueron estadísticamente significativas (p = 0,002). En el caso del grupo control a los tres meses de seguimiento la adhesión a la dieta mediterránea prácticamente no cambió (8,96; DE: 1,85), no encontrándose diferencias estadísticamente significativas antes y después del seguimiento (p = 0,167). Es decir, el grupo de intervención aumentó su adhesión a la dieta Mediterránea 2 puntos (intervalo de confianza (IC) 95%: 1,11 a 2,89) en comparación con un aumento de 0,21 puntos en el grupo control (IC 95%: -0.07 a 0,49). Esta diferencia en el aumento de adhesión al patrón de Dieta Mediterránea de 1,82 puntos (IC 95%: siendo estas diferencias 1,09 a 2,65) entre el grupo de intervención y el grupo control fue estadísticamente significativa (p < 0,001).

La mejora de adhesión a un patrón de dieta mediterránea en el grupo control se debió fundamentalmente al aumento de consumo de legumbres, verduras y hortalizas, frutos secos, y preferencia por carnes blancas (pollo, pavo y conejo) en vez de ternera, cerdo, hamburguesas o salchichas (tabla II).

Tabla II

Adhesión a la dieta mediterránea tres meses después de finalizar el programa de Educación Nutricional (EN), en función del grupo de educación al que fueron asignados

	Grupo EN		*Grupo control*		*Cambios en porcentaje tras la intervención*			
Cuestionario de adhesión a al dieta mediterránea	*Basal n = 13*	*Tras intervención n = 13*	*Basal n = 24*	*Tras intervención n = 24*	*Grupo EN*	*Grupo control*	*Grupo EN vs Grupo control*	*Valor p*[a]
1. Utilizan principalmente aceite de oliva para cocinar	9 (69,2%)	9 (69,2%)	22 (91,7%)	22 (91,7%)	0	0	0	NA
2. Consumen 4 ó más cucharadas de aceite de oliva	7 (53,8%)	8 (61,5%)	22 (91,7%)	22 (91,7%)	7,7	0	7,7	0,351
3. Consume 2 o más raciones de verdura u hortalizas al día	3 (23,1%)	7 (53,8%)	14 (58,3%)	15 (62,5%)	**30,7**	**4,2**	**26,5**	**0,042**
4. Consume 3 ó más piezas de fruta al día	9 (69,2%)	12 (92,3%)	15 (62,5%)	16 (66,7%)	23,1	4,2	18,9	0,115
5. Consume menos de 1 ración al día de carnes rojas, hamburguesas, salchichas o embutidos	12 (92,3%)	12 (92,3%)	24 (100%)	24 (100%)	0	0	0	NA
6. Consumen menos de 1 ración al día de mantequilla, margarina o nata	11 (84,6%)	12 (92,3%)	23 (95,8%)	23 (95,8%)	7,7	0	7,7	0,351
7. Consume menos de 1 bebida carbonatada y/o azucarada al día	11 (84,6%)	11 (84,6%)	20 (83,3%)	21 (87,5%)	0	4,2	-4,2	1,000
8. Bebe 1 vaso o más de vino al día	2 (15,4%)	3 (23,1%)	9 (37,5%)	9 (37,5%)	7,7	0	7,7	0,351
9. Consume 3 raciones de legumbres a la semana	1 (7,7%)	5 (38,5%)	2 (8,3%)	3 (12,5%)	**30,8**	**4,2**	**26,6**	**0,042**
10. Consume 3 o más raciones de pescado-mariscos a la semana	7 (53,8%)	8 (61,5%)	11 (45,8%)	11 (45,8%)	7,7	0	7,7	0,351
11. Consume menos de 2 veces por semana repostería comercial	7 (53,8%)	8 (61,5%)	17 (70,8%)	18 (75,0%)	7,7	4,2	3,5	1,000
12. Consume 3 o más veces por semana frutos secos	3 (23,1%)	8 (61,5%)	9 (32,1%)	9 (32,1%)	**38,4**	**0**	**38,4**	**0,003**
13. Consume preferentemente carne de pollo, pavo o conejo en vez de ternera, cerdo, hamburguesas o salchichas	4 (30,8%)	8 (61,5%)	10 (43,5%)	10 (43,5%)	**30,7**	**0**	**30,7**	**0,011**
14. Consume 2 o más veces por semana vegetales cocinados, la pasta, arroz u otros platos aderezados con salsa de tomate, ajo, cebolla o puerro elaborada a fuego lento con aceite de oliva	8 (61,5%)	8 (61,5%)	12 (52,2%)	12 (52,2%)	0	0	0	NA

EN: Educación Nutricional.
aChi-cuadrado de Pearson.

Por último, el grado de satisfacción de los participantes con el programa de Educación Nutricional, fue evaluado por 12 de los 13 participantes incluidos en el programa de intervención. Todos los aspectos fueron valorados muy positivamente a excepción de la duración del proyecto que hubieran deseado que se hubiera alargado en el tiempo (fig. 1).

Discusión

Una intervención en educación nutricional de 3 meses de duración con seis sesiones grupales y una sesión de motivación individual consiguió una mejora significativa en los hábitos alimentarios y en el grado de adhesión a un patrón de Dieta Mediterránea en personas mayores de 65 años residentes en los apartamentos tutelados del Ayuntamiento de Pamplona (Navarra).

Es importante resaltar que las personas que participaron en el proyecto EDUMAY, al igual que ocurre en otros estudios[6,7], no son conscientes de las deficiencias o posibles mejoras que podrían realizar para mejorar su alimentación, ya que al comienzo del programa casi todos ellos pensaban que su alimentación era correcta.

Sin embargo, los resultados evidenciaron que, su dieta podría mejorar en varios aspectos ya que la puntuación media de adhesión al patrón de Dieta Mediterránea al inicio de la intervención fue de 7,38 (DE: 1,56) y de 8,75 (DE: 1,62) en el grupo de intervención y el grupo control, en una escala de 14 puntos.

Los resultados obtenidos ponen de manifiesto que al inicio del programa los participantes seguían un buen patrón de Dieta Mediterránea en cuanto al consumo de grasas saludables ya que un elevado porcentaje de participantes utilizaba aceite de oliva, y la ingesta de grasas saturadas era baja, ya que más del 80% evitaba el consumo de ciertos alimentos como mantequilla, margarina, nata, carnes rojas, embutidos y hamburguesas.

Por el contrario, alrededor del 50% de los participantes no consumía o consumía pocas verduras y hortalizas. Esta cifra es muy superior al 16,7% publicado previamente en el estudio de Cuervo y colaboradores[6]. Además, el consumo de legumbres y de frutos secos era el aspecto de la dieta que debía mejorar un mayor número de personas. Por ello, el programa de Educación Nutricional se centró en las propiedades de las legumbres, los frutos secos, las verduras y hortalizas; y se propusieron diferentes recetas en función de la estación del año.

El programa de Educación Nutricional consiguió una mejora de la adhesión de los participantes a la Dieta Mediterránea, debido fundamentalmente al aumento del consumo de frutos secos, carnes blancas (pollo, pavo y conejo), legumbres y verduras y hortalizas, siendo las diferencias entre grupo de intervención y grupo control estadísticamente significativas.

A pesar de que la mejora en el grado de adhesión a la Dieta Mediterránea puede considerarse como moderada, existen varias razones que la justifican. En primer lugar, está la dificultad de modificar las costumbres ali-

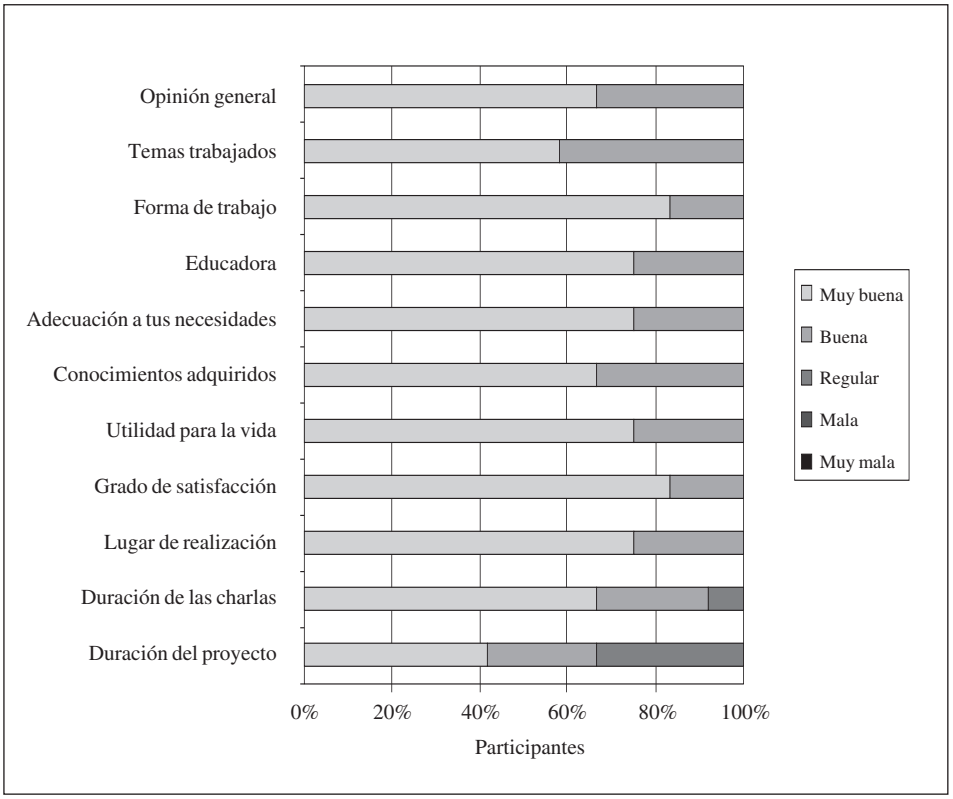

Fig. 1.—Valoración de los participantes sobre diferentes aspectos del programa de Educación Nutricional.

mentarias en personas mayores en un corto período de tiempo, ya que tienen costumbres muy arraigadas. En segundo lugar, los participantes ya mostraban al inicio un seguimiento bastante bueno del patrón de Dieta Mediterránea, con un promedio algo mayor de siete puntos sobre un total de catorce. No obstante aunque mejorar esta puntuación no parecía sencillo, se consiguió un incremento en la adhesión a dicho patrón dietético de forma significativa después de los tres meses de intervención, mediante las sesiones grupales y una sesión individual. Además, puesto que al inicio del estudio se constató que los participantes consumían grasas saludables con un alto consumo de aceite de oliva, durante la intervención se insistió más en la disminución del consumo de grasas saturadas, como carnes rojas o embutidos, que en incrementar el de grasas saludables.

Nuestros resultados son coherentes con estudios anteriores de intervención dietética[15,16], que consiguieron una disminución de la grasa total y un aumento del consumo de frutas y verduras, pescado y aceite de oliva. Asimismo, se puede afirmar que nuestros hallazgos son coincidentes con los obtenidos en el estudio PREDIMED, un ensayo aleatorizado multicéntrico realizado en España, en varones mayores de 55 años y mujeres mayores de 60 años con factores de riesgo cardiovascular con el objetivo de comprobar los efectos de la Dieta Mediterránea sobre la prevención primaria de la enfermedad cardiovascular[15]. Estos resultados muestran que los participantes mejoraron su adhesión a la Dieta Mediterránea, tras 12 meses de intervención promoviendo este patrón dietético, mediante sesiones de educación grupal e individual. Sin embargo, en este estudio mejoraron más aspectos de la dieta. Hay que tener en cuenta que en el estudio publicado por Zazpe y colaboradores[15], se obsequiaba a los participantes con aceite de oliva y frutos secos según el grupo de intervención al que fueron asignados, por lo que resulta más sencillo que mejorara el consumo de uno de estos alimentos.

En definitiva, el programa de Educación Nutricional, llevado a cabo con los residentes de los AT del Ayuntamiento de Pamplona, ha conseguido pequeñas mejoras en el patrón de Dieta Mediterránea, eficaz en la prevención primaria cardiovascular[7,9-11] y asociado a una mayor longevidad[9].

Sin embargo, el estudio presenta varias limitaciones. En primer lugar, la principal limitación es el pequeño tamaño de la muestra. La potencia estadística fue baja, pero debido a que se realizó en los AT del Ayuntamiento de Pamplona, no se pudo obtener un mayor número de participantes.

En segundo lugar, los participantes eran voluntarios, por lo que se presupone que tienen un mayor interés por mejorar su salud y aprender aspectos relacionados con la misma que el resto de residentes de los Apartamentos Tutelados a los que se ofreció el proyecto. El seguimiento se realizó a los tres meses siguientes de finalizar el programa de Educación, por tanto, para cerciorarse de que las mejoras obtenidas gracias al programa continúan a lo largo del tiempo, debería de volver evaluarse en un futuro. También es cierto que la adhesión inicial a la Dieta Mediterránea era inferior en el grupo de intervención que el grupo control, por lo que los participantes del grupo de intervención podían presentar una mejoría de mayor magnitud tras la intervención.

Por el contrario el estudio presenta varias fortalezas. En primer lugar, es un diseño cuasi-experimental llevado a cabo por la misma persona, lo que permite una mayor comparabilidad entre los grupos. Además, se trata de un estudio basado en una educación muy práctica para la vida real, con revisión de la alimentación de cada participante y con menús al alcance de todos los participantes y recetas sencillas que ellos mismos pueden preparar; siguiendo así una de las recomendaciones fundamentales para la promoción de la salud en la asistencia primaria.

Como resumen, y a pesar de las limitaciones encontradas, podemos afirmar que esta intervención ha conseguido ciertos cambios positivos en el autocuidado de los participantes y fue muy positivamente evaluado por los mismos.

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Original / *Cáncer*

The influence of nutritional status and disease on adiponectin and TNF-α levels in colorectal cancer patients

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Abstract

Background: **The aim of this study was to evaluate the association between adiponectin and tumor necrosis factor-α (TNF-α) serum levels in colorectal cancer (CRC) patients and compare these levels to clinical stage and nutritional status.**

Methods: **A total of 79 patients were enrolled in the study (39 with CRC and 40 in the control). Nutritional status was assessed by Patient-Generated Subjective Global Assessment (PG-SGA), body mass index (BMI), and phase angle (PhA). Adiponectin and TNF-α serum concentrations were determined using an enzyme-linked immunosorbent assay.**

Results: **Serum adiponectin levels were higher among CRC patients (p = 0.001). TNF-α serum levels were not significantly different between the groups, but patients with stage III or IV CRC had higher levels of TNF-α than those with lower stage disease (p = 0.037). The three tools used for the assessment of nutritional status (BMI, PhA, and PG-SGA) demonstrated that patients with a more severe nutritional deficit had higher adipocytokine levels, although these differences were significant only to TNF-α, when distributed PhA in tertiles.**

Conclusions: **Adiponectin levels were higher among CRC patients. Although TNF-α serum levels from CRC patients did not differ significantly to the control group, CRC patients with stage III or IV had higher levels compared to those with stage I and II tumors. Nutritional status, as determined by BMI, PhA, and PG-SGA, demonstrated that patients with a greatest nutritional deficit, had higher levels of adipocytokines; however, these differences were significant only for TNF-α, when distributed PhA in tertiles.**

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Key words: *Adipocytokines. Colorectal Cancer. Nutrition Assessment.*

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INFLUENCIA DEL ESTADO NUTRITIVO Y LA ENFERMEDAD SOBRE LAS CONCENTRACIONES DE ADIPONECTINA Y TNF-α EN PACIENTES CON CÁNCER COLORRECTAL

Resumen

Antecedentes: **El propósito de este estudio fue evaluar la asociación entre las concentraciones séricas de adiponectina y de factor de necrosis tumoral-α (TNF-α) en paciente con cáncer colorrectal (CCR) y comparar estas concentraciones con el estadio clínico y el estado nutritivo.**

Métodos: **Se reclutó a un total de 79 pacientes en el estudio (39 con CCR y 40 en el grupo control). Se evaluó el estado nutritivo mediante la Evaluación Global Subjetiva Generada por el Paciente (PG-SGA), el índice de masa corporal (IMC) y el ángulo de fase (AF). Se determinaron las concentraciones séricas de adiponectina y de TNF-α mediante un inmunoensayo de absorción ligado a enzima.**

Resultados: **Las concentraciones séricas de adiponectina fueron superiores en los pacientes con CCR (p = 0,001). Las concentraciones séricas de TNF-α no fueron significativamente distintas entre los grupos pero los pacientes con CC en estadios III o IV tuvieron mayores concentraciones de TNF-α que aquellos con un menor estadio de la enfermedad (p = 0,037). Las tres herramientas empleadas para evaluar el estado nutritivo (IMC, AF y PG–SGA) demostraron que los pacientes con un déficit nutricional más pronunciado presentaban mayores concentraciones de adipocitocina, aunque algunas diferencias sólo fueron significativas para el TNF-α cuanto se distribuyó el AF en terciles.**

Conclusiones: **Las concentraciones de adiponectina fueron superiores en pacientes con CCR. Aunque las concentraciones séricas de TNF-α de los pacientes con CCR no diferían significativamente de las del grupo control, los pacientes con CCR en estadios III o IV tuvieron concentraciones superiores en comparación con aquellos con tumores en estadios I y II. El estado nutritivo, determinado por IMC, AF y PG-SGA, demostró que los pacientes con un mayor déficit nutricional tenían concentraciones superiores de adipocitocinas; sin embargo, estas diferencias sólo fueron significativas para el TNF-α cuando el AF se distribuyó en terciles.**

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Palabras clave: *Adipocitocinas. Cáncer colorrectal Evaluación nutricional.*

Abbreviations

CRC: Colorectal cancer.
BMI: Body mass index.
PG-SGA: Patient-Generated Subjective Global Assessment.
SGA: Subjective Global Assessment.
PhA: phase angle.
TNF-α: Tumor necrosis factor-α.
TNM: Tumor-node-metastasis.
ELISA: Enzyme-linked immunosorbent assay.

Introduction

Colorectal cancer (CRC) has a complex etiology that includes the interaction of environmental and genetic factors. Recent studies reported that obesity is associated with an increased risk of CRC, although the mechanisms underlying this relationship remain to be fully elucidated[1]. Such mechanisms, however, include different distributions of body fat, alterations in hormonal status, obesity-related inflammation, and metabolic disturbances[2]. In particular, the increased adipose tissue in obesity causes an alteration of adipocytokine secretion, which may influence cancer initiation and progression[1,2]. Furthermore, there is evidence that several adipocytokines, (adiponectin, leptin, and TNF-α) have the potential to mediate the relationship between adiposity and colorectal neoplasma[3].

Tumor cells and tumor-associated leukocytes may also produce inflammatory cytokines such as TNF-α[4]. This cytokine has a possible role in all the steps involved in cancer initiation and progression, including cellular transformation, promotion, survival, proliferation, invasion, angiogenesis, and metastasis[4,5]. Additionally, TNF-α administration promptly lead to reduction of adiponectin expression and secretion[6]. Adiponectin may in turn induce anti-angiogenesis and anti-tumor activity[6]. Serum levels of adiponectin are associated with the activation of apoptotic enzymes in the caspase cascade, modulation of the expression of several apoptosis related genes in myelomonocytic cells, and reduction of tumor neovascularization[4].

Food intake and energy homeostasis are regulated by a complex network of peripheral mediators, including adipocytokines, changes in which can interfere with nutritional status[6]. Several studies demonstrated that adiponectin is inversely correlated with body weight.[7] and the decreased production of adiponectin in obese subjects can stimulate cancer progression through changes in insulin levels, inflammation, and angiogenesis[6-9]. However, the relationship between these cytokines or after weight loss in cancer patients has not been clearly established[7].

BMI, PhA, and PG-SGA are measures commonly used to determine nutritional status. BMI, which is easy to assess, has been the most widely used in epidemiological studies and clinical practice; however, it is relatively insensitive for the diagnosis of undernutrition[10-12]. PhA represents the electrical current stored by cell membranes[10], and its use has been studied in several diseases, including cancer[12,13]. The PG-SGA[14] is recommended as the standard method for the nutritional assessment of cancer patients by the Oncology Nutrition Dietetic Practice Group of the American Dietetic Association[15,16]. It identifies symptoms commonly seen during the treatment of cancer and includes a physical examination for the subjective assessment of nutritional status[16].

Some studies have demonstrated an association among adiponectin and TNF-α serum levels, nutritional status, and clinicopathological variables in CRC patients[17], but these studies involved heterogeneous patient groups and lacked a control group[7]. The aim of this study was to evaluate the association between adiponectin and TNF-α serum levels in CRC patients and determine if they are truly associated with the clinical stage and nutritional status.

Patients and methods

Subjects

This cross-sectional study involved outpatients treated by the Oncology Group from the Gastroenterology Division of the Federal University of Sao Paulo, between July 2010 and November 2011. The study was approved by the local Ethics Committee (Protocol 0826/10), and all patients signed an informed consent form. A total of 79 individuals were enrolled in the study, 39 of whom were CRC patients –the case group and 40 were healthy volunteers– the control group.

Data collection

Data on gender, age, treatment, site, and tumor stage were obtained from the medical records. The nutritional evaluation and collection of the blood sample for measuring adiponectin and TNF-α serum levels were performed at the same time. All patients were classified according to the tumor-node-metastasis (TNM) staging system[18].

BMI was calculated as weight (kg) divided by height (m^2). The subjects were classified according to the World Health Organization criteria[19] as undernourished (BMI < 18.5 kg/m^2), well nourished (BMI, 18.5-24.9 kg/m^2), and overweight/obese (BMI ≥ 25 kg/m^2).

The PhA was calculated as the ratio between resistance (R) and reactance (Xc), determined using the Biodynamics 450® bioimpedance analyzer with the standard protocol. R and Xc were measured directly in Ohms (Ω) at a single frequency of 50 kHz and 800 μA. The measurements were performed after at least 4 hours of fasting, with the patient lying in the supine position with his/her arms and legs extended to approxi-

mately 45° from the body. All procedures and controls for other variables affecting the validity, reproducibility, and precision of the measurements were performed according to the National Institutes of Health guidelines.[20] The PhA was calculated using the following equation: PhA = arctan (Xc/R) × (180/3.14).

The validated Portuguese version of the scored PG-SGA was used to assess nutritional status[21]. PG-SGA consists of two sections: in the first, information on weight history, food intake, nutrition impact symptoms, and functional capacity is collected, and in the second section, diagnosis, disease stage, age, components of metabolic demand (sepsis, neutropenic or tumor fever, corticosteroids), and physical examination were provided by the nutritionist. This analysis classified patients into three categories: (A) well-nourished, (B) moderately undernourished or suspected of being undernourished, and (C) severely undernourished.

Adipocytokine assays

Blood samples were collected in the morning in the fasting state. The serum samples were clotted and centrifuged at 2000 × *g* for 10 minutes and immediately frozen at –80° C for further analysis. Adipocytokine levels were measured using enzyme-linked immunosorbent assay (ELISA) kit (R&D Systems, MN, USA), adiponectin levels (with the sample diluted 4,000-fold) using the Duoset ELISA kit (DY1065), and TNF-α using the Quantikine ELISA kit (HSTA00D). The analytical methodology and technical procedures were performed according to the manufacturer's protocol.

Statistical analysis

The sample size had been calculated, considering the incidence of CCR in Brazil and the number of new cases in our Hospital.

Data are presented as percentages or mean ± SD. Differences between frequencies were assessed by chi-square test. Student's unpaired *t*-test and ANOVA test were used for normally distributed variables. Appropriate nonparametric tests (Mann Whitney *U*-test and Kruskal-Wallis test) were employed for all the other variables. The sample has been considered nonparametric for the study of adiponectin and TNF-alfa serum levels for the control and cancer group.

For the evaluation of PhA, a cutoff value was established for the population studied because of the lack of specific values for cancer patients. The PhA was divided by the distribution measured according to the proportion of observed frequencies for both groups. The data were separated into tertiles and values of the first tertile were defined as predictors of undernutrition. The analysis of variance was used to compare the classification of these tertiles for each group.

SPSS 20.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis, and values of $p < 0.05$ were considered statistically significant.

Results

There was no statistically significant difference with respect to gender, age and BMI between the groups. The majority of CRC patients had stage IV tumors (53.8%); 51.3% were not treated, 46.2% were undergoing chemotherapy, and 41% had undergone surgery for tumor resection (table I).

The mean serum levels of adiponectin were higher in CRC patients ($p = 0.001$) while TNF-α serum levels were similar between the groups ($p = 0.259$). Tumor stages I and II were analyzed together due to the small proportion of patients with stage I tumors. Compared to patients with stages I and II tumor, those with stage III or IV tumors had higher levels of TNF-α ($p = 0.037$) (table II).

The prevalence of moderate or severe undernutrition, as determined using the PG-SGA, was 69.2% in the case group. Only 7.7% of the CRC patients were undernourished as per their BMI, and none of the control group individuals were undernourished. No significant differences were found between the groups on

Table I
Characteristics of the patients in both groups

Parameters		*Case group*	*Control group*	*p*
Age	(yr ± SD)	61.0 ± 10.6	60.4 ± 9.2	0.765
Gender	Male	25 (64.1)	26 (65)	0.879
N (%)	Female	14 (35.9)	14 (35)	
Stage	I	2 (5.2)		
N (%)	II	5 (12.8)		
	III	11 (28.2)		
	IV	21 (53.8)		
BMI (mean ± SD)		23.9 ± 3.3	23.9 ± 2.4	0.893

Table II
Adiponectin and TNF-α segum levels among the groups and mean values according to the stage of disease for case group

Adipocytokine	*Case group (mean ± SD)*	*Control group (mean ± SD)*	*p**	*STAGE I and II mean ± SD*	*STAGE III and IV mean ± SD*	*p**
Adiponectin (μg/mL)	4.6 ± 2.1	3.6 ± 2.5	0.001	3.9 ± 1.1	4.8 ± 2.3	0.314
TNF-α (pg/mL)	3.7 ± 7.3	3.6 ± 5.1	0.259	1.2 ± 0.7	4.2 ± 7.9	0.037

* Mann Whitney.

the basis of PhA, although more subjects in the case group were in the first tertile (table III).

The mean of adiponectin (p = 0.337) and TNF-α (p = 0.128) levels was higher in undernourished cancer patients than in the other subjects; however, these differences were not significant. Difference on adiponectin level was observed between the groups according to the BMI classification only among the normal weight subjects (p = 0.009) (table IV).

The mean serum level of adiponectin (p = 0.073) and TNF-α (p = 0.005) in the case group was higher among patients in the first tertile of PhA; however, these differences were significant only TNF-α (table V).

Furthermore, based on the PG-SGA, there was no difference in adipocytokine levels between groups, even with the higher number of patients judged to be moderately or severely undernourished by this method (table VI).

Table III
Nutritional assessment results: BMI categories, Patient-Generated Subjective Global Assessment (PG-SGA) categories and phase angle in both groups

Parameters	*Case group*	*Control group*	*p*
BMI (kg/m²)	N (%)	N (%)	0.062
Undernourished (<18.5 kg/m²)	3 (7.7)	0 (0)	
Normal weight (18.5-24.9 kg/m²)	21 (53.8)	30 (75.0)	
Overweight/Obesity (≥ 25 kg/m²)	15 (38.5)	10 (25.0)	
PG – SGA	N (%)		
Severely Undernourished	3 (7.7)		
Moderately Undernourished	24 (61.5)		
Well Nourished	12 (30.8)		
Phase Angle	Mean ± SD (N)		
First tertile	5.1 ± 0.6 (n = 20)	6.0 ± 0.4 (n = 5)	0.161
Second tertile	6.4 ± 0.3 (n = 11)	6.8 ± 0.1 (n = 15)	0.294
Thirth tertile	7.6 ± 0.4 (n = 8)	7.8 ± 0.6 (n = 20)	0.794

Table IV
Adiponectin and TNF-α serum levels in both groups according to the BMI classification

BMI		*Case group mean ± SD*	*Control group mean ± SD*	*p**
Undernourished (<18.5 kg/m²)	Adiponectin	6.4 ± 1.7 (n = 3)		
	TNF-α	9.8 ± 14.8 (n = 3)		
Normal weight (18.5-24.9 kg/m²)	Adiponectin	4.3 ± 1.3 (n = 21)	3.6 ± 2.7 (n = 30)	0.009
	TNF-α	2.3 ± 1.8 (n = 21)	4.1 ± 5.8 (n = 30)	0.559
Overweight/Obesity (BMI ≥ 25 kg/m²)**	Adiponectin	4.8 ± 2.9 (n = 15)	3.4 ± 1.7 (n = 10)	0.292
	TNF-α	4.4 ± 9.8 (n = 15)	2.2 ± 1.9 (n = 10)	0.375

**The maximum value observed was 32,8 kg/m² in Case Group and 29,5 kg/m² in Control Group.
* Mann Whitney.

Table V
Adiponectin and TNF-α serum levels and percentiles of PhA in both groups

PhA		*Case group mean ± SD*	*Control group mean ± SD*	*p**
First tertile	Adiponectin	5.2 ± 2.5 (n = 20)	6.2 ± 5.5 (n = 5)	0.634
	TNF-α	5.9 ± 9.7 (n = 20)	3.5 ± 4.1 (n = 5)	0.812
Second tertile	Adiponectin	4.10 ± 1.1 (n = 11)	3.26 ± 2.0 (n = 15)	0.411
	TNF-α	1.3 ± 0.7 (n = 11)	5.1 ± 7.5 (n = 15)	0.055
Third tertile	Adiponectin	3.9 ± 1.8 (n = 8)	2.9 ± 1.2 (n = 20)	0.172
	TNF-α	1.2 ± 0.7 (n = 8)	2.6 ± 2.6 (n = 20)	0.036

* Mann Whitney.

Table VI
Adiponectin and TNF-α according to the PG-SGA in case group

PG-SGA		*Case group mean ± SD*	*p**
Well nourished	Adiponectin	4.9 ± 3.3 (n = 12)	0.762
Moderately undernourished	Adiponectin	4.4 ± 1.2 (n = 24)	
Severely undernourished	Adiponectin	5.3 ± 2.7 (n = 3)	
Well nourished	TNF-α	4.4 ± 10.8 (n = 12)	0.225
Moderately undernourished	TNF-α	2.4 ± 2.4 (n = 24)	
Severely undernourished	TNF-α	10.3 ± 14.5 (n = 3)	

*Kruskal-Wallis.

Discussion

To our knowledge, this is the first study to investigate the relationship between nutritional status determined using 3 different parameters (BMI, PhA, and PG-SGA) and serum levels of adiponectin and TNF-α in CRC patients. Among the CRC patients, the adipocytokine levels were also compared with the clinical stage.

We found that patients in the case group had higher serum levels of adiponectin. When compared to BMI, this difference was observed in patients with normal weight. Gonullu et al[22], in contrast, reported a lower level of adiponectin in CRC patients than in a control group (5.5 ± 5.2 μg/mL *vs* 6.2 ± 3.0 μg/mL, p = 0.030), although these groups exhibited no overall difference in BMI. These differences among the studies might reflect a higher proportion of undernourished individuals in the case group included in our study, and the inclusion of individuals with morbid obesity in the study of Gonullu et al.[22]

Adiponectin serum levels are inversely correlated with body weight in non-cancer patients, with low levels commonly observed in obese subjects[7,8]. Hillenbrand et al[8] found lower levels of adiponectin in obese patients without cancer, compared to those with CRC. Low adiponectin levels have also been described in advanced lung cancer patients with severe weight loss[9]. However, this correlation between weight loss in patients with lung or intestine cancer and adiponectin levels described by these authors[8,9] was not confirmed in a further independent study[17]. In our study, the adiponectin levels were higher in malnourished CRC patients, as classified by BMI, compared to those with a BMI ≥ 18.5 mg/m^2, but this difference was not statistically significant. The means were not compared for different categories within the control group because there were no undernourished control subjects. The different findings of our study and some previously published studies might be due to the different nutritional status of the enrolled patients.

We also found that patients with a stage III or IV tumor had higher serum adiponectin levels than patients with stage I and II tumors, although this difference was not significant. Gonullu el al [22] found higher serum levels of this adipokine in stage II cancer patients than in those with stage IV tumors (7.58 ± 5.0 μg/mL *vs* 1.92 ± 2.09 μg/mL). In contrast, Kumor et al[6] did not find an association between the serum concentration of adiponectin and the clinical stage.

TNF-α is considered an important promoter of various cytokines, and it has a known role in chronic inflammation, angiogenesis, tissue remodeling, tumor growth, and metastasis[23,24]. Paradoxically, this cytokine may also have a pro-apoptotic action, promote inhibition of tumor angiogenesis, and activate anti-tumor im-

munity[4]. Studies have shown that excess TNF-α can cause organ dysfunction and progression of cancer, including gastrointestinal tumors.[4,25,26] TNF-α increases lipolysis in adipocytes and consequently, the levels of circulating free fatty acids.[27] An overweight condition represents an expansion of the adipose tissue with an increased production of inflammatory factors and cytokines, especially TNF-α, which plays an important role in the pathophysiology of obesity.[4,26] In this study, we found no significant difference in serum TNF-α levels between the groups, in agreement with the findings of a previous study[28], although Guadagni et al[29] found higher serum levels of TNF-α in cancer patients.

We also found that serum values of TNF-α were higher among patients with advanced disease (stage III and IV). These findings were similar to those described by Guadagni et al[29], who also found higher TNF-α levels in patients with metastatic CRC. These results confirm that TNF-α may be involved in cancer progression.[8] In findings similar to those for adiponectin, TNF-α serum levels in malnourished CRC patients were also higher, although not significantly higher, than those in the non-cancer controls. Similarly, Hillenbrand et al[8] found a slight but not statistically significant elevation of TNF-α in CRC patients with a median BMI ≤ 27.1 kg/m^2 compared to obese or healthy controls.

In addition to the BMI, adipokine levels also associated with PhA and PG-SGA. PhA has been shown to provide a good estimate of the body compartment and can be used as a nutritional marker[30,31]. The levels of adiponectin and TNF-α with respect to different tertiles showed that the cancer patients in the first tertile had higher levels of adiponectin, however only TNF-α levels were significant. Similar findings were observed in relation to BMI, whereby malnourished patients had higher levels of adipokines; however, these differences were not statistically significant. These results suggest that worse nutritional status may cause higher levels of adiponectin and TNF-α.

A recent study in our institution using PG-SGA found that this was the method with a higher sensibility for determining nutritional status in CRC patients[32]. However when analyzed the PG-SGA classification with adipocytokines, no differences were observed among the groups, although these adipocytokines in undernourished patients was higher than in well nourished. Correia et al[33] reported that gastric cancer patients with TNF-α serum levels in excess of 8.72 pg/mL had a higher risk of malnutrition, according to the PG-SGA.

This study has some limitations, including the small number of CRC patients and the inclusion of underweight subjects in the case group. Although the control group consisted of individuals without cancer or gastrointestinal disease, the mean age of these subjects, matching that of the case group, may have favored the inclusion of individuals with inflammatory conditions, such as atherosclerosis and type II diabetes, which can also affect the serum levels of adipokines. The differences between serum levels of adiponectin and TNF-α in some studies may be a consequence of the variation of this cytokine with clinical stage and body weight.

In summary, the serum level of adipocytokine may be elevated in CRC patients, and we found that serum adiponectin levels were higher among CRC patients. TNF-α serum levels did not differ significantly between CRC patients and control subjects, but patients with stage III or IV CRC had higher levels compared to those with stage I and II tumors. The three measures used to indicate nutritional status (BMI, PhA, and PG-SGA) demonstrated that patients with a greater nutritional deficit had, on an average, higher levels of adipocytokines; however, these differences were not significant. Further studies with a greater number of patients are necessary to fully elucidate the relationship between adiponectin and TNF-α levels and the nutritional status and disease stage of CRC patients, and to determinate the pathophysiological role of adipokines in this cancer.

Conflict of Interest Statement

The authors have not declared any conflicts of interest.

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Original / *Deporte y ejercicio*

Estudio piloto de la efectividad de una intervención basada en juegos sobre el estado nutricional y la fuerza muscular en niños

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Resumen

Introducción: **La malnutrición por exceso es una constante en países en vías de desarrollo, Chile no es una excepción ya que existe una marcada tendencia hacia el sobrepeso y obesidad en la población escolar. La fuerza muscular ha sido asociada con un adecuado estado de salud cardiovascular y metabólica en la población escolar. Se necesitan intervenciones efectivas, que utilicen herramientas lúdicas y que permitan mejorar el estado nutricional y la capacidad física de los escolares.**

Objetivo: **Valorar la efectividad de una intervención basada en juegos realizados dentro de la jornada escolar de los niños para mejorar el estado nutricional y la fuerza muscular.**

Método: **156 escolares de 7 a 15 años, pertenecientes a dos colegios municipalizados con jornada escolar completa, participaron de un programa piloto basado en juegos recreativos dinámico durante 45 minutos de lunes a viernes durante 3 meses, en el recreo más extenso de la jornada escolar.**

Resultados: **Al finalizar la intervención se observó una modificación estadísticamente significativa en el estado nutricional, donde destaca un aumento de niños que alcanza el estado nutricional normal. En aquellos que fueron clasificados previamente como obesos se logra modificar su estado nutricional hacia sobrepeso ($p < 0,001$). Se observó una disminución de la fuerza muscular del tren inferior al término del estudio ($p < 0,001$).**

Conclusiones: **Se demostró el impacto positivo de una intervención basada en juegos recreativos dinámicos durante los recreos escolares, con modificación positiva en el estado nutricional, pero sin mejoría de la fuerza muscular de los escolares.**

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Palabras clave: *Obesidad infantil. Desorden nutricional en niños. Actividad física. Fuerza muscular.*

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PILOT STUDY ABOUT THE EFFECTIVITY OF AN INTERVENTION BASED ON GAMES IN NUTRITIONAL STATUS AND MUSCLE STRENGTH ON CHILDREN

Abstract

Introduction: **The overnutrition is a constant on developing countries; Chile is not an exception because it has a marked tendency to overweight and obesity in schoolchildren. The muscular strength has been associated with cardiovascular and metabolic health status in scholars. Effective interventions using games are needed to improve the nutritional status and physical fitness in school children.**

Objective: **To assess the intervention effectiveness based on games played at school time to improve the nutritional status and physical fitness in schoolchildren.**

Method: **156 students aged between 7 to 15 years, attending to two public schools with full school day, to which a pilot program was applied. This pilot program was based on dynamic recreational games during 45 minutes from monday to friday for 3 months in the largest playtime of the school day.**

Results: **At the end of the intervention, we observed a significant modification on children nutritional status, which highlights an increase in the number of children that reached the normal nutritional status ($p < 0.001$). We also observed a significant number of obese children who reached overweight nutritional status ($p < 0.001$). We also observed a decrease of leg muscular strength at the end of the study.**

Conclusions: **We found a positive effect of a program based on dynamic recreational games in the largest school playtime, improving nutritional status. However, we didn't observed modifications in the muscular strength.**

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Key words: *Childhood obesity. Child nutrition disorders. Physical activity. Muscle strength.*

Introducción

La obesidad es un problema de salud pública a nivel mundial y la importancia de ser estudiada y controlada durante la niñez y adolescencia está fundamentada en su impacto biopsicosocial[1,2]. En Chile la prevalencia de obesidad infantil se incrementa año tras año, así los escolares de 6 años que ingresaron a primer año de educación primaria en el año 2004, presentaron una prevalencia de obesidad de 17,3%, mientras que en los preescolares asistentes a jardines de la Junta Nacional de Jardines Infantiles, fue 10,6% en el año 2005[3]. En el año 2011 se ha visto que los menores de 6 años presentan un 21,7% de obesidad y los escolares de educación primaria un 22,1%[4].

