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Editorial

Trabajos Originales

Nutrición artificial

Pediatría

Nutrición en el anciano

Obesidad y síndrome metabólico

Valoración nutricional

Epidemiología y dietética

Otros

Revisiones

Artículo Especial

Notas Clínicas

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Sumario

Vol. 35 Mayo-Junio N.º 3

sumario

Nutrición Hospitalaria

Sumario

Vol. 35 Mayo-Junio N.º 3

sumario

Nutrición Hospitalaria

Sumario

Vol. 35 Mayo-Junio N.º 3

sumario

Nutrición Hospitalaria

Sumario

Vol. 35 Mayo-Junio N.º 3

sumario

Revisiones

Artículo Especial

Notas Clínicas

Nutrición Hospitalaria

Órgano Oficial

Sociedad Española de Nutrición Parenteral y Enteral ▮ Sociedad Española de Nutrición ▮ Federación Latino Americana de Nutrición Parenteral y Enteral ▮ Federación Española de Sociedades de Nutrición, Alimentación y Dietética

Summary

Vol. 35 May-June No. 3

summary

Nutrición Hospitalaria

Summary

Vol. 35 May-June No. 3

summary

Nutrición Hospitalaria

Summary

Vol. 35 May-June No. 3

summary

Nutrición Hospitalaria

Summary

Vol. 35 May-June No. 3

summary

Reviews

Special Article

Case Reports

ISSN (electrónico): 1699-5198 - ISSN (papel): 0212-1611 - CODEN NUHOEQ S.V.R. 318

Nutrición Hospitalaria

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Pan y sal: ¿un binomio indisoluble?

Bread and salt: an indissoluble binomial?

Pérez-Farinos y cols. (1) describen el contenido de sal en el pan en España de acuerdo con un amplio muestreo de 1.137 panes de tres tipos, incluido el integral. La principal conclusión del estudio es que los niveles de sal en el pan en 2014 se mantienen en los niveles de 2008, cuando, a través de la estrategia NAOS, se había conseguido reducir dichos niveles en un 25% (1). No se observan diferencias ni geográficas ni según el tipo de pan. El estudio pone en evidencia la sostenibilidad del éxito logrado con el acuerdo entre la administración sanitaria española y el sector del pan en la reducción del aporte de sal en el mismo.

La hipertensión arterial, estrechamente relacionada con el consumo de sal, es la principal causa de mortalidad en el mundo, responsable de un 13-14% de las muertes (2). Reducir el consumo de sal en la población constituye una de las maneras más fáciles, más eficientes y más rentables de reducir la carga de las enfermedades cardiovasculares y costes en atención sanitaria, lo que conllevaría a una mejora muy importante en la salud pública (3). La existencia de evidencia científica contundente impulsó al Ministerio de Sanidad español a desarrollar una estrategia encaminada a reducir el consumo de sal en la población a los niveles recomendados por la OMS/FAO (5 g/día a nivel poblacional) (1).

La medición de la excreción urinaria de sodio en 24 h se considera el método de referencia para obtener la información sobre las ingestas de sodio en estudios poblacionales, debido a los frecuentes problemas de infraestimación observados en muchos estudios basados en encuestas dietéticas (4). Además, al igual que sucede con el azúcar y las bebidas azucaradas, el centrar la monitorización de la reducción de la sal solo en el pan hace que no puedan analizarse compensaciones hacia otros alimentos que a menudo se producen cuando se reduce un ingrediente de un alimento. Esto se ha visto con la sal, aunque en mucha menor medida que con el azúcar y los edulcorantes bajos o sin calorías (6,7).

En relación con las tendencias de la excreción de sodio urinario en España, Maldonado-Martín y cols. (8) describieron una excreción urinaria de sodio de 24 h de 136,3 ± 63,3 mmol/24 h en niños y niñas de 6 a 14 años de Almería en 2002 (antes del inicio de la Estrategia NAOS), similar al valor de 132,7 ± 51,4 mmol/24 h (cantidad que equivale a una ingesta de sal de 7,8 ± 3,1 g/día) obtenido por Aparicio y cols. en 2014 (9), en una muestra de escolares de 7 a 11 años, en el mismo periodo que el estudio de Pérez-Farinós y cols. (1).

La media de excreción urinaria de 24 h de sodio de 168 mmol/día (ingesta de 9,8 g de sal/día) obtenida en el estudio de Ortega y cols. (4) en población adulta española de 2009, tras la entrada en vigor del acuerdo de reducción de la sal en el pan, es parecida a la obtenida 25 o 30 años antes en Manresa: 165,4 mmol/día (9,7 g de sal/día) y en Torrejón 175,6 mmol/día (10,3 g de sal/día), ambas poblaciones incluidas en el estudio Intersalt (10); periodo en el que el consumo de pan era considerablemente superior. Los datos disponibles no permiten apoyar por tanto una tendencia clara a la reducción en el consumo total de sal en España, si bien es factible que este se haya producido pero quede atenuado por el incremento del sobrepeso y la obesidad (que se relacionan con mayores excreciones urinarias de sodio) (4).

Distintas iniciativas han puesto de relieve una vez más el valor potencial de las estrategias nacionales de reducción de la ingesta de sal y su capacidad para reducir sustancialmente la epidemia de enfermedades no transmisibles que afecta de manera global tanto a países desarrollados como en desarrollo de todo el mundo (11). Coaliciones que aglutinen diversas instituciones: agencias gubernamentales, organizaciones no guberna-

editorial

mentales, académicos y la industria alimentaria, son las que ofrecen la forma más efectiva de avanzar en los programas nacionales de reducción del consumo de sal, siempre que dispongan de un fuerte liderazgo y de la colaboración de la industria. La mayoría de países del mundo, incluida España, tienen una ingesta media de sal que supera en 1-2 g/persona/día la ingesta requerida para una salud óptima. En la gran mayoría de estos países, la implementación de un programa nacional de reducción de sal sería una de las formas más simples y rentables de mejorar la salud pública (11,12).

En la línea del trabajo de Pérez Farinós y cols. (1), es necesario asegurar la implementación de estrategias de reducción de sal en España, y evaluaciones sólidas de los programas en curso para garantizar que la reducción del 30% del consumo medio de sal de la población se alcance en 2025, lo que a su vez evitará miles de muertes en nuestro país (11). Además de sobre el pan, deben ejercerse acciones sobre otros alimentos como las carnes procesadas y los embutidos (que representan un 30% del aporte de sal en nuestro país) y sobre el uso del salero de mesa presente, de forma incomprensible, en la práctica totalidad de las mesas de la geografía española, tanto en los hogares como en el sector de la restauración.

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Nutrición Hospitalaria

Trabajo Original

Nutrición artificial

Early nutrition support therapy in patients with head-neck cancer

Soporte nutricional precoz en pacientes con cáncer de cabeza y cuello

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Abstract

Background: weight loss is commonly observed in head-neck cancer patients, affecting 75-80% of them during their treatment period; weight loss is severe in 30-50% of cases. According to ESPEN publications, nutritional assessment in cancer patients should be frequently performed and nutrition support therapy must be started when any deficiency is observed.

Objective: to evaluate the effect of early nutrition support (ENS) in nutritional markers and treatment response in patients with head-neck cancer receiving radiotherapy (RT).

Patients and methods: one hundred and two patients with head-neck cancer and more than two points in the malnutrition screening tool (MUST) before receiving RT were included. ENS was provided to all patients consisting in nutrition counselling, oral supplements and/or enteral nutrition.

Results: one hundred and two patients were included; 76% had a stage IV of disease. At the end of RT, after ENS, a slightly decreased body mass index (BMI) with an increased fat-free body mass was observed ($p < 0.001$); biochemical nutrition parameters remained stable despite decreased oral intake. Less than 40% of patients had severe epithelitis or mucositis; 92% of patients received the total amount and doses of originally planned RT sessions, while 22.8% required RT-sessions interruption. Patients with caloric malnutrition had a lower fulfillment of RT than those without caloric malnutrition ($p < 0.001$). Mortality was related to lower Karnosfsky, higher weight loss before RT and higher grade of mucositis/epitelitis ($p < 0.05$).

Conclusions: patients who receive ENS keep their nutritional condition instead of associated effects due to RT. ENS represents an efficient treatment and could prevent malnutrition associated comorbidities in oncologic patients.

Key words:

Head-neck cancer. Nutrition. Radiotherapy.

Resumen

Antecedentes: la pérdida de peso es un síntoma frecuente en el cáncer de cabeza y cuello (CCC), afecta a un 75-80% de los pacientes y es severa en un 30-50% de los casos. Según las publicaciones de la ESPEN, la valoración nutricional puede realizarse periódicamente y se debe comenzar el soporte nutricional cuando se observe algún déficit nutricional.

Objetivo: evaluar el efecto del soporte nutricional precoz (SNP) en marcadores nutricionales y la respuesta terapéutica en pacientes con CCC que reciben radioterapia (RT).

Pacientes y métodos: se incluyeron 102 pacientes con CCC que tuviesen al menos dos puntos en la escala de *screening* nutricional (MUST) antes de recibir RT. Todos los pacientes recibieron SNP, que consistió en asesoramiento nutricional y suplementos orales o nutrición enteral.

Resultados: se incluyeron 102 pacientes, el 76% de ellos en estadio IV de la enfermedad. Al final de la RT, después de recibir SNP, se observó una disminución discreta en el índice de masa corporal (IMC) acompañada de aumento de la masa libre de grasa ($p < 0,001$); los parámetros bioquímicos nutricionales permanecieron estables a pesar de la disminución en la ingesta. La incidencia de mucositis o epitelitis severa fue menor al 40%; el 92% de los pacientes recibieron la totalidad de las sesiones de RT planeadas, mientras que solo el 22,8% interrumpió parcial o totalmente la RT. Aquellos pacientes con desnutrición calórica previa tuvieron un menor cumplimiento terapéutico ($p < 0,001$). La mortalidad se relacionó con el índice de Karnosfsky, con una mayor pérdida de peso previa a la RT y mayor grado de mucositis o epitelitis ($p < 0,05$).

Conclusiones: aquellos pacientes que reciben SNP mantienen su estado nutricional a pesar de los efectos asociados con RT. El SNP representa una estrategia terapéutica eficiente para prevenir complicaciones relacionadas con la nutrición en pacientes oncológicos.

Palabras clave:

Cáncer de cabeza y cuello. Nutrición. Radioterapia.

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INTRODUCTION

Head and neck cancer includes oral cavity, pharynx, larynx, hypopharynx and paranasal sinus (1). The majority are squamous cell carcinomas, affecting specially men, with a male to female ratio ranging from 2:1 to 4:1 (2). Some risk factors have been described, including alcohol abuse, smokeless tobacco and papilloma virus (VPH) infection (3). Its incidence is approximately 550,000 cases and 300,000 deaths per year (1). In Europe, during 2012, 250,000 new cases and 63,500 deaths were reported (4).

Treatment goals include local disease control and increase of the survival with minimal adjacent tissue damage; more than 60% of patients with head-neck cancer can be cured with surgery and/or radiotherapy (RT). Treatment options are determined by the disease localization, extension and histology. Patients with stage I and II are treated with surgery or radiotherapy (curative rate 77-91%), while stages III and IV require the combination of extensive surgery, radiotherapy or chemoradiation (curative rate ranges 25-61% depending on tumor localization) (2).

Malnutrition affects 30-50% of patients with head-neck tumors, especially those localized in the oropharynx or the hypopharynx; around 30% have severe malnutrition during the six months prior to diagnosis. Chemotherapy worsens the nutritional condition due to tract digestive system related symptoms including taste loss, mucositis, xerostomia, nauseas and vomits (5). Malnutrition in head-neck cancer patients has been related to a higher rate of postsurgical complications, worse treatment response and higher tumor recurrence. Malnutrition increases the risk of infections, treatment related toxicity and decreases quality/expectative of life (6). Several studies have suggested more treatment interruptions and worse treatment effectiveness related to mucositis (7); fat-free body mass loss has been proposed as the responsible for the increase in mortality and worse prognosis related to malnutrition in cancer patients (8).

Early nutrition support (ENS) seems to improve the outcome in patients with gastrointestinal tract and head-neck tumors who receive RT (5), suggesting that maintaining body weight stable avoids deterioration in nutritional status (5). International guidelines suggest early dietary counselling and oral supplements for avoiding treatment related weight loss and not-planned interruptions in RT (9); even the improvement in nutritional status could be related to decreased RT toxicity (5).

Based on this, our aim was to evaluate the effect of early nutritional support using dietary counselling, oral supplements or enteral nutrition on anthropometric, biochemical markers and RT tolerance in patients with head-neck cancer.

PATIENTS AND METHODS

PATIENTS

The Ethics Committee of the Hospital Universitario Reina Sofía (Cordoba, Spain) approved the study, which was conducted in accordance with the Declaration of Helsinki and according to national and international guidelines. Every individual or family member accepted the informed consent before inclusion into the study. We included both sex patients, older that 18-years old, with minimal two points in the malnutrition screening tool (MUST) (10). All patients had a head-neck cancer requiring RT and they were evaluated minimal in two different occasions in our outpatient clinic before the inclusion into the study. All the evaluated patients that fulfilled the inclusion criteria were included. Patients were treated according to the current guidelines for head-neck cancer (11,12). Radiotherapy consisted in external radiation using high-energy photon beams (4-6 MV) generated by a linear accelerator. The total doses was 46-70 Gy divided in 1.8-2 Gy per day, five days per week (doses per week: 10 Gy). RT tolerance was measured using the oncology toxicity grading (RTOG) as follows (9):

- Grade 0: none.
- Grade 1: asymptomatic, mild symptoms.
- Grade 2: local symptoms; intervention is required.
- Grade 3: severe without life threatening effect.
- Grade 4: life threatening, urgent intervention is required.
- Grade 5: death related to adverse effect.

For our analysis, the five levels of the RTOG were combined in three different groups as follows: good tolerance, grades 0-1; regular tolerance, grades 2-3; and bad tolerance, grades 4-5.

CLINICAL EVALUATION

Anthropometric evaluation included body mass index (BMI) calculated as weight (kg)/height (m^2). The percentage of weight loss (%EWL) was calculated using the following formula: (initial weight –follow-up weight)/(initial weight– ideal body weight) x 100; the ideal body weight was calculated for a BMI of 21 kg/m^2 in women and 23 kg/m^2 for men (13,14). The mean Karnofsky index (KI) (15) was calculated for each patient.

Mucositis evaluation was performed according to the World Health Organization (WHO) classification (16):

- Grade 0: none.
- Grade I (mild): oral soreness erythema.
- Grade II (moderate): oral erythema, ulcers, solid diet tolerated.
- Grade III (severe): oral erythema, ulcers, liquid diet only.
- Grade IV (life-threatening): oral erythema, ulcers, oral alimentation impossible.

Epithelitis evaluation was performed following the scale:

- Grade 0: no change from baseline, asymptomatic.
- Grade 1: follicular faint or dull erythema epilation, dry desquamation, decreased sweating.
- Grade 2: bright erythema, confluent moist desquamation, pitting edema.
- Grade 3: ulceration, hemorrhage, necrosis.

This scale was adapted from the toxicity criteria of the Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer (17).

Anemia was also divided in four different groups according to the hemoglobin (Hb) level:

- Grade 0: Hb > 11 GM%.
- Grade 1: Hb 11-9.5 GM%.
- Grade 2: Hb 9.5-7.5 GM%.
- Grade 3: Hb < 7.5 GM%.

NUTRITIONAL INTERVENTION

All patients received nutritional counselling based on the Mediterranean diet (18), oral supplements/enteral nutrition and a close follow-up by a nutritionist in our hospital. The volume of enteral nutrition per day was adjusted according to the basal situation of the patient, and was modified according to the food intake and the presence of RT related complications.

STATISTICAL ANALYSIS

Normality distribution of the data was determined using the Kolmogorov-Smirnov test. Continuous variables were presented as mean ± standard deviation. Categorical variables were reported in percentage values. Univariate analysis in continuous variables was performed using the Wilcoxon test. Chi-squared compared categorical data. Cox regression curves were performed for the evaluation of mortality associated variables. Statistical analyses were performed using SPSS statistical software v15. Data in graphs are expressed as mean ± SEM. p-values < 0.05 were considered as statistically significant.

RESULTS

A total of 102 patients with head-neck cancer were included in the study. The clinical features of patients are summarized in table I. In our group, 47.9% of patients were active smokers and 42.1% had active alcohol abuse. Otalgia and oral ulcer were the most prevalent symptoms (23.5% and 20.6% respectively), related to the most common primary tumor localization (oropharynx, 34.3%; larynx, 21.4%). A stage IV of disease was observed in 76% of patients when included; stage IVa was the most prevalent (63%). The mean Karnofsky index (KI) was 89.2%.

Early nutritional support was systematically performed in all patients before RT. More than 55% had decreased or different oral intake before RT but almost 90% of the included patients had abnormal oral intake after RT. At that moment, enteral nutrition was the only support in 26.6% of patients (Table II) while more than 20% required a feeding tube. A non-clinically significant decreased BMI was observed after RT ($p < 0.001$), with an increase in fat-free body mass ($p < 0.001$). Interestingly, biochemical markers including albumin, prealbumin and transferrin remained stable after the treatment period (Table II).

In our group, more than 55% of patients tolerated well the RT, 92% of cases attended to all the originally planned RT sessions and only 27.7% of patients interrupted the RT schedule, while 29.7% required hospitalization. More than 60% of patients had grade 0-1 mucositis and epithelitis and more than a half tolerated the RT treatment adequately (Table III).

In our study, eight patients died. These patients characteristically had lower KI (81.25% *vs* 90.18%; $p < 0.01$), higher weight loss before RT (19.9 *vs* 4.6%; $p < 0.001$), higher grade of mucositis ($p < 0.05$) and higher epithelitis ($p < 0.05$). There were no significant differences between age or initial biochemical nutrition parameters.

Table I. General characteristics of the studied population

Characteristic	Total 100% (n = 102)
Sex: male	79.4% (81)
Age (years old)	64.06 ± 10.81
Smoke habit	
Active	47.9% (48)
Ex-smoker	30.9% (32)
Alcohol abuse at diagnosis	
Active	42.1% (40)
Previous	22.1% (21)
Symptoms	100% (102)
Otalgia	23.5% (24)
Oral ulcer	20.6% (21)
Dysphonia	19.6% (20)
Odynophagia	16.7% (17)
Others: (epistaxis, polyp, hemoptysis)	8.7% (9)
Dyspnea	5.8% (6)
Cervical nodule	3.9% (4)
Histologically confirmed localization	
Oropharynx	34.3% (35)
Larynx	21.4% (32)
Salivary glandules	11.8% (12)
Oral cavity	7.8% (8)
Hypopharynx	7.8% (8)
Nasopharynx	4.9% (5)
Metastasis of unknown primary tumor	1.9% (2)
Stage of disease	
Stage I	4.3% (4)
Stage II	3.3% (3)
Stage III	16.3% (15)
Stage Iva	63% (58)
Stage IVb	13% (12)
*Previous treatment**	
Surgery	52.9% (54)
Concomitant or induction chemotherapy	63.7% (65)

**Radiotherapy was a therapeutic option in all included patients.*

Table II. Nutritional support before and during RT in head-neck cancer patients

Characteristic	Before RT (102)	End of RT (94)	p
BMI (kg/m^2)	25.99 ± 5.10	25.43 ± 7.37	< 0.001
Fat-free body mass (%)	73.42 ± 9.38	74.34 ± 14.42	< 0.001
Albumin (g/dl)	3.91 ± 0.59	3.77 ± 0.44	0.339
Prealbumin (mg/dl)	23.88 ± 5.60	23.03 ± 5.89	0.797
Transferrin(mg/dl)	231.12 ± 52.51	203.16 ± 61.55	0.319
Lymphocytes (mm^3)	1,738.38 ± 762.81	1,140.45 ± 1,030.65	< 0.001
Oral intake			0.200
Normal	42.6% (43)	10.1% (10)	
Less than usual	26.7% (27)	32.6% (31)	
Crushed only	21.8% (22)	24.1% (23)	
Liquids only	3% (3)	6.3% (6)	
Oral supplements only	5.9% (6)	26.6% (24)	
Feeding system			0.007
Oral	90.1% (92)	78.3% (74)	
Feeding tube	9.9% (10)	21.7% (20)	
PEG	0% (0)	0% (0)	
Enteral nutrition*	63% (74)	97.6% (92)	0.041
Number or oral supplements per day			0.032
Less than two		4.8%(5)	
Two	32% (33)	15.5% (15)	
Three	51.5% (53)	48.8% (46)	
Four	7.2% (7)	17.9% (17)	
More than five	2.1% (2)	13.1% (12)	
Enteral nutrition formula			0.125
Normocaloric-normoproteic	6.5% (7)	7.2% (7)	
Normocaloric-hyperproteic	4.9% (5)	19.3% (18)	
Hypercaloric-hyperproteic	81.5% (83)	73.5% (69)	

*PEG: percutaneous enteral gastrostomy. *Enteral nutrition refers to oral supplements or total enteral nutrition.*

Interestingly, patients with previous caloric malnutrition (defined as minimal body weight loss in the last three months of 5%), had a higher non-completion rate of RT compared to those patients without caloric malnutrition (66.5 *vs* 97.8%, respectively; $p < 0.001$). Those patients requiring induction or concomitant chemotherapy had more non-desired RT interruptions ($p < 0.05$) and higher number of hospitalizations ($p < 0.05$) (data non-shown).