En la población infantil, un mayor nivel de fuerza muscular y de masa libre de grasa, se han asociado con mejor salud cardiovascular y con niveles altos de contenido mineral óseo[5]. Adicionalmente se ha demostrado que los ejercicios de contra-resistencia incrementan el tamaño de las fibras musculares, la fuerza muscular y la función neuromuscular, contribuyendo a disminuir el tejido adiposo a nivel abdominal[6,7]. La relación entre fuerza muscular y salud infantil se ha explicado por el aumento de la fuerza muscular, la cual permite mantener un adecuado control del metabolismo energético, habiéndose demostrado que una mayor masa muscular es capaz de producir un mayor gasto energético, tanto en una condición de reposo, como durante la realización de ejercicio físico[8]. Un adecuado nivel de masa libre de grasa permite la realización de las actividades de la vida diaria[9], además de preservar y prevenir patologías en la edad adulta[10] tales como osteoporosis, osteoartritis y sarcopenia[7].

En adultos, la dosis-respuesta apropiada para generar una adaptación en el tejido muscular, ha sido dilucidada considerando la duración, la frecuencia semanal, el tipo de actividad y la intensidad del trabajo físico, siendo esta última la variable más importante para inducir los cambios metabólicos[11,12]. Para niños y adolescentes la Organización Mundial de la Salud (OMS) señala en sus guías de actividad física para la población de 6 a 17 años que este grupo etario debe realizar actividad física de moderada a vigorosa por lo menos 60 minutos al día, los 7 días de la semana[13]. Sin embargo, para lograr esta recomendación se requiere de iniciativas novedosas y atractivas para esta población, dónde se debe analizar el lugar más apropiado para aumentar el nivel de actividad física, es así como el colegio surge como una buena alternativa para implementar programas que incrementen el gasto energético de los estudiantes. El objetivo de este artículo es valorar la efectividad de una intervención basada en juegos, realizados dentro de la jornada escolar para mejorar el estado nutricional y la fuerza muscular.

Material y método

Selección de la muestra

En este estudio piloto se realizó una intervención con un plan de actividad física basada en juegos, realizados 5 días a la semana durante 12 semanas, al interior de dos establecimientos educacionales municipalizados de enseñanza básica, con jornada escolar completa, pertenecientes a la comuna de Llanquihue (Chile) durante el recreo de mayor duración (45 minutos). El diseño de este estudio es cuasi-experimental, con pre y post *test*, sin grupo control.

La selección de la muestra fue por conveniencia, 2 escuelas fueron invitadas a participar y a su vez se invitó a los padres y alumnos a participar de manera voluntaria. Comenzaron el estudio 160 sujetos, de los cuales 4 abandonaron el estudio, por lo tanto el análisis se realizó con 156 niños (64 mujeres y 92 hombres) con edades entre los 7 y 15 años.

Los criterios de exclusión del estudio fueron: embarazo, lesión músculo-tendinosa y cualquier patología que impidiera la realización de actividad física. El protocolo de estudio fue aprobado por el Comité de Ética e Investigación en Seres Humanos de la Facultad de Medicina de la Universidad de Chile (registro 125-2012).

Evaluación del estado nutricional

En el establecimiento educacional, se evaluó el peso corporal (kg), con una balanza digital (TANITA, HD 313, EEUU); la estatura (m) fue determinada utilizando un estadiómetro. El cálculo del índice de masa corporal (IMC) se realizó de acuerdo a la fórmula: peso (kg)/[estatura (m)]^2. Los protocolos de medición utilizados corresponden a la norma técnica chilena[14], para determinar su peso el niño o adolescente debe estar descalzo, con un mínimo de ropa, para determinar su estatura se situó descalzo sobre un piso plano y horizontal, de espalda al instrumento de medición, manteniendo la cabeza cómodamente erguida. El estado nutricional se clasificó por el Z-IMC según OMS[15], para esto se consideró la maduración sexual, la que fue establecida por auto-reporte utilizando las fotografías de los estadios de maduración puberal.

Evaluación de fuerza muscular

Para la evaluación de la fuerza muscular en niños han sido propuestas diferentes pruebas físicas. En el caso de las extremidades superiores, se utilizó la prueba de dinamometría manual (DM) que tiene por objeto evaluar la prensión máxima de ambas manos. Esta prueba es válida y confiable para esta población[17,18], antes de su aplicación es necesario considerar el tamaño de la mano y el género[19,20]. Se utilizó un dinamómetro modelo Smedley de 100 kg (TTM, Tokio), mantenien-

do el brazo al costado del cuerpo, con el codo extendido manteniendo la prensión máxima por dos segundos, tanto con la mano derecha como con la izquierda. Para el análisis se consideró el mayor valor de prensión obtenida en ambas manos y luego estos valores se promediaron[5,21,22]. La fuerza fue además expresada en términos relativos al peso corporal, como un cociente[21] (CDM). En cuanto a la evaluación de la fuerza de las extremidades inferiores, se utilizó la prueba de salto largo a pies juntos[9,17,18,21,22,24-26], la que consiste en saltar de manera horizontal desde una línea delimitada la mayor distancia posible con los pies juntos, se realizaron tres intentos y fue considerado el mejor salto alcanzado (SM). Además la fuerza se expresó en términos relativos a la estatura, como un cociente[23] (CSM).

Característica de la intervención

Esta fue una intervención piloto, basada en juegos recreativos, pre-deportivos y deportivos dinámicos que involucrasen todos los segmentos corporales. Esta intervención se realizó en un contexto lúdico, durante el recreo más extenso de las 2 escuelas, con una duración de 45 minutos los 5 días hábiles de la semana.

Análisis estadístico

Los resultados fueron sometidos a análisis estadístico descriptivo e inferencial, siendo aplicada la prueba de normalidad de Shapiro Wilk a las variables cuantitativas. Para determinar las diferencias pre y post test, se utilizó la prueba de Wilcoxon para muestras pareadas. Para comparar las modificaciones del estado nutricional se utilizó la prueba de simetría.

Las diferencias fueron consideradas estadísticamente significativas toda vez que $p < 0,05$. Estos análisis fueron realizados con el programa estadístico STATA 12,1 (Stata Corp, College Station, TX).

Resultados

Se estudiaron 156 niños (64 mujeres y 92 varones). Los que se distribuyeron al inicio del estudio en categorías de peso normal (n = 21), sobrepeso (n = 20) y obesidad (n = 115), no habiéndose encontrado individuos con déficit nutricional. Se observó una disminución de la frecuencia de obesidad desde 73% al inicio a 64% al final del estudio, y además se encontró un aumento del número de niños con un peso apropiado desde un 13,5% inicial a un 21,2% al finalizar la intervención ($p < 0,001$), además se observó que en los niños que presentaban sobrepeso al inicio del estudio (12,8%), la mitad de ellos (n = 10) finalizaron el estudio con peso normal y sólo uno de ellos empeoró su condición de salud y finalizó el estudio en el grupo de los niños con obesidad ($p < 0,001$) (tabla I).

En la tabla II, se presentan los resultados de todos los participantes del estudio antes y después de la intervención. Se observa una disminución de la fuerza muscular específicamente en la prueba de SM, que es estadísticamente significativa ($p < 0,001$).

En la tabla III, se presentan los datos agrupados por género, en las variables antropométricas no se observan diferencias entre hombres y mujeres, destacando en los hombres un aumento significativo para el peso corporal ($p = 0,013$), y la estatura ($p < 0,001$), sin presentarse estas diferencias en las mujeres. Respecto al IMC se presentan diferencias por género, donde las mujeres presentaron un mayor IMC en comparación con los varones tanto al inicio ($p = 0,021$) como al término de la intervención ($p = 0,030$). En cuanto a la fuerza muscular y analizando por género la prueba de DM, los hombres presentaron mayor fuerza máxima al inicio de la intervención en comparación con las niñas ($p = 0,040$). Sin embargo, no se observaron diferencias significativas al término del estudio, el CDM se comportó de manera similar a la fuerza absoluta al analizar por género, donde los varones presentaron un mayor cociente tanto al inicio ($p = 0,040$) como al término de la intervención ($p = 0,044$), lo mismo que fue observado para SM y CSM tanto al inicio como al término de la intervención ($p < 0,001$).

Discusión

Se observó un aumento significativo del peso corporal y la estatura durante el período de la intervención, pero al analizarse por IMC y categorizando por el puntaje Z del

Tabla I
Movilidad del estado nutricional pre y post intervención

	Total	*Estado nutricional post-intervención*			
Estado nutricional pre-intervención	*Pre-intervención*	*Peso normal*	*Sobrepeso*	*Obesidad*	*p value*
Peso normal	21 (13,5)	21 (13,5)	0	0	
Sobrepeso	20 (12,8)	10 (6,4)	9 (5,8)	1(0,6)	
Obesidad	115 (73,7)	2 (1,3)	14 (8,9)	99 (63,5)	
Total	156 (100)	33 (21,2)	23 (14,7)	100 (64,1)	<0,001

Número de sujetos como valor absoluto y cómo % entre paréntesis, prueba de Simetría para calcular valor de *p*.

Tabla II
Características de la muestra pre y post intervención

	Pre		*Post*		
	Mediana	*Percentil 25-75*	*Mediana*	*Percentil 25-75*	*p value*
Peso (kg)	47,5	35,4-62,3	48,4	36,9-62,6	< 0,001
Estatura (m)	1,42	1,30-1,53	1,43	1,31-1,54	< 0,001
IMC (kg/m^2)	23,6	19,9-27,6	23,7	19,9-27,8	< 0,05
Perímetro de cintura (cm)	73,0	65,5-81,0	74,1	66,0-84,5	0,057
DM (kg)	18,0	13,9-24,9	18,5	13,2-25,4	0,413
CDM	0,39	0,33-0,46	0,39	0,31-0,48	0,764
SM	117	103-140	115,5	101-136	< 0,001
CSM	0,84	0,76-1,02	0,81	0,74-0,98	< 0,001

DM: Dinamometría de mano (kg), CDM: Cociente dinamometría mano (DM (kg)/peso (kg)), SM: salto máximo (cm), CSM: Cociente de salto máximo (SM (cm)/estatura (cm), Test de Wilcoxon para calcular valor de *p*.

Tabla III
Características al inicio y el término del estudio por género

	Pre intervención			*Post intervención*		
Media (desviación estándar)	*Mujeres (n = 64)*	*Varones (n = 92)*	*p value*	*Mujeres (n = 64)*	*Varones (n = 92)*	*p value*
Peso (kg)	50,9 (17,1)	49,5 (18,4)[a]	0,435	51,4 (17,3)	50,2 (18,7)[b]	0,527
Estatura (m)	1,40 (0,13)	1,43 (0,16) [a]	0,303	1,41 (0,13)	1,45 (0,16)[b]	0,272
IMC (kg/m^2)	15,1 (5,3)	13,4 (5,4)	0,021	15,1 (5,4)	13,1 (5,1)	0,030
Perímetro de cintura (cm)	74,3 (11,3)	73,6 (12,2)	0,535	72,7 (21,7)	70,6 (23,9)	0,257
DM (kg)	10,8 (8,0)	18,0 (6,3)	0,040	11,3 (9,9)	18,3 (7,1)	0,044
CDM	0,36 (0,10)	0,43 (0,11)	0,004	0,36 (0,10)	0,43 (0,14)	0,004
SM (cm)	110,8 (11,1)[a]	134,3 (34,6)[a]	< 0,001	108,9 (11,0)[b]	131,0 (34,0)[b]	< 0,001
CSM	0,79 (0,15)[a]	0,93 (0,10)[a]	< 0,001	0,77 (0,15)[b]	0,90 (0,10)[b]	< 0,001

DM: Dinamometría de mano (kg), CDM: Cociente dinamometría mano (DM (kg)/peso (kg)), SM: salto máximo (cm), CSM: Cociente de salto máximo (SM (cm)/estatura (cm)), [a; b]: diferencia significativa sobre el mismo género comparando entre pre y post intervención con un valor de $p < 0,05$.

IMC, se observó un cambio positivo hacia la categoría de peso normal. Cuando se analizó la información por género se observó que los varones son los que muestran una mayor movilidad entre las categorías de IMC. Sin embargo, los niños que continuaron en la categoría de obesidad se hicieron aún más obesos, aumentando su perímetro de cintura de manera significativa, además del peso corporal e IMC. Esta situación es compleja desde el punto de vista sanitario porque los niños obesos tienen mayor riesgo de padecer enfermedades crónicas no transmisibles como diabetes tipo 2[27], dislipidemias y osteoartritis, entre otras patologías, habiéndose demostrado que el riesgo de padecerlas se duplica en los que tuvieron exceso de peso en la niñez y es aún mayor si éste se mantuvo en la adolescencia[28]. Nguyen y cols, en el año 2010[29], encontraron una relación directa entre diabetes mellitus tipo 2 y obesidad donde un 80,3% de los diabéticos desarrolló previamente sobrepeso u obesidad.

En las mujeres, se observó un aumento significativo del perímetro de cintura al término del estudio, este hecho puede estar influenciado por el crecimiento. Sin embargo, estudios prospectivos han demostrado que el aumento de la grasa abdominal actúa como un factor de riesgo independiente para el desarrollo de diabetes tipo 2 y de enfermedades cardiovasculares, tales como hipertensión, enfermedad coronaria y accidentes cerebrovasculares[30,31], situación que ha sido observada en niños y adolescentes en distintos estudios[32,33,34]. Una debilidad de la presente intervención piloto es que en ella sólo se intervino en la cantidad de actividad física realizada en el contexto escolar, dejando sin control la dieta y la actividad física en el tiempo libre.

La fuerza muscular tanto en mujeres como en varones mostró una disminución en extremidades inferiores. Este hecho pudiera estar más asociado al mayor peso corporal de los niños. Otra causa de este fenómeno podría radicarse en una desmotivación presentada por los alumnos con obesidad al realizar los juegos y las evaluaciones de la condición física junto con sus compañeros. En este trabajo además se expresaron los valores de fuerza muscular como cocientes[23], lo que sería una forma más adecuada de expresar la fuerza en grupos con diferentes estados nutricionales, porque ha sido demostrado que niños con sobrepeso u obesidad presentan mayor nivel de fuerza absoluta[22], por tanto la utilización de este cociente sería más adecuado para realizar un tamizaje de una población. Esto es relevante debido a que en adultos se ha demostrado que la fuerza

máxima de la extremidad superior es un potente predictor de morbilidad y mortalidad[35, 36].

El hecho más preocupante e interesante como línea de estudio es que los niños que continuaron siendo obesos aumentaron su IMC y perímetro de cintura (datos no presentados en la presente investigación). Por lo anterior es probable que un programa de intervención en niños obesos muestre mejores resultados si es que se realiza con apoyo clínico especializado y con intensidades de trabajo programadas individualmente, de acuerdo a la condición física de cada niño.

Durante este estudio, se observó un efecto positivo sobre el estado nutricional de los niños, aumentando la proporción de niños con peso normal. Una de las limitaciones del estudio es que se desarrolló en los momentos de tiempo libre de los niños, los cuales constituyen un espacio de esparcimiento y donde los niños podían decidir el hecho de participar o no en las actividades propuestas. Por lo anterior, es posible que este tipo de intervención pueda ser más exitoso si se aplica como una actividad dentro del currículum, junto con una intervención en educación alimentaria que incluya a los niños con sus padres y/o apoderados.

Conclusión

Durante las 12 semanas en que se efectuó una intervención en los recreos escolares durante 45 minutos, basada en juegos recreativos dinámicos, se observó una modificación positiva en el estado nutricional de los escolares. No se observaron cambios significativos en la fuerza muscular después del periodo de intervención.

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Original / *Valoración nutricional*

Diseño y validación de un cuestionario para evaluar el comportamiento alimentario en estudiantes mexicanos del área de la salud

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Resumen

Introducción: **El comportamiento alimentario (CA), que establece la relación del ser humano con los alimentos, influye en el consumo de nutrimentos y por tanto contribuye al estado de salud o enfermedad de la población, incluso en jóvenes universitarios. Existen algunos instrumentos validados para evaluar el consumo de alimentos y nutrimentos, pero son escasos los que valoran el CA.**

Objetivo: **Diseñar y validar un cuestionario para valorar el CA en estudiantes universitarios mexicanos.**

Métodos: **Con base en la literatura existente y se diseñó un cuestionario para evaluar el CA. Se determinó su lógica y validez de contenido mediante la evaluación por expertos. Se aplicó en dos ocasiones con un intervalo de 4 semanas a 333 estudiantes del sexto semestre de dos licenciaturas (Medicina y Nutrición) de la Universidad de Guadalajara. Se determinó su reproducibilidad mediante el coeficiente de correlación intraclase. Su validez de constructo y consistencia interna se calculó a través del análisis Rasch, tanto para la dificultad de los ítems como para la habilidad de los sujetos.**

Resultados: **El cuestionario quedó integrado por 31 preguntas con opción de respuesta múltiple. El coeficiente de correlación intraclase fue de 0,76 para la reproducibilidad del instrumento. Se obtuvo un alfa de Cronbach de 0,50 para la habilidad de los sujetos y de 0,98 para la consistencia interna de los ítems. El 87,1% de los sujetos y el 89,8% de los ítems tuvieron valores de INFIT y OUTFIT dentro de los valores aceptables.**

Conclusiones: **El presente cuestionario tiene el potencial de medir a bajo costo y de forma práctica aspectos del CA en universitarios, con el propósito de establecer o dar seguimiento a acciones correctivas o preventivas.**

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Palabras clave: *Comportamiento alimentario. Hábitos de alimentación. Estudiantes. Cuestionario. Validación.*

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DESIGN AND VALIDATION OF A QUESTIONNAIRE TO ASSESS DIETARY BEHAVIOR IN MEXICAN STUDENTS IN THE AREA OF HEALTH

Abstract

Introduction: **The dietary behavior (DB) establishes the relationship between the human being and foods and has an influence on nutrient intake and, therefore, it contributes to the health or disease status of a population, even among college students. There exit some validated instruments to assess food and nutrients intake, but there are very few assessing DB.**

Objective: **To design and validate a questionnaire to assess DB in Mexican college students.**

Methods: **According to the literature and Reasoned Theory, a questionnaire assessing DB was designed. Its logic and content validity was determined by expert assessment. It was applied on two occasions with a 4-week interval to 333 students from the University of Guadalajara coursing the sixth semester of Medicine or Nutrition. The reproducibility was assessed by means of the interclass correlation coefficient. The construct validity and the internal consistency were calculated by Rasch analysis, for both the difficulty of the items and the subjects' capability.**

Results: **The questionnaire finally included 31 questions with multiple choice answers. The interclass correlation coefficient of the instrument was 0.76. The Cronbach alpha was 0.50 for the subjects' capability and 0.98 for the internal consistency of the items. 87.1% of the subjects and 89.8% of the items had INFIT and OUTFIT values within acceptable limits.**

Conclusions: **The present questionnaire has the potentiality of measuring at low cost and in a practical way aspects related with DB in college student with the aim of establishing or following-up corrective or preventive actions.**

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Key words: *Dietary behavior. Dietary habits. Students. Questionnaire. Validation.*

Abreviaturas

CA: Comportamiento alimentario.
CUCS: Centro Universitario de Ciencias de la Salud.
TRI: Teoría de Respuesta al Ítem.
INFIT: Ajuste cercano.
OUTFIT: Ajuste lejano.
MNSQ: Media cuadrática sin estandarizar.
ZSTD: Media cuadrática estandarizada.
UdG: Universidad de Guadalajara.

Introducción

Las alteraciones metabólicas se presentan cada vez a edades más tempranas y favorecen el desarrollo de enfermedades crónicas degenerativas, cuyas complicaciones se encuentran entre las tres primeras causas de muerte a nivel mundial, tanto en países desarrollados como en vías de desarrollo[1].

En los últimos años, la evidencia científica ha mostrado que la alimentación juega un papel determinante en el proceso salud-enfermedad. Tanto la ingestión de ciertos alimentos y nutrimentos, como la práctica de algunos comportamientos alimentarios, pueden favorecer o prevenir alteraciones a nivel metabólico y, por lo tanto, contribuir al desarrollo o prevención de enfermedades crónicas no transmisibles[2-5]. Por ello, es importante evaluar de manera estandarizada la ingestión nutrimental, así como el comportamiento alimentario (CA). El CA es un conjunto de acciones asociadas a la manera de alimentarse, que incluye el qué, cómo, por qué y para qué se ingieren determinados alimentos. Por tanto, este concepto comprende la selección, preparación, preferencias de ingestión de alimentos, creencias y horarios en la toma de los alimentos, entre otros[6-8].

Existen diferentes instrumentos para estudiar la alimentación. Sin embargo, la mayoría de ellos se enfocan a la determinación del consumo de alimentos y/o nutrimentos de forma cuantitativa pero no incluyen específicamente aspectos del CA de los sujetos[9-11]. La información nutricional cuantitativa obtenida a través de los instrumentos ya existentes, sumada a la valoración del CA, permitirá el estudio del proceso alimentario y nutricional de forma más integral. Esto puede facilitar el diseño y la dirección de intervenciones dietéticas y nutricionales específicas, con el propósito de que sean eficaces para lograr una alimentación más saludable, tanto a nivel individual como en grupos poblacionales.

Actualmente, los jóvenes son una población de riesgo para desarrollar enfermedades crónico-degenerativas. De acuerdo con la Encuesta Nacional de Salud y Nutrición 2012 de México, en la población de adultos jóvenes (20 a 29 años), existe una prevalencia de obesidad abdominal del 43,9% en hombres y del 63,6% en mujeres, así como una prevalencia de hipertensión del 11,8% en hombres y del 7,9% en mujeres[12]. Respecto a la ingestión nutrimental, los datos publicados hasta el momento muestran que los jóvenes (incluyendo universitarios del área de la salud) presentan un consumo con características poco saludables como el exceso de consumo de sal, grasas saturadas y azúcares añadidos procedentes especialmente de alimentos procesados y bebidas azucaradas[13-15]. Sumado a lo anterior, los universitarios del área de salud serán los futuros profesionales de la salud, quienes serán promotores de una alimentación saludable, y cuya práctica profesional será más coherente si su CA va en esa dirección.

Objetivos

El presente estudio tiene como objetivo diseñar y validar un cuestionario para evaluar el CA en estudiantes universitarios mexicanos del área de la salud, como parte de una estrategia para evaluar y mejorar la alimentación y salud cardiovascular de la población en diversos países de América Latina de la Red Iberoamericana para el Estudio del Síndrome Metabólico (RIBESMET, www.ribesmet.com.org).

Métodos

Diseño del estudio

El estudio consistió en dos fases. La primera incluyó el proceso de planeación y desarrollo de un instrumento para evaluar el CA en estudiantes universitarios y la segunda consistió en la validación de contenido y lógica, así como la reproducibilidad, la consistencia interna y la validez de constructo del instrumento diseñado.

Planeación y desarrollo del instrumento

Para el diseño del instrumento se consideró el procedimiento implementado en publicaciones anteriores[16-18]. Se realizó una búsqueda de la literatura científica relativa a CA, y también su relación con enfermedades crónico degenerativas, y se seleccionaron los temas a incluir en el cuestionario, los cuales fueron: tiempos de comidas, preferencias de consumo de alimentos y bebidas, forma de preparación de los alimentos, lectura de etiquetas nutricionales, consumo de alimentos fuera del hogar, saciedad, seguimiento de dietas terapéuticas o especiales, y percepción de una alimentación saludable, barreras al cambio y creencias. Posteriormente, dichos temas o dominios fueron explorados a través de una entrevista semi-dirigida, en 10 estudiantes del área de la salud. La información obtenida durante las entrevistas se analizó de acuerdo a la Teoría Fundamentada[19], y con ésta se desarrolló la primera versión del cuestionario de CA, que incluyó 42 preguntas con opción de respuesta múltiple.

Esta primera versión del instrumento se aplicó a un grupo piloto de 10 estudiantes del área de la salud (diferentes a los entrevistados) para evaluar el nivel de com-

prensión y la claridad de los ítems. De acuerdo con las recomendaciones obtenidas durante esta aplicación, se realizaron cambios referentes a la redacción y al acomodo de los ítems; se eliminaron 11 preguntas y algunas opciones de respuesta que fueron confusas. Al finalizar dicho procedimiento, se obtuvo un cuestionario de 31 preguntas con opción de respuesta múltiple.

Validación de contenido y lógica del instrumento

Para comprobar la validez de contenido y lógica, se realizó una evaluación del cuestionario depurado, por parte de un grupo de expertos (15 profesionales de la salud con experiencia en el área clínica y de investigación, quienes evaluaron el instrumento de manera independiente). Cada experto contestó 9 preguntas relacionadas con el contenido y forma del cuestionario, con una escala de Likert de 1 a 5 (1 = en total desacuerdo, 2 = en desacuerdo, 3 = no estoy seguro, 4 = de acuerdo, 5 = totalmente de acuerdo).

Para completar el proceso de validación (reproducibilidad, validez de constructo y consistencia interna), entre abril y junio del 2010, se aplicó el instrumento previamente revisado por expertos, a estudiantes de sexto semestre de dos Licenciaturas (Medicina y Nutrición) del Centro Universitario de Ciencias de la Salud (CUCS) de la Universidad de Guadalajara (UdG), México.

Sujetos

El tamaño de la muestra se calculó en 403 sujetos, considerando la inclusión de más de 10 sujetos por cada ítem del instrumento y estimando una pérdida de 30% en el re-test[20]. Se invitó a participar a toda la generación de estudiantes inscritos en el sexto semestre de las Licenciaturas de Medicina (n = 350) y Nutrición (n = 60) del CUCS de la UdG. Todos los estudiantes invitados aceptaron colaborar voluntariamente en este trabajo. No obstante, 26 alumnos no asistieron el día de la primera aplicación del instrumento. Además, se excluyeron 51 alumnos que no fueron localizados para contestar el test por segunda ocasión. Por tanto, este análisis incluye 333 voluntarios (Nutrición n = 58, 17,4% y Medicina n = 275, 82,6%).

Aplicación del cuestionario

El estudio se condujo de acuerdo a lo establecido en la Declaración de Helsinki. Se obtuvo la aprobación del Comité de Ética del CUCS y todos los participantes firmaron de forma voluntaria una hoja de consentimiento informado. Los participantes contestaron en dos ocasiones el cuestionario de CA de manera autónoma, en un aula del CUCS o del Hospital Fray Antonio Alcalde de la UdG, en presencia de los responsables de esta investigación. Se determinó un plazo de cuatro semanas entre ambas aplicaciones, por considerarse un periodo de tiempo lo suficientemente prolongando como para que los estudiantes no recordaran las respuestas proporcionadas en la primera administración, y lo suficientemente corto como para que no hubieran realizado cambios sustanciales en su CA.

Análisis de datos

- *Descriptivos*. Para el análisis descriptivo, las variables cuantitativas se expresan como media (desviación estándar), así como terciles; se utilizó la prueba t-test para valorar diferencias entre estas variables. Las variables cualitativas se presentan como frecuencia (porcentaje). Para la validación, cada pregunta del cuestionario fue calificada como "saludable" o "no saludable" en función de la literatura (anexo I). No obstante, el propósito del cuestionario es explorar o dar seguimiento a diferentes aspectos del CA, donde cada opción de respuesta puede aportar información valiosa para ello. Por tanto, en el uso práctico del cuestionario calificar cada pregunta como aquí se realiza es opcional.
- *Reproducibilidad (Test-retest)*. Para determinar la reproducibilidad del instrumento, se calculó la concordancia entre test y re-test mediante el coeficiente de correlación intraclase. Para este subapartado y los análisis descriptivos, se utilizó el paquete estadístico SPSS versión 19.0 para Windows (SPSS, Chicago, IL, U.S.A.).
- *Validez*. Este subapartado se divide en dos campos. El primero de *contenido y lógica* corresponde a la evaluación obtenida de los expertos. El segundo es la *consistencia interna* y la *validez de constructo*. La consistencia interna se determinó mediante el coeficiente de confiabilidad alfa de Cronbach, tanto para la dificultad de los reactivos como para la habilidad de los sujetos, y se consideró como respetable un índice superior a 0,70[21]. Asimismo se calcularon los índices de separación para los ítems y para los sujetos y, se consideró un valor > 2,0 como adecuado. Ambos estadísticos se determinaron utilizando el modelo matemático Rasch, el cual se fundamenta en la Teoría de Respuesta al Ítem (TRI)[22]. Se utilizó este modelo para la validación debido a que el cuestionario está constituido por preguntas y respuestas múltiples nominales, lo cual demanda considerar el constructo de los ítems así como las habilidades de los sujetos para seleccionar la respuesta más saludable.

Para validar el constructo, se determinaron dos estadísticos que permiten la valoración de la habilidad de las personas y la dificultad de los ítems: INFIT (ajuste cercano) es un estadístico de ajuste con información ponderada (por las varianzas individuales), sensible a patrones de respuestas no esperados por el modelo

Anexo I

Listado de bibliografías utilizadas para determinar las respuestas saludables al cuestionario para la validación

1. Campos S, Doxey J, Hammond D. Nutrition labels on pre-packaged foods: a systematic review. *Public Health Nutr* 2011; 14 (8): 1496-1506.
2. Duffey KJ, Gordon-Larsen P, Steffen LM, Jacobs DRJr, Popkin BM. Drinking caloric beverages increases the risk of adverse cardiometabolic outcomes in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Clin Nutr* 2010; 92 (4): 954-9.
3. Duffey KJ, Steffen LM, Van Horn L, Jacobs DRJr, Popkin BM. Dietary patterns matter: diet beverages and cardiometabolic risks in the longitudinal Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Clin Nutr* 2012; 95 (4): 909-15.
4. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Fruit and vegetable intakes, C-reactive protein, and the metabolic syndrome. *Am J Clin Nutr* 2006; 84 (6): 1489-97.
5. Farshchi HR, Taylor MA, Macdonald IA. Beneficial metabolic effects of regular meal frequency on dietary thermogenesis, insulin sensitive, and fasting lipid profiles in healthy obese women. *Am J Clin Nutr* 2005; 81 (1): 16-24.
6. Fulkerson JA, Farbakhsh K, Lytle L, Hearst MO, Dengel DR, Pasch KE, et al. Away-from-home family dinner sources and associations with weight status, body composition, and related biomarkers of chronic disease among adolescents and their parents. *J Am Diet Assoc* 2011; 111 (12): 1892-7.
7. Kim HY, Lee NR, Lee JS, Choi YS, Kuak TK, Chung HR, et al. Meal skipping relates to food choice, understanding of nutrition labeling, and prevalence of obesity in Korean fifth grade children. *Nutr Res Pract* 2012; 6 (4): 328-33.
8. Mekary RA, Giovannucci E, Willett WC, van Dam RM, Hu FB. Eating patterns and type 2 diabetes risk in men: breakfast omission, eating frequency, and snacking. *Am J Clin Nutr* 2012; 95 (5): 1182-9.
9. Min C, Hwayoung N, Kang YS, Hea JS, Hyun WB, Won OS, et al. Skipping breakfast is associated with diet quality and metabolic syndrome risk factors of adults. *Nutr Res Pract* 2011; 5 (5): 455-63.
10. Serra-Majem L, Bautista-Castaño I. Etiology of obesity: two "key issues" and other emerging factors. *Nutr Hosp* 2013; 28 (Supl. 5): 32-43.
11. Smith KJ, Blizzard L, McNaughton SA, Gall SL, Dwyer T, Venn AJ. Daily eating frequency and cardiometabolic risk factors in young Australian adults: cross-sectional analyses. *Br J Nutr* 2012; 108 (6): 1086-94.

Rasch que afectan respuestas a reactivos cercanos al nivel de habilidad medida de la mayoría de los estudiantes; y OUTFIT (ajuste lejano) es un estadístico no ponderado, sensible especialmente a los comportamientos extremos no esperados por el modelo Rasch que afectan respuestas a reactivos lejanos al nivel de habilidad medida de la mayoría de los sujetos. La unidad determina el ajuste perfecto entre los datos observados y los calculados por el modelo. Con base en los resultados de estos estadísticos, la depuración de ítems se realizó por la presencia de alguno de los siguientes criterios:

- Ítems cuyo valor de INFIT y OUTFIT en su expresión de media cuadrática sin estandarizar (MNSQ) sea > 1,3 y en su expresión de media cuadrática estandarizada (ZSTD) sea > 2,0, que indica que las respuestas observadas se encuentran por encima del punto de corte superior establecido teóricamente por el modelo Rasch. Esto sugiere que las respuestas se deben al azar y no a la habilidad de los sujetos.
- Ítems cuyo valor de INFIT y OUTFIT en su expresión de MNSQ sea < 0,7 y ZSTD sea < -2,0. Estos valores por debajo del punto de corte inferior esperado por el modelo Rasch, indican que hay dependencia en las respuestas de los ítems, es decir, la respuesta de un ítem podría afectar la respuesta a otros ítems (no habría autonomía entre las respuestas).

Para confirmar la validez de constructo, se graficó la alineación esperada por el modelo Rasch de la dificultad de los ítems y de la distribución de la habilidad de los sujetos en logits (logaritmo de la dificultad del ítem en relación con la habilidad de los sujetos; ajuste perfecto, valor cero).

Los análisis de este apartado se realizaron con el software WINSTEPS® versión 3.8.0 para Windows (WINSTEPS, Chicago, IL, U.S.A.).

Resultados

Desarrollo del instrumento

La versión final del cuestionario de CA consistió en 31 ítems de opción de respuesta múltiple, e incluyó preguntas sobre selección, preparación, horarios de toma de alimentos, preferencias de ingestión de alimentos, creencias y barreras al cambio (anexo II).

Validez de contenido y lógica

En la tabla I se muestran los resultados de la encuesta realizada al grupo de expertos (n =15) para evaluar la validez lógica y de contenido del cuestionario. En cada una de las 9 preguntas evaluadas por los expertos se obtuvo puntuación promedio igual o mayor a 4,5 (de 5 máxima), de manera que el promedio de puntuación total fue de 42,5 (de 45 puntos posibles).

Anexo II
Cuestionario de comportamiento alimentario validado

CUESTIONARIO DE COMPORTAMIENTO ALIMENTARIO
Por favor marque una única opción

1. ¿Qué factor consideras más importante al elegir un alimento para su consumo?
   ❑ a. Su sabor
   ❑ b. Su precio
   ❑ c. Que sea agradable a la vista
   ❑ d. Su caducidad
   ❑ e. Su contenido nutrimental

2. Me es difícil leer las etiquetas nutrimentales:
   ❑ a. Por falta de tiempo
   ❑ b. Porque no me interesa
   ❑ 5 c. Porque no las entiendo
   ❑ d. Por pereza
   ❑ e. Sí las leo y las entiendo

3. Si evitas algún alimento, ¿Por qué motivo lo haces?
   ❑ a. Porque no me gusta
   ❑ b. Por cuidarme
   ❑ c. Porque me hace sentir mal
   ❑ d. No suelo evitar ningún alimento

4. ¿Cuál es la preparación más habitual de tus alimentos?
   ❑ a. Fritos (Incluye empanizados y capeados)
   ❑ b. Al vapor o hervidos
   ❑ c. Asados o a la plancha
   ❑ d. Horneados
   ❑ e. Guisados o salteados

5. ¿Quién prepara tus alimentos con mayor frecuencia durante la semana?
   ❑ a. Yo
   ❑ b. Mi mamá
   ❑ c. Los compro ya preparados
   ❑ d. Otro:_____

6. ¿Qué haces normalmente cuando te sientes satisfecho?
   ❑ a. Dejo de comer sin problema
   ❑ b. Dejo de comer pero me cuesta hacerlo
   ❑ c. Sigo comiendo sin problema
   ❑ d. Sigo comiendo pero me siento mal de hacerlo

7. ¿Qué haces con la grasa visible de la carne?
   ❑ a. La quito toda
   ❑ b. Quito la mayoría
   ❑ c. Quito un poco
   ❑ d. No quito nada

8. Habitualmente mastico cada bocado más de 25 veces:
   ❑ a. Totalmente en desacuerdo
   ❑ b. En desacuerdo
   ❑ c. Ni de acuerdo ni en desacuerdo
   ❑ d. De acuerdo
   ❑ e. Totalmente de acuerdo

¿Registra las horas y personas con las que habitualmente ingieres alimentos durante el día?

9. Entre semana		10. El fin de semana	
Hora	Con quién	Hora	Con quién
1. _____	_____	1. _____	_____
2. _____	_____	2. _____	_____
3. _____	_____	3. _____	_____
4. _____	_____	4. _____	_____
5. _____	_____	5. _____	_____
6. _____	_____	6. _____	_____
7. _____	_____	7. _____	_____

Anexo II *(cont.)*
Cuestionario de comportamiento alimentario validado

Marca la opción correspondiente de acuerdo a tu agrado para comer los siguientes alimentos

	a. Me agrada mucho	b. Me agrada	c. Ni me agrada ni me desagrada	d. Me desagrada	e. Me desagrada mucho
11. Frutas	❑	❑	❑	❑	❑
12. Verduras	❑	❑	❑	❑	❑
13. Carnes y pollo	❑	❑	❑	❑	❑
14. Pescados y mariscos	❑	❑	❑	❑	❑
15. Lácteos	❑	❑	❑	❑	❑
16. Pan, tortillas, papa, pasta, cereales	❑	❑	❑	❑	❑
17. Frijoles, garbanzos, lentejas	❑	❑	❑	❑	❑
18. Alimentos dulces	❑	❑	❑	❑	❑
19. Huevo	❑	❑	❑	❑	❑
20. Almendras, nueces, pistaches, semillas, etc.	❑	❑	❑	❑	❑
21. Bebidas alcohólicas	❑	❑	❑	❑	❑
22. Alimentos empaquetados	❑	❑	❑	❑	❑

23. ¿Qué sueles beber en mayor cantidad durante el día?
- ❑ a. Agua fresca
- ❑ b. Agua natural
- ❑ c. Refresco, jugos o tés industrializados
- ❑ d. Leche
- ❑ e. Otro: _____

24. ¿Qué sueles ingerir habitualmente entre comidas?
- ❑ a. Dulces
- ❑ b. Fruta o verdura
- ❑ c. Galletas o pan dulce (bollería)
- ❑ d. Yogurt
- ❑ e. Papitas, churritos, frituras, etc.
- ❑ f. Cacahuates u otras semillas.
- ❑ g. Nada

25. ¿Qué incluyes habitualmente en tu tiempo de comida principal durante el día?

	a.	b.
25.1. Botana (aperitivo)	sí ❑	no ❑
25.2. Sopa o caldo u otro entrante	sí ❑	no ❑
25.3. Plato fuerte	sí ❑	no ❑
25.4. Carne, pescado, pollo o mariscos	sí ❑	no ❑
25.5. Arroz, pasta o frijoles	sí ❑	no ❑
25.6. Verduras o ensalada	sí ❑	no ❑
25.7. Tortillas, pan "salado", bolillo o tostadas	sí ❑	no ❑
25.8. Postre	sí ❑	no ❑
25.9. Fruta	sí ❑	no ❑
25.10. Bebida	sí ❑	no ❑
25.11. Bebida endulzada	sí ❑	no ❑
25.12. Bebida sin endulzar	sí ❑	no ❑

26. ¿Con que frecuencia comes alimentos fuera de casa?
- ❑ a. Todos los días
- ❑ b. 5 a 6 veces a la semana
- ❑ c. 3 a 4 veces a la semana
- ❑ d. 1 a 2 veces a la semana
- ❑ e. Una vez cada 15 días
- ❑ f. Una vez al mes
- ❑ g. Menos de una vez al mes

27. ¿Con qué frecuencia crees que comes alimentos en exceso?
- ❑ a. Todos los días
- ❑ b. 5 a 6 veces a la semana
- ❑ c. 3 a 4 veces a la semana
- ❑ d. 1 a 2 veces a la semana
- ❑ e. Una vez cada 15 días
- ❑ f. Una vez al mes
- ❑ g. Menos de una vez al mes

Anexo II *(cont.)*
Cuestionario de comportamiento alimentario validado

28. ¿Qué haces o estarías dispuesto a hacer para cuidar tu cuerpo?
- ❑ a. Cuidar mi alimentación
- ❑ b. Seguir un régimen dietético temporal
- ❑ c. Hacer ejercicio
- ❑ d. Cuidar mi alimentación y hacer ejercicio
- ❑ e. Tomar suplementos dietéticos o productos herbolarios
- ❑ f. Nada

29. ¿Qué consideras que te hace falta para mejorar tu alimentación?
- ❑ a. Más información
- ❑ b. Apoyo social
- ❑ c. Dinero
- ❑ d. Compromiso o motivación personal
- ❑ e. Tiempo
- ❑ f. Nada, creo que mi alimentación es saludable
- ❑ g. No me interesa mejorar mi alimentación

30. Consideras que tu dieta es:
- ❑ a. Diferente cada día
- ❑ b. Diferente solo algunas veces durante la semana
- ❑ c. Diferente solo durante los fines de semana
- ❑ d. Muy monótona

31. ¿Crees que eres capaz de utilizar un consejo de nutrición para mejorar tu estado de salud?
- ❑ a. Totalmente en desacuerdo
- ❑ b. En desacuerdo
- ❑ c. Ni de acuerdo ni en desacuerdo
- ❑ d. De acuerdo
- ❑ e. Totalmente de acuerdo

Nota: A continuación se enlistan las respuestas "saludables" sugeridas por los autores con base en lo reportado en la literatura, no obstante no se descarta que las otras respuestas puedan ser de utilidad para quien lo aplica, dependiendo el propósito del uso del cuestionario.
1 = e, 2 = e, 3 = b, 4 = b/c, 5 = a, 6 = a, 7 = a/b, 8 = d/e, 9 = Al menos 3 tiempos de comida al día, 10 = Al menos 3 tiempos de comida al día, 11 = a/b, 12 = a/b, 13 = a/b, 14 = a/b, 15 = a/ b, 16 = a/b, 17 = a/b, 18 = d/e, 19 = a/b, 20 = a/b, 21 = d/e, 22 = d/e, 23 = b, 24 = b, 25.1 = b, 25.2 = a/b, 25.3 = a, 25.4 = a, 25.5 = a/b, 25.6 = a, 25.7 = a/b, 25.8 = b, 25.9 = a, 25.10 = a, 25.11 = b, 25.12 = a, 26 = f/g, 27 = f/g, 28 = d, 29 = f, 30 = a, 31 = d/e.

Tabla I
Resultados de la encuesta aplicada a un grupo de expertos para determinar validez lógica y de contenido del cuestionario de CA

	*Calificación**	
Preguntas	*Media*	*DE*
1. Las preguntas son sencillas y claras en cuanto a redacción.	5,0	0,0
2. Con estas preguntas se pueden evaluar aspectos del CA.	4,5	0,7
3. El orden de las preguntas facilita la exploración del CA.	4,5	0,7
4. Las opciones de respuesta son sencillas y claras en cuanto a redacción.	5,0	0,0
5. Las opciones de respuesta son adecuadas a las preguntas.	4,5	0,7
6. Es adecuado administrar este cuestionario de forma autónoma.	5,0	0,0
7. Esta herramienta puede contribuir a caracterizar CA de un individuo o población.	4,5	0,7
8. Este cuestionario es original para evaluar el CA.	4,5	0,7
9. Recomendaría esta herramienta para valorar CA de un individuo o población.	5,0	0,0
Promedio de la puntuación obtenida	4,7	0,7
Puntuación total de la evaluación (puntuación máxima 45 puntos)	42,5	0,7

CA, Comportamiento Alimentario; DE, Desviación Estándar. *Puntaje máximo de la calificación de cada pregunta fue 5.

Aplicación del cuestionario y análisis descriptivo

Para la validación del cuestionario de CA se incluyeron 333 estudiantes de 20 ,5 ± 3,2 años de edad promedio, de los cuales 59.8% fueron del sexo masculino. Al responder el cuestionario de CA, el promedio de respuestas saludables de la población de estudio fue de 17,4 ± 3,1 de las 31 totales. El mínimo de respuestas saludables fue 8 y el máximo de 27. En el análisis por terciles se obtuvo: el primer tercil entre 8-15 puntos, el segundo entre 16 y 18 puntos y el tercer tercil entre 19 y 27 puntos ($p < 0,001$). Las preguntas referentes a las preferencias alimentarias fueron las que presentaron las frecuencias más altas (> 90%) de respuestas saludables. Los ítems con baja frecuencia (< 4%) de respuestas saludables fueron los referentes al consumo de comida en la calle y la percepción de necesidades para lograr mejorar su alimentación.

Reproducibilidad test-retest

El coeficiente de correlación intraclase del cuestionario completo fue de 0,76, $p < 0,001$ (datos no mostrados en tabla).

Consistencia interna y validez de constructo

En la tabla II se muestran los resultados generales de la habilidad de los sujetos y de la dificultad de los ítems obtenidos por el análisis Rasch. La confiabilidad para la habilidad de los sujetos fue de 0,50 (alfa de Cronbach), mientras que para la dificultad de los ítems fue de 0,98 (alfa de Cronbach). Para la habilidad de los sujetos se obtuvo una media de INFIT MNSQ de 1,0 (0,29) y de OUTFIT MNSQ de 1,05 (0,83) con un índice de separación de 0.9. Para la dificultad de los ítems se obtuvo una media de INFIT MNSQ de 1,0 (0,05) y de OUTFIT MNSQ de 1,04 (0,23), con un índice de separación de 10,3.

En la tabla III se muestran los estadísticos de ajuste INFIT y OUTFIT para cada uno de los ítems del cuestionario (ordenados en función de su grado de dificultad en logits). De los 31 ítems evaluados, 26 (83,9%) tuvieron ajustes de INFIT u OUTFIT MNSQ entre 0.7 y 1,3 y, ZSTD entre -2,0 y 2,0. Los ítems R3, R10, R12, R14 y R27 no se ajustaron a los valores calculados por el modelo Rasch. Al analizar el ajuste de la habilidad de cada uno de los sujetos al modelo, 89,8% de los sujetos evaluados tuvieron valores de INFIT y OUTFIT entre los rangos antes mencionados (datos no mostrados en tablas).

En la figura 1 se muestra el mapa de la distribución de las habilidades de los sujetos y dificultad de los ítems de acuerdo a lo esperado por el modelo Rasch. Del lado izquierdo de la línea vertical los "#" y "." indican la ubicación de los sujetos de acuerdo a su habilidad (en logits): en la parte superior se encuentran los sujetos con mayor habilidad para contestar el cuestionario, mientras que en la parte inferior se localizan los sujetos con menor habilidad. Del lado derecho de la línea vertical (fig. 1) se encuentran ubicados los 31 ítems de acuerdo a su grado de dificultad (en logits): en la parte superior se encuentran los ítems con mayor dificultad, y en la parte inferior los ítems con menor dificultad.

De acuerdo a las alineaciones de sujetos e ítems en la figura 1, se confirma que las habilidades de la mayoría de los estudiantes se encontraron ubicadas por encima de la media de cero logits para seleccionar la opción saludable de las preguntas del cuestionario, y una tercera parte se ubicó por debajo del cero. La distribución de dificultad de los ítems presentó un comportamiento normal, cubriendo las diferentes habilidades de la población evaluada. Los huecos entre los ítems que se observaron en la figura son menores a un logit en la mayoría de los casos. Los espacios más pronunciados en su separación son los correspondientes a los ítems R25 y R12, los cuales encontramos en los extremos de la figura.

Tabla II
Resumen de los resultados de la habilidad de los sujetos y de la dificultad de los ítems obtenidos a través del análisis Rasch

	Habilidad en logits	*Error estándar*	*INFIT*		*OUTFIT*	
			MNSQ	*ZSTD*	*MNSQ*	*ZSTD*
Habilidad de los sujetos (n = 333)						
Media	0,44	0,47	1,00	0,00	1,05	0,00
DE	0,68	0,02	0,29	1,20	0,83	1,10
Índice de confiabilidad alfa de Cronbach	0,50	Índice de Separación	0,93			
Dificultad de los ítems (31 ítems)						
Media	0,00	0,16	1,00	-0,10	1,04	0,10
DE	1,77	0,06	0,05	1,10	0,23	1,40
Índice de confiabilidad alfa de Cronbach	0,98	Índice de separación	10,31			

INFIT, ajuste cercano; OUTFIT, ajuste lejano; MNSQ, media cuadrática sin estandarizar; ZSTD, media cuadrática estandarizada; DE, desviación estándar.

Tabla III
Valores INFIT y OUTFIT de cada ítem de acuerdo a su nivel decreciente de dificultad, obtenido a través del análisis Rasch

Nº, ítem	Descripción	Dificultad en logits	Error estándar	INFIT		OUTFIT	
				MNSQ	ZSTD	MNSQ	ZSTD
R25	Frecuencia de consumo de alimentos fuera de casa	3,56	0,25	1,00	0,10	0,97	0,00
R28	Qué necesitas para mejorar la alimentación	2,70	0,18	0,97	-0,20	0,97	-0,10
R19	Agrado por el consumo de alimentos dulces	2,42	0,16	1,04	0,40	1,03	0,20
R1	Razón que motiva a comprar un alimento	2,30	0,16	0,89	-1,10	0,74	-2,00
R26	Lugar en el que consultan consejos de nutrición	1,78	0,14	1,04	0,60	1,06	0,70
R23	Alimento que suelen consumir entre comidas	1,74	0,14	0,98	-0,30	0,94	-0,60
R24	Motivo por el que evitan algún alimento	1,53	0,13	1,03	0,60	1,03	0,40
R11	Configuración habitual de las comidas	1,49	0,13	0,97	-0,40	0,95	-0,60
R8	Consumo habitual de merienda	1,42	0,13	1,00	0,00	1,06	0,80
R3	Persona que prepara los alimentos	1,41	0,13	1,10	1,70	1,24	3,00
R29	Frecuencia de consumo de alimentos en exceso	1,19	0,12	1,03	0,60	1,02	0,40
R10	Presencia de horarios de comida establecidos	0,85	0,12	0,86	-3,90	0,83	-3,80
R6	Consumo habitual del almuerzo	0,77	0,12	1,01	0,30	1,01	0,20
R4	Preparación habitual de los alimentos	0,17	0,12	0,97	-0,80	0,96	-0,80
R2	Lectura de etiquetas nutricionales	0,16	0,12	0,96	-1,10	0,95	-1,20
R27	Dietas realizadas para perder peso	0,07	0,12	1,11	3,10	1,19	4,00
R21	Bebida habitual a lo largo del día	-0,80	0,12	0,95	-1,30	0,94	-1,10
R5	Consumo habitual del desayuno	-0,86	0,13	0,96	-0,60	0,90	-1,10
R31	Eliminación de grasa visible de la carne	-0,86	0,13	1,02	0,30	1,08	0,90
R20	Agrado por el consumo de huevo	-0,86	0,13	0,97	-0,30	0,97	-0,30
R18	Agrado por el consumo de leguminosas	-0,87	0,13	0,95	-0,80	0,88	-1,30
R30	Reacción al sentirse satisfecho	-0,93	0,14	1,02	0,40	1,08	0,80
R22	Tiempo dedicado a la comida	-1,20	0,15	0,97	-0,30	0,98	-0,10
R15	Agrado por el consumo de pescado	-1,29	0,15	1,03	0,30	1,17	1,30
R9	Consumo habitual de la cena	-1,75	0,17	1,00	0,10	0,93	-0,30
R13	Agrado por el consumo de verduras	-1,94	0,19	0,97	-0,20	0,82	-0,90
R14	Agrado por el consumo de carnes	-2,09	0,20	1,06	0,50	1,55	2,40
R16	Agrado por el consumo de lácteos	-2,25	0,21	1,02	0,20	1,01	0,10
R17	Agrado por el consumo de cereales	-2,39	0,22	1,00	0,10	1,11	0,50
R7	Consumo habitual de la comida	-2,56	0,24	1,00	0,10	0,97	0,00
R12	Agrado por el consumo de frutas	-3,61	0,38	1,03	0,20	2,03	1,90

INFIT, ajuste cercano; OUTFIT, ajuste lejano; MNSQ, media cuadrática sin estandarizar; ZSTD, media cuadrática estandarizada.

Discusión

La evaluación del CA permite orientar posibles intervenciones para mejorar la alimentación de la población, y así lograr un estado nutricional más saludable y prevenir enfermedades. En particular, en los estudiantes universitarios, la evaluación continua del CA es de especial relevancia pues su alimentación suele ser poco saludable, y les confiere potencial riesgo a su desempeño académico y al desarrollo de alteraciones metabólicas a corto plazo[13-15]. En este sentido, el presente trabajo aporta un instrumento auto-aplicable y práctico para evaluar aspectos del CA (selección, preparación, horarios de toma de alimentos, preferencias de ingestión de alimentos, creencias y barreras al cambio) en estudiantes universitarios, que resultó con índices de reproducibilidad y validez satisfactorios de acuerdo a la TRI[22].

La validación de cuestionarios en el área de nutrición con escalas de Likert se ha realizado a través de la Teoría Clásica del Test (que sólo considera para la validación, índices cuantitativos de evaluación para los ítems), y entre ellos se encuentran los cuestionarios diseñados hasta la fecha para evaluar alguna característica del CA[17-18,22-24]. El presente estudio realizó la evaluación de la validez de constructo y consistencia interna del cuestionario de CA utilizando el método Rasch según la TRI, ya que éste método permite evaluar de forma conjunta la habilidad de los sujetos (para elegir las opciones de respuestas saludables del cuestionario) y la dificultad de los ítems (constructo y adecuación para

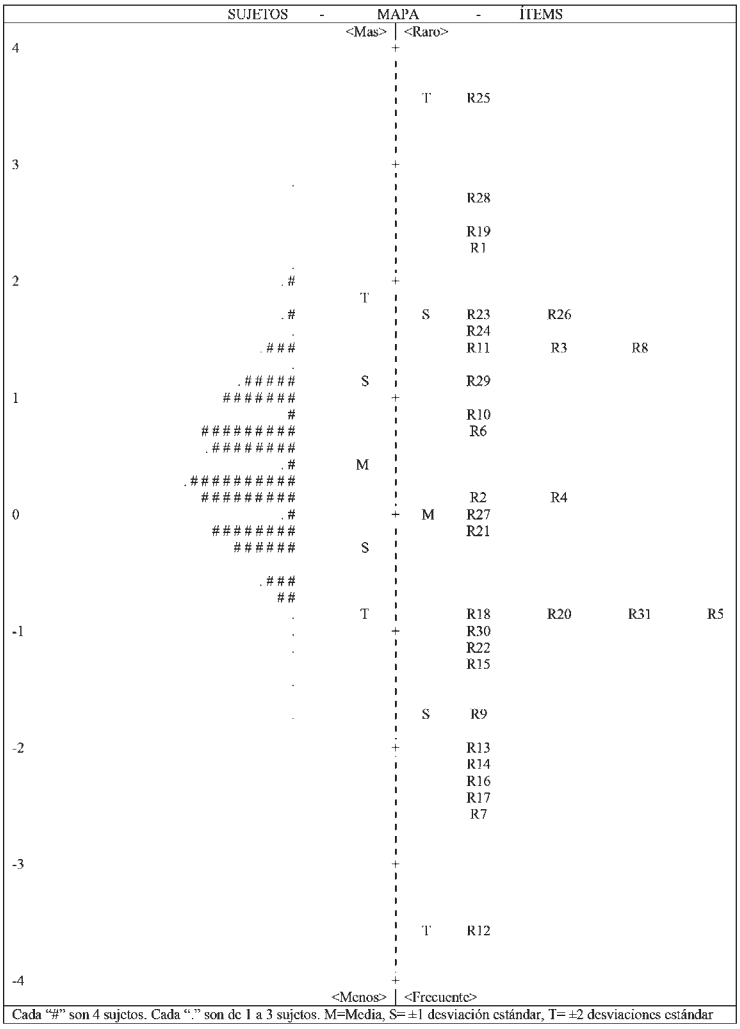

Fig. 1.—Mapa de ubicación de habilidad de los sujetos y dificultad de los ítems en logits.

medir el CA en estudiantes) expresándolos en la misma escala (logits). Asimismo, posibilita la obtención de la validez de constructo de cada uno de los ítems del instrumento y no sólo en conjunto, considerando que cada ítem aporta al CA[25]. Debido a la naturaleza del concepto que evalúa este cuestionario (CA), y a que su diseño incluyó respuestas de opción múltiple nominal y no de escala de Likert u otra escala ordinal como en el caso de otros instrumentos, fue esencial considerar para su validación tanto el constructo de los ítems como las características de habilidad de los sujetos. Dicha determinación se armoniza con la de otros autores que han validado cuestionarios para medir fenómenos de la misma naturaleza como emociones, fatiga, relaciones, etc[26-28].

El análisis test-retest (reproducibilidad) del cuestionario de CA, brindó un coeficiente de correlación intraclase de 0,76. De acuerdo a la literatura, se considera adecuado un índice de reproducibilidad a partir de 0,70[26-29]. Esto sugiere que este cuestionario de CA diseñado por nosotros tiene una adecuada estabilidad temporal. Esto coincide con trabajos previos de diseño y validación de instrumentos para valorar hábitos de alimentación, que han mostrado coeficientes de reproducibilidad entre 0,60 y 0,90 con intervalos de tiempo entre las dos aplicaciones de 2 a 4 semanas[18,24].

Las evaluaciones de validez de contenido y de lógica del cuestionario de CA por parte de un grupo de expertos fueron favorables. La mayoría de los profesionales encuestados contestaron con puntuaciones máximas, demostrando que estuvieron de acuerdo en el diseño, la redacción y la utilidad de las preguntas del cuestionario para evaluar el CA. Este tipo de evaluación posterior al diseño de los cuestionarios se ha reportado en otros estudios de validación tanto de alimentación como en otras áreas[16-18].

En la consistencia interna del cuestionario de CA, se obtuvo un alfa de Cronbach de 0,98 para la dificultad de los ítems. Estos resultados son superiores a los obtenidos en estudios de validación de cuestionarios simi-

lares[18,23,24], e indican que el instrumento tiene una confiabilidad adecuada para la medición del CA en estudiantes universitarios. El alfa de Cronbach obtenido para la habilidad de los sujetos fue de 0,50. Esto sugiere que la población valorada presentó una distribución variada de habilidades para seleccionar las opciones de respuestas saludables del test, y se corrobora con la puntuación media obtenida por los sujetos al responder el cuestionario (17 respuestas deseables de 31 totales). En la misma dirección, los resultados de los índices INFIT y OUTFIT y de la figura 1 sugieren que el cuestionario tiene la capacidad de discriminar a los estudiantes con diversos grados de habilidad para responder al cuestionario.

Respecto a la valoración del constructo del instrumento, se observó que los valores de INFIT y OUTFIT se encontraron dentro del rango esperado por el modelo Rasch y el índice de separación (10,3) fue superior a 2,0 para la dificultad de los ítems. Esto indica que el conjunto de ítems que compone el cuestionario de CA tiene unidimensionalidad, es decir, mide el mismo constructo. Otros estudios de validación que han utilizado el análisis Rasch encontraron resultados similares en la validez de constructo de sus instrumentos[25,30]. Cinco de los 31 ítems (R3, R10, R12, R14, R27), de forma individual, no se ajustaron al modelo calculado por el análisis Rasch. Sin embargo, estos ítems son esenciales para la evaluación del constructo (CA) que se desea medir, por lo que de acuerdo a lo propuesto por la TRI, se revisaron y se mejoró su redacción y diseño. Además Así, los resultados de validez presentados hasta el momento fueron calculados con dichos ítems en su formulación original, ello sugiere que su desajuste a lo esperado por el modelo Rasch no impacta de forma negativa en la confiabilidad global del cuestionario.

En relación a la habilidad de los sujetos, los valores de INFIT y OUTFIT se observaron dentro de los valores esperados; sin embargo, el índice de separación (0,9) fue inferior a 2,0. Esto indica que los sujetos evaluados presentaron habilidades heterogéneas para responder al cuestionario. Esto concuerda con los demás resultados de este trabajo al respecto discutidos en párrafos anteriores.

Reconocemos que existen otros métodos por los cuales el CA puede ser valorado, como la observación directa o la entrevista personalizada, pero demandan tiempo y habilidades del aplicador, requisitos que en ocasiones no son factibles en la investigación o práctica profesional diaria. La propuesta de este cuestionario (anexo 2) válido y confiable es evaluar algunos aspectos del CA de forma accesible, auto-aplicable, a bajo costo y rápida en estudiantes universitarios. Los análisis de los datos derivados de este instrumento permitirán obtener información relevante y útil para plantear estrategias y acciones específicas para mejorar la alimentación de esta población, con posibilidad de impactar en su rendimiento como estudiantes y en su estado de salud actual, así como en la etapa adulta. Asimismo, podrá ayudar a evaluar la eficacia de estas intervenciones. Si además del CA se desea conocer otros aspectos de la alimentación de los sujetos de estudio, se sugiere la aplicación de este cuestionario en combinación con otros instrumentos validados para evaluar la ingestión nutricional. De esta forma, se obtendrá una perspectiva amplia sobre el qué se ingiere (alimentos y nutrientes), el cómo y por qué se ingieren.

En nuestro conocimiento, este es el primer cuestionario validado para evaluar el CA en población universitaria mexicana que podrá contribuir al diseño de intervenciones y de otros cuestionarios en el área de la nutrición. Una limitación del presente trabajo es haber incluido solamente alumnos de las carreras de Medicina y Nutrición de una sola institución, haciendo difícil su generalización para ser utilizado en otras poblaciones. Sin embargo, por razones de factibilidad se decidió realizar el presente estudio en esta población. Nuevos estudios definirán la utilidad del cuestionario en otros grupos poblacionales.

En conclusión, se desarrolló y validó un instrumento con índices de reproducibilidad (ICC 0.76) y validez (alfa de Cronbach 0.98) satisfactorios de acuerdo a la TRI para medir el CA en estudiantes universitarios.

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Adherence to the Mediterranean diet by nursing students of Murcia (Spain)

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Abstract

Introduction: **The Mediterranean diet is recognized as one with the healthiest dietary patterns; however, this diet is deteriorating and being abandoned even in the Mediterranean countries themselves. Generally speaking, dietary habits get fixed during adolescence although during the college phase, students may experience important changes in their lifestyles. The KIDMED index is recognized as a good tool to assess adherence to the Mediterranean diet (AMD).**

Objective: **The aim of this study was to assess AMD in college students and to evidence possible variations throughout the college period assessing differences between the college years.**

Method: **A cross-sectional study with 213 alumni in first grade and 105 in fourth grade was carried out. The students were classified by gender, type of residence (parents' home or out of the parents' house) and body mass index (BMI) (< 25 or > 25).**

Results: **The BMI for the whole sample was 24.35 ± 2.71 in men and 22.54 ± 3.25 in women (p < 0.001). The mean score in AMD was 7.0 ± 1.9, with 43% of the students showing good adherence. In general, a low intake of fruits, vegetables, rice or pasta was observed, foods that are included in the base of the dietary pyramid. Consumption of olive oil and legumes was very high and a direct relationship was observed between overweighed people (BMI > 25) and the habit of not having breakfast usually. No significant differences were observed between the student of first and fourth grades although those students in the fourth grade living away from the parental house had higher AMD level than the other students (p < 0.001).**

Conclusions: **Educational programs promoting the intake of the different groups of food are recommended, was well as strategies promoting the consumption of fruits and vegetables within the university area and the healthy habit of having breakfast.**

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Key words: *Mediterranean diet. Nursing. College students. Nutrition.*

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ADHERENCIA A LA DIETA MEDITERRÁNEA DE ESTUDIANTES DE ENFERMERÍA EN MURCIA (ESPAÑA)

Resumen

Introducción: **La dieta Mediterránea está reconocida como una de los patrones dietéticos más saludables pero, incluso en los propios países mediterráneos se está produciendo un deterioro y abandonando de la misma. Los hábitos dietéticos quedan establecidos generalmente durante la adolescencia pero durante el periodo universitario los estudiantes pueden sufrir cambios importantes en su estilo de vida. El índice KIDMED está reconocido como una buena herramienta para la evaluación de la adherencia a la dieta mediterránea (ADM).**

Objetivo: **El propósito de este estudio ha sido evaluar la ADM de estudiantes universitarios y evidenciar posibles variaciones a lo largo de la etapa universitaria valorando diferencias entre los cursos.**

Método: Se llevó a cabo un estudio transversal con 213 alumnos de primer curso y 105 de cuarto curso. Se clasificó a los estudiantes por sexo, tipo de residencia (en casa con sus padres o fuera de casa) e índice de masa corporal (IMC) (< 25 o > 25).

Resultados: El IMC para la muestra completa fue de 24,35 ± 2,71 en hombres y 22,54 ± 3,25 en mujeres (p < 0,001). La puntuación media de ADM fue de 7,0 ± 1,9, habiendo un 43% de estudiantes que mostraban una adherencia Buena. En general, se observó un bajo consumo de frutas, verduras y arroz o pasta, alimentos que están encuadrados en la base de la pirámide alimentaria. El consumo de aceite de oliva y legumbres resultó muy elevado y se encontró relación directa entre personas con sobrepeso (IMC > 25) y el hecho de no desayunar habitualmente (p < 0,05). No se han encontrado diferencias significativas entre alumnos de primero y cuarto curso aunque los alumnos de cuarto y que vivían fuera de casa presentaron un nivel de ADM mejor que el resto (p < 0,001).

Conclusiones: **Se recomiendan programas educacionales para motivar el consumo de los diferentes grupos de alimentos en general y especialmente estrategias para fomentar el consumo de frutas y verduras en el espacio universitario así como la práctica saludable del desayuno.**

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Palabras clave: *Dieta mediterránea. Enfermería. Universitarios. Nutrición.*

Introduction

It is well documented that healthy eating habits and lifestyles are closely associated with the prevention of chronic diseases such as diabetes, obesity, Alzheimer's, hepatic steatosis and several cardiovascular diseases[1-3]. The first scientific reference dates from 1953, when L. Allbaugh[4] compared eating habits and lifestyles Greece and the USA, although it was A. Keys who first applied the name of "Mediterranean Diet" (MD) to some healthy dietary habits found around the Mediterranean region[5-7].

The MD can be described as the dietary pattern widely followed in countries as Spain, Greece, Italy and Morocco which, has been included by the UNESCO in the intangible cultural Heritage of Humanity, as a nutritional prototype of worldwide value[8]. The traditional MD is characterized by a high intake of vegetables (legumes, cereals, olive oil, seeds, fruits and nuts); a moderate intake of fish, seafood and ethanol (principally wine during meals), low-to-moderate intake of dairy products (cheese and yogurt) and eggs and a low intake of meat, accompanied by other habits such as the "siesta" (after-meal nap)[9]. In addition, these foods are normally consumed in season, in fresh or minimally processed form, which increases the availability and utilization of micronutrients and antioxidants[10]. Some of the benefits of MD has been recently demonstrated in the PREDIMED study[11] when Spanish investigators confirmed that MD supplemented with extra-virgin olive oil or nuts reduce the incidence of major cardiovascular events among persons at high cardiovascular risk.

Dietary habits are usually acquired at home watching what our parents cook and eat, especially at an early age. Attending university may lead to changes in habits and lifestyle as a result of many factors: some university students no longer live with their parents, students must adapt to stress and emotional challenges, while physical activity tends to be overlooked[12]. It has been claimed that such changes in the university period may have a significant impact on health, accompanied by the increase risk of developing chronic diseases such as obesity, diabetes, cancer and heart disease[13].

To evaluate the degree of adherence to the Mediterranean diet (AMD) several indexes have been developed[14-16]. However, they are not easy to apply and require many data. Nowadays the most widely accepted index for evaluating AMD is the KIDMED index[10], whose usefulness has been corroborated many times[17-19].

The University of Murcia is member of REUS (Red Española de Universidades Saludables-Spanish Association of Health Conscious Universities), and it is hoped that the present study will provide useful data for evaluating the need for nutritional educational programmes to establish healthy eating habits and lifestyles for students during their university course.

Eating and life style habits may suffer changes during a student's life at university. Such a comparison between different years has been made previously in other places as Zagreb[20], North Carolina[21] and Minnesota[22] but not in Spain.

Students studying many degrees could have been evaluated, but we considered that health sciences students should have higher perception of healthy dietary habits and therefore follow better dietary patterns. Student nurses, particularly those studying to be nutrition nurses are destined to work closely with patients and could influence the dietary habits of these patients[23].

The aim of this study, therefore, was to evaluate the AMD of nursing students and to compare the results found for first and fourth year students at the University of Murcia analyzing several related factors.

Methods

Subject

The cross-sectional study was designed to evaluate and compare the eating habits among undergraduate nursing students from the University of Murcia. The sample comprised 318 students, 213 from the first academic year (48 males and 165 females) and 105 from the fourth year (26 males and 69 females). Students were classified according gender, residence (family or non family, including shared flat, hall of residence, etc) and body mass index (BMI) (normal weight, overweight or obese).

This study did not need ethical approval because no invasive procedures were necessary. All students volunteered for the study.

Methods

To assess the AMD between first and fourth year nursing degree students, a self-administered questionnaire KIDMED was used. Development of the KIDMED[10] index was based on principles sustaining the Mediterranean dietary patterns as well as on those that undermine it. The questionnaire is based on 16 questions and the index ranges from 0 to 12. Four questions denote a negative connotation with respect to the Mediterranean diet and assign a value of **-**1, while the rest of the questions have a positive aspect and they are given a score of **+**1. The sums of the values from the administered test were classified into three levels: (1) 8-12, optimal Mediterranean diet; (2) 4–7, improvement needed to adjust intake to Mediterranean patterns; (3) 0-3, very low diet quality.

Statistical analysis

The statistical software package IBM SPSS Statistics v19.0 (SPSS Inc.; Chicago, Illinois USA) was used for the analysis of data. Chi-square analysis was

performed to evaluate relationships between qualitative variables and Student-t test to compare quantitative variables between groups. Differences were considered significant at $p < 0.05$.

Data were grouped according to degree years (1st or 4th), gender, residence (familiar or other) and BMI status (BMI > 25 or BMI < 25).

Results

The distribution of volunteers is shown in table I. Most of the volunteers were female (77.5%), lived at home with their families (76.3%) and had BMI < 25 (79.7%).

The results for BMI are shown for the total sample, according to year, gender and residence (table II). As was expected, there was significant differences between men and women, with men having a higher BMI in both years ($p < 0.001$).

The results for the KIDMED test for the total sample and grouped according to categories are shown in table III. As regards the total sample, 43.4% of all students had a good AMD score and only 3.1% poor AMD, with an average index of 7.0.

Differences between genders were statistically significant, with men consuming more pasta/rice ($p < 0.001$), nuts ($p < 0.05$), dairy products for breakfast and fast-food ($p < 0.001$) but fewer vegetables ($p < 0.001$). As regards place of residence, the consumption of fast-food ($p < 0.01$) and sweets/candies ($p < 0.05$) was greater for students living at home. In the case of BMI, overweight students showed a higher consumption of a second piece of fruit/day and a lower consumption of sweets/candies ($p < 0.001$) but they also skipped breakfast more often ($p < 0.01$).

First year students

In first year students, statistically significant differences existed between males and females regarding the consumption of vegetables ($p < 0.05$) and sweets every day ($p < 0.001$), women showing higher values (75.8% *vs* 58.3% and 18.8% *vs* 8.3%, respectively). In contrast, males usually took more dairy products (97.9% *vs* 85.5%) and went more than once a week to a fast-food restaurant (41.7% *vs* 21.2%) with $p < 0.001$ (table IV).

As regards where students lived (familiar or not), no statistical differences were found in the adherence to the Mediterranean diet pattern, but students who live away from seemed to show a higher adherence (41.1% *vs* 36.7% showed a good AMD). In contrast, we observed that legumes were consumed more frequently by students living at home ($p < 0.05$) (table IV).

Overweight students (BMI > 25) tended to have a healthier diet, following a Mediterranean pattern, than students with BMI below 25. This could explain some of the statistical differences we found in our study; for instance, overweight people consume a second fruit per day ($p < 0.05$) and but not sweets/candies frequently ($p < 0.001$).

Fourth year students

As shows table IV there were some differences in the AMD regarding fourth year students (table IV). For example, men consumed fewer vegetables but more pasta/rice, nuts and go more often to fast-food restaurants, in all cases with significant differences.

AMD tended to be better in those student living away from home (8.13 *vs* 6.82; $p < 0.001$) being more students in the good AMD quality group (68.8% *vs*

Table I
Description and distribution of sample

			Gender		*Residence*		*BMI*	
	Total	*Age (median)*	*Male*	*Female*	*With family*	*Others*	*< 25*	*> 25*
1º	213	19	48 (22.5%)	165 (77.5%)	158 (76.3%)	49 (23.7%)	164 (77.7%)	47 (22.1%)
4º	105	22	36 (34.3%)	69 (65.7%)	73 (69.5%)	32 (30.5%)	88 (83.8%)	17 (16%)
Total	318		84 (26.4%)	234 (73.6%)	231 (74.0%)	81 (26.0%)	252 (79.7%)	64 (20.3%)

Table II
BMI of students by categories

		Gender		*Residence*	
Year degree	*Total*	*Male*	*Female*	*With family*	*Others*
1º	23.12 ± 3.46	24.48 ± 3.47	22.72 ± 3.07***	22.93 ± 3.32	23.79 ± 3.91
4º	22.81 ± 2.65	24.16 ± 2.16	22.10 ± 2.62***	22.29 ± 2.51	23.04 ± 2.70
Total	23.02 ± 3.21	24.35 ± 2.71	22.54 ± 3.25***	22.82 ± 3.20	23.34 ± 3.25

*** $P < 0.001$ of significant difference.

Table III
Results for KIDMED test for total students and by categories

			Gender		Residence		BMI	
		Total	*Male*	*Female*	*Familiar*	*Others*	*< 25*	*> 25*
Takes a fruit or fruit juice every day		76.7	78.6	76.1	74.5	81.5	77.0	76.6
Has a second fruit every day		43.1	46.4	41.9	39.8	50.6	40.1	56.3***
Has fresh or cooked vegetables regularly once a day		68.6	52.4	74.4***	68.4	67.9	68.3	68.8
Has fresh or cooked vegetables more than once a day		24.2	15.5	27.4*	25.1	22.2	22.2	31.3
Consumes fish regularly (at least 2-3 times per week)		58.5	52.4	60.7	58.9	58.0	51.7	64.1
Likes legumes and eats them more than once a week		92.8	95.2	91.9	93.5	90.1	93.3	90.6
Consumes pasta or rice almost every day (5 or more times		38.1	54.8	32.1***	39.8	33.3	38.9	34.4
Has cereals or grains (bread, etc.) for breakfast		78.9	77.4	79.5	79.2	77.8	77.4	84.4
Consumes nuts regularly (at least 2-3 times per week)		41.5	51.2	38*	39.8	45.7	41.7	40.6
Uses olive oil at home		97.8	98.8	97.4	97.4	98.8	98.0	96.9
Skips breakfast		17.0	21.4	15.4	17.7	14.8	15.1	25*
Has a dairy product for breakfast (yoghurt, milk, etc.)		88.4	95.2	85.9***	88.3	87.7	89.7	82.8
Has commercially baked goods or pastries for breakfast		11.9	14.3	11.1	11.7	12.3	12.3	10.9
Goes more than once a week to a fast-food (hamburger)		23.6	41.7	17.1***	26.4	13.6**	23.4	23.4
Takes two yoghurts and/or some cheese (40 g) daily		60.1	56.0	61.5	58.4	63.0	58.3	67.2
Takes sweets and candy several times every day		12.6	9.5	13.7	14.7	7.4*	15.5	0***
Total punctuation (0-12)		7.0 ± 1.9	6.9 ± 2.0	7.1 ± 1.9	6.9 ± 1.9	7.3 ± 2.0	7.0 ± 1.9	7.3 ± 2.0
KIDMED Index	Poor (≤ 3)	3.1	6.0	2.1	3.0	3.7	2.8	4.7
	Average (4–7)	53.5	50.0	54.7	56.3	46.9	55.6	43.8
	Good (≥ 8)	43.4	44.0	43.2	40.7	49.4	41.7	51.6

* P < 0.05 of significant difference.
** P < 0.01 of significant difference.
*** P < 0.001 of significant difference.

39.7%; p < 0.01). These differences are mainly related to intake of fruits and nuts, both of which showed significant differences.

In the case of BMI, it is significant that overweight students tended to skip breakfast more than the rest of the students (14.8% *vs* 35.3%; p < 0.05).

Comparison between first and fourth year students

No statistical differences in the degree of AMD were seen between first and fourth year students although adherence was greater in fourth year students (40.8% *vs* 48.6%) (table IV).