DISCUSSION

The majority of patients with head-neck cancer have locally advanced disease at diagnosis. For this reason, treatment is usually aggressive, with a therapeutic goal of achieving a cure while minimizing toxicity (6). Patients are frequently malnourished prior to the beginning of treatment. Malnutrition in head-neck cancer affects 30-50% of patients (6,7,19); since malnutrition has been related to higher post-operative complication rates, worse treatment response and higher tumor recurrence, early nutritional intervention is required (6). Enteral nutrition is based on the use of oral supplements or gastro-enteric tube feeding; its goal is to guarantee and, if possible, increase the nutrients intake when oral intake is not adequate or safe (9).

Our studied population presented the most common risk factors and staging at diagnosis that are currently described in head-neck cancer patients (2,20). It represents, then, an appropriate group of patients for analyzing results and driving conclusions.

It is well known that some nutritional parameters should be controlled in cancer patients in order to initiate early interventions and to prevent excessive deficits (21). Nutritional evaluation should be performed frequently and ENS should be initiated when deficits are detected (level of evidence C); according to

Table III. Treatment evolution under early nutrition support in head-neck cancer patients

Characteristic	n = 102
Treatment tolerance-ROTG	
Good	53.0% (52)
Regular	16.3% (16)
Bad	26.5% (26)
Dead	8.2% (8)
Complete RT schema	92% (94)
Non-organized RT interruption	22.8% (23)
Duration of non-organized RT interruption (mean in days)	5.37 ± 4.22
Hospitalization need	29.7% (28)
Mucositis	
Grade 0	3.2% (3)
Grade 1	18.1% (17)
Grade 2	43.6% (41)
Grade 3	31.9% (30)
Grade 4	3.2% (3)
Epithelitis	
Grade 0	25.5% (24)
Grade 1	40.4% (38)
Grade 2	27.7% (26)
Grade 3	6.4% ()
Anemia	
Grade 0	90.1% (64)
Grade 1	2.8% (2)
Grade 2	7% (5)
Grade 3	0% (0)

the current guidelines, enteral nutrition with standard formulas should be initiated if malnutrition is detected or if oral intake has decreased during the last 7-10 days (9). Intensive early nutrition support with regular follow-up helped attenuate the natural weight loss history of treatment in our study group, as it has been previously reported (5). ESPEN guidelines suggest nutritional counseling and oral supplements use in patients under chemo-radiotherapy for avoiding weight loss (9,21); oral, enteral or parenteral route may be used depending on the clinical situation of each patient and specially, the level of function of the gastrointestinal tract (21).

Energy requirements in cancer patients should be similar to those of healthy subjects; protein intake should be above 1 g/kg/day, or even above 1.5 g/kg/day (21). Clinical features and treatment options in head-neck tumors may make reaching these goals difficult, suggesting the importance and necessity of nutritional supplements in these group of patients.

A slightly decrease in weight loss and BMI (< 0.6 kg/m^2) was observed in our patients, whereas serum proteins and nutritional markers remained stable. Only lymphocytes were decreased, which could be probably related to chemotherapy effects or to the tumor itself (22). Despite body weight loss, an increase in fat-free body mass was observed. Similar results have been reported in randomized studies evaluating early and intensive nutrition intervention in patients with gastrointestinal and head-neck tumors (5) and advanced stage IV solid tumors (23).

It is well known that RT is associated with acute side effects (whose incidence increases when concomitant or induction chemotherapy is administered), especially oral mucositis (24,25). In our group, the incidence of severe mucositis was lower than 10%, contrasting with other studies reporting mucositis rates of 89-97% in head-neck cancer patients receiving RT (26). The incidence of severe mucositis (grades 3-4) has been reported in 34-53% of patients depending on the RT method (26). Interruption rates of 86% have been also described, especially due to mucositis (27). Interestingly, a four-fold decrease in non-organized interruptions has been observed in our study group.

Oral mucositis has been related to unscheduled breaks or delays in RT administration (24,25). Unscheduled RT interruptions were observed only in 22% of the evaluated patients; this rate tends to be higher in other reports (28). Even RT interruption rates of 36% exclusively due to mucositis have been previously described (27). Remarkably, it has been suggested that when inadvertent or deliberated gaps in RT occur, reduced tumor control may result because of accelerated tumor clonogen repopulation (28). Based on this, nutritional counseling and oral supplements use are recognized as important tools to reduce weight loss and avoid treatment interruptions in patients receiving chemo-radiotherapy (9).

Compared to clinical guidelines which suggest the use of standard supplements (9,21), we mostly used specific enteral formulas depending on the patient's nutritional status, daily oral intake and regular use of the nutrition supplements. In our group, previous caloric malnutrition and combined chemo-radiotherapy was related to worse treatment adherence and fulfillment; probably in these cases, enteral nutrition and/oral supplements should be started earlier, since the diagnosis is performed.

A limitation of this study was the number of participants, the absence of a control group and the absence of other anthropometric and nutritional markers (for example, dynamometry or tomography guided fat-free mass measuring). Despite this, the ENS in our group showed relevant clinical benefits.

In conclusion, treatment in head-neck cancer patients requires a multidisciplinary approach including ENS. Enteral nutrition should be started previous to the systemic treatment and kept during and after it, in order to decrease weight loss. This strategy would allow to decrease treatment interruptions and systemic related complications and improve quality of life. Nutritional advice and oral supplements should be started earlier in previous malnourished patients and in those receiving combined chemo-radiotherapy or induction chemotherapy. Randomized, large studies are required to confirm and increase these results.

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Nutrición Hospitalaria

Trabajo Original

Nutrición artificial

Epidemiology of home enteral nutrition: an approximation to reality

Epidemiología de la nutrición enteral domiciliaria: una aproximación a la realidad

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Abstract

Introduction: home enteral nutrition (HEN) has undergone an important development; however, there is a notable lack of information with regard to its incidence and characteristics.

Objectives: our aim was to assess the state of HEN in our area.

Methods: an observational, prospective study, involving all patients who had initiated HEN in the Nutrition Unit during a year. Epidemiological, functional, and nutritional evolution of the patients was described and incidence of HEN was calculated.

Results: HEN incidences totalled 229/100,000 inhabitants/year. The HEN population in our area was characterized by the aged and a high frequency of comorbidity and functional limitations. Neurological and oncological diseases accounted for 50% of indications. The remaining cases were malnourished patients who had received short periods of HEN after hospitalization or a hip fracture. Oral supplements (60%) with standard and hypercaloric formulas were used the most. At baseline, 75% of the patients suffered from malnutrition. During the follow-up, patients showed weight gain (1.6%), an increase in the percentage of normal weight and overweight (from 74% to 82.7%, $p = 0.001$) and a reduction in pressure ulcers (15.7% *vs* 10.3%, $p < 0.001$). The median duration of HEN was 8.5 months. Only a quarter of the patients experienced complications (mostly mild gastrointestinal complications); 43.1% had died at the end of the follow-up.

Conclusions: in our area, the HEN incidence was much higher than those described in the literature. HEN appears to be a safe therapy with few complications that improves the nutritional status of the patients, even with short periods of administration.

Key words:

Malnutrition. Nutritional support. Home enteral nutrition.

Resumen

Introducción: la nutrición enteral domiciliaria (NED) ha experimentado un importante desarrollo, aunque aún existe una notable carencia de información acerca de su incidencia y características.

Objetivos: evaluar el estado de la NED en nuestra área.

Métodos: estudio observacional y prospectivo que incluyó a todos los pacientes que iniciaron NED en el periodo de un año. Describimos su evolución epidemiológica, funcional y nutricional y calculamos la incidencia de NED.

Resultados: la incidencia de NED alcanzó los 229/100.000 habitantes/año. La población con NED se caracterizó por ser añosa, con una elevada frecuencia de comorbilidad y limitación funcional. Las enfermedades neurológicas y oncológicas representaron el 50% de las indicaciones. El resto fueron pacientes malnutridos que recibieron periodos cortos de NED tras una hospitalización o fractura de cadera. Los suplementos orales con fórmulas estándar o hipercalóricas fueron los más utilizados (60%). Al inicio, el 75% de los pacientes tenía malnutrición. En el seguimiento, los pacientes lograron aumento de peso (1,6%) y mayor porcentaje de normopeso o sobrepeso (de 74% a 82,7%, $p = 0,001$). Las úlceras por presión se redujeron (15,7% *vs.* 10,3%, $p < 0,001$). La duración mediana de NED fue 8,5 meses. Solo una cuarta parte de los pacientes experimentaron complicaciones, la mayoría de ellas gastrointestinales y leves. El 43,1% había fallecido al final del seguimiento.

Conclusiones: en nuestra área, la incidencia de NED es más elevada respecto a lo descrito en la literatura. La NED es un tratamiento seguro con pocas complicaciones que mejora el estado nutricional de los pacientes, incluso con periodos cortos de administración.

Palabras clave:

Malnutrición. Soporte nutricional. Nutrición enteral domiciliaria.

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INTRODUCTION

The field of home enteral nutrition (HEN) has undergone a huge development in recent decades, leading to a reduction in the frequency of malnutrition and its serious consequences. Health care at home provides medical services in a more comfortable and familiar environment.

Despite the growing importance of HEN, there is still a notable lack of information about its epidemiology and characteristics, which can be explained both by the absence of obligatory registries and the large differences among HEN organizations in different countries or regions.

Obligatory records would offer valuable information about HEN frequency and characteristics, including the most frequent indications, complications and outcomes of patients. Also, registries could help estimate the consumption of resources needed by this therapy and its impact on the health system. However, HEN records are rare and often voluntary, which limits the reliability of their data. In 2009, a systematic review found only eleven home artificial nutrition (HAN) records published between 1987 and 2007 (60% home enteral nutrition and 40% home parenteral nutrition) in eight different countries (Australia, Germany, Italy, Japan, Spain, Sweden, the UK and the US). They all had limitations and heterogeneity in data collection, making it difficult to obtain representative information (1).

In Spain, the HAN group of the Spanish Society of Parenteral and Enteral Nutrition (NADYA-SENPE) has conducted an annual record since 1994. Although useful, it is a voluntary record and it offers only a limited view of the magnitude of HAN in our country (2-14).

The uncertainty about HAN, especially in the home enteral nutrition (HEN) area, can also be explained by the lack of definition of common criteria. Thus, in some countries it includes only those therapies administered by tubes or ostomies, while other countries consider oral treatments too when a certain amount of calories is exceeded (15,16). This fact makes comparison between records from different countries almost impossible.

The time limitation in which professionals can include data has forced the records to focus on collecting information about those patients who cover more than 75% of their requirements with HEN, thereby creating an underestimation of the actual frequency of HEN. In the UK the number of patients in recent records has dropped due to the lack of time available to dietitians to enter data and the problem of obtaining patients' written consent (17). All these difficulties account for the main motivation of this study.

OBJECTIVE

The aims of this study were to assess the status of HEN in our area, with regard to its incidence and characteristics; to weigh the importance of HEN as a therapy; and to detect fields in need of improvement in our practice. We hypothesized that voluntary registries underestimate the real frequency of HEN, and we hope to offer a more realistic vision of HEN that includes all patients regardless of the administration route or the percentage of calories provided.

METHODS

This is a prospective, observational, two-year study performed at the Complejo Hospitalario Universitario of Santiago de Compostela (CHUS), a tertiary university hospital in Galicia (Spain).

In Spain, HEN is financed by our public health system. However, HEN organization exhibits important organizational differences between autonomous communities. In our region, nutrition units are the main prescribers of HEN, although other specialist physicians may be prescribers as well. Regarding the dispensing of HEN products, in most communities this takes place in the pharmacy offices, but in Galicia it is carried out through hospital pharmacies. This peculiarity has allowed us to better control patients with HEN and has enabled us to obtain a more accurate estimate of the incidences.

INCLUSION AND EXCLUSION CRITERIA

All the patients who started HEN in the period from October 15, 2009 to October 14, 2010 at the CHUS were included in the incidence study, regardless of the type of nutrition or prescriber department.

For the descriptive study of the characteristics and the evolution of HEN, those treatments prescribed and monitored by other hospital services were excluded because of the difficulties in proper data collection.

INCIDENCE OF HEN

All new HEN prescriptions during the study period were included, regardless of the type of artificial nutrition (enteral nutrition by tube or ostomy, oral supplements, thickeners or protein modules). To avoid loss of patients, the HEN dispensing registries of the Hospital Pharmacy Department were reviewed.

Therefore, the incidence of HEN in our health area was calculated as the ratio between the patients who started HEN in the study period (both prescribed by a Nutrition Unit and by other hospital departments) and the total adult population of the area (aged > 14 years), according to the last report of our regional healthcare service (SERGAS) (18).

DESCRIPTIVE STUDY OF HEN PATIENTS AND CHARACTERISTICS

Baseline variables

At the first visit, epidemiological data, medical history, functional status and percentage of patients in nursing homes were regis-

tered. Regular home medication was also collected, with a focus on drugs that may interfere with nutritional status.

Nutritional screening tests were initially carried out, including the Malnutrition Universal Screening Tool (MUST) and the Mini Nutritional Assessment (MNA) (only in patients aged ≥ 65 years), in order to assess the risk of malnutrition. Then, a complete nutritional assessment with anthropometry (weight, height, body mass index, percentage of weight loss and tricipital skinfold) and laboratory tests (levels of albumin, prealbumin, transferrin and protein bound to retinol [PBR]) was performed. Both the nutritional screening tests and the complete evaluation were performed by the Nutrition Unit staff when the patient's situation permitted it. Patients were weighed standing barefoot on a Seca 220® mechanical scale with a precision of 0.1 kg. Height was measured with a measuring rod (Seca 220®) with a precision of 0.1 cm. A John Bull® skinfold caliper was used to determine tricipital skinfold.

Nutritional classification of patients followed the Spanish Society of Enteral and Parenteral Nutrition (SENPE) and Spanish Society of Medical Documentation (SEDOM) definitions (19).

The indication, type, administration route and calories provided by HEN were also described. When HEN provided less than 1,000 kcal/day, it was considered as supplementary nutrition. When it provided ≥ 1,000 kcal/day, it was defined as complete nutrition.

Follow-up variables

The patients were followed until October 15, 2011, to evaluate their evolution and modifications in nutritional support. During routine patient visits, changes in clinical and functional status, medication and HEN were recorded. The appearance of complications (gastrointestinal, mechanical, metabolic and infectious complications) with nutritional support (both patient-reported and those registered in the electronic medical history), the episodes of attendance at the Emergency Service and hospitalizations related to HEN were also registered.

At the end of the follow-up period, a final assessment of nutritional status was conducted, and duration of nutrition was calculated. In cases where HEN had been suspended, the cause of treatment discontinuation was investigated by contacting patients, with special interest in recording cases of death.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS 19.0 (SPSS Inc., Chicago, IL, USA). The normal distribution of quantitative variables was examined by the Kolmogorov-Smirnov test. Variables matching normal distribution were presented in terms of mean and standard deviation (SD), and those without normal distribution were presented in terms of median and interquartile range (IQR). Quantitative variables with normal distribution were compared using the Student's t test. Quantitative variables without normal distribution were compared using the Mann-Whitney and Wilcoxon tests for independent or related samples, respectively. Categorical variables were expressed as percentages and compared to the Chi-squared test. A p value lower than 0.05 was considered as statistically significant.

ETHICAL ISSUES

The study was conducted according to ethical principles grounded in the latest update of the Declaration of Helsinki. The Ethics and Clinical Research Committee of Lugo-Santiago approved the study protocol, and patient anonymity was preserved.

RESULTS

INCIDENCE OF HEN

During the study period, 788 new patients started home enteral support in our health area (85% of them monitored by the Nutrition Unit). The reference population was the 342,694 adult patients in the area (18).

The incidence of HEN in this sanitary area resulted in 229 cases/100,000 inhabitants/year, regardless of the type of HEN and the prescriber department.

BASELINE CHARACTERISTICS OF PATIENTS

Only 573 of the 788 incidents of HEN patients were finally included in the descriptive study. The main reason for exclusion was the lack of prospective data among patients whose HEN treatment was prescribed and monitored by other hospital services. Also, patients who were not registered in the recruitment period were excluded, although HEN was prescribed in the Nutrition Unit (Fig. 1).

Of the 573 patients included in the registry, 59.7% were women. The median age was 79 (IQR 87) years, with 78.6% of patients over 65 years. The distribution of patients by age was represented in figure 2.

We found high levels of comorbidity (Table I). The median number of home treatments was six (IQR 19) drugs, and 35.9% of patients reported taking medications associated with nutritional risk, especially corticosteroids, anti-Parkinson drugs or digoxin.

About 80% of the patients reported mobility limitations, with 15% of patients being bed-ridden and 20.4% experiencing pressure ulcers. A total of 60.3% needed a home caregiver, and 19.7% were living in nursing homes.

Nutritional screening with MUST was performed in 326 patients, in which it was found that 94.5% were at high-risk of malnutrition. MNA was carried out in 180 of 447 patients older than 65 years with available data, and the percentages of malnutrition or risk of malnutrition were 77.8% and 21.7%, respectively. At baseline, the complete nutritional assessment showed that 78% of the patients were malnourished, mainly with protein or mixed malnutrition (42% and 26%, respectively).

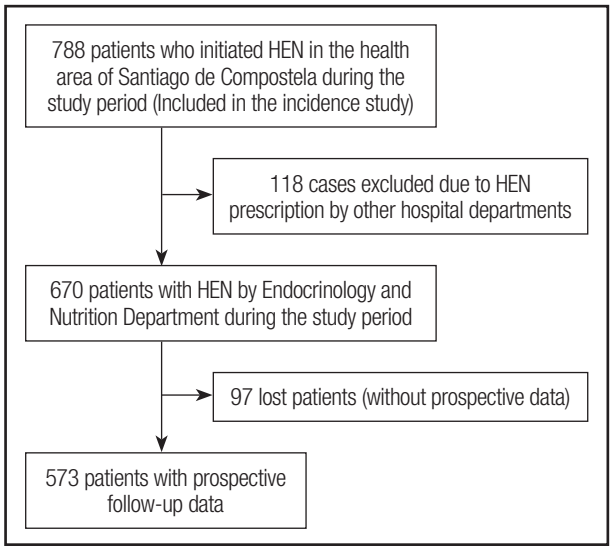

Figure 1.

Flowchart of study patients.

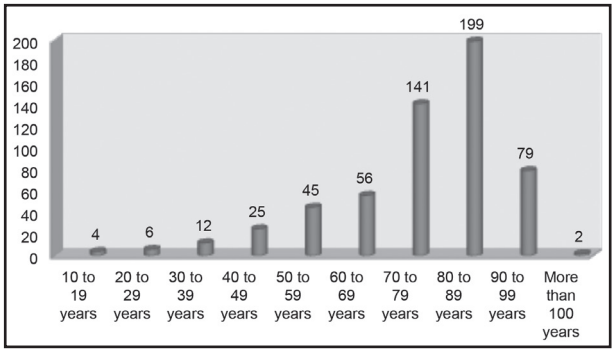

Figure 2.

Distribution of patients by age.

HEN INDICATIONS AND CHARACTERISTICS AT FIRST VISIT

Neurological and oncological diseases, which are the most common indications of HEN, accounted for almost 50% of indications in the registry. In 35% of cases, HEN was prescribed due to a neurodegenerative or neurovascular disease that affects swallowing or intestinal motility. Mechanical disorders, especially those caused by head and neck cancer or surgery, represented 11.9% of HEN indications. The remaining cases were malnourished patients who received short periods of HEN after hospitalization or after a hip fracture.

The oral route was the most used (69.2%), followed by enteral administration by tube (25.1%). Only 29 patients (5%) had a gastrostomy at the first visit. Among patients with HAN by enteral access, bolus by gravity was the most common form of administration (95.9%). Continuous infusion pumps were used in six cases and bolus administration by syringe was used in one case.

Table I. Baseline characteristics of the patients

Women (%)	59.7%
Age (median [IQR])	79 (87) years
Patients over 65 years (%)	78.6%
Comorbidities (%):	
Neurological diseases	51.7%
Digestive problems	32.1%
Cardiac pathology	30.2%
Respiratory diseases	28.8%
History of neoplasia	28.4%
Diabetes	19.7%
Functional situation (%):	
Normal	8%
Mobility limitations	82%
Bed ridden	15%
Pressure ulcers (%)	20.4%
MUST (n = 326) (%):	
High risk of malnutrition	94.5%
MNA (n = 180) (%):	
Malnutrition	77.8%
Risk of malnutrition	21.7%
Complete nutritional assessment:	
Malnutrition (%):	78%
Protein malnutrition	42%
Mixed malnutrition	26%

The type of nutritional support is summarized in table II.

High-calorie and standard (normoproteic and isocaloric) diets were the most reported in the present study (32.5% and 32.1%, respectively), while high-protein and special formulas accounted for a third of the total prescriptions.

With regard to energy intake, 38.8% of patients received more than 1,000 kcal/day, and their median intake was 1,500 (IQR 1,560) kcal/day. The remaining 61.2% of patients received less than 1,000 kcal/day, with a median intake of 600 (IQR 827) kcal/day.

Table II. Type of home nutritional support at the beginning and end of the follow-up

Type of nutritional support	Initial (%)	Final (%)
Oral supplements (< 1,000 kcal)	59.3	56.5
Oral enteral nutrition (> 1,000 kcal)	5.4	8.6
Nutrition by enteral access	31.1	29.5
Thickener	3.4	3.6
No data	0.5	1.6

EVOLUTION OF PATIENTS

Of the 573 patients initially enrolled in the study, 304 patients only had a first visit. Therefore, follow-up data were available in 269 patients. In this group, gender and age distribution were similar to baseline. The median duration of HEN was 8.5 (IQR 22.2) months and was slightly higher in patients with enteral nutrition (by tube or ostomy) than in those with oral nutrition (10.6 *versus* 8.7 months; $p = 0.010$). The type of HEN at the end of the study period is summarized in table II. Oral route of administration was still the most common (70%). Enteral access by nasogastric tube accounted for 18%, gastrostomy accounted for 12% and one patient had a jejunostomy.

Regarding the nutritional evolution of the patients, we found that 75% maintained or increased their weight during follow-up, with a mean weight gain of 1.6% (mean initial weight 60.1 [SD 13.3] kg *vs* final weight 61.1 [SD 11.7] kg; $p = 0.008$). The percentage of patients with normal or overweight rose from 74% to 82.7% ($p = 0.001$) at the end of the study. In the elderly, nearly half had a normal MNA result and the remaining were predominantly at risk but had not established malnutrition. The complete nutritional evaluation obtained an increase in the group of patients with normal assessment, from 23.2% to 67.2%, although this difference did not reach statistical significance.

In the subgroup of patients with follow-up, a significant reduction in the percentage of pressure ulcers was observed (15.7% at baseline *vs* 10.3% at final visit, $p < 0.001$). However, no changes in patients' functional status were detected.

During the study period, the 74.7% of followed-up patients did not experience any complication associated with HEN. A total of 64 patients reported 105 episodes of HEN complications, mostly mild digestive problems (Fig. 3). In addition, 104 hospitalizations in 68 patients were registered (16 bronchial aspirations, seven admissions for placement gastrostomy and one admission for refeeding in a patient with eating disorders). The index of hospitalizations related to HEN was 0.083 episodes/patient/year.

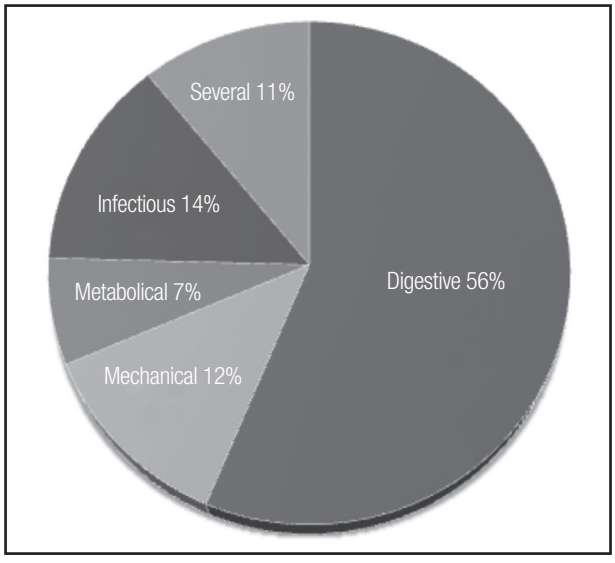

Figure 3.
Complications registered during follow-up.

At the end of the study period, home nutritional support was active in 24.4% of the 573 patients included at baseline (mainly patients with underlying neurological diseases: 46.2%); the rest had already discontinued it. Discontinuation of treatment was due to patients' death in 56.8% cases, to clinical improvement in 32.5%, to loss of follow up in 5.7% and to transfer to another health area in 3.6%.

At the end of the study, the percentage of deaths was 43.1% (247/573), including those 246 patients who had maintained HEN until death, and one patient who had previously been lost to follow-up but who had also died at the end of the study.

DISCUSSION

This paper presents the results of a systematic HEN registry, which has allowed us to calculate the actual incidence of home enteral nutritional support in our health area, including all forms of HEN, regardless of caloric intake or route of administration.

The first epidemiological data about HEN in Europe date from the late 90s, when a survey conducted in eight European countries (Belgium, Denmark, Spain, France, Italy, Poland and the UK) found a mean incidence of HEN of 163 cases/million inhabitants/year (20). However, it also highlighted the existing disparities among the countries surveyed and the big difference with the prevalence reported in the US, about ten times higher (up to 1,660 cases/million in Medicare beneficiaries, or 415 cases/million in the general population) (21,22).

Comparing our epidemiological data with international registries, we found a frequency of HEN that was clearly higher than those described in Europe and the US, but closer to the Medicare population data. This could be explained because the Medicare population includes mainly people ≥ 65 years or disabled, and HEN funding in Medicare is more similar to our public health system (20-22).

In an Italian study in Treviso, with a similar size population to ours, only 655 patients were included in the HEN registry over a period of five years, resulting in an incidence 6.9 times lower than that obtained in our study (23). These marked differences may be due to exclusion in the register of patients with oral nutritional support.

In Spain, the last NADYA record reported a much lower prevalence (80.58 to 90.51 cases/million inhabitants) (14), and studies in other Spanish regions also showed a lower frequency of HEN than ours. However, in recent years a clear increase in HEN incidence and prevalence has been observed, especially in oral nutritional support (24,25). Thus, the prevalence of HEN described in a previous study of our region was 1,034 cases/million, which is in line with the results obtained in our area a decade later (26).

CHARACTERISTICS OF REGISTRY POPULATION

The characteristics of HEN patients in terms of age, functional status or condition clearly depend on the characteristics of the registries and the definition of HEN used, which favors heterogeneity, making comparison between records a real challenge.

Our study found a marked aging that was not present in other registries, such as the US record, with an average age that was 15 to 20 years lower (between 61 and 65 years) (22). In other European studies, the percentage of HEN patients older than 65 years was slightly above 50%, while our data was close to 80% (20). However, the last Spanish NADYA record described a HEN population with a median age somewhat higher (73 years) (14), and the Treviso (Italy) registry population appeared to be most similar to ours, with an average age of 77.4 years and a percentage of patients over 65 years of 81.3% (23).

In Europe, neurological diseases are the most common pathologies reported in HEN registries, accounting for 45 to 50% of the total indications. They are followed by malignant tumors, especially head and neck cancer and esophageal tumors (25 to 35%) (17,20). Spanish records data exhibit similar results (60.5% neurological indication, followed by neck and head tumors) (14). By contrast, in US HEN registries, the proportion is reversed, involving 60% cancer patients and 40% neurological patients (22). The peculiarities of the records are probably what explain these disparities. For example, the latest data from the UK showed a downward trend in the percentage of neurological patients, probably as a result of the decrease in indications of nutritional support in patients with advanced dementia (17). In our population, the inclusion of all types of home nutritional support, including thickeners, modules and supplements, likely explains the different pathology distribution found. Neurological diseases and cancer accounted for only half of the indications. The rest were predominantly cases in which patients received perioperative nutrition after a hip fracture or cases of malnourished or at risk of malnutrition patients, including elderly people who did not meet their requirements with a traditional diet, mainly after hospitalization. In Spain, the latter two indications are not reimbursed by the national health system, but both have been included in our clinical practice following the recommendations of the guidelines of the European Society of Parenteral and Enteral Nutrition (ESPEN) Geriatrics (grade of recommendation A) (27).

NUTRITION THERAPY FEATURES

The route of administration of nutritional support is very influenced by the characteristics of the registry. Due to this fact, it is understandable that our results, with a clear predominance of the oral route and only 30% of patients undergoing other enteral accesses, differ from those data recorded in traditional voluntary HEN registries. Thus, the British record directly excludes oral nutrition, reporting just tube feeding/ostomy patients (75% and 17.5%, respectively) (17,28). In the US, only treatments expected to last more than three months are financed, thereby explaining the high prevalence of gastrostomies (550/million population in 1998) (22). Also, in other European countries, the frequency of percutaneous endoscopic gastrostomies (PEG) is high (about 58.2% of patients with HEN), followed by NGT (29.3%) (20). The Spanish NADYA registry takes into account only patients with ≥ 900 kcal/day, thus excluding most patients with oral supplements (11). In the last Spanish record published, the NGT rate represented approximately 50% of the cases, and gastrostomies accounted for 42% (14). However, the authors have warned about the limited usefulness of the registry for evaluating nutrition routes, because this data is not available in many patients. In addition, the apparent decline in the oral route (64% in 2007 *vs* 10% in 2010) seems to reflect a tendency to include only cases of HEN by NGT/ostomy due to work overload and limited time in clinical practice.

NUTRITIONAL EVOLUTION

At baseline, our study population showed a high percentage of malnutrition (over 75%), especially protein or mixed malnutrition. It was probably related to the patients' profiles, which mostly included acute diseases or acute exacerbations of chronic diseases. This would explain the impact on protein reduction and even the frequency of pressure ulcers (present in one out of every five patients), although other studies have found an even higher prevalence (23).

Nutritional support can improve patients' nutritional status regardless of their underlying pathology. In particular, oral supplementation, which is the most common HEN subtype in our study, is recommended, with a high degree of evidence, for elderly malnourished people, people who are at risk and the frail elderly. However, while some studies have found improvement in various nutritional parameters, even with small volumes of supplements (29-34), others have failed to demonstrate this nutritional improvement. The stage of disease at which treatment is started seems also to be a determining factor in the effect of HEN (35-37).

In our area, a small weight gain was achieved in HEN patients (+ 1.6%), which is slightly lower than that described by a review of studies performed in elderly patients with oral supplementation (around 2.2%) (29). However, it was enough to maintain or increase their initial weight in 75% of patients. The distribution of BMI, the nutritional assessment and the presence of pressure ulcers also experienced a marked improvement during follow-up.

TREATMENT EVOLUTION

Despite the spread of artificial nutrition, not many HEN registries detail the development of complications. In 2003, the NADYA-SENPE Spanish group published a specific study with a rate of complications/patient/year of 0.16, with gastrointestinal (62.5%) and mechanical complications (33.2%) predominating (38). These data are consistent with those published in a Galician (Spain) study (0.18 complications/patient/year, especially digestive and

infectious complications) (26) and also with those of our study, except for a lower percentage of mechanical complications, which is expected because most of our patients were receiving oral HEN. Most episodes were mild and were frequently resolved by the patient or their caregiver or by contacting the Nutrition Unit, without treatment interruption. However, the use of enteral access by NGT/ostomy may involve mechanical complications, requiring further consultation to solve them (39). Therefore, HEN appears to be a safe therapy, with a low risk rate of complications and an index of hospitalizations that is lower than other records (0.083 episodes/patient/year *vs* 0.3 to 0.4 episodes/patient/year complications in our study *vs* US records, respectively) (22).

FINAL SITUATION

HEN duration is one aspect that depends on the age and conditions of the patients included in the registry. In our area, at the end of the study period, only 24.4% of patients continued with active HEN. Most of these had neurological diseases and little chance of recovery. These results are similar to the US registry results, with 25% neurological patients and 6% oncological patients with active HEN (22).

As in the US and Canadian records (40), in our population the high percentage of short treatments and patients with a single visit was remarkable (53%). This reflects the high mortality rate found in HEN patients but also the high rate of patients with temporal indication of nutrition, which is suspended after patient amelioration (e.g., postoperative supplementation after hip fracture). As in other records, the most important causes of suspension were death or clinical improvement (10-14).

LIMITATIONS AND STRENGTHS

We have to point out as a limitation that our data represent the particular situation of HEN in our area, and they may not be extrapolated to other populations. Although we could only include in the analysis patients who had been prescribed HEN by the Nutrition Unit (due to lack of prospective data from the group in which HEN was prescribed by other hospital departments), we consider that our sample is representative of the HEN situation in our media, including more than 70% of the incident population.

As strength, this registry has shown the real situation of HEN in the health area of Santiago de Compostela, allowing us to obtain an accurate incidence estimate (including all prescriptions) and offering a realistic view of the HEN, not available in other voluntary registries.

In conclusion, HEN incidence in our area is clearly superior to that described in other epidemiological studies. The characteristics of both patients and nutrition differ from those reported in voluntary records (which usually include only certain subgroups of patients). This shows the existence of an aging and multi-pathological population that requires HEN, mainly in the form of oral supplements, during short periods until the resolution of the situation that motivates the nutrition indication.

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ARÁN

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Trabajo Original

Pediatría

Assessment of micronucleus and oxidative stress in peripheral blood from malnourished children

Evaluación de micronúcleos y estrés oxidante en sangre periférica de niños desnutridos

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Abstract

Introduction: malnutrition is one of the most common health problems among children in underdeveloped countries, including Mexico. Previous studies have indicated increased genetic damage in malnourished humans and animal models, but the essential mechanisms remain unclear. In the present study, we assessed the effects of malnutrition on the frequency of micronucleus (MN) in reticulocytes (RET) from the peripheral blood of well-nourished uninfected (WN), well-nourished infected (WNI), moderately malnourished infected (UNM) and severely malnourished infected (UNS) children. Moreover, lipid peroxidation and the antioxidant status were evaluated to investigate the role of oxidative processes in malnutrition-associated genotoxicity.

Methods: the antioxidant status of the study population was determined by measuring superoxide dismutase (SOD) in the red blood cells and glutathione peroxidase (GPX) in whole blood.

Results: the UNS and UNM groups have increased percentages of MN-RET compared to the WNI group. Moreover, the data showed a significant increase in lipid peroxidation and a decrease in erythrocyte SOD activity and GPX activity in the malnourished group compared to the well-nourished infected children.

Conclusion: the data suggest that the antioxidant system was impaired in the cells of malnourished children and that oxidative stress causes a significant increase in DNA damage, as evaluated by the MN-RET frequency.

Key words:

Oxidative stress. Malnourished children. Micronuclei. Glutathione peroxidase. Superoxide dismutase.

Resumen

Introducción: la desnutrición es uno de los principales problemas de salud entre los niños de los países en desarrollo, incluido México. Estudios previos han mostrado que existe un incremento en el daño genético en humanos y modelos animales desnutridos, pero los mecanismos por los que se desencadena aún son poco claros. En el presente estudio, evaluamos los efectos de la desnutrición en la frecuencia de micronúcleos (MN) en reticulocitos (RET) de sangre periférica de niños bien nutridos no infectados (WN), bien nutridos infectados (WNI), desnutridos moderados infectados (UNM) y con desnutrición severa e infecciones (UNS). Asimismo, se evaluaron la lipoperoxidación y la capacidad antioxidante para investigar el papel del proceso oxidativo en la genotoxicidad asociada a la desnutrición.

Métodos: la capacidad antioxidante de la población de estudio fue determinada midiendo la superóxido-dismutasa (SOD) en los eritrocitos y glutatión peroxidasa (GPX) en sangre completa.

Resultados: los niños UNS y UNM tienen alto porcentaje de MN-RET comparados con el grupo WNI. Además, los datos mostraron un incremento significativo en la lipoperoxidación y disminución en la actividad de SOD y GPX en el grupo de niños desnutridos comparados con el grupo de niños bien nutridos infectados.

Conclusión: los datos sugieren que el sistema antioxidante está deteriorado en las células de los niños desnutridos y que el estrés oxidante causa un incremento significativo en el daño al ADN, el cual se refleja en el incremento en la frecuencia de RET-MN.

Palabras clave:

Estrés oxidante. Niños desnutridos. Micronúcleos. Glutatión peroxidasa. Superóxido-dismutasa.

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INTRODUCTION

Malnutrition (also known as undernutrition) is one of the most common health problems among children in developing countries, including Mexico. Malnutrition remains a major cause of morbidity and mortality, with the greatest impact in low-income countries. Epidemiological studies have shown that malnutrition produces a complex cycle of infection, altered nutrition and decreased immune resistance, which in turn promotes a state of malnutrition that favors the occurrence of more severe and frequent infections.

Numerous studies have associated malnourishment with DNA damage, for instance, increased frequencies of both sister chromatid exchange and chromosomal aberrations, as well as an increased frequency of micronuclei, were observed in malnourished rats (1,2). Our group has previously reported the relationship between DNA damage magnitude (assessed by the micronuclei frequency) and malnutrition grade in undernourished children (3). Even though these results provide strong support for malnutrition-induced genotoxicity, the mechanisms underlying DNA damage in malnourished organisms have not been elucidated.

Oxidative stress, defined as a disturbance in the pro-oxidant/antioxidant balance that favors pro-oxidants (4), has been demonstrated in several diseases. This damage is often called oxidative damage, and has been defined as the biomolecular injury caused by the attack of reactive species upon the constituents of living organisms (5). In particular, reactive oxygen and nitrogen species (ROS/RNS) are the major oxidants that react with DNA and lead to the formation of various lesions, including oxidized bases, abasic sites, and/or DNA strand breaks (6).

There is a large body of experimental evidence suggesting that oxidative processes may substantially contribute to the genotoxicity associated with various pathological conditions, such as diabetes mellitus (7), cancer (8) and other immunological responses (9).