As regards individual questions (table IV) there were statistical differences in the consumption of cereal or grains for breakfast and the daily consumption of sweets and candy: 75.6% of first year students had cereal or bread for breakfast, while 85.7% of fourth year volunteers did so (p < 0.05), while 16.4% of first year students ate sweets several times a day *vs* 4.8% of fourth year students (p < 0.001).

Discussion

The mean BMI recorded is 23.02 with significant differences between gender (24.35 for males and 22.54 for females; p < 0.001) (table II). These results are slightly higher than those for other regions of Spain such as Soria[24], Galicia[25], Navarra[26] or Balearic Islands[27] and closer to others studies developed in Murcia[28]. These are also in line with some official studies where the prevalence of obese people is higher in southern regions of Spain[29]. On the other hand, the BMI in our study was similar to that described for medical students in northern Greece, another Mediterranean region[30], and significantly lower than that described for students in North Carolina, USA[21].

The KIDMED index showed that 43.4% of students as a whole had a good AMD score, which is higher than the 33% recorded in Galicia[25] and the 28.4% mentioned for the University of Navarra[26]. At the same time the prevalence of students with a poor AMD was 3.2%, much lower than for Galicia (23.0%) and Navarra (9.1%). Such differences may due to the different dietary culture since in the Mediterranean area of Spain, including Murcia, the MD is still more closely followed that in northern regions.

Analysis of the different items identified several negative aspects in our population. For example one in four students does not consume fruits regularly and fewer than half have a second piece. The consumption of vegetables is even worse: one in three students does not consume vegetables daily and only one in four consumes them twice per day. Fruits and vegetables have a very important mission in the body as regulators of the metabolism and both are included in the Mediter-

Table IV
Results for KIDMED test of 1st and 4th year for total students and by categories

		First year							Fourth year						
			Gender		Residence		BMI			Gender		Residence		BMI	
		Total	Male	Female	Familiar	Other	< 25	> 25	Total	Male	Female	Familiar	Other	< 25	> 25
Takes a fruit or fruit juice every day		78.4	85.4	76.4	77.8	77.6	79.3	76.6	73.3	69.4	75.4	67.1	87.5*	72.7	76.5
Has a second fruit every day		43.2	47.9	41.8	42.4	42.9	40.2	55.3*	42.9	44.4	42.0	34.2	62.5**	39.8	58.8
Has fresh or cooked vegetables regularly once a day		71.8	58.3	75.8**	71.5	71.4	70.1	76.6	61.9	44,4	71.0**	61.6	62.5	64.8	47.1
Has fresh or cooked vegetables more than once a day		24.4	18.8	26.1	25.9	20.4	22.0	31.9	23.8	11,1	30.4*	23.3	25.0	22.7	29.4
Consumes fish regularly (at least 2-3 times per week)		56.3	50.0	58.2	58.2	51.0	54.9	61.7	62.9	55.6	66.7	60.3	68.8	61.4	70.6
Likes legumes and eats them more than once a week		93.4	97.9	92.1	95.6	85.7*	93.3	93.6	91.4	91.7	91.3	89.0	96.9	93.2	82.4
Consumes pasta or rice almost every day (5 or more times per week)		37.1	43.8	35.2	39.2	30.6	39.0	29.8	40.0	69,4	24.6***	41.1	37.5	38.6	47.1
Has cereals or grains (bread, etc.) for breakfast		75.6	77.1	75.2	75.9	73.5	73.2	83.0	85.7	77.8	89.9	86.3	84.4	85.2	88.2
Consumes nuts regularly (at least 2-3 times per week)		40.4	43.8	39.4	41.1	36.7	39.0	44.7	43.8	61,1	34.8**	37.0	59.4*	46.6	29.4
Uses olive oil at home		97.7	97.9	97.6	97.5	98.0	97.6	97.9	98.1	100.0	97.1	97.3	100	98.9	94.1
Has breakfast everyday		16.4	18.7	15.8	16.5	16.3	15.2	21.3	18.1	25.0	14.5	20.5	12.5	14.8	35.3*
Has a dairy product for breakfast (yoghurt, milk, etc.)		88.3	97.9	85.5***	88.6	85.7	89.0	85.1	88.6	91.7	87.0	87.7	90.6	90.9	76.5
Has commercially baked goods or pastries for breakfast		12.7	14.6	12.1	12.0	14.3	13.4	10.6	10.5	13.9	8.7	11.0	9.4	10.2	11.8
Goes more than once a week to a fast-food (hamburger)		25.8	41.7	21.2***	27.8	16.3*	26.8	21.3	19.0	41,7	7.2***	23.3	9.4	17.0	29.4
Takes two yoghurts and/or some cheese (40 g) daily		59.2	50.0	61.8	58.2	59.2	57.3	66.0	61.9	63.9	60.9	58.9	68.8	60.2	70.6
Takes sweets and candy several times every day		16.4	8.3	18.8*	18.4	12.2	20.7	0.0***	4.8	11.1	1.4	6.8	0.0	5.7	0.0
Total punctuation (0-12)		6.9±1.9	6.9±1.8	7.0±2.0	6.7±2.0	7.0±1.9	6.8±1.9	7.5±1.9**	7.2±1.9	6.9±2.3	7.4±1.6	6.8±1.7	8.1±1.8***	7.3±1.7	6.9±2.4
KIDMED Index	Poor (≤3)	3.3	4.2	3.0	6.1	2.5	3.0	4.3	2.9	8.3	0.0	4.1	0.0	2.3	5.9
	Average (4–7)	55.9	52.1	57.0	57.1	56.3	59.1	42.6	48.6	47.2	49.3	56,2	31.3**	48.9	47.1
	Good (≥8)	40.8	43.8	40.0	36.7	41.1	37.8	53.2	48.6	44.4	50.7	39.7	68,8**	48.9	47.1

* P < 0.05 of significant difference.
** P < 0.01 of significant difference.
*** P < 0.001 of significant difference.

ranean diet pattern. They are cheap, easy to find and not perishable so there is no logical reason to avoid them as a snack or in meals. This finding should serve as a reminder concerning student's knowledge of the benefits to be gained from eating fruits and vegetables and any perceived negative factors should be analysed on attempt to avoid them.

The consumption of pasta and rice was also less than recommended. These products are the base of the food pyramid as energy suppliers and should be consumed almost daily.

Skipping breakfast is a practice not to be recommended because breakfast is essential to provide energy and nutrients to start the day. Some studies have confirmed the relation between skipping breakfast and lower attention capabilities[31].

Another negative finding was that almost one in four students goes more than once a week to fast-food restaurant, a well established practice in students, especially at weekends. Fast food restaurants are cheap, they offer quick service and the food is standardized, attributes which seem to be appreciated for students. But fast food is not exempt of harmful effects related with saturated fats, salt, sugar and energy levels. Information in this respect should be given to students to improve their dietary habits even eating out.

But our study also found positive aspects. The consumption of olive oil was high. Almost all students use it at home, even for cooking. It is important to extend the use of this fat over others to increase levels of oleic fatty acid and antioxidants[32].

Another positive aspect was the consumption of legumes (92.8%), dairy products for breakfast (88.4%) and the low consume of commercial bakery goods for breakfast.

In the study developed in Galicia several findings were similar results to ours: e.g. the consumption of 1 piece of fruit/day, fish 2-3 times/week, cereal/grains and dairy products for breakfast (also tendency to skip breakfast), yoghurt or cheese daily and olive oil.

In other respects there were important differences. In our study males are more likely to consume a second piece of fruit/day, legumes, pasta/rice and nuts but also to go more often to fast-food restaurants, while they consume fewer sweets/candies. Females consume more vegetables and nuts than their Galician counterparts[25].

Comparing with the findings for Navarra[26], students from Murcia are more likely to consume a second piece of fruit/day, legumes, nuts and olive oil. Males have a higher consumption of fast-food and lower consumption commercially baked goods for breakfast, and sweets and candies. Females consume more pasta/rice and yoghourt/cheese.

Other studies have evaluated dietary patterns but with different tests. A study developed at Hacettepe University in Turkey reported that dairy products, cereals and fruits/vegetables were consumed daily by only 22.3%, 48,5% and 25.2% of students respectively, while consumption of nuts was between 8.0-25.9% (depending on intake frequency/week). Only 25.9% of students were reported to have breakfast every day[33]. All these data are much lower than data from our results.

Other study developed in Zagreb pointed to a similar consumption of fruits, cereals and dairy products, while in the case of vegetables consumption is higher in our students[20].

If we analyse the results of KIDMED test bearing in mind where the students live (with their families or not), we found that students living away from home go to fast-food restaurants less and consume fewer sweets/candies ($p < 0.05$). It seems that students living on their own have less money to spend and so tend to eat out less often.

When AMD scores are compared between normoweight (BMI < 25) and overweight (BMI > 25) students, we find that the second group tends to score higher for almost all items. There is a higher consumption of a second piece of fruit/day (56.3% *vs* 40.1%) and lower consumption of sweets and candies (0% *vs* 15.5%) both with statistically significant differences ($p < 0.005$). However, is that overweight students are more likely to report to skip breakfast (25% *vs* the 15.1%; $p < 0.05$). The KIDMED test scored averaged 7.0 for students with BMI < 25 and 7.3 for students with BMI > 25. These differences as a whole suggest that at least some of the overweight students may be on a diet in an attempt to lose weight. This would explain the fact that they tend to skip breakfast more than the other students (in order to take fewer calories) despite the fact that many authors think this is a poor practice[34, 35].

While quite similar in both groups of students, the BMI was slightly lower in fourth year students (table III), suggesting that university students tend to be aware of their bodies and image, and therefore take increasing care on their dietary pattern and take physical activity.

Although physical activity was not evaluated, the KIDMED score was slightly higher in fourth year students, and there is an increment of students included in good AMD group (48.6% *vs* 40.8%). Although these differences are not significant, the data suggest that students learn better dietary patterns over these three years. This was especially borne out by differences which were significant; for example, the higher consumption of cereals for breakfast ($p < 0.05$) and lower consumption of sweets/candies ($p < 0.001$).

If we compare the different years according to where students live, we find that in the case of fourth year students, those who live away from home have a higher AMD score than others (8.1 and 6.8, respectively; $p < 0.001$) increasing the good AMD group in detriment to the medium AMD group ($p < 0.01$). The score was also higher for first year student living away from (8.1 *vs* 7.0; $p < 0.001$). At first sight, students should have a better diet when they live at home because their parents

presumably have a greater perception of good dietary patterns, as described by several authors[36,37]. On the other hand, if we consider that the MD is slowly being eroded at home, students who are responsible for their own, are free to choose between different options of food and can therefore express better their knowledge of good dietary patterns. This knowledge grows during a student's time at university. The difference between 1st and 4th year students living away from home mainly lies in the consumption of a second piece of fruit/day and fish ($p < 0.05$), legumes and nuts ($p < 0.01$), and fewer sweets/candies ($p < 0.001$).

The rest of the items pointed to no significant differences between first and fourth years, whether by gender or by BMI.

Conclusions

According to our study dietary patterns are better in student nurses from Murcia than in other regions, although several practices should be improved. The consumption of fruits, vegetables and pasta/rice should be increased, taking account their position at the base of the food pyramid. The AMD was similar for both years. Perhaps this reflects a lost opportunity to improve students' awareness of what a healthy diet is during their stay at university, which could become a place where healthy dietary patterns are improved and established. We found that students living on their own are receptive to nutritional information and improve their dietary patterns. Additional research is necessary to evaluate negative factors and to identify ways to improve the dietary pattern in the whole university population. We suggest strategies to improve knowledge of dietary patterns based on an approach to healthier foods: for example, vending machines with fruit, lower prices for fruit in canteens and educational programs about the importance of breakfast. These are just a few examples that could be taken into account.

Studies like this, focus on determine the status of a diet on a population should be complemented with long term and interventional studies. Cross-functional groups are required and also trained staff to follow volunteers almost daily. But these studies are not easy to perform and founds are usually difficult to achieve. Private companies of food industry should also be participants providing products in this kind of studies[38].

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Original / *Valoración nutricional*

Prevalencia de riesgo de desnutrición evaluada con NRS-2002 en población oncológica mexicana

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Resumen

Objetivos: **Los pacientes hospitalizados tienen un riesgo alto desnutrición, especialmente aquellos con cáncer. Existen herramientas que evalúan el estado nutricional en pacientes hospitalizados como el Nutritional Risk Screening 2002 (NRS-2002), el cual usamos en el presente trabajo en población mexicana con cáncer durante su hospitalización, para determinar la prevalencia de riesgo de desnutrición y los factores del NRS 2002 que más se asocian al riesgo nutricional.**

Métodos: **Se evaluó el estado nutricional de pacientes con cáncer con el tamizaje NRS-2002, durante su ingreso hospitalario. Se utilizó pruebas estadísticas no paramétricas, la prueba t de student, correlación de Pearson y Spearman, y ANOVA para contrastar las variables que se asocien con riesgo nutricional y por medio de modelos de regresión logística se determinó los ítems del cuestionario de mejor predicción de riesgo de desnutrición en población oncológica mexicana.**

Resultados: **El riesgo nutricional se presentó en el 50,2% de los pacientes durante su ingreso hospitalario. Los factores que más se asocia al riesgo nutricional fueron género, edad, niveles de IMC menores a 20,5, pérdida de peso e ingesta de alimentos y el cáncer hematológico ($p < 0,05$). El modelo que mejor predijo la presencia de riesgo de desnutrición en nuestra población fueron las mismas variables categorizadas que utiliza la presente encuesta de tamizaje NRS-2002 ($p < 0,05$).**

Conclusiones: **La prevalencia de desnutrición en el paciente con cáncer es alta y el NRS-2002 es una herramienta confiable en la predicción de riesgo de desnutrición en población oncológica mexicana.**

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Palabras clave: *Paciente oncológico. Desnutrición. Nutritional Risk Screening 2002 (NRS 2002). Evaluación nutricional. Riesgo nutricional.*

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PREVALENCE OF NUTRITIONAL RISK EVALUATED WITH NRS-2002 IN MEXICAN ONCOLOGY POPULATION

Abstract

Objective: **Hospitalized patients have high risk of malnutrition, specially those with cancer. There are some screening tools that lead to the detection of malnutrition in hospitalized patients, as Nutritional Risk Screening 2002 (NRS-2002), which we used in Mexican population with cancer at the moment of hospital admission to determine the prevalence of malnutrition risk, and to determine as well as the best predictive item to measuring nutritional risk in our population.**

Methodology: **Nutritional status in cancer patients with NRS 2002 during hospital admission was assessed. To the analysis of variable non statistical parametric tests, student-t test, Pearson and Spearman test, as well as ANOVA test were used. To determine the best item for predicting nutritional risk in Mexican population with cancer, a logistic regression test was applied.**

Results: **Of our population, 50.2% of were classified as patients in nutritional risk at hospital admission. Gender, age, normal levels of IMC lower than 20.5, food intake, weight loss and hematological cancer were associated with nutritional risk ($p < 0.05$). The best model of logistic regression for predicting nutritional risk were the same used by NRS-2002 questionnaire ($p < 0.05$).**

Conclusion: **Malnutrition prevalence is high in cancer patients and NRS-2002 is a reliable tool for predicting nutritional risk in Mexican population with cancer.**

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Key words: *Oncology patient. Malnutrition. Nutritional risk screening 2002 (NRS 2002). Nutritional risk. Nutritional assessment.*

Introducción

La desnutrición consiste en una deficiencia de energía, proteínas y otros nutrimentos que causan efectos adversos medibles en la composición y función de los tejidos y órganos, que causan un importante efecto negativo sobre la evolución final del paciente[1]. Los pacientes hospitalizados tienen un mayor riesgo de presentar desnutrición a medida que se prolonga su estancia hospitalaria y a su vez influye tanto en el tratamiento antineoplásico como en los riesgos de complicaciones, la mortalidad y costos de atención[2]. La prevalencia de desnutrición en pacientes oncológicos hospitalizados oscila entre el 20-50%[3-7]. Los estudios en pacientes oncológicos realizados previamente en nuestro hospital reportan una prevalencia de desnutrición entre el 18 y 37%, lo cual afecto el tiempo de estancia hospitalaria y evidentemente en incremento de los costos de atención[8,9]; y éstos pueden podrían llegar a ascender en países europeos de 1.9 hasta a más de los 170 billones de euros anuales, cuando se podrían ahorrar estas cantidades si tan solo pudieran prevenir el deterioro de la situación nutricional de los pacientes[10,11]. Debido a esto, la valoración nutricional es una herramienta clave para la detección temprana de aquellos pacientes con desnutrición o en tienen riesgo de desarrollarla y disminuir la incidencia de desnutrición y sus costos de atención.

Para la detección de desnutrición se han propuestos distintos técnicas o métodos, como valoraciones antropométricos, bioquímicas y tamizajes de valoración de riesgo de desnutrición[12,13]. Estos últimos son métodos más aplicados por su validez y facilidad de aplicación a fin de detectar el riesgo de que un paciente ingrese al hospital con con un estado nutricional deficiente para posteriormente, ser sometido a una valoración nutricional que permita determinar el tipo de intervención nutricional más conveniente[13]; los más usados en los pacientes adultos están el Mini Nutritional Assessment, Malnutrition Universal Screening Tool (MUST) y Nutritional Risk Screening 2002 (NRS-2002)[14-16]. El NRS-2002, propuesto por Kondrup y colaboradores, es recomendado por la ESPEN, ha sido validado en países Europeos y orientales, presenta una especificidad y sensibilidad > 80% en pacientes de distintas patologías y edades, así como en mayores de 60 años[15,17]. Este cuestionario consta de 2 etapas de valoración en las cuales reúne datos del Índice deMasa Corporal (IMC), pérdida de peso, ingesta energética y severidad de la enfermedad de base a fin de tomar en cuenta todas las características iniciales del paciente para que puedan entrar en una de las categorías de diagnóstico[18,19]. Esta encuesta de escrutinio se utilizó en el presente estudio con el objetivo de evaluar la prevalencia de riesgo de desnutrición en los pacientes oncológicos Mexicanos y determinar si los ítems utilizados por este tamizaje son los mejores para predecir el riesgo de desnutrición en nuestra población para poder sentar las bases a fin de aplicarse de manera rutinaria en el hospital a pacientes oncológicos.

Material y métodos

El presente estudio es de tipo transversal y descriptivo, aprobado por el comité de ética e investigación del Hospital General de México y fue realizado en un lapso de 18 meses. Se tomaron en cuenta a todos los pacientes que ingresaron al servicio de oncología para ser hospitalizados, que presentaran una edad mayor a 18 años, sin importar el tipo de cáncer diagnosticado, morfología o etapa clínica en el momento en que ingresaron al hospital.

Tamizaje nutricional

Tras la hospitalización de los pacientes, un grupo de nutriólogos realizó el cuestionario de Tamizaje del riesgo nutricional 2002 (NRS-2002) que consta de 2 etapas: La primera etapa consta de un "Tamizaje inicial" que consta de 4 preguntas (¿l IMC es menor a 20,5?, ¿El paciente ha perdido peso en los últimos 3 meses?, ¿El paciente ha reducido su consumo alimenticio durante la última semana?¿Presenta una enfermedad severa?) que, en caso de considerarse positiva alguna de ellas se pasa a la segunda etapa de valoración de riesgo nutricional final que con base al estado nutricional (Valoración de la pérdida de peso, el IMC y la ingesta dietética), "severidad de la enfermedad" (valora el tipo de padecimiento, enfermedad de base o procedimiento médico al que será sometido el paciente) y, si el paciente es mayor a 70 años establece una puntuación extra para poder determinar la presencia de riesgo de desnutrición del paciente a padecer desnutrición.

Se evaluó el IMC de los pacientes según los criterios de la Organización Mundial de la Salud (OMS)[20]; la pérdida de peso respecto al peso habitual se clasificó como leve, a una pérdida mayor al 5% en tres meses, moderada, a una pérdida mayor al 5% en 2 meses y severa, a una pérdida mayor al 5% en un mes o más del 15% en 3 meses; y la ingesta de alimentos respecto a la habitual se clasificó como ingesta normal aquella entre 71-100%, disminución leve a una ingesta entre el 51-70%, disminución moderada entre el 26-50% y disminución severa entre el 0 y 25%.

Análisis estadístico

Los datos obtenidos fueron acomodados en una base de datos y se analizaron por medio del programa SPSS (Statistical Product and Service Solution) versión 20 para Windows. La descripción de los datos obtenidos se realizó a través de medias ± desviación estándar, y porcentajes respecto al total de la población.

Para el análisis de los datos de los pacientes evaluados en la segunda etapa del tamizaje nutricional se utilizó la prueba Ji cuadrada para contrastar variables nominales, U de Mann-Withney para el contraste de variables ordinales, la prueba t de student para el con-

traste de variables escalares, y correlación de Pearson y Spearman para determinar la fuerza de asociación entre variables. Se utilizó del análisis de varianza (ANOVA) y la prueba *Post-Hoc* para determinar la relación entre el riesgo nutricional y el tipo de cáncer.

Se realizó un modelo estadístico de regresión logística para determinar si los datos de la encuesta de tamizaje nutricional NRS-2002 son los más predictivos de riesgo de desnutrición en nuestra población de pacientes con cáncer.

Se utilizó un 80% de poder del estudio y un 95% de confianza para determinar diferencias significativas entre variables por medio de valores de $p < 0,05$.

Resultados

Durante los 18 meses del estudio 444 pacientes fueron evaluados durante las primeras 24 horas de su ingreso hospitalario. Las características generales de los pacientes se describen en la tabla I. Del total de pacientes el 61,1% fueron mujeres con edad promedio de 50,45 ± 12,52 años y el 39,9% hombres con edad promedio de 48,13 ± 18,79 años. El IMC se evaluó en el total de los pacientes y se observó que al ingreso hospitalario el 7.2% presentó desnutrición y el 50,7% presentó un estado nutricional normal, ambos con similar proporción entre sexos; por otro lado el 24,1% presentó sobrepeso y 18% obesidad, observándose una mayor proporción en el sexo femenino, lo cual se corroboró con los valores puntuales de IMC que indican que los pacientes de sexo masculino ingresan con valores de IMC significativamente menores a los del femenino ($p < 0,05$) (tabla II).

En cuanto al tamizaje de riesgo nutricional con NRS-2002, los resultados de la primera etapa muestran que el 25,5% no contestaron afirmativamente a ninguna pregunta de la primera etapa, es decir, sin sospecha de riesgo nutricional y el 75% continuó a la segunda etapa o tamizaje final. De los pacientes que continuaron con la evaluación, el 26% presentaron un IMC menor a 20,5, 55,6% reportaron pérdida de peso, 55,4% reportaron tener una ingesta de alimentos disminuida y 35,5% fueron considerados como "paciente grave".

La distribución de los pacientes que continuaron a la segunda etapa del tamizaje con su correspondiente puntaje final se muestran en la tabla III, y observa que el 50,2% de los pacientes (n = 223) se encontraron en riesgo nutricional o puntaje mayor a 3, y el 24,3% (n = 108) un puntaje menor a 3 para ser reevaluado semanalmente durante su estancia hospitalaria. En cuanto al riesgo nutricional y los puntos clave que evalúa el cuestionario, todos presentaron una asociación a la presencia de riesgo nutricional. El sexo femenino se asoció con una mayor riesgo nutricional en comparación con el masculino; también se asoció con un IMC en rangos normales pero con valores significativamente menores en aquellos pacientes que no presentan riesgo nutricional y sólo el 26% se encontró por debajo de 20,5; por otro lado la edad de los pacientes con riesgo nutricional presentó una media significativamente mayor que aquellos sin riesgo pese a que sólo el 10% de aquellos en riesgo nutricional presentaron una edad mayor a 70; por último la ingesta de alimentos y la pérdida de peso se asociaron significativamente al riesgo nutricional. Entre los factores que se correlacionaron con riesgo nutricional, la ingesta de alimentos ($p < 0,0001$, r = 44,3%) y IMC menor a 20,5 ($p < 0,0001$, r = 40,8%) presentaron una correlación débil, mientras que la pérdida de peso correlacionó moderadamente ($p < 0,0001$, r = 64,9%). Por último al analizar el tipo de cáncer que más se asocia a la presencia de riesgo nutricional al ingreso hospitalario se encontró que el tipo de diagnóstico más asociado fue el cáncer hematológico ($p < 0,0001$).

Discusión

El presente estudio según nuestros conocimientos, es el primero en México que utiliza el NRS para evaluar el riesgo de desnutrición en población oncológica lo cual permite establecer una comparación más uniforme con la obtenida en otros países.

La desnutrición es un problema común, y varía según el método que se utilice para determinarla, el tipo de población estudiada y el país de origen, de ahí la dispersión de valores encontrados en la literatura. Por medio de valores de IMC, la prevalencia de desnutrición resulto muy baja (7,2%), por lo que el IMC no resulta ser por si sólo una herramienta muy útil en la detección

Tabla II
Diagnóstico nutricional de IMC por sexo del total de pacientes evaluados

IMC	*Total N = 444 (%)*	*Masculino n = 177 (%)*	*Femenino n = 267 (%)*	*Valor de p e IC*
Desnutrición severa (IMC <16-18,49)	32 (7,2)	16 (3,6)	16 (3,6)	
Normal (IMC 18,5-24,99)	225 (50,7)	109 (24,5)	116 (26,1)	p < 0,0001
Sobrepeso (IMC 25-29,99)	107 (24,1)	39 (8,8)	68 (15,3)	
Obesidad (IMC >30)	80 (18)	13 (2,9)	67 (15,1)	

IMC = índice de masa corporal, IC = Intervalo de confianza.

Tabla III
Tamizaje de riesgo nutricional NRS-2002 aplicado a los pacientes del servicio de oncología

	Evaluación semanal SCORE < 3 n = (%)	*Riesgo nutricional SCORE > 3 n = (%)*	*Valores de p*
Puntuación de la población			
0[a]	113 (25)	–	
1	12 (2.7)	–	–
2	96 (21.6)	–	–
3	–	76 (17.1)	–
4	–	130 (29.3)	–
5	–	16 (3.6)	–
6	–	1 (0.2)	–
Muestra total de la segunda evaluación	108 (24.3)	223 (50.2)	–
Sexo			
Femenino	81 (18.2)	125 (28.2)	0.001[b]
Masculino	27 (6.1)	98 (22.1)	
IMC (kg/m^2)	27.12 ± 5.14	22.81 ± 4.65	< 0.0001[d] IC = 3.19-5.41
IMC ≥20.5	0	86 (26)	<0.0001[b]
Edad	46.82 ± 13.26	52.33 ± 15.57	0.02[d] IC = -8.94,-2.08
Edad ≥ a 70 años	0	33 (10)	<0.0001[b]
Pérdida de peso			
Sin pérdida	50 (11.3)	44 (9.9)	< 0.0001[c]
Leve	58 (13.1)	39 (8.8)	
Moderada	0	43 (9.7)	
Severa	0	97 (21.8)	
Ingesta de alimentos			
Ingesta normal	35 (7.9)	57 (12.8)	< 0.0001[c]
Disminución leve	73 (16.4)	41 9.2)	
Disminución moderada	0	75 (16.9)	
Disminución severa	0	50 11.3)	

IC = Intervalo de confianza.
[a] Frecuencia de pacientes que no pasaron a la segunda etapa del tamizaje nutricional.
[b] Contraste de variables con la prueba Chi-cudrada..
[c] Contraste de variables con la prueba U de Mann-Whitney.
[d] Contraste de variables con la prueba t-student.

de desnutrición, además de que se reporta en la literatura una baja sensibilidad para poder evaluar el estado nutricional. [21,22] Por otro lado al reclasificar nuestros resultados de IMC con valores establecidos por el tamizaje (IMC < 20,5) el porcentaje aumenta considerablemente hasta un 26%, siendo los varones los más asociados a estos porcentajes lo cual coincide con algunas publicaciones que indica que el sexo masculino es un factor de riesgo de desnutrición, mientras otras no concuerdan con estos datos[23,24].

En cuanto al riesgo nutricional nuestros datos arrojaron valores elevados (50,2%) en pacientes con cáncer, sin embargo, este resultado no muy comparable a otros estudios ya que la mayoría son realizado en población general o de otras patologías distintas a la nuestra. Minetras que en México, Landa-Galván HV y cols. en población de nuestro mismo hospital, encontraron una prevalencia de riesgo de desnutrición del 45,2%, en pacientes hepatopatas[25], en otros países de Sudamérica, las prevalencias reportadas por el cuestionario NRS 2002 son distintas desde un 39% en Brasil y 57% de riesgo de desnutrición Argentina[27]. Sin embargo pese a que estos estudios evalúan el NRS 2002, no son aplpicados en población con el mismo diagnóstico a la nuestra.

En cuanto a los países del continente europeo y occidente, las prevalencias reportadas son menores los que reportamos en México y Latinoamérica, posiblemente debido a las condiciones socioeconómicas que presenta cada país. En población hospitalizada en general la prevalencia varía desde 38 a 67%[17,28,29], Sherhat G A y cols.[19] reportaron en Turquía en el 2009 una prevalencia de 31,2% en pacientes con cáncer gástrico; Bosetti

F y cols.[30] en Italia en el 2012 una prevalencia de 32% en cáncer en general; en China en el mismo año un estudio reportan el 22% en pacientes con leucemia[31]; y un estudio en Romania en el 2013, realizado en población similar a la nuestra, es decir con cáncer, reportaron que una prevalencia menor a la nuestra, dando como resultado que el 31,3% de su población con el cuestionario NRS 2002 presento riesgo de desnutrición[32].

El cuestionario de Tamizaje NRS-2002 tiene el propósito de diferenciar a los individuos que se encuentren en alto riesgo de presentar problemas nutricionales o que presentan un estado nutricional deficiente, de aquellos pacientes con buen estado nutricional.

Una de las fortalezas de nuestro estudio es el análisis de los ítems que conforma el cuestionario de NRS 2002 el cual mostro el conjunto de sus ítems muestra ser un buen modelo de predicción de desnutrición en nuestra población, a excepción del tipo de cáncer ya que pueda deberse a que aunque haya distintos tipos de cáncer en nuestro estudio no deja ser no deja ser una patología de misma naturaleza, además de que en general el cáncer es un factor de riesgo de desnutrición[23]. Debido a esto a la hora de relacionar directamente el tipo de cáncer con el riesgo nutricional el cáncer de hematológico es uno de los que mayor puntaje de riesgo de desnutrición presentó, y esto coincide con el mismo cuestionario NRS 2002 que da un puntaje extra al tipo de cáncer hematológico[16].

La desnutrición debería ser evaluada de forma sistemática en todos los hospitales, tal y como ocurre con otros signos de exploración. En el caso de los pacientes hospitalizados es imprescindible contar con un sistema de tamizaje capaz de detectar el riesgo nutricional de los pacientes, y de fácil aplicación por cualquier personal de la salud para poder identificar de manera temprana problemas relacionados el estado nutricional y brindar un soporte nutricional adecuado a la situación del paciente, y así evitar complicaciones.

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Conflicto de interés

Los autores no reportamos ningún conflicto de interés en la publicación de este estudio.

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Original / *Otros*

Composición corporal y variabilidad del ritmo cardiaco en pacientes con enfermedad pulmonar obstructiva crónica candidatos a rehabilitación respiratoria

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Resumen

La composición corporal es una metodología no invasiva, que nos entrega información acerca de la distribución de tejidos en la estructura corporal, además es un indicador del riesgo de mortalidad en pacientes con Enfermedad pulmonar obstructiva crónica. La variabilidad del ritmo cardiaco es una técnica que nos entrega información de la condición fisiológica autonómica, siendo reconocida como un indicador que se encuentra disminuido en una serie de enfermedades. El propósito de este estudio fue evaluar la composición corporal y la Variabilidad del ritmo cardiaco. La metodología utilizada es la de Debora Kerr (1988) avalada por Sociedad Internacional para avances en Cineantropometría para composición corporal y para Variabilidad del ritmo cardiaco los lineamientos descritos por la American Heart Association (1996). Se empleó equipamiento Roscraff, caliper Slimguide y reloj Polar RS 800CX. Se evaluaron 14 pacientes candidatos a rehabilitación respiratoria: Edad 76 ± 9,9 años; IMC 26,7 ± 3,9 kg/m²; Masa Muscular 26,1 ± 6,3 kg; Masa Ósea 8,1 ± 1,3 kg; Masa Adiposa 16,4 ± 3,6 kg; VEF1 54 ± 14 %. Un mayor perímetro de cintura e índice Cintura Cadera se asoció a una menor Variabilidad del ritmo cardiaca global. El componente óseo se relacionó positivamente con la Variabilidad del ritmo cardiaco y los pacientes con un mayor Volumen espiratorio forzado en el primer segundo presentaron un menor componente de alta frecuencia en la Variabilidad del ritmo cardiaco. En estos pacientes, la Variabilidad del ritmo cardiaco en forma global se encuentra reducida y se asocia con parámetros de riesgo cardiovascular.

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BODY COMPOSITION AND HEART RATE VARIABILITY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE PULMONARY REHABILITATION CANDIDATES

Abstract

Body composition is a non-invasive method, which gives us information about the distribution of tissues in the body structure, it is also an indicator of the risk of mortality in patients with chronic obstructive pulmonary disease. The heart rate variability is a technique that gives us information of autonomic physiological condition, being recognized as an indicator which is decreased in a number of diseases. The purpose of this study was to assess body composition and heart rate variability. The methodology used is that of Debora Kerr (1988) endorsed by the International Society for advances in Cineantropometría for body composition and heart rate variability of the guidelines described by the American Heart Association (1996). Roscraff equipment, caliper Slimguide and watch Polar RS 800CX was used. , BMI 26.7 ± 3.9 kg / m²; Muscle Mass 26.1 ± 6.3 kg ; Bone Mass 1.3 kg ± 8.1 76 ± 9.9 years Age : 14 candidates for pulmonary rehabilitation patients were evaluated , Adipose mass 16.4 ± 3.6 kg ; FEV1 54 ± 14%. Increased waist circumference and waist hip ratio was associated with a lower overall heart rate variability. The bone component was positively related to the variability of heart rate and patients with higher forced expiratory volume in one second had lower high-frequency component in heart rate variability. In these patients, the heart rate variability is reduced globally and is associated with cardiovascular risk parameters.

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Key words: *Anthropometry. Chronic obstructive pulmonary disease. Heart rate variability.*

Introducción

La enfermedad pulmonar obstructiva crónica es una patología prevalente en la atención primaria. En las salas de atención respiratorias del adulto, donde prestan servicios Kinesiólogos, presentando un porcentaje importante de consulta e ingreso diario.

Con el aumento de tabaquismo en nuestro país esperamos que esta patología tenga aun mayor incidencia en la población, y ser un motivo de consulta más frecuente.

Es la rehabilitación respiratoria una de las terapias que demuestra disminuir los síntomas, mejorar la calidad de vida, reducir las exacerbaciones, restringir las hospitalizaciones y evitar las consecuencias sistémicas propias de la Enfermedad pulmonar obstructiva crónica. Acompañada de una terapia broncodilatadora óptima, así como también, de las distintas intervenciones de las disciplinas que cuenta la atención primaria como son medicina, nutrición, enfermería y psicología.

Por esto, se realizó una indagación representativa de 14 pacientes candidatos a rehabilitación respiratoria, para definir como se encontraba la Variabilidad del ritmo cardiaco, además de un perfil de la morfoestructura, junto con las variables espirométricas funcionales, solicitadas para evaluar el ingreso a dicho programa.

Con esta exploración se espera ayudar a optimizar la evaluación de los pacientes ingresados a programas de rehabilitación pulmonar, para así evitar posibles eventos cardiovasculares, los cuales se podrían prevenir con este tipo de evaluaciones.

Sujetos y métodos

Se estudió una muestra de 14 pacientes respiratorios con Enfermedad pulmonar obstructiva crónica (EPOC), todos seleccionados para realizar rehabilitación pulmonar, pertenecientes a la sala de Enfermedades respiratorias del adulto ERA del Centro de salud San Ramón.

Todos los sujetos fueron informados del contenido de la investigación y se les pidió el consentimiento para participar en la misma. El estudio contó con la aprobación del Departamento de salud comunal.

Los criterios seguidos para ser ingresados al programa de rehabilitación pulmonar fueron:

a) Estar ingresado a la Sala de enfermedades respiratorias del adulto con diagnostico de Enfermedad pulmonar obstructiva crónica.
b) Mantener controles y examen al día.
c) Estar controlado y compensado de sus enfermedades crónicas.
d) Electrocardiograma normal.
e) Volumen espiratorio forzado en el primer segundo entre 50% y 65%.
f) Evaluación y autorización médica para ingresar al programa.
g) No poseer contraindicaciones al ejercicio.
h) Prestar el consentimiento informado.

Este estudio es de tipo no experimental, descriptivo, de diseño transversal, correlacionar con un muestreo no probabilístico, presenta las variables Composición corporal, Variabilidad del ritmo cardiaco y Espirometría; la metodología usada fue: Para valorar la composición corporal se utilizó la metodología de Débora Kerr (1998); Para evaluar la Variabilidad del ritmo cardiaco se utilizó el método de la American Heart Association (1996) de análisis lineal en dominio del tiempo y dominio de la frecuencia. Materiales: Kit antropométrico Roscraff, Canadá; Caliper Slimguide; Pesa electrónica Gama capacidad 150 kg ± 0,1 kg; además Software Polar precisión performance®, Software Kubios, Finlandia, Software G- Stat 20, España, Espirómetro Micro Medical.

Resultados

Se estudió una muestra de 14 pacientes respiratorios edad 76 ± 9,9 años, talla 159,2 ± 8,8 cm., peso 67,9 ± 12,4 kg, Índice de masa corporal 26,7 ± 3,9; Pacientes con Enfermedad pulmonar obstructiva crónica, de los cuales todos estaban seleccionados para realizar rehabilitación pulmonar, pertenecientes a la sala de Enfermedades respiratorias del adulto del Centro de salud San Ramón, de los cuales uno fue descartado por presentar requerimiento de oxígeno al momento de la evaluación.

En la tabla I la media de SDNN es 23,16 ms y 5,79 para el Indice triangular RR de los pacientes con Enfermedad pulmonar obstructiva crónica.

En la tabla II la Masa muscular muestra un porcentaje medio de 38,2% en los pacientes EPOC.

Tabla I
Variabilidad del ritmo cardíaco análisis estadístico en el dominio del tiempo

Media R-R (ms)	*SDNN (ms)*	*PNN50 (%)*	*Índice triangular*
846,67 ± 93,9	23,16 ± 14,0	7,66 ± 15,2	5,79 ± 2,6

Tabla II
Composición corporal

Músculo (%)	*Músculo (kg)*	*Adiposo (%)*	*Adiposo (kg)*	*Óseo (%)*	*Óseo (kg)*
38,2 ± 3,4	26,1 ± 6,3	24,3 ± 4,5	16,4 ± 3,6	12,1 ± 1,3	8.1 ± 1,3

En la figura 1 se observa una relación positiva, estadísticamente significativa entre el porcentaje de masa ósea y el porcentaje de PNN50 de los pacientes con Enfermedad pulmonar obstructiva crónica.