Hence, an interesting working hypothesis might be that the increase in oxidative stress, resulting from elevated levels of free radicals generation and/or a reduced antioxidant response, may contribute to the DNA damage observed in malnourished children.

Increased oxidative damage results not only from increased oxidative stress but also from a failure to repair or replace damaged biomolecules, and mainly oxidative stress can result from decreased antioxidant levels (10). It was previously reported that kwashiorkor-type malnourished children present low reduced glutathione (GSH) levels (11).

Therefore, the correlation between increased oxidative damage and decreased antioxidant defense systems in malnourished children would lead to new insights into the management of this health problem.

The aim of this study was to determine if malnutrition and infection are associated with an increased micronuclei (MN) frequency in reticulocytes, since MN detection is a worldwide-validated assay used to quantify DNA damage (12). Malnutrition and infection were also correlated with erythrocyte hemolysis, as a marker of lipid peroxidation, and the antioxidant status was determined by measuring superoxide dismutase (SOD) in red blood cells and glutathione peroxidase (GPX) in whole blood.

MATERIALS AND METHODS

PATIENTS

Peripheral blood was collected from pediatric patients aged six to 72 months by simple random sampling. This study was approved by the Ethics and Biosafety Committee of the Iztapalapa Pediatric Hospital, Federal District Government, and was conducted in accordance with the Declaration of Helsinki. Signed informed consent was obtained from each participating child's parents.

Children were divided into four experimental groups based upon their nutritional and infectious status as follows: a) well-nourished healthy (uninfected) children (WN); b) well-nourished infected children (WNI); 3) moderately malnourished infected children (UNM); and 4) severely malnourished infected children (UNS).

Malnutrition degree was calculated according to the clinical signs and symptoms presented, as well as the weight-to-height deficit for Mexican children according to the tables previously published by Ramos-Galván (13). The bacterial infections were rigorously diagnosed based upon established medical criteria. Samples from children with viral diseases, birth defects, allergies and traumas were excluded. Similarly, samples with hemolysis, blood clots and/or poor cell quality/number were not included in this study. Uninfected WN children were outpatients at the same hospital and were studied as controls. The samples for the other groups were obtained during hospital admission, before treatment with drugs or supplements.

The age range, gender, weight and height, as well as infection type are described in table I for each group.

SAMPLE PREPARATION

Venipuncture blood samples were collected into heparin-containing tubes as an anticoagulant (250 U/ml, Microlab, Mexico City, Mexico), transported on ice to the laboratory and processed within three hours.

DNA DAMAGE ASSESSMENT: MICRONUCLEUS FREQUENCY

After obtaining blood samples, an aliquot (100 µl) of peripheral blood was diluted (1:2) in BBS (bicarbonate buffered saline solution: 0.9 g NaCl + 0.0444 g $NaHCO_3$ in 100 ml distilled H_2O) at pH 7.5. A 100 µl aliquot was removed from the diluted sample and fixed by vigorous shaking in cryogenic tubes containing 2 ml of ultra-cold (-70 °C) methanol (Merck Millipore, Darmstadt, Germany). The samples were stored at -70 °C for at least 24 hours prior to cell staining and further analysis.

CELL STAINING AND FLOW CYTOMETRY ANALYSIS

To process the samples, the cryogenic tubes were removed from the freezer and resuspended. A 1-ml aliquot was

Table I. Clinical characteristics of the study groups

Study group (n)	Mean + SD Age in months (range)	Mean + SD Weight in kg (range)	Mean + SD Height in cm (range)	Mean weight deficit (%)	Type of infection (n)
WN (10)	45.1 ± 16.65 (19-60)	15.47 ± 2.89 (17-22)	98.3 ± 18.49 (90-123)	< 10	No infection (10)
WNI (9)	18.44 ± 1.10 (9-41)	10.04 ± 2.55 (7-10.3)	70.22 ± 28.33 (71-105)	<10	Respiratory (6) Gastrointestinal (3)
UNM (12)	27.6 ± 23.27 (6-60)	14.14 ± 15.35 (5.3-17.5)	79.3 ± 23.11 (65-128)	28 (27-32)	Respiratory (9) Gastrointestinal (3)
UNS (10)	15.85 ± 12.2 (6-44)	5.03 ± 1.02 (4-6.1)	53.7 ± 22.10 (63-60)	51.2 (37-75)	Respiratory (6) Gastrointestinal (3) Mixed* (1)

*WN: well-nourished uninfected children; WNI: well-nourished infected children; UNM: moderately malnourished infected children; UNS: severely malnourished infected children. The number of children in each group (n), the averages and ranges for their age, weight, height, and weight deficit, as well as the number of children with specific infections. *The child presented both gastrointestinal and respiratory infections.*

removed, washed with BBS at 4 °C and centrifuged at 600 × g for five minutes at 4 °C. The pellet was resuspended, and a 25-µl aliquot was treated with 1 mg of RNase/ml and 5 µl anti-CD71-fluorescein isothiocyanate (anti-CD71-FITC) (to label the RETs and to differentiate them from erythrocytes) (15). All of the samples were incubated in the dark at 4 °C for 40 min followed by room temperature incubation for 90 min. After these incubations, 500 µl of BBS was added, and the sample was analyzed by flow cytometry. Before acquisition of the events, 2 µl (2 µg/ml) of cold IP (for detection of DNA micronuclei-specific fluorescence) was added to detect MN (14).

Flow cytometric analysis was conducted using a FACSCalibur™ flow cytometer (Becton Dickinson, Immunocytometry Systems, San Jose, CA, USA) equipped with an argon laser (488 nm excitation). The data were analyzed with the CellQuest™ Software (version 3.0.1, Becton Dickinson) for data acquisition and analysis (BD Biosciences). We followed the strategy reported by Cervantes et al. (3). Five hundred thousand events were acquired per sample. The percentages of RETs and MN-RETs were calculated according to the method proposed by Litron Laboratories (Rochester, NY, USA).

OXIDATIVE DAMAGE ANALYSIS IN ERYTHROCYTES FROM PERIPHERAL BLOOD

Evaluation of lipid peroxidation

Lipid peroxidation was assessed as an oxidative stress marker using the hemolysis assay reported by Catal F et al. (15) and modified as follows, 250mL of each sample were mixed with 2,2-azo-bis(2-amidinopropane) dihydrochloride (AAPH Cayman Chemicals, USA) for three hours. AAPH is a water-soluble azo compound that has been extensively used as a free radical generator during lipid peroxidation assays and antioxidants characterization (16,17). AAPH decomposition produces molecular nitrogen and 2 carbon radicals. The carbon radicals may combine to produce stable products or react with molecular oxygen to produce peroxy-radicals. AAPH half-life is approximately 175 h (37 °C, at neutral pH), thus the rate of free radical generation in solution is essentially constant during the first several hours.

One ml of each sample was mixed with 2 ml of phosphate-buffered saline (PBS). The mixture was centrifuged for ten minutes at 1,500 g and the plasma was eliminated. The erythrocyte pellet was washed twice with 2 PBS ml, homogenized by inversion and centrifuged after each wash. A 250 µl sample of the erythrocyte pellet was removed and placed in three polypropylene tubes. PBS (250 µl) was added to the first tube, which was the negative control. AAPH (150 mM) was added to the second tube, and 250 µl of distilled water was added to the third tube in order to hemolyze, and was used as a positive control. All tubes were incubated at 37 °C for three hours. Each hour, 5 µl of the mixture were removed and diluted (1:200) with PBS. The mixture was centrifuged for five minutes at 1,500 g. A 1,000 µl sample from the uppermost part was taken and placed in a cell. The absorbance was read at 410 nm in a Spectra UV-visible Beckman DU® 650 spectrophotometer. The percentage of hemolysis in each sample was calculated and referenced to the positive control.

ANTIOXIDANT RESPONSE IN PERIPHERAL BLOOD

Analysis of superoxide dismutase activity

SOD enzymatic activity in erythrocytes was evaluated using the quantitative *in vitro* determination of superoxide dismutase (SOD) RANSOD kit (Randox Laboratories Ltd., County Antrim, UK), according to the manufacturer's instructions.

Heparinized whole blood (500 µl) was centrifuged for ten minutes at 1,500 g and the plasma was then aspirated. The erythrocyte pellet was washed four times with 4 ml of a

0.9% NaCl solution, homogenized by inversion and centrifuged at 1,500 g for ten minutes after each wash.

The washed erythrocytes were then brought to 2.0 ml with cold redistilled water, mixed and left to stand at 4 °C for 15 minutes. One hundred µl of the diluted erythrocytes were mixed with 0.01 mM phosphate buffer. Fifteen µl of these diluted erythrocytes were removed and mixed with 1.7 ml of the Mixed Substrate (reconstituted according to the manufacturer's instructions) and 250 µl of xanthine oxidase. The absorbance was determined after 30 seconds (A_1) and three minutes (A_2) using a Beckman DU® 650 spectrophotometer at a wavelength of 505 nm and temperature of 37 °C. The activity was expressed as SOD units/ml of blood.

Analysis of glutathione peroxidase activity

GPx enzymatic activity was determined using the Paglia and Valentine method (18). GPx catalyzes the oxidation of glutathione (GSH) by cumene hydroperoxide. In the presence of glutathione reductase (GR) and NADPH, the oxidized glutathione (GSSG) is immediately converted to the reduced form with a concomitant oxidation of NADPH to $NADP^+$. The absorbance decrease at 340 nm was measured.

The GPx activity in whole blood was evaluated using the quantitative *in vitro* GPx determination RANSEL kit (Randox Laboratories Ltd., County Antrim, UK), according to the manufacturer's instructions. Fifty µl of whole blood were diluted with Ransod Sample Diluent, mixed and incubated at 37 °C for one minute. Twenty µl of diluted blood, 1 ml of mixed substrate (glutathione 4 mmol/l, glutathione reductase > 0.5 U/l, NADPH 0.34 mmol/l) and 40 µl of cumene (cumene hydroperoxide 0.18 mmol/l) were mixed. The absorbance of the mixture was determined after one minute and two minutes using a Beckman DU® 650 spectrophotometer at 650 nm. The GPx activity was expressed as U/l of blood.

STATISTICAL ANALYSIS

For each group, we calculated the mean and the standard error of the mean for the RET+ and MN-RET+ frequency, hemolysis percentages, USOD/ml in red blood cells and U/l GPx in whole blood. The frequency of MN between the study groups was compared using a Kruskal-Wallis test, followed by Mann-Whitney U test and Bonferroni multiple comparison tests. Statistical analyses were performed using NCSS version 07.1.9 and NOPANDEV software packages. Differences with a p value of less than 0.05 were accepted as statistically significant.

RESULTS

PATIENTS

Forty-one children, 17 girls and 24 boys, 6-60 months old, participated in this study and were classified in four groups as follows: a) well-nourished healthy (uninfected) children (WN); b) well-nourished infected children (WNI); c) moderately malnourished infected children (UNM); and d) severely malnourished infected children (UNS). Their age range, weight and height, as well as infection type, are described in table I.

RETICULOCYTE (RET) FREQUENCY

The RET frequencies for the individual children in the various study groups are shown in figure 1. The RET average percentage for the WN group was 1.77 ± 0.42%, which was significantly lower than the value found for the WNI group, 2.73 ± 0.43% ($p < 0.05$). The UNM group had a RET average percentage of 2.45 ± 0.41%. The UNS group showed RETs increased frequency compared with the WN and WNI groups, and had an average of 3.93 ± 0.97% ($p < 0.05$).

MN-RET FREQUENCY

The MN-RET mean frequency was 0.49 ± 0.09% for the WN group, which was significantly lower than that of the WNI group, with an average of 1.11 ± 0.2% ($p < 0.05$). These values indicate that the MN-RET frequency in the WNI group increased due to infection. The UNS group had a MN-RET higher frequency, with an average of 2.92 ± 0.48%, compared to the UNM group, which had an average of 1.69 ± 0.30%. However, this difference was not statistically significant. Moreover, the MN-RET percentage in the UNS group was significantly higher than that of the WNI group (2.92 and 1.11%, respectively; $p < 0.05$). When the MN-RET frequency was compared with those of the WN group and the UNM and UNS groups, both malnourished groups showed a statistically significant increase ($p < 0.05$ for both groups) (Fig. 2).

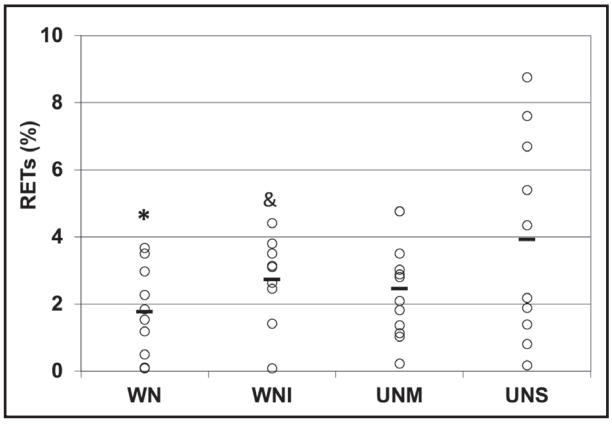

Figure 1.

Reticulocyte frequency in the peripheral blood samples from well-nourished children (WN), well-nourished infected children (WNI), moderately malnourished infected children (UNM) and severely malnourished children with infections (UNS). The data are presented as the average ± standard error. Significant differences: *WN vs WNI, UNM, UNS and WNI vs UNS ($p < 0.05$).

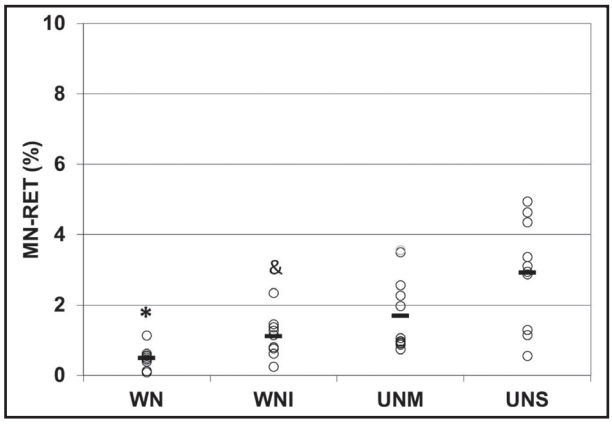

Figure 2.

Micronucleated reticulocyte frequency in the peripheral blood samples of well-nourished children (WN), well-nourished infected children (WNI), moderately malnourished infected children (UNM) and severely malnourished children with infections (UNS). The data are presented as the average ± standard error. Significant differences: *WN vs WNI, UNM, UNS and WNI vs UNM and UNS ($p < 0.05$).

OXIDATIVE DAMAGE ANALYSIS IN THE ERYTHROCYTES FROM PERIPHERAL BLOOD

The data presented in figure 3 show that the UNS group significantly increased the hemolysis percentage, with an average of 119.19 ± 31.41% compared to the UNM group, which had an average of 87.96 ± 21.37%. The hemolysis percentage was 78.63 ± 11.01% for the WN group, which was lower than that of the WNI group, with an average of 52.81 ± 14.25%. The data showed that the hemolysis percentage of the UNM and UNS groups were significantly higher than that of the WNI group ($p < 0.05$). These results suggest that the hemolysis percentages in these two groups increased due to malnutrition. Moreover our results show a positive correlation between the MN-RET frequency and lipid peroxidation ($r = -0.973$) in severe malnourished children.

ANTIOXIDANT RESPONSE IN PERIPHERAL BLOOD

Superoxide dismutase activity (SOD)

Figure 4 shows that the BNI group had a higher SOD activity compared to the BN group (362 ± 69 USOD/ml of blood and 428 ± 38 USOD/ml, respectively). Nevertheless, this difference was not statistically significant. The SOD activity determined in the UNS group blood was 230 ± 26 USOD/ml. This result was, lower than the one obtained for the UNM group (300 ± 32 USOD/ml of blood). When the SOD activity was compared among the well-nourished groups (WN and WNI) and the malnourished groups (UNM and UNS), both malnourished groups showed a statistically significant decrease ($p < 0.05$ for both groups) (Fig. 4). These data suggest that the SOD activity in the malnourished groups decreased due to malnutrition.

Glutathione peroxidase activity (GPx)

As shown in figure 5, the GPx activity determined for the UNM and UNS groups (12,480 ± 339 U/l and 11,727 ± 3,354 U/l of blood, respectively) significantly decreased compared to the WNI group (14,337 ± 1,957 U/l of blood, $p < 0.05$). The data show that the BNI group had a similar SOD activity compared to the

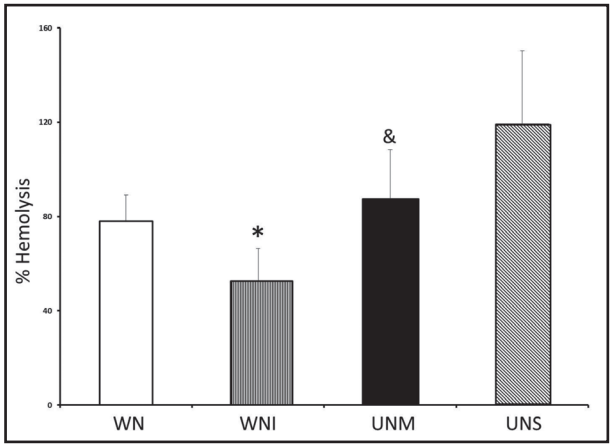

Figure 3.

Percent of hemolysis in the peripheral blood samples of well-nourished children (WN), well-nourished infected children (WNI), moderately malnourished infected children (UNM) and severely malnourished children with infections (UNS). The data are presented as the average ± standard error. Significant differences: *WNI vs UNM and UNS; UNM vs UNS ($p < 0.05$).

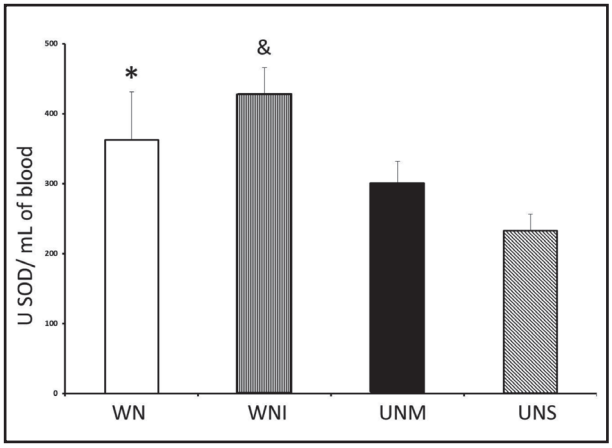

Figure 4.

SOD activity in the peripheral blood samples of well-nourished children (WN), well-nourished infected children (WNI), moderately malnourished infected children (UNM) and severely malnourished children with infections (UNS). The data are presented as the average ± standard error. Significant differences: *WN vs UNM and UNS; WNI vs UNM and UNS ($p < 0.05$).

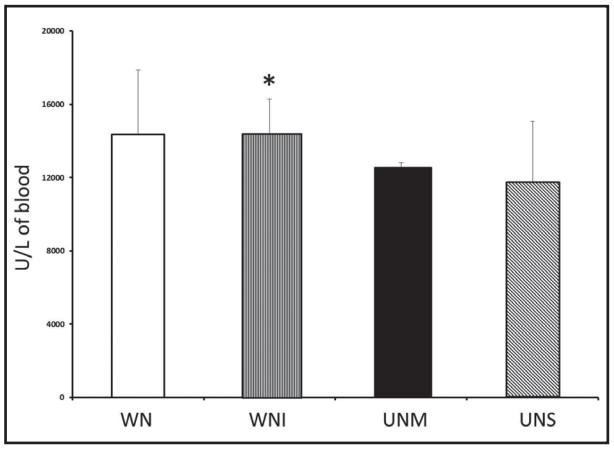

Figure 5.

GPx activity in the peripheral blood samples of well-nourished children (WN), well-nourished infected children (WNI), moderately malnourished infected children (UNM) and severely malnourished children with infections (UNS). The data are presented as the average ± standard error. Significant differences: *WNI vs UNM and UNS ($p < 0.05$).

BN group (14,354 ± 3,509 U/l of blood), suggesting that GPx activity decreased due to malnutrition.

Negative correlations were obtained between lipid peroxidation and SOD ($r = -0.762$) and between GPx and lipid peroxidation ($r = -0.700$) in severe malnourished children, supporting the fact that an energy-deficient state may result in enhanced lipid peroxidation and decreased antioxidant enzyme activities.

DISCUSSION

Protein energy malnutrition is one of the major health problems in developing countries, since the harmful effects produced by the insufficient intake of nutrients can negatively impact the organism growth and development. Recent data from Cervantes et al. (3) showed a higher MN frequency in reticulocytes from the peripheral blood of moderate and severely malnourished children compared to well-nourished infected children. Furthermore, it has been shown that malnourished rats have a high MN-RETs frequency, pointing towards an increased genetic damage during malnourishment (1). These and other studies have reported genetic damage in malnourished humans and animal models, but the essential mechanisms remain unclear.

Therefore, our aim was to correlate the DNA damage (MN-RET frequency) with the activity of antioxidant enzymes and lipid oxidative damage in well-nourished infected and malnourished infected children.

The average RET percentage for the WNI group was significantly higher than that of the WN group, suggesting that infection may increase the RETs frequency. These data are in agreement with previous reports showing that children with gastrointestinal or respiratory infections exhibit an increased RET percentage (3).

In relation to children with malnutrition and infection, the UNM average is similar to that of the WNI group, implying that moderate malnutrition does not affect circulating RETs number. However, the severely malnourished group had an increase in RETs average when compared to the WN and WNI groups, suggesting that children with severe malnutrition have hematologic alterations. An early study also reported that anemic individuals increased the circulating RETs content (19), and it is also known that anemia is often associated with malnutrition (20).

On the other hand, the 0.49% MN-RET frequency determined in well-nourished children concurs with what has been previously reported (3,21). At the same time, the MN-RETs higher frequency of WNI when compared to the WN group also coincides with previous reports (3).

Epidemiological studies have shown that most bacterial gastrointestinal infections in children from developing countries are caused by *Streptococcus pneumonia* and *Escherichia coli* (22). Therefore, the augmented frequency of MN in the WNI group may be due to molecules released by infectious agents that provoked genetic damage (23). Indeed, it has been shown that *E. coli* produces cytotoxic enterotoxins that affect protein synthesis and inhibit DNA repair (24). Moreover, it has been demonstrated that *S. pneumonia* produces a DNA recombinase, which destabilizes the host DNA and renders it susceptible to single strand breaks (25).

Our data showed a significant increase in the two malnourished infected groups compared to the WN and WNI groups. The inclusion of an undernourished uninfected child group was not possible because undernourished children frequently suffer from infections. Hence, we assumed that the comparison between the WN and WNI groups shows the changes associated with the infection, and that the comparison between the WNI and malnourished groups shows the alterations related to malnutrition.

The higher frequency of MN-RETs (DNA damage) in malnourished children cells may be attributed to several causes, such as micronutrients malabsorption (e.g., folate) and/or oxidative stress. It is known that folic acid deficiency promotes genetic damage via DNA breakage (26). Therefore, the higher MN-RET frequency observed in malnourished children might be related to a folate deficiency. Further studies will be necessary to address the relationship between levels of specific micronutrients, oxidant stress and genome stability, and additionally, to support the relation between oxidant stress and different types of malnutrition.

In relation to oxidative stress, it is known that infectious agents (e.g., bacteria) trigger an immune response in the host, which increases free radicals generation (27). Moreover, several studies have shown that serum antioxidants concentration is significantly lower in severely malnourished children (15,28) as well as increased lipid peroxidation (29), but there are no reports relating infections and oxidative stress in malnourished children.

Our data showed increased lipid peroxidation in malnourished children peripheral blood compared to WN and WNI children. This is an important factor that correlates with our findings of increased MN-RETs and DNA damage in malnourished children.

Infections in malnourished children may activate the production of free radicals, such as superoxide anions, hydrogen peroxide

and myeloperoxidase. Leukocytes and other phagocytic cells fight bacteria, parasites, and virus-infected cells by destroying them with NO, O_2, and H_2O_2 (30,31). These molecules contribute to lipids, proteins and nucleic acids oxidation. Some studies of children with kwashiorkor have demonstrated decreased concentrations of antioxidant vitamins, such as vitamin A and vitamin E, and elevated lipid peroxidation levels (32).

However, contradictory evidence has been reported by Partadiredja et al. (33), who found that malnutrition during the gestation and pre-weaning period in mice had no significant effect on lipid peroxidation. In contrast, other studies have reported an increase in lipid peroxidation following diet restriction (34-36).

Okunade et al. (37) showed that lipid peroxidation in kwashiorkor children erythrocytes was higher than the lipid peroxidation found in the well-nourished infants' erythrocytes. Lenhartz et al. (38) also confirmed excessive lipid peroxidation in kwashiorkor children. Our results agree with these results since lipid peroxidation in the UNM and UNS groups were significantly higher than in the WNl group.

Previous studies have shown that lipid peroxidation end products binding to DNA bases may create mutagenic lesions (39), supporting the relationship between DNA damage and elevated lipid peroxidation.

Oxidative damage in malnourished children may be related to impaired antioxidant system function. Our data showed an increase in SOD activity in the WNl group compared to the WN group. The SOD activity for the UNS group was lower (1.3-fold decrease) than in the UNM group. When the SOD activity was compared between the WN-WNl groups and UNM-UNS groups, both malnourished groups showed a statistically significant decrease compared to the well-nourished groups.

The same was observed in relation to GPX activity, which was significantly reduced in moderate and severely malnourished children in comparison to well-nourished infected children. Similar data have also been identified in other studies where GSH levels in malnourished children were lower when compared with the controls (15,32,40).

Moreover, Partadiredja et al. (33) reported that the changes in the GSH levels are an important indication of the anti-oxidant defense mechanisms during early life malnutrition.

Boşnak et al. (29) found that chronic inflammation may promote an imbalance between oxidant and antioxidant mechanisms in malnutrition because malnourished children are prone to developing frequent infections. They did not find a significant difference between malnourished infected children and well-nourished infected children. In contrast, in the present study, a significant difference between both groups was detected (WNI *vs* UNM and UNS). Therefore, malnutrition might be a cause of the elevated oxidant stress, which may provoke oxidative damage and increased MN formation. The damage observed may be due to the deficiency of several essential nutrients required for protein synthesis that are associated with DNA integrity, impaired DNA repair mechanisms, or unavailability of molecules necessary to protect cells against DNA oxidative damage.

In conclusion, the data from this study support that moderate and severe malnutrition in children is associated with increased MN-RET frequency. Negative correlations were obtained between lipid peroxidation and SOD-GPx activities in severe malnourished children, supporting the fact that an energy-deficient state may result in enhanced lipid peroxidation and decreased antioxidant enzyme activities. Hence, malnutrition may be considered as a pro-oxidant condition because it increases the levels of lipid peroxidation and decreases antioxidant activity.

Therefore, increased oxidative stress may represent a mechanistic link between malnutrition and genotoxicity.

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Trabajo Original

Pediatría

Physical activity values in two- to seven-year-old children measured by accelerometer over five consecutive 24-hour days

Valores de actividad física en niños de dos a siete años, medidos mediante actimetría durante cinco días consecutivos las 24 horas diarias

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Abstract

Introduction: interpretation of accelerometer-derived physical activity in preschool children is confounded by differences in cut-off points.

Aim: the purpose of this study was to analyze physical activity in 2-to-7-year-old children to establish reference values for daily activity.

Methods: observational study in children aged 2-7 years, without chronic diseases and whose parents provided informed consent. The main variable was physical activity, measured continuously over 120 hours (three workdays and two weekend days) by accelerometer. Secondary variables were weight status (body mass index [BMI] Z-score) and gender. The relationship between the main variable and secondary variables was determined through the t-test, ANOVA and the Pearson correlation coefficient. A multivariate model was used to obtain the standard deviation (SD) of all possible combinations of values, constructing percentiles of normality ($x \pm SD$ and $x \pm 2 \cdot SD$).

Results: one hundred and thirty-six children (35% of municipality children) were included in the study (54.4% of them were girls). Their weight status distribution was: 25 underweight (18.4%), 54 normal weight (39.7%), 12 risk of overweight (8.8%), 22 overweight (16.2%) and 23 obese (16.8%). The median age was 5.7 years and the mean physical activity was 592 counts/minute. The boys undertook more physical activity ($p = 0.031$) and the underweight and normal-weight children undertook more physical activity than the overweight and obese children ($p = 0.012$). There were no significant differences according to age. The multivariate analysis showed significant differences ($p < 0.001$) according to gender and weight status. In boys, physical activity decreased as weight status increased. In contrast, the girls in the extreme BMI groups obtained higher levels of physical activity.

Conclusion: overweight and obese preschool children had lower levels of physical activity than normal weight children. Physical activity levels were higher in boys.

Key words:

Preschool child.
Physical activity.
Pediatric obesity.
Normal distribution.

Resumen

Introducción: la interpretación de la actividad física medida mediante actimetría en preescolares es confusa debido a los diferentes puntos de corte.

Objetivo: el objetivo de este estudio fue analizar la actividad física en niños de dos a siete años para establecer valores de actividad física diaria.

Método: estudio observacional en niños de dos a siete años, sin enfermedades crónicas y cuyos padres hubieran firmado el consentimiento informado. La variable principal fue la actividad física, medida durante 120 horas ininterrumpidas (tres días laborables y dos días festivos) mediante actímetros. Las variables secundarias fueron el estado de peso (puntaje z de índice de masa corporal [IMC]) y el sexo. La relación entre la variable principal y las variables secundarias fue determinada mediante el test-t, ANOVA y el coeficiente de correlación de Pearson. Se utilizó un modelo multivariable para obtener estándares de desviación en todas las posibles combinaciones de valores, construyendo percentiles de normalidad ($x \pm DE$ y $x \pm 2 \cdot DE$).

Resultados: participaron en el estudio 136 niños (35% de los niños del municipio); el 54,4% fueron chicas. La distribución de estado de peso fue: 25 niños con bajo peso (18,4%), 54 normopeso (39,7%), 12 en riesgo de sobrepeso (8,8%), 22 con sobrepeso (16,2%) y 23 con obesidad (16,8%). La media de edad fue 5,7 años y de actividad física, 592 cuentas/minuto. Los chicos realizaron mayor actividad física ($p = 0,031$) y los niños con bajo peso y normopeso realizaron mayor actividad física que los niños con sobrepeso y obesidad ($p = 0,012$). No hubo diferencias significativas respecto a la edad. El análisis multivariable mostró diferencias significativas ($p < 0,001$) respecto al sexo y el estado de peso. En los niños, la actividad física decreció cuando aumentó el peso. Por el contrario, las niñas en grupos de IMC extremos obtuvieron mayores niveles de actividad física.

Conclusión: los preescolares en situación de sobrepeso y obesidad presentaron niveles menores de actividad física que los niños normopeso. Los niveles de actividad física fueron mayores en los chicos.

Palabras clave:

Preescolar.
Actividad física.
Obesidad pediátrica.
Distribución normal.

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INTRODUCTION

The global prevalence of overweight and obesity in preschool-age children has increased dramatically since 1990, from approximately 4% in 1990 to 7% in 2010 (1). Furthermore, obesity was more prevalent in children aged 4-5 years (18.3%) and overweight was more prevalent in children aged 8-9 years (25.5%) (2). This great increase in the incidence of overweight and obesity at early ages results in a high prevalence of metabolic syndrome (3). Consequently, obesity is related to decreasing quality of life (4) and to increased healthcare costs due to associated comorbidities, equivalent to 7% of the gross domestic product in developed countries (5).

During childhood and adolescence, environmental factors are the main causes of obesity, due to the energy imbalance caused by a high-energy intake (6) and/or a low level of physical activity (7). Thus, it is crucial to promote preventive interventions in early childhood to impact on lifestyle and prevent the development of overweight and obesity (7).

Over the past decade, a large body of empirical studies has described the correlates and determinants of physical activity in preschoolers (8-11). Though several tools exist to estimate physical activity approximately, these tools are not so effective at providing a more accurate determination, whether daily or over a certain period (12). For example, physical activity questionnaires obtain a subjective estimation of physical activity. In this field, accelerometry has been shown to be the most reliable method to record the quantity and level of physical activity that each subject performs in each period (13). Accordingly, accelerometers are considered to be the gold standard for free-living physical activity assessment (14).

A meta-analysis of several studies reporting accelerometry-derived daily physical activity levels of preschool-age children concluded that is necessary to develop physical activity guidelines for this range of age due to the confusion between several different cut-off points applied in the literature (15). Consequently, an equation based on these cut points in preschoolers was created (16).

Furthermore, physical activity levels have been assessed in different ways. Some authors define these levels following cut points using ROC curves over 3-7 minutes performing different physical activities in three different sessions (17). Others have measured physical activity levels in various ways: for three minutes using interclass correlation coefficients to modify Children's Activity Rating Scales, obtaining different cut points for three-, four-, and five-year-old children (18); for 20 minutes using the standard deviation (SD) of the counts and VO_2, random-coefficient models and multivariate models for gender, race, age, height, quadratic terms for age and height and interactions between these variables and accelerometry counts, determining moderate-to-vigorous physical activity cut points at 420 counts/15 seconds and vigorous physical activity cut points at 842 counts/15 seconds (19); and for an average of 100 minutes, constructing physical activity cut points by ROC analysis, specifically to determine sedentary behaviors at < 1,100 counts/minute (20). A more recent study determined physical activity cut points for preschoolers during a physical exercise session over four consecutive days (during activity time) using the Children's Activity Rating Scales and ROC curve and the ANOVA and Chi-squared test to determine differences between physical activity cut points, obtaining light physical activity at 373 counts/15 seconds, moderate physical activity at 585 counts/15 seconds and vigorous physical activity at 881 counts/15 seconds (21).

Nevertheless, these physical activity levels have recently been revised. The authors concluded there is a need to unify these cut points to determine the true physical activity of these children through methodological studies to advance the understanding of physical activity in this age group (22). Previous studies have focused on analyzing the amount of time that children spend each day in moderate-to-vigorous physical activity, not their total daily physical activity (23). Thus, physical activity such as playing games or in park areas that does not involve moderate-to-vigorous physical activity is not included in these activity measurements though it could be important in the quantification of total physical activity at the end of the day.

Determining reference values for this population is difficult because the variables that could influence physical activity do not use the same time period to determine cut points, or the same hours per day and the same days per week to analyze the physical activity of the children, even though some authors indicate the need to obtain data for ten hours per day to be considered as a valid day (23). The choice of accelerometer cut points can result in large discrepancies (21). Also, determining true physical activity in children requires recording over more days, with the best option being the analysis of consecutive days (8) and throughout the entire day. For this reason, we examined physical activity in two- to seven-year-old children, 24 hours per day over five consecutive days (three workdays and two weekend days) with the aim of establishing daily reference values without the influence of variables. The hypothesis of this study was that by measuring physical activity during this period accurate physical activity levels of preschool children would be obtained.

MATERIALS AND METHODS

STUDY POPULATION

Rafal is a small town of 3,091 inhabitants in Alicante, Spain. It is situated in a rural area in which most of the population lives off the cultivation of fruits and vegetables and the production of wine. Consequently, access to food representative of the Mediterranean diet, such as fruit and vegetables, is not an issue. The socioeconomic status of the families was medium-low, and 22.5% were children of immigrant parents, mostly of Moroccan origin.

STUDY DESIGN AND PARTICIPANTS

We undertook a cross-sectional observational study with quantitative analysis between September 2014 and June 2015, inviting

the entire population of children aged between two and seven years (through their parents), either from the pediatric office at the health center, the school or the two kindergartens in the municipality. The parents of all the children read and signed the consent form. Children were excluded if they had any disease, such as diabetes or Down syndrome, which could result in lack of control with the accelerometer.

A nutritionist took the children to the multipurpose classroom in small groups of four. The children who were measured in the pediatric examination room were accompanied by their parents. Weight and height were recorded with the children in underwear and without shoes. Next, accelerometers were placed on the abdominal area of the participants, and the nutritionist explained that the accelerometer could only be removed to aquatic activities (swimming or bathing). The parents helped during this time to ensure the accelerometers remained in place without interruptions and to record the time the child went to bed and woke up as well as any interruption during this period.

VARIABLES AND MEASUREMENTS

The main outcome variable in this study was 24-hour-per-day physical activity. Physical activity was measured for 120 uninterrupted hours (three workdays and two weekend days) by accelerometer (counts/minute), validated to determinate physical activity in this age range (12,24,25). The data procedure was recorded every 15 epochs to maximize opportunities to more accurately capture the sporadic nature of young children's physical activity (26). A valid day may include at least ten hours per day (23), and a minimum of four consecutive days (three weekdays and one weekend day) were required to include a child (27). Half an hour of consecutive zeros was established as inactivity. To determine non-wear time as aquatic activity or some periods of time that children refuse to wear the accelerometer, these periods of time were compared with parent's reports, as well as sleep time, at night and day (27), which was excluded to calculate the mean of counts/minute of the sample.

Secondary variables were weight status (determined by the body mass index [BMI] Z-score), gender, and age. BMI (kg/m^2) was calculated from the weight and height parameters obtained, and the BMI Z-score was calculated in relation to age and gender using the Seinaptraker program (28), based on the Orbegozo Foundation standards (29). Children under five years were classified by BMI Z-score into five subgroups: underweight Z-score < -1, normal-weight Z-score ([-1]-1), risk of overweight Z-score > 1 to ≤ 2, overweight Z-score > 2 to ≤ 3 and obesity Z-score > 3. On the other hand, children over five years were classified by BMI Z-score into four subgroups: underweight Z-score < -1, normal-weight Z-score ([-1]-1), overweight Z-score > 1 to ≤ 2 and obese Z-score > 2, according to World Health Organization (WHO) recommendations (30).

Auxological parameters were measured by two trained nutritionists. Tools used were: Seca® weighing-scales (761 Class IIII, accuracy 0.5 kg), a Harpenden stadiometer (Holtain Ltd., Crymych, Dyfed, UK), which accurately determines height within 0.1 cm, and 13 accelerometers (Actigraph™ GT1M and ActiLife program).

SAMPLE SIZE

Sample size was calculated to estimate the mean of our main variable, counts per minute (cpm). Since the analysis was carried out in volunteers, sample size was calculated *a posteriori.* As the sample was selected from the total study population (n = 391) with an expected SD of 170 cpm (31), an accuracy in the determination of the population mean of 23.07 cpm was obtained.

STATISTICAL ANALYSIS

The descriptive analysis was performed through absolute and relative frequencies for qualitative variables, while the mean and SD were used for quantitative variables. The relationship between the main variable and secondary variables was calculated using the t-test, ANOVA and the Pearson correlation coefficient. A linear regression model was constructed with the dependent variable of physical activity (in cpm) and the independent variables of weight status, age and gender, considering possible interactions between them. Non-significant interactions were eliminated from the model. The goodness-of-fit of the model was obtained through ANOVA. The model was used to obtain the SD from all the possible combinations of values (for example, children with childhood obesity). With each of the SD, normal percentiles were computed ($x \pm SD$ and $x \pm 2 \cdot SD$). For each relevant parameter its associated confidence interval (CI) was calculated. The type I error was set at 5%. IBM SPSS Statistics 24 software was used.

In the ANOVA and normal distribution test and the determination of percentiles of normality for daily physical activity, the BMI groups of risk of overweight and overweight were unified due to the sample size of risk of overweight children.

ETHICAL ISSUES

The study protocol was approved by the Ethics Committee of the University of Alicante prior to initiation (18 March, 2014). The researchers informed the parents about the study, the ethical principles and confidentiality, and written consent was provided by the parents of the participants.