En la figura 2 se observa una relación negativa, estadísticamente significativa entre los cm. de perímetro de cintura y los ms. de SDNN de los pacientes con Enfermedad pulmonar obstructiva crónica.

Discusión

La enfermedad pulmonar obstructiva crónica es una dolencia que va en aumento en la población chilena, debido al aumento del tabaquismo. Por tanto es importante conocer la repercusión de está en el organismo, ya que es una enfermedad Multisistémica[1]. Asi tambien, es importante conocer el comportamiento de la Variabilidad del ritmo cardiaco en reposo y la morfoestructura en estos pacientes[2]. En este sentido la American Heart Association (1996) plantea que la Variabilidad del ritmo cardiaco tiene usos clinicos, que permiten evaluar el estado de salud cardiovascular. Ademas la Variabilidad se ve disminuida en la enfermedad pulmonar obstructiva crónica[3]. Asi como tambien, la morfoestructura se encuentra afectada por la Enfermedad pulmonar obstructiva crónica[4]. Ademas la atrofia musculo esqueletica esta relacionada con la disminución de calidad de vida, aumento del uso de los recursos de salud y una sobrevida empeorada en EPOC avanzados[5].

En el grupo de pacientes evaluados, todos presentan una Enfermedad pulmonar obstructiva crónica diagnosticada de forma clínica con informe de espirómetro. Al revisar las patologías crónicas, gran cantidad de pacientes presenta al menos una patología como la Hipertensión arterial o Diabetes mellitus tipo 2, por lo tanto es necesario evaluar el estado de salud cardiovascular[6].

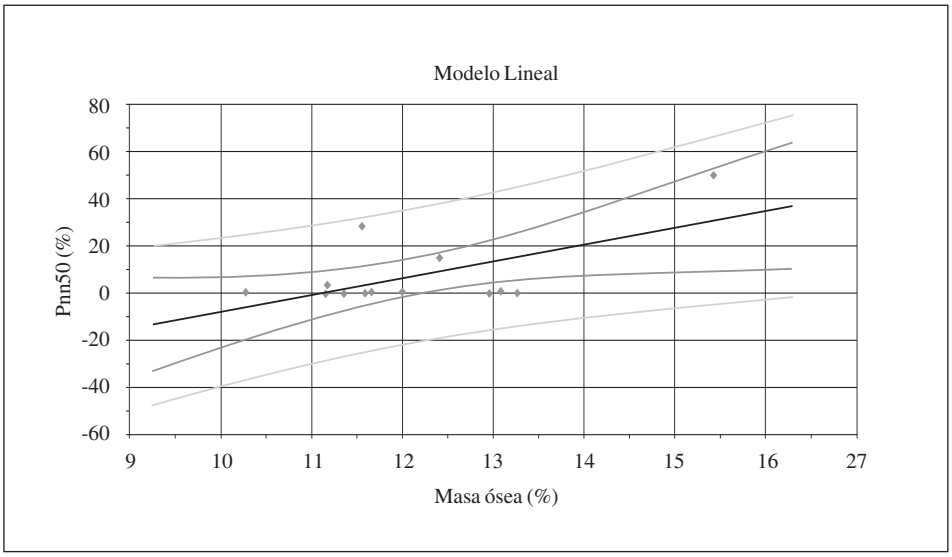

Fig. 1.—Relación entre masa ósea en porcentaje-Número de pares de intervalos RR adyacentes que difieren por más de 50 milisegundos en el registro completo dividido por el número total de intervalos RR (PNN50) en porcentaje de pacientes con EPOC; coeficiente de correlación r Pearson: 0,612; P : 0,0255 (n = 13).

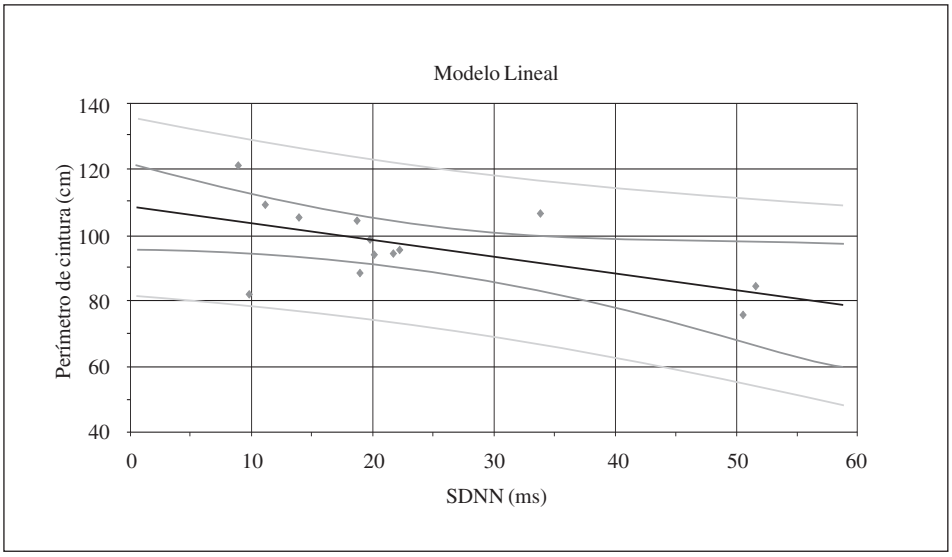

Fig. 2.—Relación entre perímetro de cintura en centímetros-Desviación de todos los intervalos RR (SDNN) en milisengundos en pacientes EPOC; Coeficiente de correlación r Pearson: -0,5667; p: 0,0435 (n = 13).

Los parámetros para informar la Variabilidad vienen dados por American Heart Association – Circulation (1996). Donde un valor SDNN menor a 50 ms (Media de la muestra: 23,16 ms) además de un valor de índice triangular RR menor a 15 (Media de la muestra: 5,79) indican una Variabilidad del ritmo cardiaco altamente disminuida[7].

Estos pacientes son sedentarios, con un sentimiento de temor frente a la sensación de disnea. Por lo tanto están en un círculo patológico de sedentarismo – desacondicionamiento[8].

La relación entre el porcentaje de Masa ósea y el PNN50, que representa la influencia parasimpática del corazón[9]. Tiene relación con el sistema de sostén que es el esqueleto. Igualmente es un sistema de anclaje para la masa muscular. Al tener un sostén mayor se puede tener una masa muscular mayor[10].

Así también un SDNN mayor, indica que existe mayor Variabilidad en el sistema nervioso autónomo, presentando mejor parámetro de salud cardiovascular[11]. La relación entre el perímetro de cintura y el SDNN. El perímetro de cintura según las tablas chilenas de riesgo cardiovascular indica: para varones un valor mayor a 102 cm y para las mujeres de 88 cm actualmente muestra un mayor riesgo de presentar un evento cardiovascular en el futuro. Consiguientemente, a mayor perímetro menor Variabilidad, representado por un SDNN más bajo[12].

La Antropometría representa una herramienta de apoyo a la labor del Kinesiólogo tanto para el monitoreo del entrenamiento, nutrición y prevención de lesiones en este tipo de pacientes[13-15]. La Variabilidad del ritmo cardiaco constituye una variable de gran valor pronóstico y valoración del riesgo cardiovascular[16-19]. Además el índice de masa corporal es un indicador que debe ser mejorado con medidas antropométricas[20,21].

Conclusiones

La Variabilidad del ritmo cardiaco se encuentra reducida en este grupo de pacientes. La Variabilidad está asociada con parámetros antropométricos de riesgo cardiovascular en esta muestra de pacientes. Un mayor perímetro de cintura se asoció con una menor Variabilidad del ritmo cardiaco. Un índice de cintura – cadera mayor se relacionó con una Variabilidad del ritmo cardiaco disminuida. El componente óseo se relacionó con el componente parasimpático de la Variabilidad del ritmo cardiaco.

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Original / *Otros*

Hypomagnesaemia in critically ill patients with haematological malignancies

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Abstract

Introduction: **There is currently little information regarding the incidence of hypomagnesaemia and its impact on the prognosis of critically ill patients with haematological malignancies.**

Objective: **This study sought to describe the incidence of hypomagnesaemia in critically ill patients with haematological malignancies admitted to an oncological intensive care unit (ICU).**

Methods: **A total of 102 critically ill patients with haematological malignancies, who were 18 years of age and admitted to the ICU between January 2008 and April 2011, were included in this study. Hypomagnesaemia was defined as a serum magnesium concentration below 1.7 mg/dl.**

Results: **The incidence of hypomagnesaemia at admission or during the first 24 hours of stay in the ICU was 22.5% (23/102). The hospital mortality rates of patients with and without hypomagnesaemia were 47.8% and 60.7%, respectively.**

Conclusion: **The incidence of hypomagnesaemia in critically ill patients with haematological malignancies was 22.5%. Mortality in the ICU and in the hospital was similar in patients with and without hypomagnesaemia.**

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Key words: *Hypomagnesaemia. Critically ill patients. Haematological malignancies. Intensive care unit. Mortality. Outcome.*

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HIPOMAGNESEMIA EN PACIENTES HEMATOLÓGICOS CRÍTICAMENTE ENFERMOS

Resumen

Introducción: **En la actualidad existe poca información relacionada con la incidencia de hipomagnesemia y su impacto en el pronóstico de pacientes hematológicos críticamente enfermos.**

Objetivo: **Describir la incidencia de hipomagnesemia en pacientes hematológicos ingresados a en una unidad de cuidados intensivos (UCI) oncológica.**

Métodos: **Se incluyeron 102 pacientes con enfermedad hematológica, mayores de 18 años, ingresados en la UCI entre enero 2008 y abril 2011. Se definió hipomagnesemia como concentración sérica de magnesio inferior a 1,7 mg/dl.**

Resultados: **La incidencia de hipomagnesemia al ingreso o durante las primeras 24 horas de estancia en la UCI fue del 22,5% (23/102). La mortalidad hospitalaria de los enfermos con y sin hipomagnesemia fue del 47,8% y 60,7%, respectivamente.**

Conclusión: **La incidencia de hipomagnesemia en pacientes hematológicos críticamente enfermos fue del 22,5%. La mortalidad en UCI y en el hospital fue similar en los enfermos con y sin hipomagnesemia.**

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Palabras clave: *Hipomagnesemia. Enfermedades hematológicas. Unidad de cuidados intensivos. Mortalidad. Pronóstico.*

Introduction

Electrolyte abnormalities are a common medical problem in critically ill patients. During their stay in the intensive care unit (ICU), these patients have alterations in serum sodium, potassium, magnesium, chlorine and phosphorus. The normal plasma concentration of magnesium is between 1.7 and 2.3 mg/dl. Its absorption occurs in the gastrointestinal tract at the level of the jejunum and ileum, and 80% of magnesium is excreted by 80% glomerular filtration, with 60% of this being reabsorbed in the proximal tubule[1]. The observed rate of hypomagnesaemia in critically ill patients is 60%[2]. Hypomagnesaemia is defined as serum magnesium values below 1.7 mg/dl. Most episodes of hypomagnesaemia in critically ill patients are asymptomatic; however, when serum magnesium values are less than 1.2 mg/dl signs, then symptoms occur, such as lethargy, confusion, coma, convulsions, ataxia, nystagmus, prolongation of the QT on the electrocardiogram, and atrial and ventricular arrhythmias. Additionally, hypokalemia can occur simultaneously. Causes of hypomagnesaemia in critically ill patients with haematological malignacies include: administering total parenteral nutrition for an extended period of time, nasogastric suction, diarrhoea, vomiting and the use of certain drugs (loop diuretics, aminoglycosides, cyclosporine, amphotericin B, cisplatin)[3]. At present, there is little information regarding the incidence of hypomagnesaemia and its impact on the prognosis of critically ill patients with haematological malignancies. The aim of this study was to describe the incidence of hypomagnesaemia in haematological oncology patients admitted to the ICU.

Methods

This study is a sub -analysis of an observational prospective cohort study conducted between January 1, 2008 and April 30, 2011, which was previously approved by the Bioethics Committee of Instituto Nacional de Cancerologia (INCan), and the need for informed consent was waived[4]. The INCan is located in Mexico City, Mexico. The ICU at INCan is a mixed unit with six adult medical–surgical beds that are exclusively used for oncology patients. At least one intensivist and six nurses are on duty 24 hours a day (eight-hour shifts). The nurse - patient ratio is 1:1. Daily review of patients admitted to the ICU is performed by a multidisciplinary team that include medical staff and nurses, oncologists, haematologists, surgeons, infectious disease specialists and nutritionists. Approximately 300 patients per year are admitted to the ICU[5].

All patients over 18 years with haematologic malignancies admitted to the ICU during the study period were included. The demographic, clinical and laboratory variables were collected during the first day of ICU stay. The length of stay in the ICU, and the total length of hospital stay were recorded. Hypomagnesaemia was defined as a serum magnesium concentration below 1.7 mg/dl.

Statistical Analysis

Continuous variables were expressed as the mean ± standard deviation or as the median and interquartile range if the distribution of data was not normal.

To compare continuous variables Student's t- test or the Mann Whitney U test according to the sampling distribution was used. For the analysis of categorical variables, the chi-square test or the Fisher exact test was used. Survival curves were estimated by the Kaplan- Meier method. Survival data were compared using the log-rank test (log -rank test). In all cases, a value of $p < 0.05$ was considered statistically significant. SPSS 21.0 was used to analyse data.

Results

One hundred two patients with haematological malignancies were included in this study. The incidence of hypomagnesaemia at admission or during the first 24 hours of ICU stay was 22.5% (23/102). Eighty-seven patients required mechanical ventilation (85.2%). Of the patients who had magnesium concentrations below 1.7 mg/dl, none had arrhythmias during their stay in the ICU (table I).

The median serum magnesium level for the entire group of patients was 2.1 mg/dl, with the medians of the normal magnesium and hypomagnesaemia group at 1.5 and 2.2 mg/dl, respectively ($p < 0.001$). Patients with hypomagnesaemia had lower serum potassium levels compared with patients with normal serum magnesium (table II).

The hospital mortality in patients with and without hypomagnesaemia was 47.8% and 60.7%, respectively (table I). Figures 1 and 2 show the survival curves of critically ill patients with and without hypomagnesaemia during the ICU stay and hospital stay.

Discussion

Hypomagnesaemia is a common finding in hospitalised patients. The present study shows that 22.5% of patients with haematological malignancies admitted to the ICU have a serum magnesium concentration below 1.7 mg/dl. Different authors have reported a prevalence of hypomagnesaemia between 20 and 61%[6-9]. Other studies[7-9] have presented a prevalence of hypomagnesaemia higher than that found in our study. Similar to the results of this work, Reinhart et al.[6] reported that the incidence of hypomagnesaemia was

Table I
Clinical characteristics of critically ill patients with haematological malignancies with and without hypomagnesaemia

Variables	*Hypomagnesaemia (Yes) n = 23*	*Hypomagnesaemia (No) n = 79*	*p*
Age, years, mean ± SD	47.3 ± 18.8	41.6 ± 17.6	0.186
Men, n (%)	14 (60.8)	39 (49.3)	0.331
Female, n (%)	9 (39.1)	40 (56.6)	
APACHE score, mean ± SD	18.4 ± 7.2	17.2 ± 5.4	0.491
SOFA score, mean ± SD	10 ± 4	9.7 ± 3.8	0.746
Length of stay in ICU (days), median (IQR)	2 (2-11)	4 (1-9)	0.497
IMV, n (%)	20 (86.9)	67 (84.8)	0.990
Arrhythmias, n (%)	0(0)	3 (3.7)	0.999
ICU mortality, n (%)	11(47.8)	36 (45.5)	0.848
Hospital mortality, n (%)	11(47.8)	48 (60.7)	0.279

SD = standard deviation, APACHE II = Acute Physiology and Chronic Health Evaluation, SOFA = Sequential Organ Failure Assessment, ICU = intensive care unit, IQR = interquartile ranges IMV = invasive mechanical ventilation.

Table II
Other biochemical variables in critically ill patients with haematological malignancies with and without hypomagnesaemia

Variables	*Hypomagnesaemia (Yes) n = 23*	*Hypomagnesaemia (No) n = 79*	*p*
Sodium, mEq/L	*138.2* ± 6	*139.1* ± 5.8	0.523
Potassium, mEq/L	3.8 ± 0.80	4.2 ± 0.88	0.04
Chlorine, mEq/L	109.7 ± 6.9	110.1 ± 6.9	0.826
Phosphorus, mEq/L	4.5 (3.6-5)	4 (2.5-5)	0.234
Creatinine, mg/dL	0.9 (0.55-1.5)	0.9 (0.58-1.5)	0.968
Glucose, mg/dL	119 (104-137)	125 (101-159)	0.575

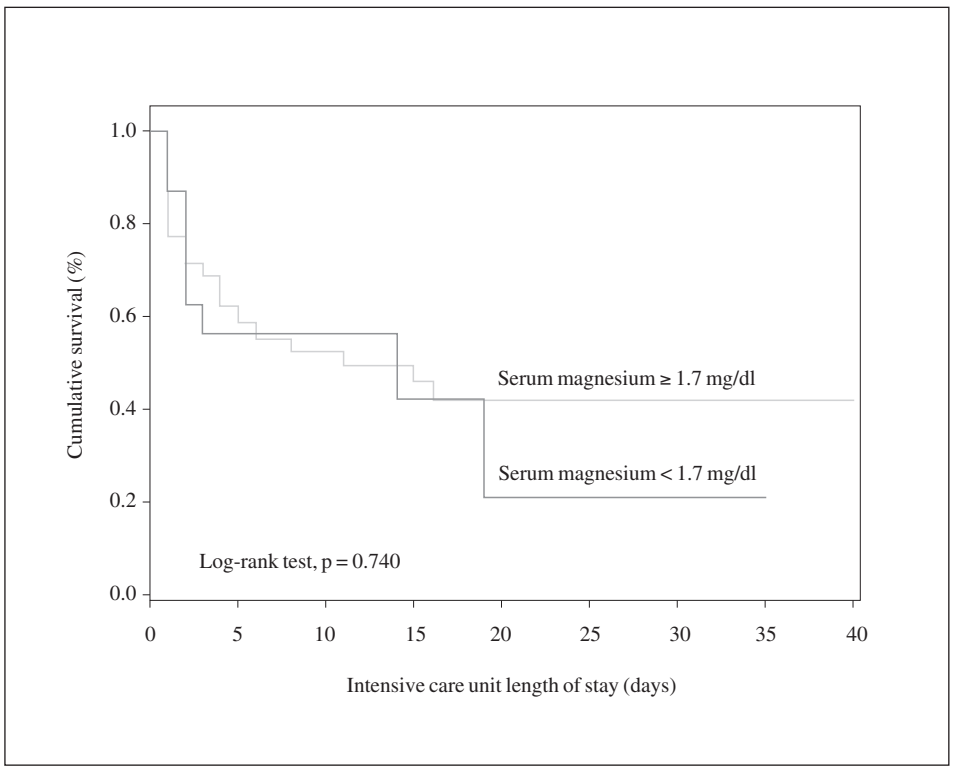

Fig. 1.—Shows the survival curves of critically ill patients with haematological malignancies with and without hypomagnesaemia during the stay in the intensive care unit.

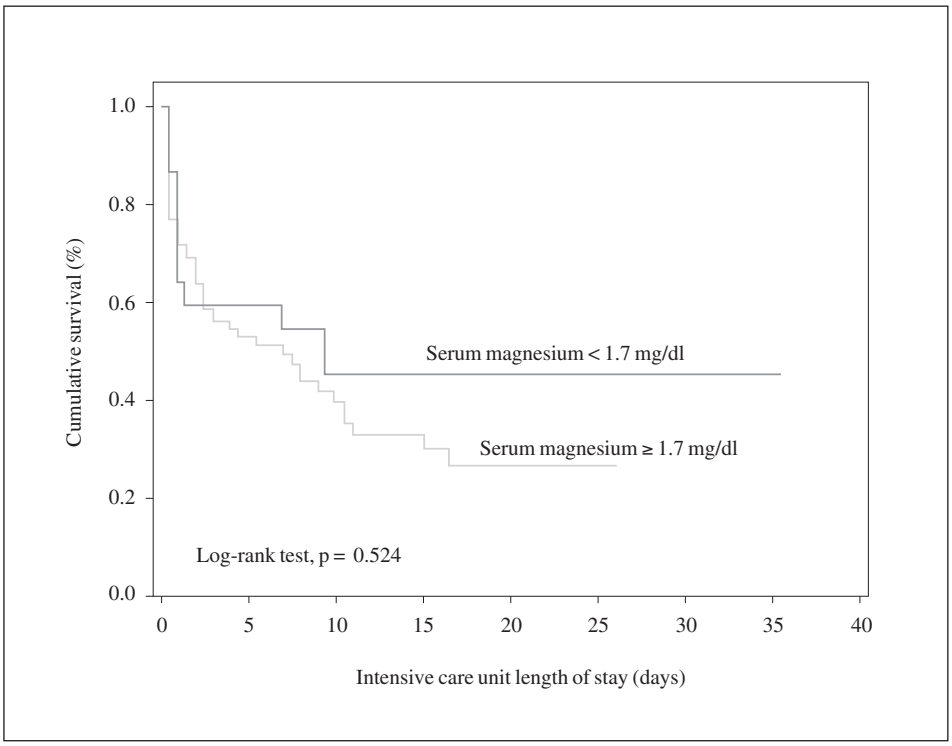

Fig. 2.—Shows the survival curves of critically ill patients with haematological malignancies with and without hypomagnesaemia during the hospital stay.

20% in critically ill patients admitted to the ICU, and the mean concentrations of magnesium were less than that found in our group of patients with haematologic malignancies. Although it has been reported that hypomagnesaemia is a risk factor for the development of arrhythmias[3], in our study, the group of patients with hypomagnesaemia did not experience serious arrhythmias during their stay in the ICU. Often, patients with hypomagnesaemia have hypokaalemia[10]. The patients in our study with hypomagnesaemia had significantly lower potassium levels. The association between hypomagnesaemia and mortality varies from study to study. Soliman et al.[13] reported that critically ill patients, on admission or during their stay in the ICU, develop low serum magnesium and, have a mortality of 19 to 35%, respectively. The study by Safavi et al.[12] showed a significant difference in the ICU mortality between patients with and without hypomagnesaemia at admission (55% *versus* 33%). Limaye et al.[14] reported that the mortality rate in critically ill patients with hypomagnesaemia is significantly higher than in patients without hypomagnesaemia (57% versus 31%). Agus[15] reported that magnesium correction does not improve the prognosis of patients with hypomagnesaemia. In our study, no statistically significant difference was observed in the mortality rate in the ICU and in the hospital between the groups with and without hypomagnesaemia.

The present work has the following limitations: the sample is relatively small and the experience of a single centre is presented.

Conclusions

The incidence of hypomagnesaemia in critically ill patients with haematological malignancies was 22.5%. The patients who presented with hypomagnesaemia also had potassium concentrations significantly lower than patients without hypomagnesaemia. Mortality in the ICU and in the hospital was similar in patients with and without hypomagnesaemia.

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Conflict of interest

The authors declared that they have no conflict of interest.

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The calcium concentration of public drinking waters and bottled mineral waters in Spain and its contribution to satisfying nutritional needs

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Abstract

Introduction: **A sufficient intake of calcium enables correct bone mineralization. The bioavailability of calcium in water is similar to that in milk.**

Objective: **To determine the concentration of calcium in public drinking water and bottled mineral water.**

Methods: **We used ion chromatography to analyse the calcium concentrations of public drinking waters in a representative sample of 108 Spanish municipalities (21,290,707 people) and of 109 natural mineral waters sold in Spain, 97 of which were produced in Spain and 12 of which were imported.**

Results: **The average calcium concentration of public drinking waters was 38.96 ± 32.44 mg/L (range: 0.40-159.68 mg/L). In 27 municipalities, the water contained 50-100 mg/L of calcium and in six municipalities it contained over 100 mg/L. The average calcium concentration of the 97 Spanish natural mineral water brands was 39.6 mg/L (range: 0.6-610.1 mg/L). Of these, 34 contained 50-100 mg/L of calcium and six contained over 100 mg/L. Of the 12 imported brands, 10 contained over 50 mg/L. Assuming water consumption is as recommended, water containing 50-100 mg/L of calcium provides 5.4-12.8% of the recommended intake of calcium for children aged one to thirteen, up to 13.6% for adolescents, 5.8-17.6% for adults, and up to 20.8% for lactating mothers. Water with 100-150 mg/L of calcium provides 10-31% of the recommended dietary allowance, depending on the age of the individual.**

Discussion: **Public drinking water and natural mineral water consumption in a third of Spanish cities can be considered an important complementary source of calcium.**

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Key words: *Calcium. Public drinking water. Natural mineral water. Water softening. Nutritional requirements.*

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CALCIO EN EL AGUA DE CONSUMO PUBLICO Y AGUAS MINERALES NATURALES EN ESPANA Y SU CONTRIBUCION EN CUBRIR LAS NECESIDADES NUTRICIONALES

Resumen

Introducción: **Una adecuada ingesta de calcio condiciona una buena mineralización ósea.**

Objetivo: **Determinar el contenido en calcio en aguas de bebida.**

Métodos: **En 2012 se analizaron las concentraciones de calcio, por cromatografía iónica, de aguas de consumo público de una muestra representativa de 108 poblaciones españolas que abastecen a 21.290.707 personas, así como de 109 aguas minerales naturales comercializadas en España (97 españolas y 12 importadas).**

Resultados: **La concentración media de calcio en aguas de consumo público fue de 38,96 ± 32,44 mg/L (rango: 0,40-159,68 mg/L). En 27 poblaciones el agua contiene entre 50-100 mg/L de calcio y en 6 fue superior a 100 mg/L. La concentración media de calcio de las 97 marcas españolas de aguas fue de 39,6 mg/L (rango: 0,6-610,1 mg/L), 34 de ellas contenían entre 50-100 mg/L de calcio, mientras que en 6 de ellas más de 100 mg/L. De las 12 marcas importadas, 10 contenían más de 50 mg/L. Asumiendo una ingesta de agua recomendada, si el agua contiene entre 50-100 mg/L de calcio, ésta aportaría entre 5,4-12,8% de la ingesta de calcio recomendada para los niños de 1-13 años, hasta el 13,6% en adolescentes, entre 5,8-17,6% en adultos, y hasta el 20,8% en madres lactantes. El agua conteniendo 100-150 mg/L de calcio aportaría entre 10-31% de las recomendaciones según la edad.**

Discusión: **El agua de consumo público de un tercio de ciudades españolas y de aguas minerales naturales puede ser considerada como una fuente complementaria importante de calcio ingerido.**

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Palabras clave: *Calcio. Agua de bebida. Agua mineral natural. Ablandamiento del agua. Necesidades nutricionales.*

Abbreviations

PDW: Public drinking waters.
NMW: Natural mineral waters.
EU: European Union.
EFSA: European Food Safety Agency.
IOM: Institute of Medicine.
RDA: Recommended Dietary Allowances.
PTH: Parathyroid hormone.

Introduction

Sufficient calcium consumption is important for maintaining correct bone health and preventing osteoporosis[1,2]. It may also help to prevent obesity[3], insulin resistance[4] and other chronic illnesses associated with the immune and neuromuscular system[5].

The United States Institute of Medicine (IOM) recently set the recommended dietary allowances (RDA) for calcium. These ranges from 700 to 1,000 mg/day for children aged between one and nine and from 1,000 to 1,300 mg/day for adolescents and adults[6] (table I). These daily allowances are not met by the entire Spanish population[7], especially at two key stages of bone metabolism: infancy and menopause. Representative studies of the Spanish population found that the calcium consumptions of 76.7% of children of school age[8] and 79.6% of menopausal women[9] were insufficient.

Where recommended daily intake is not satisfied via food consumption, medical calcium supplements may be taken[10]. However, administering these supplements involves practical difficulties[11] as well as cardiovascular risks[12] that have not yet been fully determined.

Table I
Recommended Dietary Allowance (RDA) and Tolerable upper intake levels (UL)[6]

Age	*RDA (mg/day)*	*UL (µg/day)*
0 – 6 months	200 (*)	1,000
6 – 12 months	260 (*)	1,500
1 – 3 years	700	2,500
4 – 8 years	1,000	2,500
9-13 years	1,300	3,000
14-18 years	1,300	3,000
14-18 years Pregnant/ Lactating mothers	1,300	3,000
19-50 years	1,000	2,500
19-50 years Pregnant/ Lactating mothers	1,000	2,500
51-70 years (Men)	1,000	2,000
51-70 years (Women)	1,200	2,000
> 70 years	1,200	2,000

(*) Adequate intake.

For this reason, in recent years much interest has been generated in calcium-enriched foods (milk, yoghurt, cereals, fruit juices, etc.) and other sources of calcium. The calcium present in drinking water should therefore also be considered since its bioavailability from drinking water is similar to that from dairy products[13]. When recommendations regarding types of drinking water are reviewed, however, their calcium concentrations are rarely considered important[14]. For example, neither Spanish[15] nor European[16] regulations on public drinking water (PDW) refer to the concentration of this mineral. The Codex rule[17] for natural mineral waters (NMW) also does not mention calcium concentration and Spanish and European regulations on bottled water only indicate that these beverages can be described as calcic if they contain over 150 mg/L of calcium.

Few studies have determined the calcium concentration of Spanish PDW and NMW[18,19]. Even fewer studies have analysed how frequent and continuous consumption of calcium may prevent osteoporosis or other chronic illnesses[20]. In this study, therefore, we analyse the calcium concentration of the PDW and NMW consumed in Spain and evaluate their contribution to the recommended dietary intake of this mineral.

Material and methods

During 2012 we selected PDW samples from 108 of the 144 Spanish cities with a population of over 50,000 inhabitants (total population of 21,290,707, or 45.3% of the total Spanish population). These cities were selected at random so that they would represent all Spanish geographical regions. The number of inhabitants in each city was taken from the de jure population figures by municipalities recorded for 2012 by the Spanish Statistical Office[21]. In each of the cities studied, we collected three two-litre samples of PDW in opaque plastic bottles after allowing the water to flow from the tap for at least three minutes. These samples were taken from private homes or public establishments that were without domestic filters or reverse osmosis systems. Similarly, three bottles (with different bottling dates) of 97 Spanish brands of NMW and 12 brands of imported NMW were acquired from supermarkets or grocery stores in various Spanish cities. From the full list of 151 Spanish NMW recognized by the EU[22], we selected 97 samples of the most consumed Spanish brands that also represented the geographical regions with the most springs. The locations of the springs of the NMW are shown in figure 1. For both types of sample (PDW and NMW), the bottles were stored in the dark and at ambient temperature until they were analysed.

Calcium concentrations were determined by ion chromatography (EPA method 300.7) using the Dionex DX-120 ion chromatograph with Fluka 39865 standard calibration solution. Sample calibrations and concentrations were obtained using PeakNet 5.10d

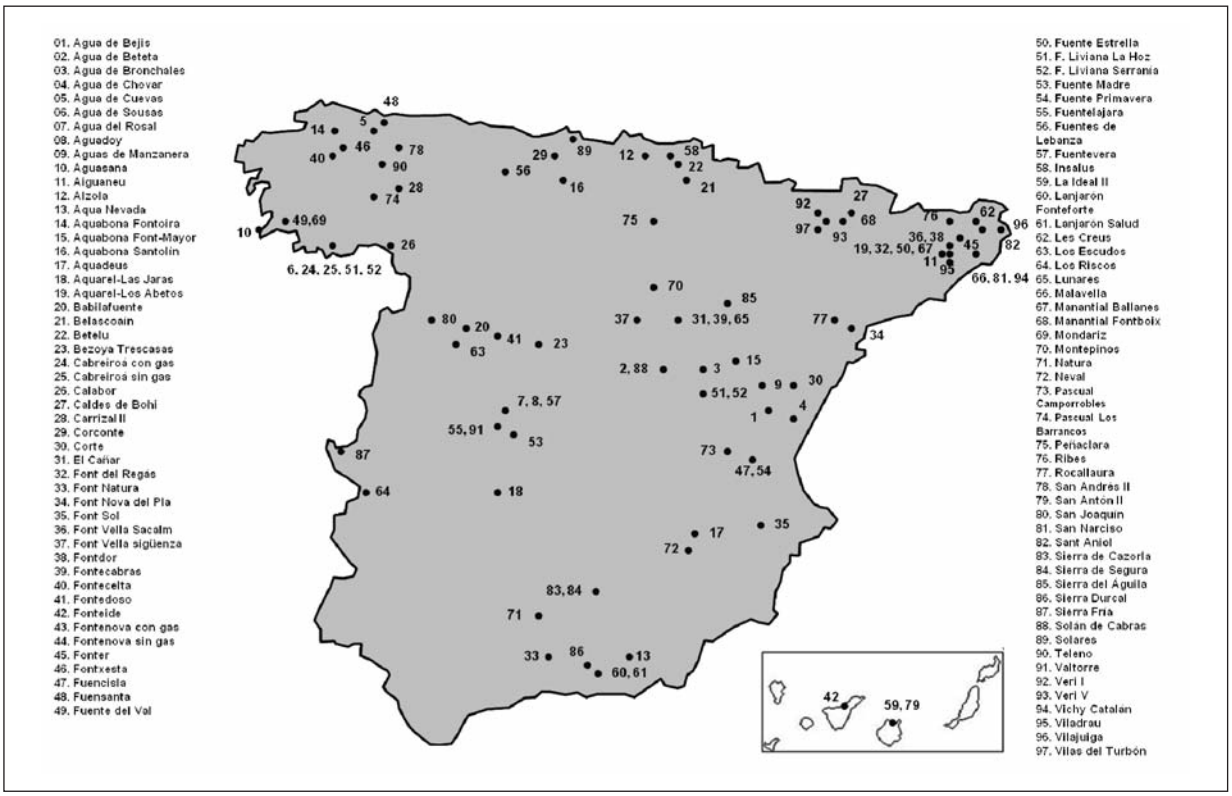

Fig. 1.—Sources of Spanish natural mineral waters.

–SE and the 4110-B method recommended by the American Public Health Association, the American Water Works Association, and the Water Environment Federation[23].

Results

Table II shows the average calcium concentration in the PDW of the 108 Spanish cities studied. The average calcium concentration for all cities was 38.96 ± 32.44 mg/L, ranging from 0.40 mg/L in San Vicente del Raspeig to 159.68 mg/L in Girona.

In 48 of the 108 cities, the calcium concentration was below 25 mg/L. In 27 cities, it was between 25 and 50 mg/L and in another 27 cities, which supply 3,726,377 people it was between 50 and 100 mg/L. Finally, in 6 other cities, home to almost one million people, the calcium concentration was over 100 mg/L (table III).

Figure 2 shows the Spanish cities where the calcium concentrations in the PDW were determined.

Tables IV and V show the calcium concentrations in mg/L of the 109 NMW brands studied (97 Spanish brands and 12 imported brands, respectively). The average calcium concentration of the Spanish NMW brands was 39.6 mg/L and the concentration ranged from 0.6 mg/L (Aquasana®) to 610.1 mg/L (Agua de Manzanera®). Of the Spanish brands, 57 (58.76%) contained less than 50 mg/L, 34 (35.05%) contained between 50 and 100 mg/L, and 6 (6.19%) contained over 100 mg/L. The average calcium concentration of the imported NMW was 93.52 ± 47.11 mg/L, with a maximum of 158.4 mg/L and a minimum of 14 mg/L. Of the 12 brands studied, 10 had a calcium concentration of over 50 mg/L and four had a calcium concentration of over 140 mg/L.