RESULTS

We offered the entire population in this age range (391 children) the opportunity to participate, but 252 of them refused (through their parents) and two children met the exclusion criteria. Thus, the final sample included 136 children (35% of the children in this age range in the municipality).

Table I shows the weight status distribution of the sample of children studied: 25 underweight children (18.4%), 54 with normal weight (39.7%), 12 with risk of overweight (8.8%), 22 overweight (16.2%) and 23 obese (16.8%). Consequently, almost half the sample had excess weight and one in four preschool children was obese. The median age of the participants was 5.7 years (IQ 2.5) and the range of age was 2.4 to 7.3 years. Table I also shows their physical activity as recorded by accelerometer. In the entire sample, the mean was 592 cpm, with a SD of 125 cpm. Concerning gender, weight status group and age, the boys undertook more physical activity, underweight and normal-weight children undertook more physical activity in comparison with the overweight and obese groups, and there were no significant differences by age.

In the multivariate analysis (Table II), the integration of gender and weight status showed significant differences. Specifically, boys had a lower weight status than girls. From the normal distribution analysis, the mean plus two levels of SD for gender and weight status were obtained (Table III). When the number of cpm measured in a child exceeded two SD, above or below, the physical activity level was considered as abnormal. Figure 1 illustrates this distribution. In boys, physical activity decreased as weight status increased. In contrast, the girls in the extreme weight status groups (underweight and obese) undertook greater amounts of physical activity.

Table I. Descriptive and inferential analysis of physical activity in children aged two to seven years

Variable	Total n = 136 n (%)/x ± SD	Cpm x ± SD/r	p-value
Cpm	N/A	592 ± 125	N/A
Gender:			
Boys	62 (45.6)	618 ± 135	0.031
Girls	74 (54.4)	571 ± 113	
Weight status:			
Underweight	25 (18.4)	604 ± 128	0.012
Normal weight	54 (39.7)	627 ± 118	
Risk of overweight*	12 (8.8)	555 ± 154	
Overweight	22 (16.2)	563 ± 130	
Obese	23 (16.9)	538 ± 114	
Age (years)	5.5 ± 1.5	-0.064	0.458

*Cpm: counts per minute; n (%): absolute frequency (relative frequency); N/A: not applicable; r: Pearson correlation coefficient; x ± SD: mean ± standard deviation. *This category of weight status includes only children under five years.*

DISCUSSION

A significant association was found between a higher level of physical activity and a healthier weight status and gender. The multivariate regression model produced curves of normal physical activity values for both genders and considering weight status.

Table II. Multivariate analysis of physical activity in children aged two to seven years

Variable	B (95% CI)	p-value
Intercept	567.3 (494.8, 639.7)	< 0.001
Weight status*	1.26 (-25.2, 27.7)	0.925
Boys	191.2 (82.5, 299.8)	< 0.001
Boys · Weight status*	-52.4 (-90.4, -14.4)	0.007

*B: regression coefficient; CI, confidence interval. *: defined as: 1, underweight; 2, normal weight; 3 and 4, risk of overweight and overweight; and 5, obese. Goodness-of-fit of the model (ANOVA test): $F = 6.35$, $p < 0.001$.*

The relationship between physical activity and weight status has been shown in school-age youth (32) and preschool children (9). However, it is difficult to compare physical activity between studies due to the considerable variation of prevalence estimates used to quantify this physical activity (22). A review concluded that a valid day may include at least ten hours per day, eliminating inactive hours in which children were asleep and aquatic activities (23).

In our case, we measured 120 consecutive hours distributed over workdays and weekend days, eliminating an average of ten hours of total inactivity (sleep). The mean physical activity in our sample was approximately 1,000 cpm. This value situates our sample in the light activity category, according to recent studies (19,33,34), and confirms that young children are not achieving an adequate amount of physical activity (27). However, we believe that uninterrupted physical activity measurements afford children and their families more freedom of activity, trying to measure a more accurate physical activity. When only a short period in which children are doing physical exercise is measured, these children could be forced to do more physical activity than they normally would during a day, resulting in a biased measurement. Furthermore, most authors have focused their studies on quantifying the number of minutes that preschool children spend in moderate-to-vigorous physical activity, following public health recommendations (15,16,19,21,26,35). However, a recent review concludes that the decision to select from among various cut points significantly influences the optimal levels of moderate-to-vigorous physical activity for obesity prevention in children (36). Moreover, none of the studies reviewed considered the weight status of preschool children to determine their physical activity levels or to provide physical activity level recommendations to prevent childhood obesity.

We measured total physical activity, which provides more accurate values for physical activity levels in preschool-age children during their normal daily life. Reference values are given by gender and weight status, which provide clinicians with standardized physical activity level values with which to compare their patients. Since we considered total daily physical activity, these values could be a reference, adaptable to the special needs of each group of children depending on their characteristics. According to sex,

Table III. Normal distribution of physical activity (in counts per minute) in children aged two to seven years, considering weight status and gender

Weight status	Boys					Girls				
	x-2·SD	x-SD	x	x + SD	x + 2·SD	x-2·SD	x-SD	x	x + SD	x + 2·SD
Underweight	650	679	707	736	764	519	544	569	593	618
Normal weight	620	638	656	675	693	539	554	570	585	601
Risk of overweight and overweight	574	590	605	620	636	541	556	571	586	601
Obese	508	531	554	577	600	525	548	572	596	620

X: mean; SD: standard deviation.

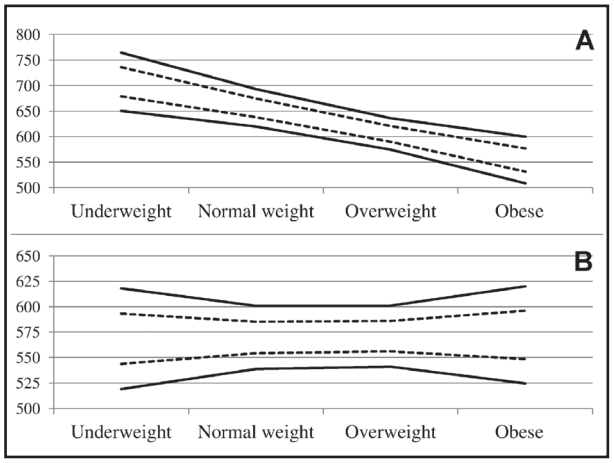

Figure 1.

Percentiles for normality for daily physical activity (counts per minute) according to the weight of the child. Thick lines denote mean ± 2 · SD, and continuous lines denote mean ± SD. *The overweight group includes children in risk of overweight and overweight, depending of their range of age.

boys were more active than girls (27) and overweight and obesity groups presented a lower amount of physical activity, especially in the boys. For this reason, activities requiring more effort in these children should be promoted during both school (37) and family time (38). This is of great importance given the epidemiologic problem in countries such as Spain, where the prevalence and incidence of obesity have constituted an alarming situation in the population in this age range during the last decades (39).

The most significant contribution of the study is the reference values obtained according to gender and weight status, which provide clinicians with the standardized daily physical activity levels of preschool-age children. Since we considered the total daily physical activity, these values could be used as a reference and adapted to the special necessities of each child depending on their weight status. In future studies, the use of accelerometers throughout the entire day is recommended to quantify physical activity and to choose an appropriate physical exercise intervention to improve weight status in preschool-age children (7,27,40).

The strength of this study is the evidence shown about the association between the level of daily physical activity in Spanish preschool children, weight status and gender. By monitoring the children 24 hours per day and measuring workdays and weekend days we could obtain a more accurate determination of total physical activity in preschool children. This is of great importance given the need to study the population in this age range and the need for reliable data to quantify the true level of physical activity.

The main limitation of this study is that it was carried out in a small population. Therefore, it is necessary to replicate the study in other communities before the results can be extrapolated to the general population in this age range.

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ETHICAL STANDARDS

All human and animal studies have been approved by the appropriate Ethics Committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

In addition, all people gave their informed consent prior to their inclusion in the study.

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ARÁN

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Trabajo Original

Pediatría

La obesidad infantil y su asociación con el sentimiento de infelicidad y bajos niveles de autoestima en niños de centros educativos públicos

Childhood obesity and its association with the feeling of unhappiness and low levels of self-esteem in children of public schools

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Resumen

Introducción: los niños con exceso de peso corren mayor riesgo de sufrir alteraciones psicosociales.

Objetivo: el propósito de esta investigación fue relacionar la condición de sobrepeso y obesidad con los niveles de autoestima y felicidad en escolares de centros educativos públicos.

Métodos: participaron 364 escolares (180 niños y 184 niñas) de entre once y 13 años de edad (12,44 ± 1,14 años de edad). Se realizaron mediciones antropométricas y se evaluaron los niveles de autoestima y felicidad a través del Test de Autoestima Escolar (TAE).

Resultados: la autoestima escolar fue significativamente mayor en los niños ($p < 0,001$). El 55,49% ($n = 204$) de los escolares evaluados presentó exceso de peso. Los sujetos con sobrepeso y obesidad presentaron menores niveles de autoestima en comparación con los normopeso ($p = 0,032$); además, 43 escolares presentaron muy baja autoestima, existiendo relación entre los niveles de muy baja y baja autoestima ($n = 119$) y la condición de sobrepeso y obesidad ($p = 0,033$). En relación a la pregunta "¿soy una persona feliz?", una mayor proporción de escolares respondió positivamente ($n = 296$). La respuesta negativa a la pregunta se asoció con la presencia de exceso de peso ($p = 0,042$).

Conclusión: la condición de sobrepeso y obesidad se relacionó con bajos niveles de autoestima y de felicidad en escolares. Estos resultados son alarmantes, ya que la autoestima es el aprecio que uno tiene de sí mismo y la felicidad es un índice del bienestar personal subjetivo, y es un tema que concierne a las familias y a todo el sistema educativo.

Palabras clave:

Autoestima. Felicidad. Escolares. Obesidad.

Abstract

Introduction: overweight children are at increased risk for psychosocial disorders.

Objective: the purpose of this research was to relate the condition of overweight and obesity to the levels of self-esteem and happiness in schoolchildren of public schools.

Methods: a total of 364 schoolchildren (180 boys and 184 girls) were enrolled between eleven and 13 years old (12.44 ± 1.14 years old). Anthropometric measurements were performed and the levels of self-esteem and happiness were evaluated through the School Self-Esteem Test (APT).

Results: school self-esteem was significantly higher in boys ($p < 0.001$); 55.49% ($n = 204$) of the students evaluated were overweight. Overweight and obese subjects had lower levels of self-esteem compared to normal weight children ($p = 0.032$). In addition, 43 students had very low self-esteem, and a relationship between very low and low self-esteem levels ($n = 119$) and the overweight and obesity was observed ($p = 0.033$). In relation to the question "Am I a happy person?", a greater proportion of students answered positively ($n = 296$). The negative response to the question was associated with weight excess ($p = 0.042$).

Conclusion: overweight and obesity were related to low levels of self-esteem and happiness in schoolchildren. These results are alarming since self-esteem is one's appreciation of oneself and happiness is an index of subjective personal well-being and is a topic that concerns families and the entire education system.

Key words:

Self-esteem. Happiness. Schoolchildren. Obesity.

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INTRODUCCIÓN

La obesidad infantil se ha convertido en una epidemia global y en uno de los mayores desafíos de salud pública del siglo XXI (1). Su prevalencia ha aumentado en la mayoría de los países independientemente de su nivel de ingresos, incluido Chile (2). La etiología de la enfermedad es multifactorial y compleja, derivada de una interacción entre factores genéticos, biológicos y ambientales, y se asocia con varias comorbilidades que afectan a la salud física (3) y mental (4). Actualmente, existe un aumento en el interés por aspectos psicosociales derivados de la obesidad, debido a que los jóvenes obesos corren mayor riesgo de sufrir una baja autoestima, empeoramiento de la calidad de vida, deterioro en su funcionamiento social (5), mayores niveles de depresión y ansiedad (6) y también mayor probabilidad de mantener el estado de obesidad en la adultez (7). Por tal motivo, y en términos de mejorar la autoestima, la pérdida de peso es un factor importante, así como el entorno y las redes de apoyo que se generen (8).

La felicidad es un constructo complejo (9), es considerada como uno de los índices del bienestar personal subjetivo (10) y es un tema que concierne a las familias y educadores (11). Su evaluación debe ser una prioridad en el sistema escolar, ya que los niños obesos con niveles decrecientes de autoestima muestran tasas significativamente más altas de tristeza, soledad y nerviosismo y son más propensos a involucrarse en comportamientos de alto riesgo (12).

La autoestima y el sentimiento de felicidad en la escuela afectan el rendimiento académico y el desarrollo integral de los niños y pueden asociarse a factores y síntomas depresivos, así como a trastornos de la imagen corporal. Sin embargo, existe escasa información respecto a la asociación de estas variables en niños que presentan exceso de peso. Por tal motivo, el propósito de esta investigación fue relacionar la condición de sobrepeso y obesidad con los niveles de autoestima y felicidad escolar autopercibidas en niños de centros educativos públicos, determinando de esta manera si, en la muestra de estudio, la condición de exceso de peso tiene relación con no sentirse feliz o presentar baja o muy baja autoestima escolar.

MATERIAL Y MÉTODOS

El estudio es de tipo observacional, descriptivo, transversal, con muestreo aleatorio simple. Para calcular el tamaño de la muestra se estimó un margen de error del 5%. Fueron evaluados 364 escolares, 180 niños y 184 niñas, de entre 11-13 años de edad, pertenecientes a centros educativos públicos mixtos de la Región de La Araucanía (Chile).

En una primera etapa, una vez obtenido el tamaño de la muestra, se enumeró a todos los escolares y se realizó el muestreo. Posteriormente a esa muestra de estudio, se evaluaron datos respecto al curso de estudio, edad, sexo, antropometría, autoestima y felicidad.

Los criterios de inclusión fueron presentar el consentimiento informado por parte de los padres y el asentimiento del participante, estar matriculado en los colegios de estudios, tener entre 11-13 años de edad y no presentar discapacidad física o mental.

Los protocolos de la investigación se han realizado considerando las normas y principios éticos establecidos en la Declaración de Helsinki de 2013 y fueron aprobados por el Departamento de Educación Física, Deportes y Recreación de la Universidad de La Frontera (Proyecto DFP16-0013), Temuco, Chile.

PROCEDIMIENTOS

La masa corporal (kg) se midió a través de una balanza TANITA, modelo Scale Plus UM-028 (Tokio, Japón). Los escolares fueron evaluados con los pies descalzos y con pantalón corto y polera. La talla (m) se estimó con un tallímetro marca Seca® modelo 214 (Hamburgo, Alemania), graduada en mm. El índice de masa corporal (IMC), que se obtiene al dividir el peso corporal por la talla en metros al cuadrado (kg/m^2), se utilizó para estimar el grado de obesidad, determinando el estado nutricional de los participantes de acuerdo al siguiente criterio de calificación según su percentil: IMC entre p85 y < p95, sobrepeso; IMC > p95, obesidad (13). El perímetro de cadera (PC) se midió a la altura de la extensión máxima de los glúteos y la circunferencia de cintura (CC), a la altura de la cicatriz umbilical (14). Ambas mediciones fueron realizadas empleando una cinta métrica marca Seca® modelo 201 (Hamburgo, Alemania). La razón cintura-estatura (RCE) se obtiene al dividir la CC por la estatura y se utilizó como herramienta para estimar la acumulación de grasa en la zona central del cuerpo; una razón mayor de 0,55 indicaría mayor riesgo cardiometabólico (15). El índice cintura-cadera (ICC) se obtiene al dividir CC/PC y fue utilizado para determinar acumulación de grasa en la zona central del cuerpo.

Para la medición de autoestima se utilizó el TAE-Alumno: Batería de Test de Autoestima Escolar (16), vía autorreporte general para alumnos de 3.º a 8.º de Primaria en relación a una norma establecida por curso y por edad. Se aplica un punto por cada respuesta positiva y cero por cada respuesta negativa. La sumatoria del puntaje bruto se transforma a puntaje T según normas por edad y se sitúa al alumno acorde a las siguientes categorías: autoestima normal, ≥ 40 puntos; baja autoestima, 30-39 puntos; y muy baja autoestima, ≤ 29 puntos. El nivel de consistencia interna alcanzado en este cuestionario con la muestra actual fue de alfa de Cronbach = 0,81. Además, para los análisis estadísticos se utilizó la pregunta "¿soy una persona feliz?" del cuestionario, registrando la respuesta positiva o negativa de cada participante.

ANÁLISIS ESTADÍSTICO

Los datos son presentados como media ± desviación típica. La distribución normal de datos se evaluó a través de la prueba de Kolmogorov-Smirnov. Para la comparación de las variables paramétricas cuantitativas entre dos grupos se utilizó el test t de Student y cuando existían más de dos grupos se realizó un análisis de varianza (ANOVA). La prueba *post-hoc* de Bonferroni fue utilizada para detectar dónde se encontraban esas diferencias.

Para el análisis de las variables categóricas se utilizó Chi-cuadrado. Todos los análisis se realizaron con el programa estadístico SPSS para Windows v.23.0 (IBM SPSS Statictics 23.0. USA). El nivel de confianza fue del 95% ($p < 0,05$).

RESULTADOS

La autoestima escolar fue significativamente mayor en los niños ($p < 0,001$) y en relación a las variables de antropometría el PC fue mayor en las niñas ($p < 0,011$) (Tabla I).

El 55,49% (n = 204) de los escolares evaluados presentó exceso de peso (sobrepeso u obesidad). Las variables CC, PC, ICC y RCE fueron mayores en los sujetos con obesidad ($p < 0,05$). Con respecto a la autoestima, existieron diferencias significativas en la comparación por grupos, presentando los sujetos con sobrepeso y obesidad valores inferiores a los normopeso, sin diferencias entre ellos ($p = 0,032$) (Tabla II).

En la figura 1 se representan las categorías de autoestima en relación a la condición de normopeso, sobrepeso y obesidad, destacando que 43 escolares presentaron muy baja autoestima, con relación entre los niveles de muy baja y baja autoestima (n = 119) y la condición de sobrepeso y obesidad ($p = 0,033$).

En relación a la pregunta "¿soy una persona feliz?", una mayor proporción de escolares respondió positivamente (n = 296). La respuesta negativa a la pregunta se asoció con la presencia de sobrepeso y obesidad ($p = 0,042$) (Fig. 2).

DISCUSIÓN

El propósito de esta investigación fue relacionar la condición de sobrepeso y obesidad con los niveles de autoestima y felicidad en niños de centros educativos públicos, determinando de esta manera si en la muestra de estudio la condición de exceso de peso tiene relación con no sentirse feliz o presentar baja o

Tabla I. Comparación de las variables de estudio según sexo

	Total (n = 364)	Niños (n = 180)	Niñas (n = 184)	Valor p
Edad	12,44 ± 1,14	12,49 ± 1,14	12,38 ± 1,13	NS
Peso (kg)	56,87 ± 12,60	57,54 ± 13,05	55,75 ± 10,20	NS
Talla (m)	1,58 ± 0,09	1,59 ± 0,10	1,56 ± 0,07	0,003
IMC (kg/m^2)	22,84 ± 3,68	22,57 ± 4,00	23,20 ± 3,20	NS
CC (cm)	72,80 ± 9,34	73,74 ± 9,56	71,56 ± 8,95	NS
PC (cm)	89,98 ± 8,06	88,60 ± 6,96	92,45 ± 4,48	0,011
ICC (CC/PC)	0,81 ± 0,06	0,83 ± 0,03	0,78 ± 0,03	< 0,001
RCE (CC/talla)	0,46 ± 0,05	0,46 ± 0,04	0,46 ± 0,03	NS
Autoestima escolar	48,26 ± 11,97	51,61 ± 12,10	45,17 ± 11,14	< 0,001

Los valores mostrados son media ± desviación típica. Los valores p < 0,05 son estadísticamente significativos. IMC: índice de masa corporal; CC: contorno cintura; PC: perímetro cadera; ICC: índice cintura-cadera; RCE: razón cintura-estatura; NS: no significativo.

Tabla II. Comparación de variables según estado nutricional

	Normopeso (n = 162)	Sobrepeso (n = 100)	Obesos (n = 102)	Valor p
Edad	12,33 ± 1,11	12,39 ± 1,11	12,65 ± 1,23	NS
IMC (kg/m^2)	20,06 ± 1,50*	23,58 ± 1,26†	28,22 ± 2,39‡	< 0,001
CC (cm)	66,40 ± 5,02*	74,28 ± 5,27†	85,06 ± 7,89‡	< 0,001
PC (cm)	85,46 ± 4,86*	91,11 ± 5,58†	99,24 ± 7,60‡	< 0,001
ICC (CC/PC)	0,78 ± 0,06*	0,81 ± 0,05†	0,86 ± 0,06‡	< 0,001
RCE (CC/talla)	0,43 ± 0,03*	0,47 ± 0,03†	0,54 ± 0,04‡	< 0,001
Autoestima escolar	51,61 ± 12,21*	45,19 ± 10,44†	44,21 ± 13,43†	0,032

Los valores mostrados son media ± desviación típica. Los valores p < 0,05 son estadísticamente significativos. IMC: índice de masa corporal; CC: contorno cintura; PC: perímetro cadera; ICC: índice cintura-cadera; RCE: razón cintura-estatura; NS: no significativo. Diferentes letras de subíndice indican diferencia significativa (p < 0,05) en comparaciones entre grupos.

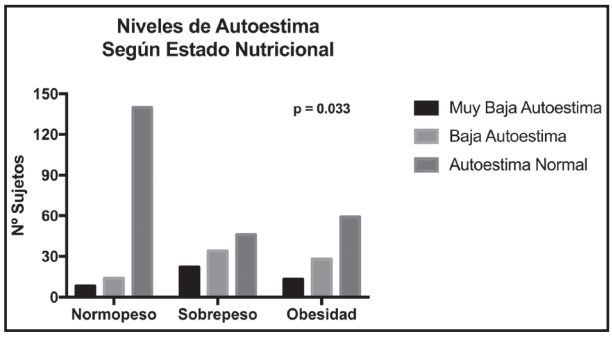

Figura 1.

Relación del nivel de autoestima con el estado nutricional.

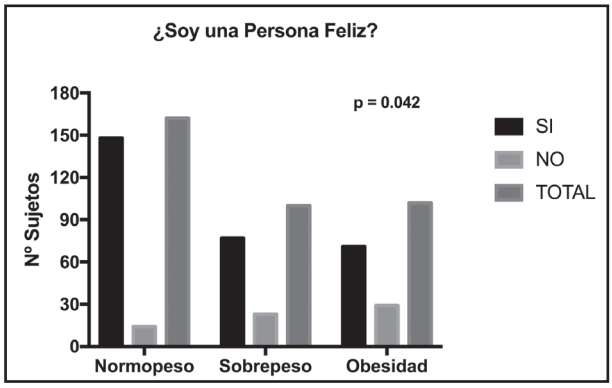

Figura 2.

roporción de escolares que responden de forma positiva y negativa.

muy baja autoestima. El principal hallazgo de la investigación fue que el exceso de peso se asocia en los escolares a no sentirse feliz, resultado preocupante debido a la elevada prevalencia de obesidad infantil.

Existe evidencia que establece una relación significativa entre IMC incrementado y disminución de la autoestima (17,18). Por tal motivo, la medición de variables antropométricas resulta necesaria para una evaluación integral de los niños que permita su comprensión de forma holística, ya que no se ha conseguido ningún progreso en la reducción de la prevalencia de la obesidad (19). En la presente investigación el IMC fue mayor en los niños. Estos resultados son diferentes a lo reportado en una muestra representativa de escolares provenientes del Congo (20), donde se obtuvieron resultados inversos. La CC igualmente fue superior en los niños, con resultados similares a los de un estudio realizado en escolares brasileños (21), donde el valor de la CC fue mayor en los niños, sin alcanzar diferencias estadísticamente significativas.

Una buena autoestima se relaciona con muchos aspectos positivos para la salud mental, como la percepción positiva de parte de los pares, logros académicos y persistencia. En cambio, una autoestima baja, sumada a problemas de cohesión familiar y menos apoyo social, genera mayores índices incluso de suicidio (22).

En la presente investigación la autoestima fue superior en los niños y estos resultados son similares a los reportados en un estudiado realizado con una muestra de estudiantes de escuelas públicas de Noruega (23,24) y en estudiantes ingleses (25).

En el presente estudio, la condición de sobrepeso y obesidad se asoció significativamente con una baja o muy baja autoestima, similar a lo reportado en una muestra de escolares, en donde aquellos clasificados con sobrepeso y obesidad tuvieron valores menores en autoestima, específicamente en las dimensiones de competencia escolar, aceptación social, competencias atléticas y apariencia física en comparación con los estudiantes clasificados como normopeso (26). En niños, se ha observado un efecto diferencial de la obesidad sobre la autoestima en problemas de externalización y percepción social relacionados con comportamientos de bullying y con ser víctimas de acoso (27).

En relación a la pregunta asociada al concepto felicidad, 296 escolares respondieron positivamente. La respuesta negativa a la pregunta se asoció con la presencia de sobrepeso y obesidad. Una muestra de 60 niños chinos de entre siete y 12 años reportó niveles significativamente menores en felicidad y satisfacción en los sujetos obesos al compararlos con sujetos normopeso. Además, presentaron una baja autoevaluación personal y un menor nivel de adaptabilidad social (28), al igual que en niños turcos, donde los clasificados como obesos reportaron valores en felicidad y satisfacción significativamente menores (29). En virtud de lo anterior, resulta preponderante el desarrollo de acciones concretas vinculadas a la atención y prevención integral de la obesidad en la etapa adolescente, ello a partir del fortalecimiento educativo y la concienciación social respecto a esta materia. Por este motivo, monitorizar el estado nutricional deberá ser una prioridad en las agendas y políticas públicas dentro del ámbito escolar (30).

Como conclusión de este estudio podemos señalar que la condición de sobrepeso y obesidad se relacionó con bajos niveles de autoestima y de felicidad en escolares. Estos resultados son alarmantes en términos psicosociales, entendiendo la trascendencia que posee la autoestima y la percepción de felicidad en la construcción identitaria de los sujetos y la configuración de las relaciones interpersonales, factores que inciden de forma directa en el desarrollo de la salud emocional, mental y social.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Pediatría

Medición del gasto energético de reposo en pacientes oncológicos pediátricos: concordancia entre calorimetría indirecta y ecuaciones predictivas

Measurement of rest energy expanditure in pediatric oncological patients: concordance between indirect calorimetry and predictive equations

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Resumen

Introducción: en el cáncer infantil, la enfermedad impacta sobre el gasto energético en reposo (GER) de manera no estimable mediante ecuaciones predictivas.

Objetivo: determinar concordancia entre medición del gasto energético en reposo por calorimetría indirecta *versus* ecuaciones predictivas.

Método: estudio observacional analítico transversal en niños de 5-15 años que reciben quimioterapia, en control ambulatorio por la Clínica Las Condes y el Hospital Dr. Sótero del Río, entre julio de 2013 y julio de 2015. Se realizó medición de GER mediante calorimetría indirecta y ecuaciones de Schofield y la Organización Mundial de la Salud (OMS). Análisis de concordancia, con punto de corte clínicamente relevante y coeficiente de concordancia del 90%.

Resultados: se incluyó a 27 niños y se realizaron 27 calorimetrías. De ellos, el 66% presentaba leucemia, el 15% presentaba tumor de sistema nervioso central y el 81% se encontraba en etapa de mantención. No se encontró diferencia significativa entre medición por calorimetría indirecta *versus* OMS (p 0,18) ni *versus* Schofield (p 0,07), ni al estratificar por estado nutricional o tipo de diagnóstico oncológico. El coeficiente de concordancia de Lin entre calorimetría y Schofield fue del 79,4% (IC 95% = 65,2-93,6) y con OMS, del 78% (IC 95% = 62,9-93,2).

Conclusiones: el nivel de concordancia entre calorimetría indirecta y Schofield y OMS respectivamente fue menor de 80%, lo cual es insuficiente e implica que en más de un 20% de los casos sería un cálculo de GER sobre o subestimado y, por lo tanto, con un aporte nutricional excesivo o deficitario. En consecuencia, es necesario contar con la calorimetría indirecta como parte de la evaluación nutricional en una población nutricionalmente de riesgo como esta.

Palabras clave:

Cáncer infantil. Calorimetría indirecta. Gasto energético en reposo. Pacientes oncológicos pediátricos.

Abstract

Introduction: in childhood cancer, the disease impacts resting energy expenditure (GER) in a way that is not estimable by predictive equations.

Objective: the aim of this study is to determine the concordance between the measurement of resting energy expenditure (REE) by indirect calorimetry in pediatric oncology patients *versus* the World Health Organization (WHO) and Schofield predictive equations.

Method: cross-sectional study in children aged 5-15 years receiving chemotherapy, in outpatient Clínica Las Condes and Hospital Dr. Sótero del Río, from July 2013 to July 2015. REE measurement was performed by indirect calorimetry and WHO and Schofield equations. Concordance analysis, with clinically relevant cut-off point and concordance coefficient of 90%.

Results: twenty-seven children were included and 27 calorimetries were performed; 66% of these children were diagnosed with leukemia, 15% with central nervous system tumor and 81% were in the maintenance stage of their treatment. There is no significant difference between indirect calorimetry measurement *versus* WHO (p 0.18) or Schofield (p 0.07), neither when stratifying by nutritional status or type of cancer diagnosis. Concordance was calculated between calorimetry and Schofield, with a concordance coefficient of Lin = 79.4% (95% CI = 65.2-93.6) and *versus* WHO = 78% (95% CI = 62.9-93.2).

Conclusion: this level of agreement, less than 80% in both cases, is insufficient. With both equations for estimating REE, there is overestimation or underestimation of energy requirements in more than 20% of cases. There is no agreement between the measurement of REE measured with indirect calorimetry *versus* its estimation with Schofield's and the WHO equations. Consequently, indirect calorimetry is required as part of the nutritional assessment in a nutritionally at-risk population such as pediatric patients with oncological pathology.

Key words:

Childhood cancer. Indirect calorimetry. Resting energy expenditure. Pediatric oncology patients.

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INTRODUCCIÓN

Durante la infancia, una adecuada nutrición es de suma importancia para el bienestar general, crecimiento y desarrollo del niño. Un factor que afecta notablemente el gasto energético es la presencia de enfermedad y los factores que influyen en esto son el tipo de enfermedad, la etapa de la enfermedad y el tipo de tratamiento que está recibiendo el paciente.

El cáncer infantil es considerado como una de las principales causas de mortalidad infantil (1). El progreso en la investigación, los métodos diagnósticos y la eficacia del tratamiento han permitido mejorar el índice de sobrevida. Sin embargo, tanto la enfermedad como su tratamiento pueden ocasionar la aparición de malnutrición por déficit, lo que repercute directamente en la función inmune, con mayor susceptibilidad a infecciones, disminución de la tolerancia a la quimioterapia, alteración en el crecimiento y desarrollo y, por lo tanto, mayor morbimortalidad en estos pacientes (2-10).

Se describe internacionalmente una incidencia de desnutrición de entre el 6% y el 50% en niños con patología oncológica (3,4), por lo que es fundamental realizar una adecuada evaluación nutricional y planificar un óptimo soporte nutricional para promover un adecuado crecimiento y desarrollo, disminuir la comorbilidad asociada y optimizar la calidad de vida de estos pacientes.

La Sociedad Americana de Nutrición Enteral y Parenteral (ASPEN) recomienda la estimación del gasto energético en reposo (GER) con calorimetría indirecta (11).

La calorimetría indirecta es un procedimiento seguro, no invasivo e indoloro, que requiere cooperación del paciente para estar tranquilo durante la realización del examen. El niño, en ayunas, debe permanecer recostado en una camilla, respirando tranquilo por un periodo de 30 minutos para lograr un registro de al menos cinco minutos del estado de equilibrio, definido como el periodo en que el consumo de oxígeno (O_2) y la eliminación de dióxido de carbono (CO_2) presentan una variación menor al 10%.

Sin embargo, con frecuencia no es posible realizar calorimetría indirecta por no contar con la disponibilidad del equipo para realizarla o por el costo asociado a este procedimiento. En estos casos se utilizan ecuaciones predictivas para estimar el GER. Estas ecuaciones son derivadas de datos de calorimetría indirecta extraídos de niños sanos y basadas en análisis de regresiones múltiples de los datos obtenidos, por lo que no son exactas (12).

La aplicación de factores de estrés y factor de actividad sobre estas ecuaciones para intentar estimar los requerimientos energéticos en niños con patología produce falta de exactitud, disparidad en la estimación de requerimientos energéticos *versus* la calorimetría indirecta y, por lo tanto, mayor riesgo de dar aportes excesivos o insuficientes en los niños críticamente enfermos (11,12).

Dado que la enfermedad impacta sobre el gasto energético en reposo de manera no estimable mediante ecuaciones predictivas, la calorimetría indirecta es la única herramienta capaz de objetivar eficazmente el gasto energético en reposo (11-18).

Así pues, dirigir la medición del gasto energético con calorimetría indirecta en un grupo seleccionado de pacientes de alto riesgo nutricional como son los pacientes con patología oncológica puede prevenir el aporte excesivo o deficiente de nutrientes y sus consecuencias deletéreas asociadas.

El uso de calorimetría indirecta permite una observación más directa, objetiva y cercana en relación temporal entre el gasto energético y el curso de la enfermedad. Estos avances se traducen en el óptimo aporte de nutrientes en forma individual, el ajuste dinámico de los aportes en base a los requerimientos durante el curso de la enfermedad y evitar potenciales complicaciones derivadas de un aporte nutricional inadecuado.

El objetivo de este estudio es determinar la concordancia entre la medición del gasto energético en reposo por calorimetría indirecta en pacientes oncológicos pediátricos *versus* ecuaciones predictivas de la OMS y de Schofield.

No se encontró literatura nacional ni internacional que comparase esta concordancia.

MÉTODOS

Se realizó un estudio observacional, analítico, transversal, de concordancia entre calorimetría indirecta *versus* dos ecuaciones predictivas, la de la OMS y la de Schofield, para la estimación de requerimientos energéticos (GER) en pacientes pediátricos en control ambulatorio del Centro del Paciente Oncológico Pediátrico de la Clínica Las Condes y el Departamento de Oncología Pediátrica del Hospital Dr. Sótero del Río, Santiago, Chile.

El estudio fue aprobado por el Comité de Ética de la Clínica Las Condes y del Hospital Dr. Sótero del Río, de acuerdo a la Declaración de Helsinki.

Se incluyó a los pacientes con patología oncológica de entre cinco y 18 años que estaban en control ambulatorio en sus centros hospitalarios respectivos, que durante los últimos 30 días habían recibido quimioterapia ya sea oral o endovenosa, sin cuadros agudos infecciosos presentes al momento de la medición y que aceptaron participar, previo consentimiento informado firmado si eran mayores de 12 años y consentimiento informado firmado por sus padres en el caso de los menores de 12 años.

Se excluyó a los pacientes que estaban hospitalizados o con necesidad de suplementación de oxígeno, drenaje pleural o escape aéreo, porque en todas estas condiciones es técnicamente imposible realizar las mediciones de gases necesarias para validar la calorimetría.

Las variables de estudio fueron la medición del gasto energético en reposo mediante calorimetría indirecta con calorímetro Quark RMR-Cosmed y su estimación a través de dos ecuaciones predictivas ampliamente utilizadas en pacientes pediátricos, la de Schofield (peso y talla) y la de la OMS, junto a las variables demográficas peso, talla, sexo, estado nutricional y diagnóstico oncológico.

Las mediciones fueron realizadas entre julio de 2013 y julio de 2015 en el Centro de Nutrición y Obesidad de la Clínica Las Condes, por una nutricionista capacitada para este procedimiento y el cálculo de GER mediante las ecuaciones OMS y Schofield, ciega al objetivo del estudio. En este mismo momento, previo a realizar la calorimetría, se pesó y midió a cada participante y con estos datos se realizó la evaluación nutricional utilizando para

la clasificación nutricional en los menores de cinco años peso/talla y en los mayores de cinco años, índice de masa corporal (IMC), de acuerdo con las curvas de crecimiento de la OMS. Se utilizaron como puntos de corte para la clasificación nutricional en los menores de cinco años: obesidad: > +2 *z-scores* para P/T; sobrepeso: > +1 *z-scores* para P/T; riesgo de desnutrición: < -1 *z-scores* para P/T; desnutrición: < -2 *z-scores* para P/T; y para los mayores de cinco años: obesidad: > +2 *z-scores* para IMC; sobrepeso: > +1 *z-scores* para IMC; riesgo de desnutrición: < -1 *z-scores* para IMC; y desnutrición: < -2 *z-scores* para IMC.

Para realizar la calorimetría indirecta se utilizó el equipo Quark RMR-Cosmed, con el paciente en ayuno durante al menos 12 horas, en decúbito supino sobre una camilla por 30 minutos y con un *canopy* o máscara transparente sobre la cabeza, y se realizó el análisis de gases respiratorios correspondiente al consumo de O_2 y la producción de CO_2, que al ser analizado por el *software* del equipo mediante ecuación de Wier otorga el GER expresado en calorías por día.

Para el análisis de los datos solo se consideraron válidas las mediciones que alcanzaron el estado de equilibrio (periodo de tiempo en que la variación del consumo de O_2 y la eliminación de CO_2 es menor al 10%) de al menos cinco minutos.

De forma simultánea se estimó el gasto energético en reposo mediante dos ecuaciones predictivas, Schofield (peso y talla) y OMS, utilizando los mismos datos de peso y talla para cada paciente. Estos resultados fueron comparados con los obtenidos por calorimetría indirecta para el análisis estadístico de concordancia.

Se exigió para efectos de este estudio un coeficiente de concordancia del 90% entre la medición del gasto energético en reposo por calorimetría indirecta *versus* fórmulas de Schofield y OMS respectivamente.

ANÁLISIS ESTADÍSTICO

El análisis estadístico se realizó con el software estadístico Stata 12 Texas Corp.

Se describieron las variables categóricas con frecuencias absolutas y porcentuales y las variables continuas con mediana e intervalo mínimo máximo, porque no distribuyeron normal. Posteriormente, se realizó la comparación entre las medianas del sistema de calorimetría *versus* la ecuación de cálculo de Schofield y calorimetría *versus* OMS, con el test no paramétrico de Mann-Whitney.

Se evaluó la concordancia entre calorimetría *versus* Schofield y calorimetría *versus* OMS con el gráfico de Bland-Altman y, finalmente, para determinar el nivel de concordancia de cada par respectivamente se calculó el coeficiente de correlación de concordancia de Lin.

El valor p de significación estadística fue < 0,05.

RESULTADOS

Se midió a 27 pacientes y se realizaron 27 calorimetrías indirectas. La edad fue de entre cinco y 15 años. La tabla I muestra las características demográficas y clínicas de los pacientes en estudio, de los cuales el 66% (n = 18) fueron pacientes con diagnóstico de leucemia, el 15% (n = 4) presentaban tumor de sistema nervioso central y el 19% (n = 5) tenía otros diagnósticos oncológicos. Es importante destacar que la mayoría de los pacientes se encontraban eutróficos (9/27 pacientes, 33%) y en etapa de mantención de su tratamiento oncológico (22/27 pacientes, 81%).