Discussion

Consuming the recommended dietary allowances for calcium is important for achieving better bone mineral density. Because of their high calcium content and high bioavailability of around 30%, the main dietary sources of calcium are milk and dairy products. The high calcium content in milk and its derivatives is similar to that of water. In an experimental study, Couzy et al.[13] compared the bioavailability of calcium from cow's milk and calcium-rich waters (467 mg/L) in 10 young women aged between 21 and 36. The rates of absorption were 25.0 ± 6.7% for milk and 23.8 ± 4.8% for water. In another experimental study, Bacciottini et al.[25] observed that the absorption of a calcium content of 3.18 mmol from water was 23.15 ± 4.06%, but this percentage does not appear to be constant. The authors of a systematic review and meta-analysis also observed that in waters with a lower

Table II
Average calcium concentration in public drinking water accosrding Spanish regions

Nº	*Autonomous community*	*Cities*	*Population*	*Average calcium concentration (mg/L)*
83	Andalusia	Alcalá de Guadaíra	70,155	25.59 ± 2.13
49	Andalusia	Algeciras	116,209	16.71 ± 1.82
44	Andalusia	Cádiz	126,766	66.38 ± 5.24
76	Andalusia	Chiclana de la Frontera	77,293	63.67 ± 6.07
12	Andalusia	Córdoba	328,428	14.27 ± 1.23
45	Andalusia	Dos Hermanas	122,943	24.02 ± 2.34
64	Andalusia	El Puerto Santa María	87,696	59.67 ± 5.67
81	Andalusia	Fuengirola	71,482	45.94 ± 3.24
19	Andalusia	Granada	234,325	27.53 ± 2.21
25	Andalusia	Jerez de la Frontera	207,532	58.29 ± 5.67
87	Andalusia	La Línea de la Concepción	64,595	18.57 ± 1.87
6	Andalusia	Málaga	568,305	31.84 ± 3.23
42	Andalusia	Marbella	134,623	27.10 ± 2.08
57	Andalusia	San Fernando	96,366	65.94 ± 5.84
86	Andalusia	Sanlúcar de Barrameda	65,805	64.29 ± 7.42
4	Andalusia	Sevilla	703,206	23.95 ± 2.16
106	Aragon	Huesca	52,059	65.5 ± 5.87
5	Aragon	Zaragoza	674,317	10.85 ± 1.21
68	Asturias	Avilés	84,242	0.88 ± 0.23
15	Asturias	Gijón	277,554	35.36 ± 3.45
21	Asturias	Oviedo	224,005	43.06 ± 4.32
108	Asturias	Siero	51,181	33.04 ± 5.23
8	Balearic Islands	Palma	401,270	101.16 ± 11.02
74	Canary Islands	Arona	78,614	6.81 ± 2.21
97	Canary Islands	Arrecife	59,127	18.67 ± 2.87
9	Canary Islands	Palmas de Gran Canaria (Las)	381,847	44.64 ± 3.54
105	Canary Islands	San Bartolomé de Tirajana	52,161	20.62 ± 2.32
39	Canary Islands	San Cristóbal de La Laguna	150,661	4.11 ± 0.65
22	Canary Islands	Santa Cruz de Tenerife	222,417	34.14 ± 3.21
90	Canary Islands	Santa Lucía de Tirajana	63,637	19.01 ± 1.76
54	Canary Islands	Telde	100,015	10.88 ± 1.07
32	Cantabria	Santander	182,700	73.62 ± 7.01
101	Cantabria	Torrelavega	55,947	54.96 ± 5.32
99	Castille and Leon	Ávila	56,855	9.82 ± 0.87
34	Castille and Leon	Burgos	178,966	15.86 ± 1.32
43	Castille and Leon	León	134,305	30.11 ± 2.98
37	Castille and Leon	Salamanca	155,619	11.98 ± 1.65
13	Castille and Leon	Valladolid	317,864	34.06 ± 3.42
102	Castille La Mancha	Cuenca	55,866	72.19 ± 7.13
63	Castille La Mancha	Talavera de la Reina	88,856	27.97 ± 2.84
71	Castille La Mancha	Toledo	82,291	11.91 ± 1.76
23	Catalonia	Badalona	219,547	50.72 ± 7.89
2	Catalonia	Barcelona	1,621,537	37.18 ± 5.34
93	Catalonia	Castelldefels	62,080	71.01 ± 9.04
98	Catalonia	Cerdanyola del Vallés	58,747	46.37 ± 5.56
65	Catalonia	Cornellà de Llobregat	86,519	82.34 ± 10.23
92	Catalonia	El Prat de Llobregat	63,418	45.79 ± 5.67
58	Catalonia	Girona	96,188	159.68 ± 18.76
96	Catalonia	Granollers	60,658	47.82 ± 5.34
16	Catalonia	Hospitalet de Llobregat	257,038	100.12 ± 12.12
41	Catalonia	Lleida	135,919	44.73 ± 5.39
77	Catalonia	Manresa	76,558	10.79 ± 9.87
46	Catalonia	Mataró	121,722	67.86 ± 7.89
104	Catalonia	Mollet del Vallès	52,484	53.1 ± 4.56
52	Catalonia	Reus	107,118	101.6 ± 18.23
80	Catalonia	Rubí	72,987	49.94 ± 7.45
69	Catalonia	Sant Boi de Llobregat	82,428	93.31 ± 8.76
47	Catalonia	Santa Coloma de Gramenet	119,717	51.18 ± 4.67
24	Catalonia	Tarrasa	210,941	88.78 ± 7.98
91	Catalonia	Viladecans	63,489	65.77 ± 6.98
94	Valencia	Alcoy	61,552	19.24 ± 2.56

Table II *(cont.)*
Average calcium concentration in public drinking water accosrding Spanish regions

Nº	*Autonomous community*	*Cities*	*Population*	*Average calcium concentration (mg/L)*
11	Valencia	Alicante	334,757	46.26 ± 4.65
82	Valencia	Benidorm	71,034	65.26 ± 6.67
33	Valencia	Castellón de la Plana	180,005	73.10 ± 7.76
20	Valencia	Elche	230,112	40.92 ± 5.21
73	Valencia	Gandía	80,020	33.93 ± 3.66
67	Valencia	Orihuela	86,164	2.77 ± 1.23
89	Valencia	Paterna	64,023	146.5 ± 13.78
85	Valencia	Sagunto	66,070	93.62 ± 12.45
103	Valencia	San Vicente del Raspeig	53,126	0.40 ± 0.12
75	Valencia	Torrent	78,543	84.05 ± 7.56
53	Valencia	Torrevieja	101,792	50.1 ± 5.23
3	Valencia	Valencia	814,208	88.71 ± 8.65
107	Valencia	Vila-real	51,205	114.68 ± 13.32
40	Extremadura	Badajoz	148,334	16.1 ± 2.13
60	Extremadura	Cáceres	93,131	15.64 ± 2.13
100	Extremadura	Mérida	56,395	43.25 ± 4.12
79	Galicia	Ferrol	74,273	5.60 ± 0.89
17	Galicia	La Coruña	246,056	9.4 ± 0.96
56	Galicia	Lugo	96,678	12.8 ± 1.03
51	Galicia	Orense	107,742	10.9 ± 1.45
59	Galicia	Santiago de Compostela	95,092	7.30 ± 0.67
14	Galicia	Vigo	297,332	2.10 ± 0.12
38	La Rioja	Logroño	152,107	96.97 ± 9.43
27	Madrid	Alcalá de Henares	204,574	13.19 ± 1.23
50	Madrid	Alcobendas	109,104	13.39 ± 1.32
35	Madrid	Alcorcón	167,967	10.03 ± 1.02
62	Madrid	Coslada	90,280	10.47 ± 1.05
29	Madrid	Fuenlabrada	197,836	10.15 ± 1.21
36	Madrid	Getafe	167,164	11.31 ± 1.46
66	Madrid	Las Rozas	86,340	10.49 ± 2.32
30	Madrid	Leganés	186,066	10.28 ± 1.03
1	Madrid	Madrid	3,255,944	13.94 ± 1.23
84	Madrid	Majadahonda	68,110	10.24 ± 0.98
26	Madrid	Móstoles	206,478	10.17 ± 1.43
70	Madrid	Pozuelo de Alarcón	82,428	10.08 ± 1.08
78	Madrid	San Sebastián Reyes	75,912	11.55 ± 1.13
48	Madrid	Torrejón de Ardoz	118,162	12.59 ± 1.34
61	Murcia	Lorca	91,906	6.32 ± 0.81
88	Murcia	Molina de Segura	64,065	1.57 ± 0.88
7	Murcia	Murcia	436,870	0.70 ± 0.41
28	Navarre	Pamplona	198,491	18.57 ± 1.76
55	Basque country	Baracaldo	98,460	32.8 ± 3.45
10	Basque country	Bilbao	354,860	31.59 ± 4.32
72	Basque country	Getxo	80,770	39.9 ± 5.67
95	Basque country	Irún	60,951	27.55 ± 3.42
31	Basque country	San Sebastián	185,357	22.53 ± 2.34
18	Basque country	Vitoria	235,661	50.43 ± 5.53

Data expressed as means ± SD.

calcium concentration (< 100 mg/L), the percentage absorbed was greater (47.5%)[26]. In summary, the absorption coefficient of calcium in water with respect to the absorption coefficient of calcium in milk ranges from 1.129 ± 0.056 to 0.985 ± 0.070. According to the bibliography, therefore, calcium in water is absorbed at least as easily as the calcium in dairy products[27]. Also, according to a review conducted in 2006, as occurs with other food sources of calcium, the calcium in water is absorbed almost 20% more if it is consumed along with other foods than if it is consumed on its own[28].

People who do not consume sufficient calcium may be given supplements usually to be taken once a day. However, as supplements with large quantities of calcium may inhibit parathyroid hormone (PTH) and bone resorption[29] more intensely but for less time, it is recommended that the doses be broken up in order to

Table III
Calcium concentration distribution in public drinking water, according the number of regions and inhabitants analyzed

Average calcium concentration (mg/L)	*Number of regions (n = 108)*	*Number of inhabitants (n = 21,290,707)*
< 25	48	10,500,978
25-50	27	6,086,510
50-100	27	3,726,377
> 100	6	976,842

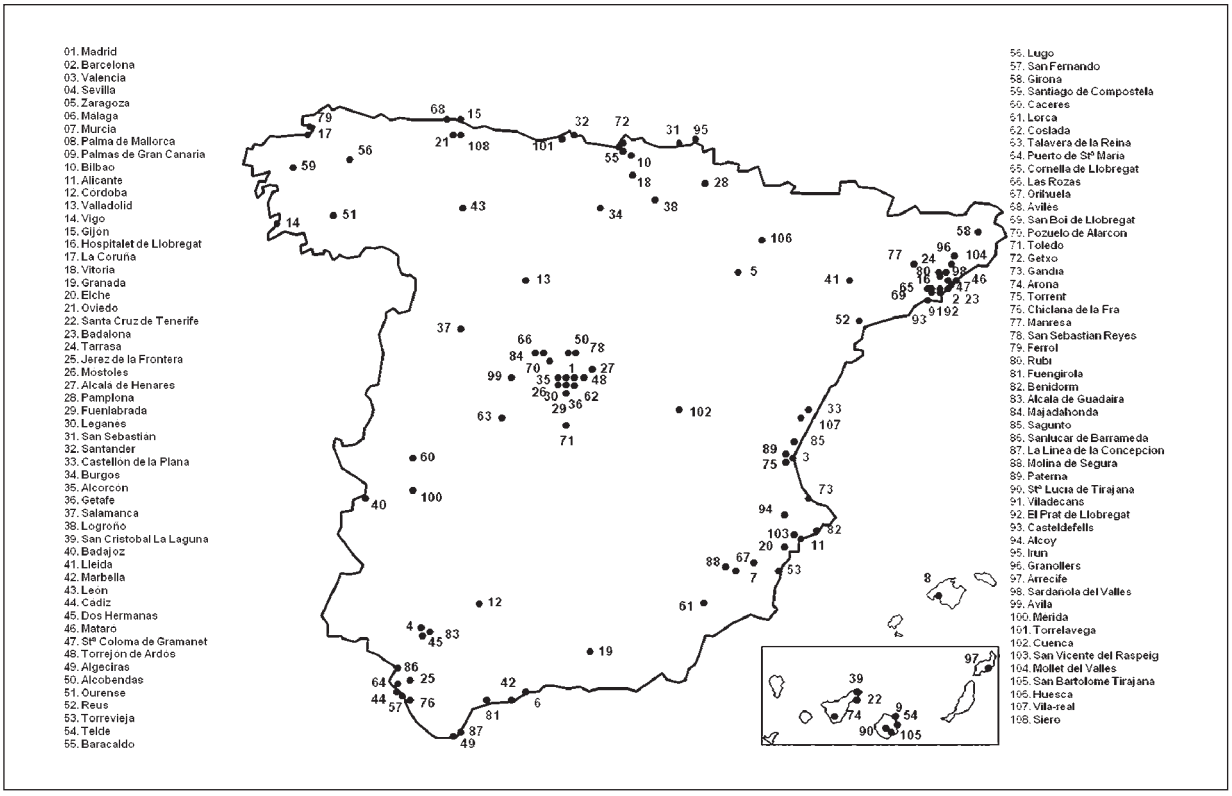

Fig. 2.—Spanish cities whose calcium concentrations of public drinking waters have been analyzed.

achieve a more sustained inhibition of bone resorption[30,31]. Water consumed throughout the day can therefore be a significant food alternative to satisfy requirements for this mineral[32]. In a six-month randomized double-blind test conducted on postmenopausal women, calcium-rich drinking water was found to have a positive effect on the biochemical parameters associated with bone metabolism[33]. In the EPIDOS cohort, a 100 mg per day increase in calcium consumption from drinking water in women aged over 75 was associated with a 0.5% increase in bone mineral density[34]. However, we should also mention that people with osteoporosis treated with bisphosphonates should take these drugs with water that is low in calcium since a tendency to form complexes with divalent cations (calcium, magnesium, iron, etc.) and a reduction in the absorption of the bisphosphonates have been reported[35].

The calcium concentrations of the PDW vary greatly and basically depend on the type of bedrock on which the aquifer lies (if the water is from a subterranean source) or on the origin of the water (if the water is from an above-ground source).

In a review of the mineral content of the PDW of 44 cities in the United States[36], the average calcium concentration in 36 cities whose PDW source was above ground was 34 ± 21 mg/L and in the eight cities whose source was subterranean it was 52 ± 24 mg/L. Calcium concentration ranged from 2 to 85 mg/L. In a descriptive transversal study of PDW in Canada, the average calcium concentration was 48.8 mg/L and the calcium concentration ranged from 1 to 135 mg/L. When the authors of that study also analysed the calcium concentration of PDW in the United States, they found that the average concentration was 50.6 mg/L and that the concentration ranged from 8.3 to 131 mg/L[35].

Table IV
Calcium content of 97 Spanish brands of natural mineral waters

Nº	Brand	Spring	Region	Bottle	Calcium in bottle label	Average calcium concentrations (mg/L)
1	Agua de Bejis®	Los Cloticos- Bejis	Bejis (Castellón)	Plastic 1,500 ml	49.7	45.8 ± 4.2
2	Agua de Beteta®	Fuente del Arca	Beteta (Cuenca)	Plastic 1,500 ml	66	65.4 ± 5.6
3	Agua de Bronchales®	Bronchales 3	Bronchales (Teruel)	Plastic 2,000 ml	3	3.2 ± 1.1
4	Agua de Chovar®	Fuente Barranco Carbón	Chovar (Castellón)	Plastic 2,000 ml	19	19.4 ± 2.4
5	Agua de Cuevas®	Fuente de Cuevas	Aller (Asturias)	Plastic 1,500 ml	45.6	51.1 ± 7.12
6	Agua de Sousas®	Sousas II	Verín (Ourense)	Plastic 1,500 ml	3.1	3.6 ± 0.5
7	Agua del Rosal®	Agua del Rosal	Calera y Chozas (Toledo)	Plastic 1,500 ml	66.2	58.8 ± 5.3
8	Aguadoy®	Aguadoy	Calera y Chozas (Toledo)	Plastic 2,000 ml	30.9	31.9 ± 2.8
9	Aguas de Manzanera®	El Salvador	Manzanera (Teruel)	Plastic 5,000 ml	705.4	610.1 ± 25.2
10	Aguasana®	A Granxa/La Granja	Baiona (Pontevedra)	Plastic 1,500 ml	0.5	0.6 ± 0.6
11	Aiguaneu®	Aiguaneu	Espilneves (Girona)	Plastic 1,500 ml	44.8	36.8 ± 3.8
12	Alzola®	Alzola	Elgoibar (Guipúzcoa)	Plastic 1,500 ml	61	59.1 ± 5.8
13	Aqua Nevada®	Aqua Nevada	El Tesorillo, Albuñán (Granada)	Plastic 1,500 ml	13	15.1 ± 1.2
14	Aquabona Fontoira®	Fontoira	Cospeito (Lugo)	Plastic 1,500 ml	42.1	41.2 ± 3.7
15	Aquabona Fuen-Mayor®	Fuen-Mayor	Cañizar del Olivar (Teruel)	Plastic 1,500 ml	75.6	76.2 ± 8.6
16	Aquabona Santolín®	Santolín	Quintanaurria (Burgos)	Plastic 1,500 ml	90.3	88 ± 8.2
17	Aquadeus®	Fuente Arquillo	El Robledo (Albacete)	Plastic 1,500 ml	71.5	69.8 ± 6.7
18	Aquarel-Las Jaras®	Las Jaras	Herrera del Duque (Badajoz)	Plastic 1,500 ml	1.9	2.3 ± 0.8
19	Aquarel-Los Abetos®	Los Abetos	Arbúcies (Girona)	Plastic 1,500 ml	34	29.5
20	Babilafuente®	Antigua Fuente del Caño	Babilafuente (Salamanca)	Glass 1,000 ml	47.7	49.7 ± 5.5
21	Belascoaín®	Belascoaín	Belascoaín (Navarra)	Plastic 1,500 ml	243	189 ± 12.8
22	Betelu®	Ama-Iturri	Betelu (Navarra)	Plastic 1,500 ml	92	74.1 ± 8.3
23	Bezoya Trescasas®	Bezoya Trescasas	Trescasas (Segovia)	Plastic 1,500 ml	4	6.6 ± 0.8
24	Cabreiroá con gas®	Cabreiroá	Verín (Ourense)	Glass 750 ml	22	20.4 ± 2.5
25	Cabreiroá sin gas®	Cabreiroá	Verín (Ourense)	Plastic 1,500 ml	9.5	9.6 ± 1.2
26	Calabor®	Calabor	Pedralba de la Pradería (Zamora)	Glass 500 ml	5.1	6.8 ± 1.5
27	Caldes de Bohi®	Font del Bou	Barruera (Lleida)	Plastic 1,500 ml	4	1.7 ± 0.6
28	Carrizal II®	Carrizal II	Cuadros (León)	Plastic 1,500 ml	38	39.6 ± 2.8
29	Corconte®	Balneario de Corconte	Soncillo (Burgos)	Plastic 1,500 ml	16	13.9 ± 1.6
30	Cortes®	Penyagolosa	Cortes de Arenoso (Castellón)	Plastic 1,500 ml	80.5	87.6 ± 7.6
31	El Cañar®	Cañar	Jaraba (Zaragoza)	Plastic 1,500 ml	96.1	90.1 ± 9.7
32	Font del Regàs®	Font del Regàs	Arbuices (Girona)	Plastic 8,000 ml	36.2	31.6 ± 5.8
33	Font Natura®	Font Natura	Loja (Granada)	Plastic 1,500 ml	70.9	62.7 ± 6.7
34	Font Nova del Pla®	Font Nova del Pla	Aiguamúrcia (Tarragona)	Plastic 1,500 ml	74	73.2 ± 7.1
35	Font Sol®	Aguas de Sierra	La Font de la Figuera (Valencia)	Plastic 1,500 ml	120.3	114.1 ± 13.7
36	Font Vella Sacalm®	Font Sacalm	Sant Hilari Sacalm (Girona)	Plastic 5,000 ml	38.5	32.2 ± 3.6
37	Font Vella Sigüenza®	Sigüenza	Sigüenza (Guadalajara)	Plastic 1,500 ml	82.8	80 ± 7.6
38	Fontdor®	Fontdor	Sant Hilari Sacalm (Girona)	Plastic 5,000 ml	26.4	24.2 ± 6.2
39	Fontecabras®	Fontecabras	Jaraba (Zaragoza)	Plastic 1,500 ml	92.3	86.6 ± 8.7
40	Fontecelta®	Fontecelta	Sarriá (Lugo)	Plastic 1,500 ml	21.3	18.2 ± 1.9
41	Fontedoso®	Fontedoso	El Oso (Ávila)	Plastic 5,000 ml	32.1	27.6 ± 2.8
42	Fonteide®	Fonteide	La Orotava (Santa Cruz de Tenerife)	Plastic 500 ml	6.4	6.8 ± 0.9
43	Fontenova con gas®	Fontenova	Verín (Ourense)	Glass 1,000 ml	12.8	10.2 ± 1.2
44	Fontenova sin gas®	Fontenova	Verín (Ourense)	Glass 1,000 ml	6.5	11.6 ± 1.8
45	Fonter®	Fonter	Amer (Girona)	Plastic 1,250 ml	32	34.3 ± 3.9
46	Fontxesta®	Fontxesta	Láncara (Lugo)	Plastic 5,000 ml	6.2	9.2 ± 1.1
47	Fuencisla®	Fuencisla	Requena (Valencia)	Plastic 1,500 ml	86.1	80.2 ± 7.8
48	Fuensanta®	Fuensanta de Buyeres	Nava (Asturias)	Plastic 1,500 ml	69	65.6 ± 5.4
49	Fuente del Val®	Fuente del Val 2	Mondariz (Pontevedra)	Plastic 1,500 ml	17.8	14.2 ± 1.8
50	Fuente Estrella®	Fuente Estrella	Arbúcies (Girona)	Plastic 1,500 ml	25.3	25.4 ± 2.9
51	Fuente Liviana®	Arroyo de la Hoz	Huerta del Marquesado (Cuenca)	Glass 1,000 ml	66.9	52.9 ± 5.0
52	Fuente Liviana®	Serranía I	Huerta del Marquesado (Cuenca)	Plastic 2,000 ml	65.4	58.4 ± 5.2
53	Fuente Madre®	Fuente Madre	Los Navalmorales (Toledo)	Plastic 1,500 ml	67.8	66.2 ± 6.4
54	Fuente Primavera®	Fuente Primavera	Requena (Valencia)	Plastic 1,500 ml	88.7	81.3 ± 7.9
55	Fuentelajara®	Fuentelajara	Belvis de la Jara (Toledo)	Plastic 5,000 ml	21.6	22.7 ± 2.5
56	Fuentes de Lebanza®	La Cueva	Lebanza (Palencia)	Plastic 1,500 ml	37.8	39.6 ± 3.8

Table IV ***(cont.)***
Calcium content of 97 Spanish brands of natural mineral waters

Nº	*Brand*	*Spring*	*Region*	*Bottle*	*Calcium in bottle label*	*Average calcium concentrations (mg/L)*
57	Fuentevera®	Fuentevera	Calera y Chozas (Toledo)	Plastic 5,000 ml	8.2	7.3 ± 0.9
58	Insalus®	Insalus	Lizarza (Gipuzkoa)	Plastic 1,500 ml	157.3	154
59	La Ideal II®	La Ideal II (El Rapador)	Firgas (Las Palmas)	Glass 750 ml	58.2	57.7 ± 5.4
60	Lanjarón Fonteforte®	Fonteforte	Lanjarón (Granada)	Glass 500 ml	41.6	50 ± 5.8
61	Lanjarón Salud®	Salud	Lanjarón (Granada)	Plastic 1,500 ml	27.2	27.4 ± 2.8
62	Les Creus®	Les Creus	MaÇanet de Cabrenys (Girona)	Glass 1,000 ml	28.6	31.5 ± 3.6
63	Los Escudos®	Montalvo V	Aldeatejada (Salamanca)	Plastic 1,500 ml	41	39.8 ± 5.1
64	Los Riscos®	Los Riscos de la Higüela	Aburquerque (Badajoz)	Plastic 1,500 ml	2.9	2.1 ± 0.3
65	Lunares®	Lunares	Jaraba (Zaragoza)	Plastic 1,500 ml	100.4	89.9 ± 8.8
66	Malavella®	Malavella	Caldes de Malavella (Girona)	Glass 750 ml	–	12.4 ± 1.2
67	Manantial Ballanes®	Ballanes	Arbúcies (Girona)	Plastic 50 ml	54.4	42.4 ± 4.8
68	Manantial Fontboix®	Fonboix	Barruera (Lleida)	Plastic 2,000 ml	6.8	7.9 ± 1.2
69	Mondariz®	Mondariz IV	Mondariz (Pontevedra)	Plastic 1,500 ml	9.3	7.4 ± 0.8
70	Montepinos®	Montepinos	Almazán (Soria)	Plastic 1,500 ml	93.8	77.6 ± 7.8
71	Natura®	Natura	Los Villares (Jaén)	Plastic 1,500 ml	39	44.9 ± 4.8
72	Neval®	Neval	Moratalla (Murcia)	Plastic 1,500 ml	41.1	46.6 ± 4.2
73	Pascual Nature Camporrobles®	Camporrobles	Camporrobles (Valencia)	Plastic 1,500 ml	68.1	64.9 ± 6.2
74	Pascual Nature Los Barrancos®	Los Barrancos	La Ribera de Folgoso (León)	Plastic 1,500 ml	24.6	25.2 ± 2.6
75	Peñaclara®	Riva Los Baños	Torrecilla en Cameros (La Rioja)	Plastic 1,500 ml	139	127.6 ± 11.7
76	Ribes®	Fontaga	Ribes de Freser (Girona)	Plastic 1,500 ml	46.6	37.6 ± 3.8
77	Rocallaura®	Agua de Rocallaura	Vallbona de les Monges (Lleida)	Plastic 1,500 ml	169	178.6 ± 14.8
78	San Andrés II®	San Andrés II	Cuadros (León)	Plastic 8,000 ml	39	35.6 ± 2.8
79	San Antón II®	San Antón II	Firgas (Las Palmas)	Glass 750 ml	16.1	16 ± 1.8
80	San Joaquín®	S. Joaquín de Huemos de Cañedo	Valdunciel (Salamanca)	Glass 750 ml	41.2	39.8 ± 4.1
81	San Narciso®	San Narciso	Caldes de Malavella (Girona)	Glass 1,000 ml	51.4	56.8 ± 6.7
82	Sant Aniol®	Sant Aniol	Sant Aniol de Finestres (Girona)	Glass 1,000 ml	90.7	87.8 ± 8.3
83	Sierra de Cazorla®	Sierra Cazorla	Villanueva del Arzobispo (Jaén)	Plastic 1,500 ml	78.6	69 ± 6.6
84	Sierra de Segura®	Fuente Blanca	Villanueva del Arzobispo (Jaén)	Plastic 1,500 ml	77.7	63.1 ± 6.5
85	Sierra del Aguila®	La Majuela	Cariñena (Zaragoza)	Plastic 5,000 ml	86.3	83.6 ± 8.8
86	Sierra Dúrcal®	Sierra Dúrcal	Dúrcal (Granada)	Glass 500 ml	36.4	35.7 ± 4.0
87	Sierra Fría®	El Chumacero	Valencia de Alcántara (Cáceres)	Plastic 5,000 ml	1.5	1.9 ± 0.7
88	Solán de Cabras®	Fuente de Solán de Cabras	Beteta (Cuenca)	Plastic 1,500 ml	56.9	54.4 ± 5.6
89	Solares®	Fuencaliente de Solares	Solares (Cantabria)	Plastic 1,500 ml	75.3	69.3 ± 5.6
90	Teleno®	Teleno	Palacios de la Valduerna (León)	Plastic 1,500 ml	6	3.6 ± 0.5
91	Valtorre®	Valtorre	Belvis de la Jara (Toledo)	Plastic 1,500 ml	22.9	21.2 ± 2.0
92	Veri I®	Veri	Bisauri (Huesca)	Plastic 5,000 ml	69	65.1 ± 6.1
93	Veri V®	Veri V	Castejón de Sos (Huesca)	Plastic 1,500 ml	31.3	28.1 ± 2.3
94	Vichy Catalán®	Vichy Catalán	Caldes de Malavella (Girona)	Glass 1,000 ml	–	17.5 ± 1.8
95	Viladrau®	Fontalegre	Viladrau (Girona)	Plastic 1,500 ml	27.7	24.4 ± 2.5
96	Vilajuïga®	Vilajuïga	Vilajuïga (Girona)	Glass 1,000 ml	85.3	74.3 ± 7.2
97	Vilas del Turbón®	Vilas del Turbón	Vilas del Turbón - Torrelarribera (Huesca)	Glass 750 ml	50.3	36.1 ± 4.2

Data expressed as means ± SD.

According to information provided by Spanish health authorities, the average calcium concentration of most of the 333 PDW analysed was below 100 mg/L and above 200 mg/L in only four PDW[19].

With regard to NMW, a review of the mineral contents of water commercialized in North America[37] found that calcium concentrations were above 100 mg/L in only four of the 28 brands analysed. However, when the same authors analysed the calcium concentrations of 20 waters sold in Europe, they found that the calcium concentration exceeded 100 mg/L in 11 of them. In a descriptive study conducted in Silesia (Poland), the average calcium concentration of 35 NMW analysed was 178.7 ± 107.3 mg/L[38]. In a study that analysed the chemical composition of 21 types of NMW sold in Saudi Arabia, the authors found that the calcium concentrations analysed in the laboratory ranged from 12 to 90 ppm, although the labels on the bottles indicated that it ranged from 6 to 40 ppm[39]. Finally, a review of calcium concentration in European NMW found that almost half of them contained over 100 mg/L. Swiss

Table V
Calcium content of 12 imported brands of natural mineral waters

Nº	Brand	Spring	Region	Country	Bottle	Label calcium	Average calcium concentrations (mg/L)
1	Badoit®	Badoit	Saint Galmier (Loire)	France	Glass 750 ml	190	140.4 ± 10.3
2	Evian®	Cachat	Evian (Haute-Savoie)	France	Plastic 1,500 ml	80	68 ± 6.0
3	Jouvence de Wattwiller®	Jouvence	Wattwiller (Haute-Rhin)	France	Plastic 1,330 ml	85	72.3 ± 7.4
4	Pedras Salgadas®	Pedras Salgadas	Vila Pouca de Aguiar (Trás-os-Montes)	Portugal	Glass 250 ml	100	96.5 ± 9.4
5	Perrier®	Perrier	Vergèze (Gard)	France	Glass 750 ml	155	145.1 ± 13.5
6	San Martino®	San Martino	Codrongianos (Sassari)	Italy	Plastic 1,000 ml	167	145.8 ± 9.9
7	San Pellegrino®	San Pellegrino	San Pellegrino Terme (Bergamo)	Italy	Glass 1,000 ml	179	158.4 ± 12.4
8	Saint Géron®	Gallo romaine	Saint Géron (Haute Loire)	France	Glass 750 ml	79.1	82.8 ± 8.6
9	Ty Nant®	Ty Nant Water	Bethania (Llanon)	United Kingdom	Glass 750 ml	22.5	24.3 ± 2.4
10	Vichy-Célestins®	Célestins	Vichy (Allier)	France	Plastic 1,250 ml	103	97.1 ± 9.6
11	Vittel®	Bonne Source	Vittel (Vosges)	France	Plastic 1,500 ml	94	77.5 ± 7.2
12	Volvic®	Clairvic	Volvic (Puy de Dôme)	France	Plastic 1,500 ml	11.5	14 ± 1.6

Data expressed as means ± SD.

NMW had the highest calcium concentrations, which ranged from 436 to 663 mg/L[20].

In the present study we also found that the European NMW consumed in Spain, which are mainly bottled in France and Italy, also generally contain higher calcium concentrations than waters obtained from Spanish sources.

The European Food Safety Agency (EFSA), in establishing the recommended dietary allowances of water, assumes that consuming water is fundamental to maintaining good hydration at all stages of life. The Agency also states that roughly 20% of our daily water requirements are provided by foods[40] (table VI).

Based on this recommended intake of water and on the recommended intake of calcium by age and gender, the percentage of recommended calcium intake provided by water according to its calcium concentration (from 25 to 150 mg/L) has been calculated (tables VIIa and VIIb). These tables show that water containing a calcium concentration of between 50 and 100 mg/L provides 5.4-12.8% of the RDA for children aged between one and 13, up to 13.6% for adolescents, 5.8-17.6% for adults, 8-16% for expectant mothers, and up to 20.8% for lactating mothers. These data should be taken into account because, according to the bibliography, calcium intake among the Spanish population is insufficient[7]. In 27 of the 108 cities analysed in this study (with a total population of 3,726,377), the calcium concentration of the water was precisely within this 50-100 mg/L range. Moreover, the calcium concentration also ranged from 50 to 100 mg/L in 34 of the 97 Spanish NMW and in six of the 12 imported NMW analysed.

According to our information, waters with a calcium concentration of between 100 and 150 mg/L provide 10-20.4% of RDA in children and adolescents and 17.6-26.4% of RDA in menopausal women. These are stages in which calcium intake is found to be lower[8-9].

Table VI
Water adequate intake according the European Food Safety Agengy (EFSA)[40]

	Adequate intake of water (mL/day)		
Age	Food*	Water and drinks	Total water
0-6 months	–	–	680
6-12 months	160-200	640-800	800-1,000
1 year	220-240	880-960	1,100-1,200
2-3 years	260	1,040	1,300
4-8 years	320	1,280	1,600
9-13 years (Men)	420	1,680	2,100
9-13 years (Women)	380	1,520	1,900
>14 years (Men)	500	2,000	2,500
>14 years (Women)	400	1,600	2,000
Pregnancy	460	1,840	2,300
Lactating women	540	2,160	2,700

* EFSA states that foods contribute approximately with the 20% of the daily recommendations for water intake; Water and other drinks provide the 80% remaining water daily recommendations.

Table VIIA
Adequacy percentage to daily calcium recommendations from water consumption (0-18 years)

		0-6 months	*6-12 months*	*1 year*	*2-3 years*	*4-8 years*	*9-13 years (M)*	*9-13 years (W)*	*14-18 years (M)*	*14-18 years (W)*
Calcium RDA (mg/day)		200 (*)	260 (*)	700	700	1,000	1,300	1,300	1,300	1,300
Daily recommended water intake (ml/day)		680	560-800	770-960	910	1,120	1,470	1,330	1,750	1,400
Adequacy percentage to daily calcium recommendations from water consumption										
Average calcium concentrations (mg/L)	25	8.7	5.4-7.6	2.7-3.4	3.2	2.8	2.8	2.5	3.4	2.7
	50	17.5	10.8-15.2	5.4-6.8	6.4	5.6	5.6	5	6.8	5.4
	100	35	21.6-30.4	10.8-13.4	12.8	11.2	11.2	10	13.6	10.8
	150	52.5	32.4-45.6	16.2-20.2	19.2	16.8	16.8	15	20.4	16.2

Abbreviations: M, men; W, women. (*) Adequate intake.

Table VIIB
Adequacy percentage to daily calcium recommendations from water consumption (≥ 19 years)

		19-50 years (M)	*19-50 years (W)*	*Pregnancy*	*Lactating mother*	*51-70 years (M)*	*51-70 years (W)*	*> 70 years (M)*	*> 70 years (W)*
Calcium RDA (mg/day)		1,000	1,000	1,000-1,300	1,000-1,300	1,000	1,200	1,200	1,200
Daily recommended water intake (ml/day)		1,750	1,400	1,610	2,100	1,750	1,400	1,750	1,400
Adequacy percentage to daily calcium recommendations from water consumption									
Average calcium concentrations (mg/L)	25	4.4	3.5	4-3	5.2-4	4.4	2.9	3.6	2.9
	50	8.8	7	8-6	10.4-8	8.8	5.8	7.2	5.8
	100	17.6	14	16-12	20.8-16	17.6	11.6	14.4	11.6
	150	26.4	21	24-18	31.2-24	26.4	17.4	11.6	17.4

Abbreviations: M, men; W, women.

Moreover, sufficient intake of calcium during pregnancy has also been found to help prevent eclampsia[41]. Consuming water with a calcium concentration of between 100 and 150 mg/L during pregnancy can provide 12-24% of the RDA of calcium. In adults, consuming water with this same calcium concentration (between 100 and 150 mg/L) can provide 11.6-26.4% of the RDA. In women over 51 years of age, whose RDA of calcium is higher (1200 mg/day), consuming water with this calcium concentration can provide 11.6-17.4% of the RDA. These figures are similar for women aged 70. This could be especially important for adults with lactose intolerance or minor digestive problems that require a lower consumption of dairy products-foods which in the west are fundamental to providing calcium, especially for people at risk of osteoporosis[42].

In the present study, the water of only 6 of the 108 cities had a calcium concentration of over 100 mg/L. The city with the highest concentration was Girona, with an average concentration of 159.7 mg/L. Of the 109 NMW analysed, only 10 had a concentration of over 100 mg/L. The calcium concentrations of five of these ten NMW were between 100 and 150 mg/L. According to the bibliography currently available, waters excessively rich in calcium are not recommended for children still on a milk diet because of the risk of their developing calcium lithiasis. For example, the use of French NMW (Hépar®) containing 550 mg/L of calcium to make up starting formulas for babies' bottles was associated with the development of coraliform renal calculus. In this case, the daily calcium intake via water was 1,750 mg/day rather than the recommended daily amount of 210 mg[43].

Another aspect that must be taken into account with calcium-rich or hard PDW waters is the softening of the water aimed at preventing the annoying encrustation associated with taps and domestic electrical appliances. Two basic methods of softening water exist: one uses ion exchange resins and the other is reverse osmosis. With ion exchange resins, the calcium is adsorbed and replaced by other ions (especially sodium). The exchange of ions continues as long as there are sufficient ions in the resin to be replaced. Most domestic water softeners use this principle. The Brita® filter, for example, removes 89.4% of the calcium contained in the water[35]. Reverse osmosis is based on the use of a semipermeable membrane that removes 94-98% of the calcium and magnesium. In countries that use desalinated water, the calcium concentration of PDW is therefore below 6 mg/L. In short, domestic filters or reverse osmosis applied to PDW in people's homes almost completely eliminate the calcium content of the water even though the benefits or detriments to the individual of doing so are unknown[44].

Finally, we should always remember that, from the nutritional point of view, water and milk should continue to be our fundamental beverages and that soda drinks, because of their low nutritional value, should be consumed only occasionally[45]. Consuming water rather than sugary drinks also helps to prevent overweight and its complications[46].

In conclusion, a third of the PDW of 108 Spanish cities and 50 of the 109 NMW sold in Spain contain over 50 mg/L of calcium. Given its bioavailability and its use as a healthy means of hydration, drinking water should be taken into account as a complementary dietary source of calcium.

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There is chronic latent magnesium deficiency in apparently healthy university students

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Abstract

Introduction: **Magnesium is an essential micronutrient for human body, and its deficiency has been associated with risk of non-communicable diseases.**

Objective: **Assessment of magnesium status, and evaluation of the frequency of magnesium deficiency in a group of healthy adults.**

Methods: **Plasma and erythrocyte magnesium levels, and magnesium intake were determined in 115 students (55 women and 60 men), from a public university in Brazil.**

Results: **The medians of magnesium concentration in plasma (0.76 mmol/L), erythrocyte (1.97 mmol/L), and of dietary daily intake (8.84 mmol/d) were low. Forty two percent of participants had plasma or erythrocyte magnesium below the limit of 0.75 and 1.65 mmol/L, respectively. A high percentage showed high probability of inadequate magnesium intake.**

Conclusions: **There was a high frequency of subclinical magnesium deficiency in the adults assessed, that could be related to low dietary magnesium intake.**

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Key words: *Magnesium deficiency. Nutritional status. Adult. Students.*

HAY DEFICIENCIA CRONICA LATENTE DE MAGNESIO EN ESTUDIANTES UNIVERSITARIOS APARENTEMENTE SANOS

Resumen

Introducción: **El magnesio es esencial, y su deficiencia ha sido asociada a mayor riesgo de enfermedades crónicas.**

Objetivos: **Evaluar el estado de nutrición de magnesio y su ingesta en adultos sanos, y determinar la frecuencia de su deficiencia en esta población.**

Métodos: **Fueron evaluados 115 adultos estudiantes de una universidad pública en Brasil, y se determinó la ingesta dietética y los niveles de magnesio en plasma y eritrocitos.**

Resultados: **Las medianas de distribución de magnesio en plasma (0,76 mmol/L), en eritrocitos (1,97 mmol/L), y la ingesta de magnesio (8,84 mmol/d) fueron bajas. Un 42% de la muestra tuvieron concentración de magnesio en plasma o eritrocitos por debajo de los respectivos 0,75 mmol/L y 1,65 mmol/L. Un alto porcentaje de ellos exhibió probabilidad de ingesta de magnesio inadecuada.**

Conclusiones: **Se observó una alta frecuencia de deficiencia de magnesio subclínica en los adultos evaluados.**

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Palabras clave: *Deficiencia de magnesio. Estado nutricional. Adulto. Estudiantes.*

Abreviations

BMI: Body mass index.
DRI: Dietary reference intake
EAR: Estimated average requirement.
NCD: Non-communicable diseases.
UFRN: Federal University of Rio Grande do Norte.

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Introduction

The role of magnesium in the incidence and progression of non-communicable diseases – NCD (type 2 diabetes, hypertension, cardiovascular diseases, metabolic syndrome, and osteoporosis) have been demonstrated elsewhere[1,2].

Although it is found in a wide variety of foods, according to current magnesium estimated average requirement (EAR, 255-265 mg/d for female and 330-350 mg/d for male adults)[1] the population of many countries may be vulnerable to chronic latent magnesium deficiency, with severe long-term consequences to their health[2,3].

According to recent Brazilian Food Survey, the prevalence of inadequacy of magnesium intake was over 70%, especially in urban areas. In Brazil, the nutritional habits and food availability vary widely among the different regions and the different income patterns of the population. However, it may be assumed that it is based on beans, polished rice, meat and meat products and less in magnesium food sources as fruits, vegetables, nuts and dairy products[4].

The aim of this study was to assess the intake and status of magnesium in apparently healthy university students from a public university in the Northeast city of Natal.

Methods

This study was approved by the Ethics Committee on Research of the Federal University of Rio Grande do Norte – UFRN (protocol # 154/03).

Subjects

A cross-sectional study was carried out in a random sample (n = 115) of apparently healthy adult students from UFRN, of both genders. The sample size was calculated considering the total of undergraduate students from this university (n = 19,847), using an expected frequency of magnesium deficiency of 9%, the highest prevalence of hypomagnesemia published in literature since 2003[5], with an error of 5%, and confidence interval of 90%.

The participants were randomly selected according to the following inclusion criteria:

1. Being a student at the UFRN.
2. Aged from 19 to 30 years; not being malnourished or obese, pregnant or lactating.
3. Not suffering from chronic or acute disease.
4. Non athlete.
5. No current history of smoking, alcoholism, drug abuse or use of vitamin-mineral supplement or medication (including contraceptives).

Study design

Participants initially completed a standard questionnaire with general information. Those who were selected according to the inclusion criteria came to the laboratory after a 12-14 h fasting, when blood samples were collected and their weight, height and dietary intake were assessed.

Anthropometric measurement

Body weight was measured using calibrated digital scales (0.1 kg precision – Plenna, São Paulo, SP, Brazil) with participants wearing light clothes and no shoes. Height was obtained (0.1 mm precision) using a square and an inextensible tape, fixed on wall with no baseboard. Body mass index (BMI) was calculated, and the participants categorized according to World Health Organization classification: < 18.5 kg/m^2 underweight, 18.5 to 24.9 kg/m^2 normal weight, 25.0 to 29.9 kg/m^2 pre-obesity, > 30.0 obesity[6]. These measurements were obtained by a trained team of nutritionists and nutrition students.

Magnesium intake

One 24-h food recall was applied by trained nutritionists. The magnesium intake was estimated with the use of the *VirtualNutri* software[7]. The prevalence of inadequacy was evaluated from: z = (EAR – mean intake of the group)/standard deviation of group[8].

Magnesium status

All glassware was demineralized prior to analyses. Plasma and erythrocyte magnesium concentrations were determined by flame atomic absorption spectrometry (AAnalyst 100; Perkin Elmer, Norwalk, CT, USA), according to previously standardized and validated protocols[9].

The method's detection limits were 0.0006 mg/dL (0.0002 mmol/L) for plasma, and 0.0003 mg/dL (0.0001 mmol/L) for erythrocytes. Precisions of 95-96% were obtained for plasma and erythrocyte analyses. The precisions were verified using secondary standards (samples of plasma and erythrocyte pools) prepared in our laboratory. The magnesium concentration reference ranges were: plasma 0.75-0.96 mmol/L,[3] and erythrocytes 1.65-2.65 mmol/L[10].

Statistical analyses

Statistical analyses were performed using SPSS software (Chicago, IL, USA) version 15.0. All data were normally distributed (Kolmogorov-Smirnov test), so the means were compared by Student t-test for independent samples. The level of significance α established was 5%.

The residual method of adjustment of magnesium intake was used to minimize the effect of energy in dietary calculations[11].

Results

The participants, aged 19 to 29 years, reported high percentage of family history of non-communicable disease (81.7%) and physical inactivity (69.8%). Men (52% of the sample) had BMI higher than women (table I).

Men and women had similar magnesium intake and status, evaluated by plasma and erythrocyte magnesium (table I). The probability of inadequate magnesium intake was 70% among women and 94% among men (figs. 1A and B).

Mean plasma and erythrocyte magnesium concentrations were close to the lower cut-off point (table 1). A considerably percentage of the participants had plasma (34%) and erythrocyte magnesium (17%) below the lower reference range (figs. 1C to 1F), and 8% had both: reduction in plasma and erythrocyte magnesium.

Discussion

Assessment of food intake followed by the adequate choice and interpretation of biochemical parameters are the main tools for the evaluation of micronutrient related nutritional status.

The frequency of inadequate magnesium intake in the population of this study was high, especially in men, where the values exceeded 90%. The 70% inadequacy found in women was similar to that shown in the 2008-2009 National Food Survey, in the same region[4]. On the other hand, a considerable percentage of both men and women had plasma but no erythrocyte magnesium below the lower limit of the reference.

The average low magnesium intake of 8.84 mmol/d observed was lower than that of healthy population of other countries[5,12,13], and is most probably due to the low consumption of magnesium food sources (whole grains, dark green vegetables, nuts). The foods that most contributed to magnesium intake were fruits (papaya, guava, orange, banana, and tomato), beans; corn couscous; coffee; milk; and chocolate powder, and are considered moderate to poor magnesium sources.

Hypomagnesemia was present in a 34% frequency, which was higher than that found in other populations of apparently healthy adults (5% in North of Mexico[12], 9% in Southern Spain)[5]. Besides, if the cutoff point of 0.85 mmol /L for plasma magnesium, recommended by Elin,[3] is used, this value would increase to 87%.

According to this author[3], due to the great inclusion of processed foods in the habitual diet in the past century, there was a reduction in magnesium intake. Thus, those individuals who have inadequate magnesium ingestion and concomitantly plasma/serum magnesium concentration between 0.75 and 0.85 mmol/L, in fact, should be classified as chronic latent magnesium deficient (or subclinical magnesium deficient). The interchangeable plasma magnesium pool has its concentrations tightly regulated through kidney excretion, and bone resorption. So, in order to maintain

Table I
Characteristics and magnesium status of the population under study, by gender

Parameters	*Unit*	*Total (n = 115)*	*Gender*		*p**
			Female (n = 55)	*Male (n = 60)*	
age	(y)	22.5 ± 2.5 (22.1)	22.3 ± 2.4 (22.0)	22.1 ± 2.4 (22.0)	0.703
BMI †	(kg/m²)	22.5 ± 2.6 (22.1)	21.5 ± 2.3 (20.9)	23.3 ± 2.5 (23.1)	< 0.001
normal weight	(%)	84.3	90.9	78.3	–
pre-obesity	(%)	15.7	9.1	21.7	–
dietary magnesium‡	(mmol/d)	8.84 ± 3.07 (8.44)	8.71 ± 3.20 (8.38)	8.95 ± 2.98 (8.71)	0.673
	(mg/d)	214.8 ± 74.7 (211.2)	211.7 ± 77.7 (203.7)	217.6 ± 72.4 (211.6)	0.673
plasma magnesium§	(mmol/L)	0.76 ± 0.06 (0.76)	0.76 ± 0.06 (0.76)	0.77 ± 0.07 (0.77)	0.213
	(mg/dL)	1.86 ± 0.16 (1.85)	1.84 ± 0.14 (1.84)	1.88 ± 0.17 (1.88)	0.213
erythrocyte magnesium§	(mmol/L)	1.97 ± 0.33 (1.94)	1.98 ± 0.33 (1.93)	1.96 ± 0.32 (1.96)	0.844
	(mg/dL)	4.79 ± 0.79 (4.72)	4.80 ± 0.81 (4.70)	4.78 ± 0.79 (4.76)	0.844
	(mmol/g Hb)	8.15 ± 2.01 (7.95)	8.27 ± 2.09 (7.97)	8.05 ± 1.95 (7.92)	0.553
	(mg/g Hb)	198.2 ± 48.8 (193.3)	201.2 ± 50.7 (193.8)	195.6 ± 47.5 (192.6)	0.553

The results are expressed as mean ± standard deviation with the median value shown in parenthesis or%
* The means were compared by Student t-test for independent samples
† BMI classifications: normal weight, 18.5-24.9 kg/m²; pre-obesity, 25.0-29.9 kg/m²
‡ Data adjusted according to the individual energy intake. The estimated average requirements for an individual aged 19-30 years are: 10.5 mmol/d (255 mg/d) for women, 13.6 mmol/d (330 mg/d) for men.
§ Normal magnesium range: 0.75-0.96 mmol/L (1.82-2.33 mg/dL)[3] for plasma; 1.65-2.65 mmol/L (4.01-6.44 mg/dL)[10] for erythrocyte.

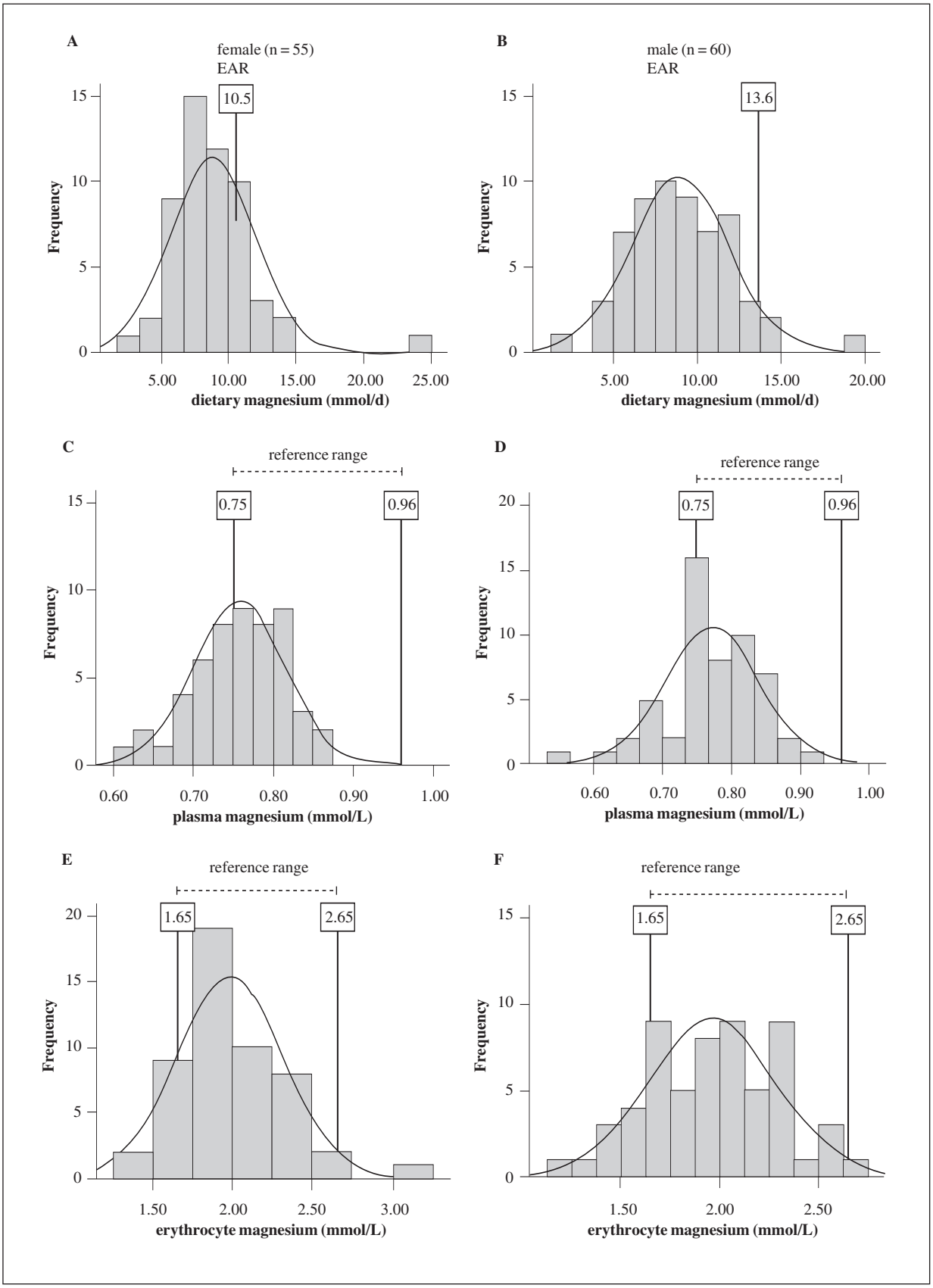

Fig. 1.—Distribution of magnesium intake, plasma and erythrocyte magnesium from participants, by gender (EAR: estimated average requirement).

plasma magnesium within the reference interval, these individuals certainly have depleted reserve (bone) compartments[3,14].

Although the plasma magnesium pool represents less than 1% of total body magnesium[14], its assessment cannot be disregarded when magnesium status is evaluated. Long-term dietary magnesium restriction could result in magnesium decompartmentalization, before clinical signs and symptoms of magnesium deficiency become evident[2,3]. Nevertheless, the detection of magnesium deficiency only by clinical signs and symptoms is difficult because they are pathognomonic for many diseases[1,14].

Although it is not completely clear how low magnesium intake predisposes to NCD[1], the magnesium deficiency observed in the present study in apparently healthy adults is worrying, due to the high frequency of family history of NCD reported by the participants, which is significant in the local population, as demonstrated in a telephone survey conducted by the Brazilian Health Ministry. In this survey, the findings showed a prevalence of 5.8% for diabetes, 24.9% for hypertension, and 18.5% for obesity[15].

In conclusion, the high frequency of subclinical magnesium deficiency in the adults assessed in this study can be attributed to their low dietary magnesium intake. Although the association of magnesium deficiency with the development of NCD is not completely understood, it is reasonable to address the focus of future research to the evaluation of magnesium status in a larger and significant sample of the Brazilian population.

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Conflict of Interest Declaration

The authors have no potential conflicts of interest that could inappropriately influence this work.

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Anthropometric, food intake differences and aplicability of low-cost instruments for the measurement of body composition in two distinct groups of individuals with short bowel syndrome

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Abstract

Introduction: **Short bowel syndrome is associated with weight loss due to nutrient, electrolyte and fluid malabsorption. In view of the pathophysiology of SBS, all patients would be expected to exhibit similar clinical signs and symptoms, whereas many variations occur probably due to the adaptive capacity of the remaining small intestine in order to compensate for the resected area.**

Objective: **To determine whether there is a difference in nutritional status and food intake between patients receiving PNT, patients who do not receive PNT but are monitored on an ambulatory basis, and control subjects, and 2) to determine body composition by two different methods, i.e., electrical bioimpedance and skin fold measurement.**

Methods: **This was a case-control study where the subjects were divided into three groups: parenteral group (PG) – adults with a history of SBS intermittently using PNT; ambulatory group (AG) – adults with a history of SBS who do not receive PNT; control group (CG) – adults with no history of intestinal resections and/or use of PNT. The volunteers were submitted to measurements of body weight, height, body composition by bioimpedance analysis and assessment of food intake using a food frequency questionnaire. Univariate analysis of variance (ANOVA) with the aid of the SAS® 9.2. software, using the PROC GLM feature. The Student t-test was used to compare the instruments for the assessment of body composition, with the aid of the PROC TTEST feature of the SAS® 9.2 software.**

Results: **Thirty-two volunteers, 19 women and 13 men, participated in the study. The PNT group consisted of 9 volunteers, 4 women and 5 men, with a mean (± SD) age of 57 ± 9 years. The nutrition status and food intake were different between the groups. There was no difference in percent body fat measured by anthropometry and bioimpedance analysis.**

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ANTROPOMETRÍA, DIFERENCIAS EN EL CONSUMO DE ALIMENTOS Y APLICABILIDAD DE INSTRUMENTOS DE BAJO COSTE PARA LA MEDICIÓN DE LA COMPOSICIÓN CORPORAL EN DOS GRUPOS DISTINTOS DE INDIVIDUOS CON SÍNDROME DEL INTESTINO CORTO

Resumen

Introducción: **El síndrome del intestino corto se asocia con pérdida de peso por la malabsorción de nutrientes, electrolitos y líquidos. A la vista de la fisiopatología del SIC, se esperaría que todos los pacientes exhibieran signos y síntomas clínicos similares, mientras que pueden ocurrir variaciones probablemente por la capacidad de adaptación del intestino delgado restante con el fin de compensar el área resecada.**

Objetivo: **Determinar si existen diferencias en el estado nutritivo y en el consumo de alimentos entre pacientes que reciben TNP, aquellos que no reciben TNP pero que están monitorizados de forma ambulatoria e individuos control, y 2) determinar la composición corporal mediante dos métodos distintos: la bioimpedancia eléctrica y la medición del pliegue cutáneo.**

Métodos: **Éste fue un estudio de casos-control en el que se dividió a los sujetos en tres grupos: el grupo de parenteral (GP) – adultos con una historia de SIC y con uso intermitente de TNP; grupo ambulatorio (GA) – adultos con una historia de SIC que no recibían TNP; grupo control (GC) – adultos sin antecedentes de resecciones intestinales ni uso de TNP. Los voluntarios fueron sometidos a mediciones del peso corporal, talla, composición corporal mediante análisis de bioimpedancia y evaluación del consumo de alimentos utilizando un cuestionario de frecuencia de alimentos. Se realizó un análisis de varianza (ANOVA) con la ayuda del programa SAS® 9.2, utilizando la aplicación PROC GLM. Se empleó el test t de Student para comparar los instrumentos de la evaluación de la composición corporal, con la ayuda de la aplicación PROC TTEST del programa SAS® 9.2.**

Resultados: **32 voluntarios, 19 mujeres y 13 hombres, participaron en el estudio. El grupo TNP estaba compuesto de 9 voluntarios, 4 mujeres y 5 hombres, con una edad media (± DE) de 57 ± 9 años. El estado nutritivo y el consumo de alimentos fueron diferentes entre los grupos. No hubo diferencias en el porcentaje de grasa corporal medida por antropometría y análisis de bioimpedancia.**

Discussion and conclusion: **Large resections, as well as the resected portions, explain the greater nutritional impairment of PG compared to AG and CG, although no significant difference in food consumption was detected between these three groups. Since the use of PNT can lead to a state of hyperhydration, the results of BIA should be interpreted with caution, in view of the fact that the lean mass determined by this method varies positively with the hydration state of an individual.**

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Key words: *Short bowel syndrome. Body composition. Food intake.*

Discusión y conclusión: **Las resecciones largas, así como las porciones resecadas, explican la mayor alteración nutricional del grupo GP en comparación con los grupos GA y GC, aunque no se detectaron diferencias significativas en el consumo de alimentos entre los tres grupos. Puesto que el empleo de TNP puede conducir a un estado de hiperhidratación, los resultados del ABI deberían interpretarse con precaución puesto que la masa magra determinada por este método varía positivamente con el estado de hidratación de un individuo.**

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Palabras clave: *Síndrome del intestino corto. Composición corporal. Consumo de alimentos.*

Introduction

Short bowel syndrome (SBS) is usually due to intestinal ischemia or necrosis, neoplasias, postoperative complications, benign causes, or inflammatory bowel disease[1-3], which culminate in extensive areas of enterectomy. The result is the loss of the absorptive area and of the processes of site-specific transport, with impaired gastrointestinal hormone secretion and, in some cases, loss of the ileocecal valve, factors that involve intense weight loss and nutrient, electrolyte and fluid malabsorption. In addition, there is gastric hypersecretion, inactivation of pancreatic enzymes, loss of bile salts with a shorter intestinal transit time, osmotic diarrhea, steatorrhea, vitamin deficiencies, hypovolemia, hyponatremia and hypokalemia, and an increased incidence of nephrolithiasis and cholelithiasis[1,3,4].

It has been reported that an intestinal length of 100 cm would be sufficient to maintain absorptive capacity and that absorption would be maintained without the need for support with parenteral nutrition therapy if the colon, ileocecal valve and at least 40 cm of the small bowel were preserved[5]. Other more conservative authors have stated that greater impairment of nutritional status associated with the risk of cholelithiasis occurs when the remaining intestine is shorter than 120 cm without the colon or shorter than 60 cm even with continuity of the colon, with the patients requiring parenteral nutrition therapy (PNT) for the recovery and/or maintenance of nutritional status[3,6] stated that usually patients with 180 cm of remaining intestine do not require PNT, whereas patients with 90 cm and the colon in continuity require PNT for approximately one year and, in agreement with[3], patients with 60 cm of remaining intestine require permanent PNT even with the colon in continuity.

In view of the pathophysiology of SBS, all patients would be expected to exhibit similar clinical signs and symptoms, whereas many variations occur probably due to the adaptive capacity of the remaining small intestine in order to compensate for the resected area[7]. Thus, SBS is not simply defined by the length of the remaining intestine, but also by mutiple factors and variables related to the postoperative period, such as extension of the resection itself, site of resection, presence of base diseases, presence or absence of the ileocecal valve, functionality of the organs of the gastrointestinal tract, and the adaptive ability of the remainig intestine, where the adaptation phase starts[7,8].

Although adaptive processes occur, the loss of nutrients is highly significant and, as a clinical consequence, these patients progress to a situation of severe protein-calorie malnutrition[3,4,9].

The objectives of the present study were: 1) to determine whether there is a difference in nutritional status and food intake between patients receiving PNT, patients who do not receive PNT but are monitored on an ambulatory basis, and control subjects, and 2) to determine body composition by two different methods, i.e., electrical bioimpedance and skin fold measurement.

Methodology

Patients

This was a case-control study[10] conducted at the University Hospital of the Faculty of Medicine of Ribeirão Preto, University of São Paulo (HCFMRP/USP). The experimental protocol was approved by the Research Ethics Committee of HCMRP/USP (protocol no. 8667/2009) and at no time did it interfere with the clinical course of the patient or with the routine of the outpatient clinic. All patients gave written informed consent to participate in the study.

The subjects were divided into three groups: parenteral group (PG) – adults with a history of SBS intermittently using PNT; ambulatory group (AG) – adults with a history of SBS who do not receive PNT; control group (CG) – adults with no history of intestinal resections and/or use of PNT. Individuals who accepted to participate in the study and who were eligible according to the inclusion criteria, were recruited for the study.

The exclusion criteria for PG and AG patients were:

1. Refusal to permit data collection.
2. HCFMRP/USP patients who did not develop SBS.
3. Patients with a resection time of less than one year at the time of data collection.
4. Unstable patients in terms of infectious aspects (changes in more than 4 of the following parameters: systolic arterial pressure, diastolic arterial pressure, body temperature, heart rate, respiratory rate, C-reactive protein, lymphocyte count, ferritin and transferrin levels).
5. Patients whose base disease for resection was cancer.
6. Patients with resection but who did not meet the criteria for SBS.
7. Patients with SBS who do not intermittently use PNT and are not monitored on an ambulatorry basis.
8. Patients with syndromes that impair cognitive function.

The exclusion criteria for CG subjects were:

1. Refusal to permit data collection.
2. Adults with a difference of ± 2 years of age compared to AG patients.
3. Adults who had undergone any type of intestinal resection.
4. Adults who had already used PNT.
5. Unstable adults in terms of infectious aspects, i.e., changes in more than 4 of the following parameters: systolic arterial pressure (considered to be normal up to 129 mmHg), diastolic arterial pressure (considered to be normal up to 89 mmHg), body temperature (minimum limit of 37°C), heart rate (100 beats/minute), respiratory rate (normal values: 12 to 22 breaths/minute)[11-13] C-reactive protein, lymphocyte count, ferritin and transferrin.

Experimental design

Data were collected in three phases, each applied in the same order for all individuals.

Phase 1 consisted of the analysis of the medical records of AG patients, with information being obtained about name, HCFMRP/USP registration number, date of birth, remaining intestine, data recorded by the surgeon, presence or absence of the ileocecal valve, time of PNT use in months, and use or not of a lipid emulsion in PNT. Phase 2 consisted of contacting the individuals eligible for participation in the study. PG patients were invited verbally during hospitalization for PNT, AG patients were contacted by telephone or letter, and CG subjects were invited by means of posters scattered around the Hospital.

Phase 3 was devoted to data collection, involving anamnesis (age, schooling, food record (Quantitative Food Frequency Questionnaire, QFFQ), anthropometric evaluation (weight (kg), height (m), body mass index (BMI) (kg/m^2), skin folds (mm), estimate of body fat based on skin folds (percentage and kg), arm circumference (cm), arm muscle circumference (cm^2), and electrical bioimpedance (percentage and kg). Data were collected in the same place by the same investigator for all groups, in a room duly prepared for this purpose in the Clinical Research Unit on the 12th floor of HCFMRP/USP.

Anthropometry

Weight and height measurements were made and used to calculate the BMI. In addition, skin folds (bicipital, tricipital, subscapular and suprailiac folds) were measured for extrapolation of percent body fat and body fat mass (kg) and arm circumference (AC) was measured in order to obtain arm muscle circumference (AMC)[14]. Bioimpedance was also performed with the Tetrapolar Bioimpedance Biomarker 2000® instrument according to preestablished protocols.

Assessment of food intake

Food intake was determined using the QFFQ, which represents a retrospective method aiming at the detailed report of food intake over a given period of time using a food list[15]. The data obtained with the QFFQ were analyzed with the Dietsys® software to evaluate the foods consumed by the study population and to determine the correlation of the size, number and frequency of the foods consumed with nutritional status assessed by the anthropometric measurements[16].

Statistical Analysis

An exploratory analysis of the data was first performed. The basic objective of this methodology is to synthesize a series of values of the same nature in order to obtain an overall view of the variation of these values, which are organized in tables with descriptive measures and plotted on graphs. Descriptive analysis of the data was performed with the aid of the SAS® 9.2 software, using the PROC MEANS feature.

Univariate analysis of variance (ANOVA) was then used[17], with the aid of the SAS® 9.2 software, using the PROC GLM feature.

The Student t-test was used to compare the instruments for the assessment of body composition, with the aid of the PROC TTEST feature of the SAS® 9.2 software.

Results

Thirty-two volunteers, 19 women and 13 men, participated in the study. The PNT group consisted of 9 volunteers, 4 women and 5 men, with a mean (± SD) age of 57 ± 9 years. Mean time since the first resection was 6 ± 4 years. Eight subjects did not have the ileocecal valve and 1 subject had it.

The ambulatory group consisted of 10 subjects, 6 women and 4 men with a mean age of 60 ± 11 years and a mean time since the first resection of 13 ± 7 years. In this group, 5 participants had the ileocecal valve, 4 did not have it, and 1 patient had no information about it in his medical records.

In both groups the remaining intestine was shorter than 1 meter and time since first resection differed significantly between PG and AG subjects ($p = 0.02$).

The control group consisted of 13 participants, 9 women and 4 men, with a mean age of 58 ± 12 years. The three groups did not differ significantly regarding age ($p = 0.79$).

Figure 1 illustrates the analysis of food intake and shows the mean values and standard deviations of the main nutrients consumed by 1.000 kcal, with no significant difference between groups regarding any of the nutrients evaluated.

The mean (± SD) values for folate (µg/1000kcal), vitamin A (IU/1000 kcal) and vitamin E (mg/1000 kcal) for PG, AG and CG were, respectively: 99 ± 34.6 µg /1,000 kcal, 4214.2 ± 3775.4 IU/1,000 kcal and 3 ± 0.72 mg/1,000

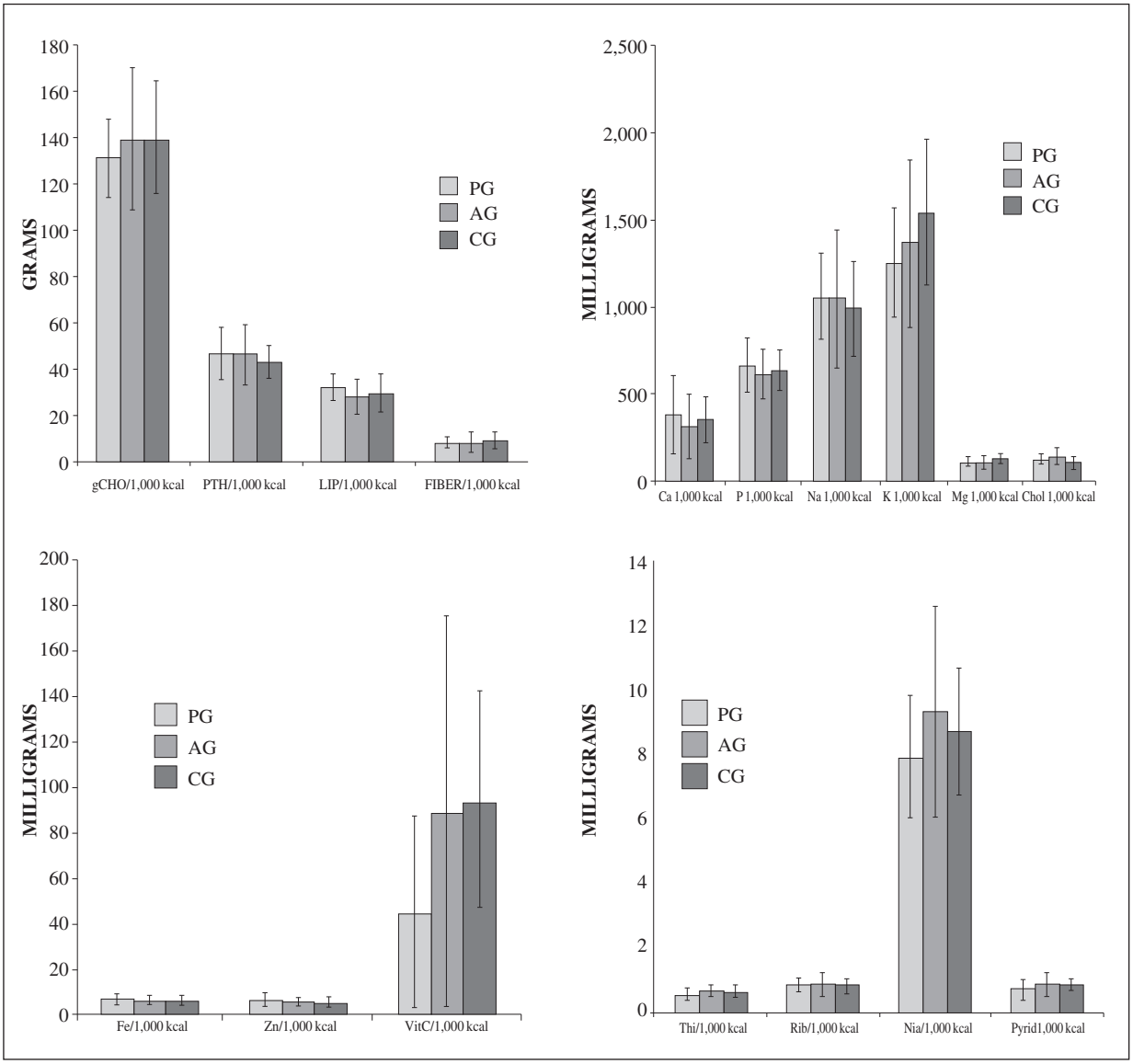

Fig. 1.—A. Mean and standard deviation of grams of carbohydrate (CH), proteins (PTH), lipids (Lip) and fibers (Fiber) per 1,000 kcal/day for each group . B. Mean and standard deviation of grams of calcium (Ca), phosphorus (P), sodium (Na), potassium (K), magnesium (Mg) and cholesterol (Chol) per 100 kcal/day for each group. C. Mean and standard deviation of milligrams of iron (Fe), zinc (Zn) and vitamin C (VitC) per 100 kcal/day for each group. D. Mean and standard deviation of milligrams of thiamine (Thi), riboflavin (Rib), niacin (Nia) and pyridoxin (Pyrid) per 100 kcal/day for each group.

kcal; 105 ± 40.5 µg /1,000 kcal, 3938.6 ± 2393.9 IU/1,000 kcal and 2.8 ± 0.7 alpha tocopherol equivalent /1,000kcal; 132.2 ± 44.2 µg/1,000 kcal, 5347.1 ± 3400.9 IU/1,000 kcal and 3.4 ± 0.9 alpha tocopherol equivalents /1,000 kcal.

The mean (± SD) values, the level of significance and the confidence interval (CI) for the data of anthropometric evaluation are given in table I.

Another variable that should be emphasized is the ileocecal valve and its possible influence on nutritional status. Figure 2 illustrates the data regarding BMI, AMC, fat mass determined with an adipometer and by bioimpedance, related to the presence or absence of the valve. The comparison of the instruments for the measurement of body composition, presented as

Table I

Mean, standard deviation, confidence interval and level of significance of the data of anthropometric assessment of the study groups

	PG	*AG*	*CG*	*p value*
BMI (kg/m²)	17 ± 2†	24 ± 5	29 ± 7†	0.0006
AC (cm)	23 ± 3†*	29 ± 5*	34 ± 6†	0.0003
AMC (cm²)	21 ± 3†	25 ± 4	27 ± 5†	0.0096
**Fat mass (kg) - Adipometer	7 ± 3†	18 ± 11	28 ± 11†	0.0008
% Body fat mass– Adipometer	16 ± 7†	28 ± 14	36 ± 10†	0.0015
***Lean mass (kg) - BIA	40 ± 7†*	40 ± 6*	48 ± 4†	0.0002
Fat mass (kg) - BIA	10 ± 4†	20 ± 8	27 ± 11†	0.0008
% Lean mass - BIA	81 ± 8†*	68 ± 7*	65 ± 7†	0.0007
% Fat mass- BIA	19 ± 8†*	40 ± 7*	35 ± 7†	0.0007
% Lean mass ACT	75 ± 4†	73 ± 2	73 ± 1†	0.0090

†P ≤ 0.05 for the difference between PG and CG. * P ≤ 0.05 for the difference between PG and AG. ** PG patient 9 could not be submitted to all anthropometric measurements with an adipometer because he was bedridden (impossibility to measure the subscapular and suprailiac skin fold). *** PG patient 7 was not submitted to BIA because she wore a pacemaker (one of the contraindications of the use of this technology). AG patient 1 was not submitted to BIA because he did not come to the hospital on the day scheduled for this evaluation.

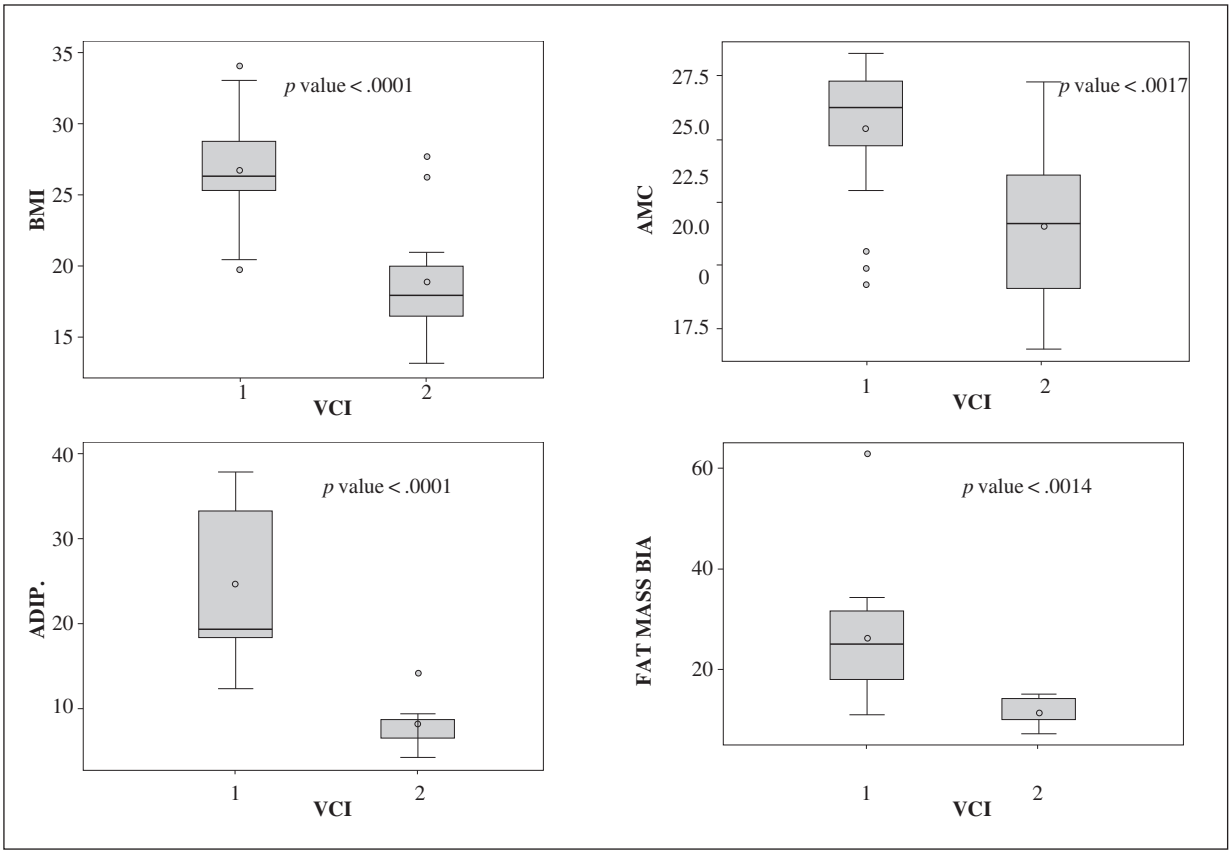

Fig. 2.—Evaluation of the influence of the presence of the ileocecal valve (identified by number 1) and its absence (identified by number 2) on the main anthropometric parameters: 2a – VCI (ileocecal valve) × BMI; 2b – VCI × AMC; 2c – VCI × amount of fat in kg determined with an adipometer; 2d – VCI × amount of fat in kg determined by BIA.

General Comparison (results of BIA and adipometer determinations without considering the group to which the subject belonged) and later presented separately for each group are listed in table II.

Discussion

The description obtained from the surgery report for intestinal resection was not well delimited regarding the remaining portions. However, there was a significant difference in time since resection between PG and AG, with this time being longer for AG. In addtion, although there were interindividual differences regarding the remaining portions, the importance of the presence of the ileocecal valve in the adaptive process and in the maintenance of nutritional status should be emphasized[18] published a case report regarding a male with only 40 cm of remaining intestine and without the ileocecal valve, with negative consequences for his nutritional status. Similarly[19], in a study on children, reported that loss of the ileocecal valve is more important regarding the presence of chronic diarrhea than the resection of the ileum or of the colon *per se*[20] also mentioned the importance of this structure in order to prevent bacterial translocation from the colon to the small bowel.

This effect is supported by the studies of Sundaram et al.[21], who stated that removal of the ileocecal valve reduces chyme emptying time from the small bowel to the colon, with a shorter time of food contact with the absorptive surface. This also increases the risk of bacterial translocation to the small bowel, causing an aggravation of nutritional status, in agreement with the results of anthropometric assessment obtained in the present study. In other words, the shorter time since the first intestinal resection (and consequently a shorter time for the adaptive process[6,8]–) and the loss of an important structure are some of the factors that may contribute to the worse nutritional status of PG subjects and a greater dependence on PNT.

Comparison of the anthropometric measures of the three groups studied here showed a moderate to severe degree of malnutrition among PG individuals compared to AG and CG individuals, as also reported in the literature. However, no significant difference in food intake was observed between groups, regardless of the nutrient involved. This agrees with data reported by Furtado et al.[22], who also detected a marked impairment of nutritional status in their SBS patients despite a similar food intake for all individuals, who live in the same region of the country and therefore have similar eating habits. Large resections definitely are a plausible explanation, since lean and fat mass depletion is one of the consequences. In addition to the similar food consumption, PG subjects receive an additional supply by means of PNT (~7 consecutive days/month), but even so their nutritional status is more impaired.

In view of this fact, the following question arises: why is it that AG individuals do not have this impairment of nutritional status even though they were also submitted to large intestinal resections? Part of this question was answered above when the preservation of the ileocecal valve was compared between groups. Another plausible answer would be the presence of an inflammatory state, i.e., possible changes in TNF-α and IL-6 levels related to the long-term use of PNT [23], which are known to act by increasing energy expenditure, anorexia, adipose and muscle reserves, and cachexia[24]. In agreement, REIMUND et. al[25] showed a positive correlation between TNF-α levels and the quantity of macronutrients infused by PNT, suggesting that the presence of this inflammatory state stimulates the catabolic pathways and increases the nutritional requirements of these individuals. Baumann et al.[26] also mentioned IL-6 and TNF-α as the main factors responsible for the increased muscle catabolism, and Bistrian et al [27] related the duration and intensity of the inflammatory state to reduction of lean body mass in individuals on dialysis.

The assessment of the nutritional status of patients with SBS is extremely important in clinical practice, since malnutrition is one of the most prevalent acute situations afer extensive resections, increasing the risk of morbidity and mortality throughout life[28].

The parameters chosen here for the assessment of body composition were based on low cost and accessibility and on the fact that they are based on noninvasive methods already established in the literature[29,30]. Although they are quite useful paameters in clinical practice, they have their limitations. However, the present study was important since, to our knowledge, there are no studies in the literature involving this type of assessment in Brazilian patients with SBS, indicating the relevance of the investigation of this population.

The data in table II permit us to infer that the two instruments for the assessment of body fat were adequate for use in this group of patients since there were no inter- or intragroup differences when the body fat mass obtained by BIA was compared to that obtained with an adipometer. Although a technique considered to be the gold standard was not used, other studies have already demonstrated the validity of both the anthropometric technique based on skin fold measurement[31,32] and

Table II
Comparison of two instruments for the measurement of body fat: adipometer and bioimpedance

General comparison (n = 32)	*p value*
	0.3929
Group comparison	*p value*
PG (n = 9)	0.1347
AG (n = 10)	0.5251

the BIA technique[33,34] compared to DXA and to doubly-labeled water, which are considered to be the gold standards. On the basis of this premise, the statement would be correct if it were not a special group of patients using PNT, which influences the hydration state since, according to its own definition, PN is an intravenous infusion of fluids and nutrients[35].

Table I presents the results discussed above. PG patients showed significantly higher mean percent lean mass values compared to AG and CG. Lean mass is a compartment known to vary positively with hydration status[36]. Thus, the lean mass value is overestimated in hperhydrated individuals[37], representing a limitation of the use of this type of instrument[36]. On this basis, BIA does not seem to be a good instrument for the assessment of body composition for patients with SBS who use PNT. However, BIA continues to be a technique of promising future and requires more studies, especially regarding the development of specific equations for different populations and the investigation of their basic assumptions in order to minimize their limitations. The skin fold technique has proved to be a good option for more reliable estimates of body composition.

Conclusion

- Time since first intestinal resection, remaining intestine and preservation of the ileocecal valve are some of the more relevant aspects for the maintenance of nutritional status in individuals with SBS.
- Large resections, as well as the resected portions and the hypothesis of the existence of an inflammatory state related to the long-term use of PNT, explain the greater nutritional impairment of PG compared to AG and CG, although no significant difference in food consumption was detected between these three groups.
- Since the use of PNT can lead to a state of hyperhydration, the results of BIA should be interpreted with caution, in view of the fact that the lean mass determined by this method varies positively with the hydration state of an individual.

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Original / *Otros*

Análisis del servicio de comedor y la opinión de los usuarios en un centro penitenciario de Cataluña

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Resumen

Introducción: **Los estudios sobre restauración colectiva se encuentran viviendo un cierto auge en España. Sin embargo, se dispone de muy poca información sobre cómo se organiza este servicio en las instituciones penitenciarias, y mucho menos aún sobre cómo es percibido por sus usuarios.**

Objetivos: **Analizar el servicio de comedor y el menú servido en la Prisión Modelo de Barcelona, y confrontarlo con la percepción de los usuarios**

Metodología: **Entrevista abierta semiestructurada con un responsable de la Subdirección de Instituciones Penitenciarias; observación del funcionamiento del comedor y otros espacios a cargo de uno de los investigadores del estudio; y administración de un cuestionario de elaboración propia adaptado al tipo de institución. La valoración nutricional y de la calidad del menú se realizó a través del programa DIAL y del índice de alimentación saludable (IAS).**

Resultados: **Los menús suministrados contienen habitualmente un exceso de grasa (41,3% del total) y un déficit en hidratos de carbono (41,7% del total) y la puntuación obtenida según el IAS es aceptable (58,4 puntos). Tres cuartas partes del los reclusos usan el comedor a diario para una de las comidas principales, empleando menos de 15 minutos de media por comida. El espacio se considera como muy ruidoso. Las raciones se consideran adecuadas, pero el sabor, la calidad y el servicio de la comida se valoran negativamente.**

Discusión y conclusiones: **Se denota una cierta brecha entre las propuestas institucionales y las prácticas y percepciones cotidianas de los usuarios. Algunos cambios en los alimentos y platos servidos en los menús, como por ejemplo la reducción de carnes y un aumento del consumo de legumbres, podrían contribuir a una mejora nutricional, de percepción y económica del menú. Una mayor variedad de alimentos y mayor posibilidad de elección tanto en el comedor como en el economato podrían ser también positivas. Una reordenación estratégica del uso del tiempo y de los espacios en el comedor que redujese la sensación de provisionalidad y el ruido podría contribuir a un mejor y más agradable uso del mismo, a la vez que contribuiría a una mejor percepción de la comida y del bienestar en general.**

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Palaabras clave: *Hábitos alimentarios. Nutrición. Prisión. Alimentación colectiva. Percepción.*

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ANALYSIS OF FOOD SERVICE AND OPINION OF ITS USERS IN A CATALAN PRISON

Abstract

Introduction: **Studies on food services are increasing actually in Spain. However, there still is very little information on how this service is organized in prisons, and even less about how it is perceived by its residents.**

Objectives: **To analyze the food service and menu in the *Modelo* Prison in Barcelona, and confront it with the perception of prisoners.**

Methods: **Semi-structured open interview with an official of the Division of Prisons, participant observation in the dining room and other spaces by one of the study researchers, and a specifically designed questionnaire adapted to this kind of institution. Nutrition and menu quality assessment was performed using the DIAL program and healthy eating index (IAS).**

Results: **The supplied menus usually contain an excess of fat (41.3%) and carbohydrate deficit (41.7 %) even if is acceptable under IAS score (58.4 points). 75% of residents uses the dining room for daily main meals, spending less than 15 minutes on average per meal. The space is considered very noisy. The portions are considered adequate, but the taste, quality and service of food are negatively valued.**

Discussion and conclusions: **Some gaps between institutional proposals and everyday practices and perceptions of users are clearly denoted. Some changes in food and dishes served in the menus –such as reducing meat and increasing consumption of legumes– could contribute to improve nutrition, perception and final cost of the menu. A greater variety of food and more possibility of choice in the dining room and in the shop could be also positive. A strategic reorganization of the use of time and space in the dining room that would reduce the feeling of discomfort and noise could contribute to a better and more enjoyable use of it, while contributing to a better perception of food and welfare in general.**

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Key words: *Food habits. Nutrition. Prison. Food services. Perception.*

Abreviaturas

IAS: Índice de Alimentación Saludable.
SIDA: Síndrome de Inmunodeficiencia Adquirida.
ON: Objetivos Nutricionales.
AMDR: Intervalo aceptable de distribución de macronutrientes (del inglés, Acceptable Macronutrient Distribution Ranges.

Introducción

El libro blanco de la Nutrición en España en su edición del 2013 recoge que "*el suministro de una dieta sana y equilibrada nutricionalmente, pero aceptable para el consumidor, son factores evidentes que deben ser considerados en cualquier operación de servicio de alimentos*"[1]. En este sentido, desde diferentes organismos e instituciones se han llevado a cabo bastantes iniciativas para controlar y mejorar la calidad nutricional de los servicios de restauración colectiva, especialmente en colegios y hospitales[2,3]. Sin embargo, se dispone de menos información sobre cómo se organiza este servicio en las instituciones penitenciarias, y mucho menos aún sobre cómo es percibido por sus usuarios, a pesar de que en España afectaba a 68.614 personas en enero de 2013 y de que se destinó un presupuesto de 219 millones de euros para la cocina[4].

Los estudios realizados en este ámbito ponen en evidencia la existencia de dificultades y retos sobreañadidos que son propios de este entorno y no así de otro tipo de instituciones[5-8]. Las comidas realizadas en la prisión son, de manera general, el único sustento durante periodos de tiempo más o menos largos y van destinadas a un colectivo con una elevada variabilidad de orígenes geográficos, creencias religiosas, entornos socioculturales, en algunos casos en situación de exclusión social[9,10]. Asimismo, es un colectivo en el que encontramos una mayor prevalencia de drogodependencia, tabaquismo o patologías como SIDA, hepatitis C o tuberculosis que en la población general[11-14].

La comida se convierte para los reclusos, en muchos aspectos, en un símbolo de la experiencia en la cárcel[15]. La imposibilidad de escoger qué, dónde y cuándo comer reafirma su pérdida de libertad y la crítica a la comida puede convertirse entonces en un reflejo de la crítica a la institución, un acto de rebelión o una forma de resistencia[16].

Así, al margen de la evidente necesidad de aplicación y seguimiento de la normativa que establece los requisitos nutricionales y de calidad de los menús servidos en los centros penitenciarios, coincidimos con otros estudios[17,18] en que es fundamental conocer cómo los usuarios perciben la alimentación en la cárcel y en qué medida se ajusta a sus preferencias alimentarias. Los desajustes entre la cantidad, composición y variedad de la comida servida y la consumida supondrán sin duda un mayor gasto económico derivado del desperdicio alimentario, así como un impacto desfavorable para la salud de un colectivo que, ya de por sí, presenta una mayor prevalencia de determinadas patologías y conductas de riesgo.

Ante esta situación, en el presente trabajo, analizamos el servicio de comedor y el menú servido en el más antiguo y principal centro penitenciario en activo de la provincia de Barcelona y lo confrontamos con la opinión y percepción de los usuarios, con el objetivo de poner en evidencia determinados aspectos que podrían ayudar a conciliar la visión de los diferentes actores implicados y, de este modo, conseguir un mejor aprovechamiento de los recursos y un mayor beneficio para la salud y el bienestar general de los usuarios.

Metodología

El estudio se llevó a cabo en el servicio de comedor de la prisión Modelo de Barcelona. La población penitenciaria de este centro se encuentra entorno a unos 1.800 individuos y está constituida principalmente por presos preventivos, es decir, en espera de sentencia firme. La recogida de datos e información sobre el servicio de comedor se llevó a cabo a través de entrevista abierta semi-estructurada[19] con un responsable de la Subdirección de Instituciones Penitenciarias; la observación personal del funcionamiento del mismo a cargo de uno de los investigadores del estudio, y la administración de un cuestionario de elaboración propia adaptado y modificado a partir del cuestionario 7 para comedores escolares del programa PERSEO[20] (anexo1). El cuestionario contenía 22 preguntas sobre el menú, las condiciones del servicio y el recinto y los aspectos organizativos del comedor. Se incluyeron preguntas abiertas, cerradas y preguntas con una escala tipo Likert con 5 niveles de valoración. Para el análisis de los datos generados por las preguntas abiertas se utilizó un análisis cualitativo genérico[21]. La participación en el cuestionario fue anónima y voluntaria y se administró, en el marco de la asignatura *Nutrición y Dietética,* a 31 de los 36 estudiantes de secundaria de la prisión.

La valoración nutricional del menú servido se realizó mediante el programa DIAL[22], a partir de los informes de los 7 menús semanales tipo correspondientes a las temporadas primavera-verano y otoño-invierno, facilitados por el representante de la administración, considerados como representativos de los que se sirven en cualquier institución penitenciaria con cocina propia, como es el caso de la Modelo. Para la determinación de las raciones habituales de consumo y los pesos de alimentos servidos en comedores colectivos se tomaron como referencia las recogidas en Carbajal y Salas-Salvadó[23, 24]. Para determinar la calidad del menú se utilizó el Índice de Alimentación Saludable (IAS) [25].

Resultados

El servicio de comedor

El servicio de comedor dispone de cocina propia y de un horno donde se confecciona a diario el pan y la

bollería. El personal está formado por cuatro cocineros profesionales, además de personal de ayuda de cocina formado por internos que son seleccionados y reciben formación específica sobre manipulación de alimentos. Este trabajo y funciones están reconocidos institucionalmente.

A excepción de los reclusos que se encuentran sancionados en "régimen cerrado" o los que están enfermos, que comen en la celda o en la enfermería respectivamente, las comidas se llevan a cabo en 3 comedores de 260 m^2 de superficie media y al que asisten una media de 250 comensales por turno, con un servicio de tres turnos diarios. Cada recluso tiene asignado un comedor en función de la galería que ocupa, y un turno de comida que viene determinado por el espacio disponible y el número de internos de la galería. El sistema de funcionamiento del comedor es el autoservicio, y se sirve en bandejas metálicas con espacios destinados a albergar los alimentos. Se consume en mesas comunitarias, con cubiertos de PVC reutilizable y se dispone de 30-40 minutos para finalizar la comida. No obstante, la información facilitada por los usuarios a través de la encuesta indica que el 87% de los reclusos participantes en esta investigación destina como máximo 14 minutos para comer.

La asistencia al comedor no es obligatoria, pero el 75% de los presos afirman realizar al menos dos comidas al día en él.

Los resultados de satisfacción con las condiciones del servicio de comedor, el recinto y el menú, se muestran en la tabla I. A excepción de la iluminación, el resto de los aspectos consultados son mal valorados por los participantes de la encuesta. La entrevista con el responsable de la subdirección de instituciones penitenciarias también coincide en considerar los comedores luminosos y bastante ruidosos.

Los peores resultados se obtienen para el sabor, considerado como malo o muy malo para el 87,5% de los participantes. Esta opinión se ratifica cuando se les consulta sobre cuál es la queja principal sobre el comedor, dónde el sabor de la comida obtiene el mayor número de respuestas (9), muy por encima del resto de quejas: variedad (4), textura (1) y temperatura (1). Las respuestas abiertas incluyen percepciones negativas sobre el proceso de descongelación de los alimentos -sobre todo de las varitas de pescado- o sobre la dureza de la carne.

Tabla I
Opiniones sobre diferentes aspectos del servicio del comedor (entorno y menús) (n = 16)

	Muy buena + buena n (%)	*Mala + muy mala n (%)*
Iluminación	6 (37,5%)	2 (12,5%)
Ruido	3 (18,7%)	10 (62,5%)
Sabor	2 (12,5%)	14 (87,5%)
Calidad	3 (18,7%)	11(68,7%)
Cantidad	2 (12,5%)	7 (43,75%)
Temperatura	2 (12,5%)	10 (62,5%)
Variedad	2 (12,5%)	8 (50%)

La disconformidad con la cantidad servida viene determinada en su mayor parte por la insatisfacción con el postre, que se considera escaso por el 68,7% de los encuestados. Este plato es además el más consumido por los reclusos puesto que sólo un 18,7% afirma dejar el postre, frente al 43,7% dicen acabarse el primer plato y el 18,7% % el segundo, a pesar que las cantidades servidas para los primeros y segundos platos se consideran "normales" por la mayoría (68,7% y 56%, respectivamente).

El gusto o sabor son los motivos más aludidos en la mayoría de los casos (11/16) para no consumir todo lo que se les sirve. La temperatura (comida fría) es el segundo motivo mencionado (4/16). Los fritos suelen ser mejor aceptados que otros modos de preparación.

El menú

El menú se elabora por los Servicios Médicos de la Cárcel con la colaboración de nutricionistas de Instituciones Penitenciarias. Se suministran obligatoriamente 3 comidas al día. Hasta hace poco, con la comida se suministraba también una pieza de bollería con el fin de ser consumida como merienda. No obstante, ante los recortes presupuestarios y el mal destino de dicha pieza en la mayor parte de los casos, que no era consumida y finalizaba desechada en la basura, se decidió eliminarla.

El menú está conformado por dos platos y postre, acompañados de pan y agua, no existiendo posibilidad de elección alguna por parte de los usuarios. Sí es posible, sin embargo, renunciar a alguno de los platos o a la guarnición. Las cantidades vienen fijadas por el espacio de las bandejas pero es posible repetir si ha quedado comida tras servir a todos los comensales.

Los menús para situaciones especiales se confeccionan a partir de un listado de alimentos permitidos y prohibidos para cada una de las situaciones, así como modos de preparación recomendados. No se dispone, no obstante, ningún menú estructurado de modo semanal.

El contenido energético y la composición nutricional diaria promedio del menú estándar se muestran en la tabla II.

El perfil calórico y la comparación con los objetivos nutricionales (ON) de la Sociedad Española de Nutrición Comunitaria y el intervalo aceptable de distribución de macronutrientes (AMDR) [26] se muestran en la tabla III y la figura 1.

La puntuación obtenida por el menú según Índice de Alimentación Saludable (IAS)[25] fue de 58,4 pudiéndose considerar entonces como aceptable (50-80), pero con la necesidad de introducir cambios para poder llegar a considerarse saludable (> 80).

Tabla II
Energía y composición nutricional diaria promedio del menús estándar

Energía y nutrientes	*Cantidad*
Energía (kcal)	2.716
Proteína (g)	116
Hidratos de Carbono (g)	268
Fibra dietética (g)	26,6
Grasa total (g)	125
AGS (g)	36,6
AGM (g)	60,7
AGP (g)	14,7
AGP + AGM/AGS	2,1
Colesterol (mg)	428

Tabla III
Puntuación del menús según el IAS

	Puntuación
Cereales y legumbres	8,4
Verduras y hortalizas	10
Frutas	2,8
Lácteos	6,5
Carnes, Pescados y Huevos	10
Energía de lípidos [%kcal]	2,4
Energía AGS [% kcal]	5,7
Colesterol [mg]	1,5
Sodio aportado por los alimentos [mg]	7
Variedad alimentos/3 días	4
Puntuación total	**58,4**

En lo que respecta a las diferentes identidades culturales o religiosas, aunque no se contemplan en las fichas de menús y adaptaciones facilitadas, desde la Subdirección de Instituciones Penitenciarias se nos informó que existen acuerdos con diferentes estamentos de distintas confesiones religiosas. Por ejemplo, siempre se respeta el Ramadán y se proporciona la comida para poder ser consumida en las horas que la religión lo permite.

Los menús para situaciones especiales se distribuyen a la vez que los normales. La cocina ya dispone del registro de dichas necesidades y sus usuarios, de modo que solo es necesario identificarse.

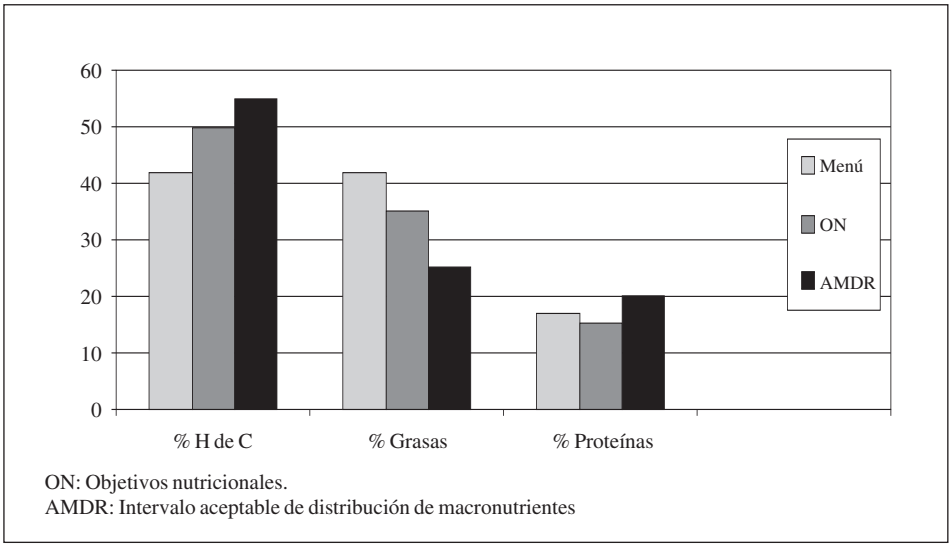
Algunos regímenes especiales se preparan aparte (alergias específicas, régimen hiposódico, sin huevo...), mientras que otros se preparan a la vez y sólo son sustituciones de una parte del plato por el producto adecuado (cambio de cerdo por pollo o pavo, por ejemplo, para los internos de credo musulmán).

Este tipo de adaptación, sin embargo, no satisface a los internos de ciertas religiones. Demandan que los alimentos sean tratados y conservados de modo especial desde la materia prima, así como cocinados y condimentados según sus preceptos. A modo de ejemplo, resaltan la necesidad de no utilizar el mismo aceite para las frituras de pavo o pescado que para cocinar los productos del cerdo.

Discusión

Del análisis del servicio de comedor y del menú servido en la prisión Modelo de Barcelona y la confrontación con la opinión y percepción de los usuarios, se ponen en evidencia determinados aspectos que muestran la brecha que existe entre las propuestas institucionales y las prácticas y las percepciones cotidianas de los usuarios. Más allá de los aspectos biológicos, la alimentación es una actividad que se da en contextos sociales concretos, que imprimen sus propias características tanto a la actividad en si como a su uso y a su percepción por parte de los individuos.

En primer lugar, a pesar de que la mayoría de los reclusos afirman usar el comedor para las comidas prin-



ON: Objetivos nutricionales.
AMDR: Intervalo aceptable de distribución de macronutrientes

Fig. 1.—Perfil calórico del menú estándar en comparación con los objetivos nutricionales (ON) y el intervalo aceptable de distribución de macronutrientes (AMDR).

cipales y podrían dedicar alrededor de 30 minutos a comer, destinan a ello, en términos generales, menos de la mitad de ese tiempo. El ambiente ruidoso del comedor o simplemente la posibilidad de utilizar su tiempo en otro tipo de actividades más satisfactorias, podrían llevar a los reclusos a pasar el mínimo tiempo posible en este espacio usando este espacio simplemente como un lugar de paso más, y no realmente como un lugar de relación.

En segundo lugar, los internos valoran mal tanto la calidad como el sabor de la comida, así como las condiciones en que llega a la mesa (temperatura, dureza...), si bien no cuestionan la cantidad, la cual cosa se refrenda por el hecho de que no acostumbran a terminarse sus raciones a pesar de que, según ellos mismos manifiestan, las consideran adecuadas. Las adaptaciones de los menús a diferentes confesiones religiosas (principalmente la musulmana) no tienen en cuenta más que superficialmente un análisis cultural[27] y tampoco resultan suficientes, en opinión de los afectados.

Hay que considerar, sin embargo, el hecho de que la aceptación de la comida por parte de los reclusos depende en gran manera del modo de preparación y de la manera en que los alimentos cocinados llegan a la mesa y sin duda, la masificación del centro del estudio[28], dificulta enormemente no tan solo la organización de las comidas sino las condiciones en las que los internos comen, por simple aritmética entre espacio y número de internos.

En cuanto al aporte energético y a las fuentes de energía del menú, en línea con otros trabajos en el mismo ámbito[5,18,29] observamos que los menús suministrados contienen habitualmente un exceso de grasa (41,3% del total) y un déficit en hidratos de carbono (41,7% del total), desde cualquier referencia con la que se comparen[26]. El exceso de lípidos coincide además con la detección de un uso excesivo de fritos y rebozados en los segundos platos. Probablemente, la intención de adaptar los alimentos y las técnicas culinarias a las preferencias de los reclusos, que parecen valorarlos, haya podido influir en este aspecto, pero debería reconsiderarse, a tenor de la elevada proporción de energía aportada por la grasa en los menús.

A esto habría que añadir que si bien el servicio de comedor supone la vía natural para el sustento alimenticio de los internos, la asistencia al mismo no es obligatoria y, en gran medida, los reclusos complementan su dieta, en función de sus apetencias, con alimentos adquiridos en el economato, cuya oferta es mayoritariamente a base de productos industriales que no requieren cocinado para su consumo (embutidos, pan de molde, enlatados, bollería industrial, galletas, snacks,...) que de manera general contribuirán al incremento en la proporción de grasa de la dieta, además de azúcares simples y/o sal.

El hecho de plantear una posible modificación y diversificación la oferta del economato hacia productos más "saludables", que incluyera fruta, por ejemplo, podría plantearse como una alternativa, pero seguramente debería tratarse con mucho cuidado, puesto que cabría la posibilidad de ser entendida como una limitación más en la libertad de elección de los reclusos, ya de por si mermadas y, por lo tanto, podría llegar a convertirse en un foco de conflicto si no se lleva a cabo con una estrategia de comunicación adecuada. Antes de proceder con cambios que afecten a la capacidad de elección, sería conveniente llevar a cabo programas de educación nutricional destinados a incidir sobre los hábitos alimentarios y realizar modificaciones en el menú ofrecido por la institución.

En este sentido, incorporar legumbres 1 ó 2 días a la semana como segundo plato, en lugar de carne, podría beneficiar la composición general del menú tanto en lo referente al incremento en proporción de glúcidos como en la disminución de lípidos del menú, gracias a su menor contenido general en grasas, grasas saturadas y la ausencia de colesterol. La calidad proteica y la disponibilidad de hierro estarán garantizadas si se sirven combinadas con cereales, vegetales y/o frutas de postre[30]. Esta sustitución también podría ser económicamente favorable y del agrado de los comensales, puesto que, son los segundos platos los que más comensales afirman dejar y los que reciben mayor número de críticas, destacando la dureza de la carne. Además podría convertirse también en un elemento, si no vehiculador, no obstaculizador de las distintas identidades alimentarias y/o religiosas, ya que en términos genéricos son considerados como *halal* o *kosher*, y son productos que pertenecen, asimismo, a distintas tradiciones culinarias[31].

La incorporación de mayor variedad de frutas y la posibilidad de escoger entre varias de ellas en cada comida, ya sea como postre, en el desayuno o recuperando la opción de la merienda, como alternativa a la bollería, redundaría también en una mejora de la puntuación del menú según el IAS y en la proporción de las fuentes de energía del mismo, a la vez que podría crear una mayor sensación de libertad de elección sobre su alimentación. Este hecho podría resultar también beneficioso a la larga, puesto que en ocasiones, la postura crítica expresada hacia la comida refleja en el fondo una crítica a la falta de libertad para escoger qué, cuándo y dónde comer[16].

Conclusiones

El hecho diario de comer y la forma y los espacios en los cuales éste se desarrolla es una de las principales experiencias que marcan la cotidianidad, tanto individual como social, de los reclusos. Si bien el servicio y el menú del comedor del centro penitenciario presentan aspectos positivos y destacables, algunos otros deberían modificarse para conseguir ofrecer un menú más saludable a la vez que una mayor aceptación por parte de los beneficiarios del mismo.

Por un lado, el exceso de fritos y de grasas presentes en los menús, atribuibles quizás a un intento de adaptar

los alimentos servidos a las preferencias de los reclusos, no cumple con las expectativas que presuntamente lo motivan. Algunos cambios en los alimentos y platos servidos en los menús, como por ejemplo la reducción de carnes y un aumento del consumo de legumbres, podrían contribuir en relación con la percepción de la comida por parte de los reclusos, tanto como una mejora genérica de la composición nutricional del menú, como en relación con la percepción de la propia salud a través de la alimentación, además de repercutir económicamente de manera positiva en los costes.

Una reordenación estratégica del uso del tiempo y de los espacios en el comedor que redujese la sensación de provisionalidad y el ruido podría contribuir a un mejor y más agradable uso del mismo, a la vez que contribuiría a una mejor percepción de la comida y del bienestar en general.

Hay que destacar, de todos modos, que cuando la rutina de la institución normaliza una situación, ésta es vivida como lo único real y posible. De hecho, los reclusos no piensan directamente, por ejemplo, en la alimentación en la prisión, a no ser que haya una pérdida de peso o un aumento (ambos casos han sido observados en la prisión Modelo) destacables. En este sentido, se observa que este hecho cobra consciencia en relación con los reclusos al ser puesto en evidencia.

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Caso clínico

Development of type 2 diabetes mellitus thirty-one years after Billroth II in a patient asking for diabetes surgery

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Abstract

Introduction: **Diabetes surgery in obese and slim patients seems to be a superior alternative to the current medical treatment. Gastric bypass is an alternative treatment for diabetes. Nevertheless, there are still doubts whether diabetes can recur if you gain weight or if the effects are maintained over time. Other questions refer to the type of surgery to make the bypass limb length or reservoir size for the resolution of the Diabetes Mellitus.**

Presentation of case: **Male patient 69-year-old came to us in order to perform tailored One Anastomosis Gastric Bypass (BAGUA) to treat his type 2 diabetes mellitus and metabolic syndrome. He has a history of peptic ulcer treated with subtotal gastrectomy and Billroth II reconstruction 49 years ago. He currently is not obese and developed diabetes 31 years after surgery.**

Discussion: **Globally there are no reports of patients with normal BMI that after performing gastric bypass developed diabetes mellitus. There are cases where obese diabetic patients after gastric bypass improve or remits the T2DM, but it relapses due to insufficient weight loss or gain it. The patient with gastric bypass Billroth II type, should not developed diabetes. He is normal weight and not had weight gain that could be linked to the development of diabetes.**

Conclusions: **The results generated by bariatric surgery are encouraging, but still do not clarify the precise way how surgery produces rapid improvement of systemic metabolism as in diabetes, but in our patient, the effect was quite different because the gastric bypass had no protective effect against diabetes.**

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Key words: *Diabetes mellitus. Tailored BAGUA. Gastric bypass. Bariatric surgery. Diabetes surgery.*

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DESARROLLO DE DIABETES MELLITUS TIPO 2 TREINTA Y UN AÑOS DESPUÉS DE BILLROTH II EN UN PACIENTE QUE SOLICITA CIRUGÍA DE DIABETES

Resumen

Introducción: **La cirugía de la diabetes en pacientes obesos y delgados parece ser una alternativa superior al tratamiento médico actual. El bypass gástrico es un tratamiento alternativo al tratamiento médico actual. Sin embargo, todavía hay dudas sobre si la diabetes puede reaparecer si hay aumento de peso o si se mantienen los efectos en el tiempo. Otras preguntas se refieren al tipo de cirugía para hacer la longitud del remanente gástrico o el tamaño del reservorio para la resolución de la Diabetes Mellitus.**

Presentación del caso: **Paciente masculino de 69 años de edad, vino a nosotros con el fin de realizar el bypass gástrico de una anastomosis a medida (BAGUA) para tratar su diabetes mellitus tipo 2 y el síndrome metabólico. Tiene antecedentes de úlcera péptica tratado con gastrectomía subtotal y reconstrucción tipo Billroth II hace 49 años. Actualmente él no es obeso y desarrolló diabetes 31 años después de la cirugía.**

Discusión: **A nivel mundial no hay reportes de pacientes con IMC normal que después de realizar un bypass gástrico desarrollaron diabetes mellitus. Hay casos en que los pacientes diabéticos obesos después del bypass gástrico mejoran o remite la DMT2, pero reaparece debido a la pérdida de peso insuficiente o reganancia de él. El paciente con un bypass gástrico tipo Billroth II, no debió desarrollar diabetes. Él tiene peso normal y no ha aumentado de peso que podría estar relacionado con el desarrollo de diabetes.**

Conclusión: **Los resultados generados por la cirugía bariátrica son alentadores, pero aún no aclaran la forma precisa cómo la cirugía produce una rápida mejoría del metabolismo sistémico como la diabetes, pero en nuestro paciente, el efecto fue muy diferente debido a que el bypass gástrico no tuvo un efecto protector contra la diabetes.**

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Palabras clave: *Diabetes mellitus. BAGUA a medida. Bypass gástrico. Cirugía bariátrica. Cirugía de diabetes.*

Abbreviations

BMI: Body Mass Index.
BAGUA: One Anastomosis Gastric Bypass.
T2DM: Type 2 Diabetes Mellitus.

Introduction

Diabetes surgery in obese and slim patients seems to be a superior alternative to the current medical treatment[1,2]. There are still doubts whether diabetes can recur if you gain weight or if the effects are maintained over time. Other questions refer to the type of surgery to make the bypass limb length or reservoir size for the resolution of the Diabetes Mellitus[3].

The first experiences come from Friedman et al.[4], who in 1955 reported cases of patients after subtotal gastrectomy Billroth II type for peptic ulcer having diabetes mellitus. Patients had ulcer healing and a marked improvement of diabetes, as manifested by the reduction or elimination of insulin requirements. The same results were found with the Greenville Gastric Bypass that nobody still practices[5].

Since then it has been investigated how duodenal exclusion can control diabetes, beginning a new alternative of treatment for diabetes mellitus, where several studies have followed-up diabetic patients after gastric bypass. Pories et al.[6] studied for 14 years to 608 patients of whom 165 were diabetic, determining that the surgery provides long-term control of diabetes.

SOS study also revealed that bariatric surgery not only cures but also prevents the onset of diabetes[7].

Nevertheless, GarcíaCaballero et al.[2] has shown that the resolution of diabetes mellitus is not only present in obese but also in normal weight patients even with C-peptide zero to whom eliminates the use of fast-acting insulin and reduces to a minimum the necessity of long-acting insulin enhancing glycemic control[8].

In this context, we have experienced a case where a man came to us asking for diabetes surgery and the preoperative study found that the patient had been operated 49 years before for Billroth II because of duodenal ulcer. The patient have always had normal BMI.

Presentation of case

Male patient 69-year-old came to us in order to perform the tailored One Anastomosis Gastric Bypass (BAGUA) to treat his type 2 diabetes mellitus (T2DM) and metabolic syndrome. He has a history of peptic ulcer treated surgically with gastrectomy and Billroth II reconstruction 49 years ago. Then he developed T2DM 18 years ago, who despite intensive medical treatment based on oral hypoglycemic and insulin has not achieved an adequate control of blood glucose. He had also arterial hypertension and dyslipidemia.

Physical examination is weight of 66 kg, height 1.70 m, BMI 22.8 and TA 181/82.

His treatment is irbesartan 300 mg, metformin 850 mg, 20 mg omeprazole, ramipril 10 mg, aspirin 100 mg, atorvastatin 20 mg, 10 mg lercanidipine, 27 IU insulin glulisine and 24 IU insulin glargine per day.

Laboratory levels are glucose 192 mg/dL, triglycerides 100 mg/dL, cholesterol 160 mg/dL, HDL 41 mg/dL, LDL, 99 mg/dL, HbA1c 7.8% and C-peptide 2.14 ng/mL.

The oesophagogram shows minimum gastroesofagic reflux, Billroth II gastrectomy with wide gastroenterostomy and fast transit to the jejunum. The duodenal afferent loop shows no fill (figs. 1 and 2).

Discussion

Globally there are no reports of patients with normal BMI that after performing gastric bypass develop diabetes mellitus. There are cases where obese diabetic patients after gastric bypass improve or remits the T2DM, but it relapses due to insufficient weight loss or gain it.

The existing series of patients worldwide usually have remission of diabetes mellitus in obese patients[6,7].

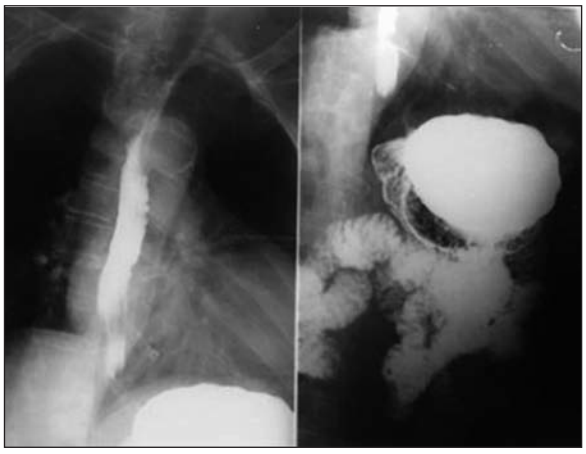

Fig. 1.—

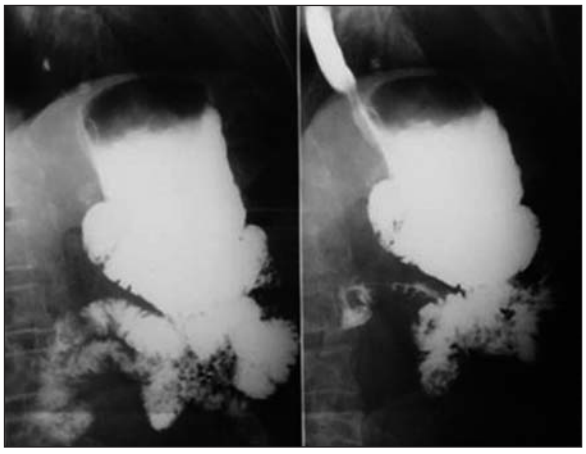

Fig. 2.—

However, there are few studies on normal weight patients. They are operated with the premise that if bariatric surgery improves diabetes in obese patients, also can be applied to normal weight patients achieving resolution of diabetes[9]. However all these studies have limitations due to their structure, type of surgical procedures, BMI, time following, etc.

Questions remain without response as either how surgery helps in diabetes or which surgical procedure is appropriate[1].

Our patient with a gastric bypass Billroth II type should not develop diabetes. He is normal weight and not had weight gain that could be linked to the development of diabetes. He has also a reorganization of the gastrointestinal tract with appropriate hormonal modulation, but he developed diabetes. The new data generated are encouraging, but still do not clarify the precise way about how bariatric surgery produces rapid improvement of systemic metabolism[10], which is the challenge for future research.

Conclusion

The results generated by bariatric surgery worldwide are encouraging, but not clear precisely how the surgery produces rapid improvement of systemic metabolism. It is well known that bariatric surgery causes improvement and/or resolution of various diseases such as diabetes, and some authors mention that gastric bypass is protective against the onset of diabetes, but in our case, the effect was very different because gastric bypass had no protective effect against diabetes.

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