Tabla I. Características clínicas y epidemiológicas de todos los sujetos

	Total sujetos: n = 27
Género n (%)	
Masculino	15 (55)
Femenino	12 (45)
Edad en años p50 (min-max)	10 (5-15)
IMC (z-score) Mediana (min-max)	0 (-3,1-+3,5)
Diagnóstico oncológico n (%)	
Leucemia	18 (66)
Tumor SNC	4 (15)
Otros tumores	5 (19)
Estado nutricional n (%)	
Eutrófico	9 (33)
Riesgo desnutrición	5 (19)
Desnutrición	3 (11)
Sobrepeso	7 (26)
Obesidad	3 (11)

En la figura 1 se muestran los valores obtenidos de la comparación entre calorimetría indirecta *versus* OMS y entre calorimetría indirecta *versus* Schofield, con valores de p.

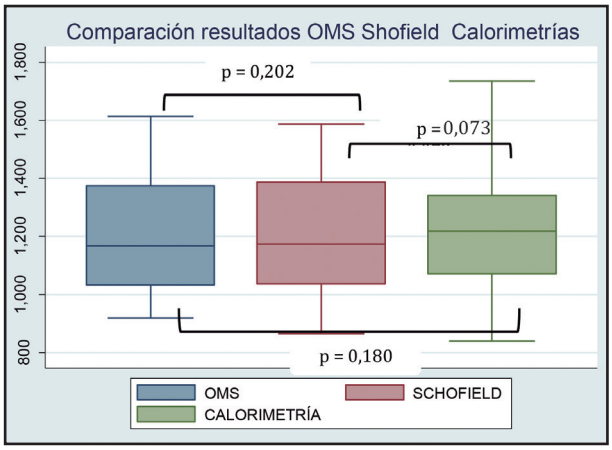

Figura 1.

Comparación entre calorimetría indirecta *versus* OMS y entre calorimetría indirecta *versus* Schofield, con valores de p.

No se encontraron diferencias estadísticamente significativas entre los resultados obtenidos por medición del gasto energético en reposo con calorimetría indirecta *versus* cálculo con fórmulas de Schofield (p = 0,07) y OMS (p = 0,18), respectivamente.

Se comparó el GER por los distintos métodos de medición, estratificado por tipo de diagnóstico oncológico y por estado nutricional, comparando los resultados obtenidos en pacientes eutróficos *versus* malnutrición por déficit (desnutrición y riesgo de desnutrición) y *versus* malnutrición por exceso (sobrepeso y obesidad). No se encontraron diferencias estadísticamente significativas en ninguno de estos grupos; sin embargo, al estratificar por edad sí se observó una diferencia estadísticamente significativa p = 0,04 (Tabla II).

Tal como se muestra en la tabla III, se calculó la concordancia entre calorimetría y Schofield, con coeficiente de correlación de concordancia de Lin = 79.4% (IC 65,2-93,6 p = 0.001), y calorimetría y OMS, con coeficiente de correlación de concordancia de Lin = 78% (IC 62,9-93,2 p = 0.001).

Al medir el GER con calorimetría indirecta y compararlo con la ecuación de la OMS, se observó una diferencia entre lo medido y lo estimado por esta fórmula de requerimientos calóricos de -23% a +27%. Nueve (33%) pacientes de 27 presentaron una diferencia mayor al 10% de los requerimientos calóricos estimados entre ambos métodos. Al comparar los resultados de la calorimetría indirecta y la ecuación Schofield (peso y talla) se observó una diferencia entre lo medido y lo estimado por esta fórmula de requerimientos calóricos de -16% a +25%. Trece (48%) pacientes de 27 presentaron una diferencia mayor al 10% de los requerimientos calóricos estimados entre ambos métodos.

Tabla III. Concordancia entre medición de GER por calorimetría indirecta *versus* ecuación de la OMS y de Schofield (peso y talla)

	CCC Lin	IC 95%	Valor p
Calorimetría *vs.* OMS	78%	62,9-93,2	0.001*
Calorimetría *vs.* Schofield	79,4%	65,2-93,6	0.001*

Valor p significativo: concordancia significativa.*

DISCUSIÓN

En el presente estudio no se encontraron diferencias estadísticamente significativas entre la medición del GER con calorimetría indirecta *versus* las ecuaciones de Schofield y la OMS, ni al estratificarlo por tipo de diagnóstico oncológico ni por estado nutricional.

En este estudio la mayoría de los pacientes son eutróficos y solo 3/27 (11%) de nuestra población estudiada presentan obesidad o desnutrición. Al comparar los resultados obtenidos entre la medición del GER con calorimetría indirecta *versus* las ecuaciones de Schofield y la OMS en pacientes eutróficos *versus* malnutrición por déficit y *versus* malnutrición por exceso no se encontraron diferencias estadísticamente significativas. Sin embargo, esta comparación tiene un valor p muy cercano a la significancia estadística, lo que puede estar influenciado por el tamaño muestral pequeño y es importante de considerar, ya que el gasto energético en reposo estimado por ecuaciones predictivas tiene baja relación con los obtenidos por calorimetría indirecta

Tabla II. Medianas de gasto energético de reposo medido por calorimetría indirecta y calculado por fórmulas predictivas, según diagnóstico nutricional, diagnóstico oncológico y edad

	Calorimetría (kcal/día) p50 (min-max)	Ecuación OMS (kcal/día) p50 (min-max)	Ecuación Schofield (kcal/día) p50 (min-max)	Valor p
Estado nutricional				0,056
Eutrófico	1.310 (839-1.453)	1.341 (919-1.604)	1.326 (865-1.587)	
Malnutrición por déficit	1.134 (1.006-1.629)	1.073 (949-1.386)	1.088 (909-1.433)	
Malnutrición por exceso	1.294 (1.044-1.735)	1.246 (935-1.614)	1.215 (877-1.560)	
Diagnóstico oncológico				0,1739
Leucemia	1.269 (1.044-1.735)	1.191(935-1.614)	1.205 (877-1.587)	
Tumor SNC	1.064 (839-1.629)	1.092 (919-1.386)	1.120 (865-1.433)	
Otros	1.105 (1.031-1.349)	1.145 (949-1.359)	1.159 (909-1.344)	
Edad				0,040*
< 10 años	1.084 (839-1.570)	1.048 (919-1.555)	1.040 (865-1.511)	
≥ 10 años	1.327 (1.070-1.735)	1.366 (1.145-1.614)	1.366 (1.159-1.587)	

*Comparación de medianas con test de Mann-Whitney. *Valor p significativo*

debido a las diferencias en composición corporal y masa magra de los pacientes (19-21).

El nivel de concordancia entre la medición del gasto energético en reposo por calorimetría indirecta *versus* ecuaciones de Schofield y la OMS es del 79,4% y 78% respectivamente, lo que concuerda con la diferencia encontrada entre lo medido por calorimetría y lo estimado por fórmula de Schofield, de -16% a +25%, y la OMS, de -23% a +27%.

Este nivel de concordancia, menor al 80% en ambos casos, es insuficiente, considerando que para efectos de este estudio se estableció como punto de corte clínicamente relevante un coeficiente de concordancia del 90% entre la medición del gasto energético en reposo por calorimetría indirecta *versus* las fórmulas de Schofield y la OMS, lo que no se cumple.

Con ambas ecuaciones para estimación del GER existe en más de un 20% de los casos una sobre o subestimación de sus requerimientos energéticos, lo que se traducirá en un inadecuado aporte de nutrientes en estos pacientes.

Además, es muy importante considerar que se trata de una población de pacientes con patología de alto riesgo nutricional y una diferencia menor o mayor al 10% de los aportes nutricionales se considera como hipo o sobrealimentación y puede incidir de forma negativa en su estado nutricional, con potenciales complicaciones metabólicas, infecciosas, mayor morbimortalidad y estadía hospitalaria.

Una limitación del estudio fue el tamaño muestral pequeño y que la mayoría de los pacientes se encontraban en fase de mantención de su tratamiento, por lo que se valoran los resultados como una primera aproximación al tema y es necesario continuar realizando estudios de concordancia para sustentar estos resultados.

Sin embargo, este estudio, al mostrar que no existe una concordancia entre la medición del gasto energético en reposo medido con calorimetría indirecta *versus* su estimación con ecuaciones de Schofield y de la OMS, en una población de alto riesgo nutricional como los pacientes pediátricos con patología oncológica, que con frecuencia presentan alteraciones en su alimentación y en su estado nutricional, contribuye a reforzar la importancia de utilizar la calorimetría indirecta para la determinación de los requerimientos energéticos en estos pacientes. De esta manera, se avanza hacia la incorporación de la calorimetría indirecta como un elemento fundamental dentro de la evaluación nutricional de los pacientes oncológicos pediátricos en las distintas fases de su tratamiento, para otorgar un adecuado, óptimo y exacto soporte nutricional, de acuerdo a sus necesidades, disminuir la comorbilidad asociada a un aporte nutricional inadecuado ya sea por déficit o por exceso, promover un adecuado crecimiento y desarrollo y optimizar su calidad de vida.

En conclusión, no existe concordancia suficiente (≥ 90%) que permita confiar en las ecuaciones de Schofield y la OMS, por lo que se debiera utilizar la calorimetría indirecta para la determinación de los requerimientos energéticos en pacientes pediátricos con patología oncológica.

Se necesitan más estudios, con mayor tamaño muestral y que consideren la composición corporal, en esta población de pacientes.

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Trabajo Original

Pediatría

Densidad mineral ósea en niños celiacos. Indicaciones de estudio y efecto de la exclusión del gluten de la dieta

Analysis of bone mineral density in children with celiac disease. Densitometry indications and effect of gluten-free diet

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Resumen

Introducción: una de las principales manifestaciones extradigestivas de la enfermedad celiaca es la disminución de la densidad mineral ósea (DMO). La densitometría ósea realizada con DXA es el método de elección para la valoración de la DMO. Las indicaciones de su uso en niños celiacos son controvertidas.

Objetivos: analizar la DMO y diversas variables clínicas-analíticas en niños celiacos cuando son diagnosticados y tras realizar una dieta sin gluten. Definir un perfil de pacientes con mayor probabilidad de presentar afectación de la DMO en base a diversas características individuales, para realizar indicaciones de DXA.

Métodos: estudio realizado en 24 niños celiacos (12 varones) (edad: 8,7 ± 3,3 años). Mediante DXA se determinó su DMO al diagnóstico y tras realizar dieta sin gluten. La DMO fue comparada en cada paciente en los dos momentos del estudio y al diagnóstico entre grupos de pacientes estratificados según criterios de gravedad dependientes de variables clínicas, analíticas e histológicas.

Resultados: la DMO fue normal en todos los pacientes estudiados en el momento del diagnóstico y tras realizar tratamiento, sin que se apreciaran diferencias entre esos dos momentos del análisis. Los niños que presentaban sintomatología cuando eran diagnosticados de enfermedad celiaca tuvieron menor DMO en columna y fémur que los asintomáticos. La calcemia tuvo correlación inversa con el tiempo de evolución de la enfermedad antes de su diagnóstico.

Conclusiones: en general, en nuestro medio, no está indicada la realización de estudio de la mineralización ósea en los niños celiacos, salvo cuando haya existido una evolución clínica prolongada antes del diagnóstico.

Palabras clave:

Exploración con absorciometría de rayos X de energía dual. Densidad mineral ósea. Enfermedad celiaca. Niños 0 a 18 años.

Abstract

Introduction: one of the main extradigestive manifestations of celiac disease is the decrease in bone mineral density (BMD). Bone densitometry performed with DXA is the method of choice for BMD assessment. Indications for its use in celiac children are controversial.

Objective: analyzing BMD and various clinical-analytical variables in celiac children when diagnosed and after a gluten-free diet. Define a profile of patients who are more likely to present BMD involvement based on several individual characteristics, to perform DXA indications.

Methods: study performed in 24 celiac children (12 boys) (age: 8.7 ± 3.3 years). Their BMD was determined at diagnosis and after a gluten-free diet using DXA. The BMD was compared in each patient in the two moments of the study and at the moment of diagnosis between groups of patients stratified according to severity criteria dependent on clinical, analytical and histological variables.

Results: BMD was normal in all patients studied at the time of diagnosis and after treatment, with no difference between the two moments of the analysis. Children who presented symptomatology when diagnosed with celiac disease had lower spine and femur BMD than asymptomatic ones. The calcemia had an inverse correlation with the time of evolution of the disease before its diagnosis.

Conclusions: in general, in our setting, the study of bone mineralization in celiac children is not indicated, unless there has been a prolonged clinical course before diagnosis.

Key words:

DXA Scan. Bone mineral density. Celiac disease. Children.

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INTRODUCCIÓN

La enfermedad celiaca (EC) es una enfermedad sistémica inmunomediada, desencadenada por el consumo de gluten y prolaminas, en individuos genéticamente predispuestos (1). Su prevalencia es muy variable dependiendo del área geográfica (2,3) y se caracteriza por la presencia de una gran variedad de manifestaciones clínicas, aunque la forma clásica de la enfermedad incluye, fundamentalmente, sintomatología digestiva (diarrea, esteatorrea, etc.). Sin embargo, es cada vez más frecuente el diagnóstico de pacientes con formas no clásicas o extradigestivas de EC (4). Uno de los síntomas extradigestivos característicos es la disminución de la densidad mineral ósea. Más del 70% de pacientes con EC tienen una pérdida de masa ósea en la edad adulta (5).

La densitometría ósea mediante absorciometría dual de rayos X (DXA) es la técnica de elección para determinar la salud del hueso y su realización puede tener indicación en el momento del diagnóstico y durante el seguimiento de enfermedades crónicas en las que la salud ósea está en riesgo, como sucede en la EC. Aunque en la edad adulta plantea menos dudas la necesidad de valorar la mineralización ósea en pacientes celiacos (6), esta indicación es más controvertida en niños con EC.

El presente estudio fue planteado con el objetivo de obtener información sobre la densidad mineral ósea de los niños celiacos cuando son diagnosticados y conocer el efecto que provoca sobre ella la realización de una dieta sin gluten. Además, se ha pretendido definir también un perfil de pacientes con mayor probabilidad de presentar afectación de la densidad mineral ósea en base a diversas características clínicas, analíticas y dependientes de la anatomía patológica, de forma que sea posible realizar indicaciones de densitometría ósea en pacientes celiacos en la edad pediátrica en función de sus características individuales.

MATERIAL Y MÉTODOS

Estudio observacional, analítico, longitudinal y prospectivo realizado en los pacientes entre tres y 14 años diagnosticados de EC en la consulta de gastroenterología infantil de un hospital de tercer nivel entre agosto de 2010 y noviembre de 2013.

En el momento del diagnóstico se recogió información sobre: forma de presentación clínica de la enfermedad y tiempo de evolución, datos antropométricos, genética de EC y diversos parámetros analíticos (hemoglobina, hierro, ferritina, calcio, fósforo, fosfatasa alcalina, serología de celiaquía) de los pacientes. La densidad mineral ósea fue valorada en dos momentos evolutivos, cuando fueron diagnosticados de enfermedad celiaca (M1) y tras un periodo de exclusión del gluten de la dieta de entre seis y 12 meses (M2).

La valoración antropométrica incluyó la medición de peso, talla, índice de masa corporal (IMC) y los z-scores de dichos parámetros. Los z-score se calcularon utilizando tablas de referencia nacionales de Fernández (2011) mediante la fórmula: z-score = (medida-media)/desviación estándar (7).

El análisis del metabolismo mineral óseo y férrico se determinó con método de espectrofotometría en analizador Cobas® 8000 de Roche. Para el estudio serológico se utilizaron kits EliA de ImmunoCap, del fabricante ThermoFisherScientific, cuyo punto de corte de normalidad para los anticuerpos antigliadina deaminada (anti-GPD) es de 10 mg/l y para los anticuerpos antitransglutaminasa (AC_TGt) es de 3 UI IgA/ml. Los anticuerpos antiendomisio (EMA) se analizaron mediante Atom Biosystems Barcelona y se consideraron títulos positivos a partir de una dilución 1/5. Para el estudio genético se manejó el kit de PCR-SSP™ para HLA-DQB1* de One Lambda. La clasificación por la que se estratificaron las biopsias digestivas fue la de Marsh modificada (8).

El diagnóstico de EC se realizó utilizando los criterios de la European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) vigentes en el momento en que los pacientes fueron atendidos en la consulta. Antes del año 2012 se aplicaron los criterios establecidos por la ESPGHAN en 1990 (9) y a partir de 2012 se utilizaron los criterios implantados por Husby y cols., que prescinden de biopsia duodenal si los pacientes cumplen todos los requisitos clínicos-analíticos (1).

La valoración de la densidad mineral ósea (DMO) se realizó mediante técnica de absorciometría de rayos X de energía dual (DXA), utilizando un densitómetro de la marca Lunar Prodigy Primo® (GE Healthcare) con software enCORE® 2009 12.1. Se realizaron tres mediciones: cuerpo total, fémur izquierdo y columna lumbar. De todas las variables resultantes se seleccionaron: la densidad mineral ósea de cuerpo total con exclusión de la cabeza (TBLH_DMO), el z-score de TBLH_DMO, el z-score de la DMO a nivel de columna lumbar (L1-L4_Z) y la DMO total a nivel del fémur (Total_fem).

Se estratificó la muestra dependiendo de si los pacientes presentaban o no características que podían implicar una mayor gravedad del proceso y, por tanto, un mayor riesgo de afectación ósea. De entre todas las variables analizadas solo fueron útiles para establecer dos grupos dicotómicos con suficiente número de pacientes la presencia de manifestaciones clínicas al diagnóstico, un tiempo de evolución al diagnóstico mayor a un año, niveles de ferritina inferiores a 15 ng/ml, IMC < -1DS, serología de EC con AC_TGt mayores de diez veces los valores normales, HLA-DQ2 homocigoto y atrofia vellositaria total (IIIC de la clasificación de Marsh modificada). Los diversos parámetros de mineralización ósea obtenidos con DXA en el momento del diagnóstico fueron comparados entre el grupo de pacientes que presentaban los mencionados factores de riesgo y el resto de los pacientes incluidos en el estudio.

Para realizar el análisis estadístico se utilizó el paquete estadístico SPSS versión 18. En la estadística descriptiva se usaron: media, desviación estándar (DS), frecuencias y rangos. Para el análisis de las variables cuantitativas dependientes e independientes se utilizaron el test de la t de Student cuando la distribución era normal y un test no paramétrico cuando no lo era (test de Wilcoxon o U de Mann-Whitney). Para conocer la correlación entre variables cuantitativas se utilizó el test de correlación de Pearson. Para todos los test se consideró que existía una diferencia significativa si el valor de $p < 0,05$.

En la realización del estudio se siguieron las normas de Helsinki de 2008 para la realización de estudios en humanos y se obtuvo el consentimiento informado de los padres de todos los pacientes (10).

RESULTADOS

Se incluyeron en el estudio un total de 24 niños celiacos (50% varones) con una edad de 8,7 ± 3,3 años. La media de edad para los varones fue de 10,1 ± 2,3 años y para las niñas, de 7,4 ± 3,6 años.

DESCRIPCIÓN DE LA MUESTRA EN EL MOMENTO DEL DIAGNÓSTICO DE LA ENFERMEDAD CELIACA

El 79,2% de los pacientes presentaba algún síntoma (vómitos, dolor abdominal, distensión abdominal, diarrea, estreñimiento, hiporexia o fallo de medro), mientras que el 20,8% restante se encontraba asintomático. El 62,5% de los pacientes iniciaron las manifestaciones clínicas ≤ 1 año antes de acudir a la consulta.

En el momento del diagnóstico los z-score del peso e IMC para todos los pacientes de la muestra se encontraron dentro de la normalidad. En cuanto al z-score de talla, existían dos pacientes con z-score < -2 DS. Las niñas tenían un z-score de peso y talla más bajo que los niños al diagnóstico, lo que se observó con resultados significativos (Tabla I).

El 25% de los pacientes presentaba sideremia menor de 60 mcg/dl. El 25% de los pacientes presentaba ferritina menor de 15 ng/ml. Se encontraron tres pacientes con cifras bajas de fosfatasa alcalina (FA). La hemoglobina, calcemia y fosforemia fueron normales en todos los niños. Los valores medios de los parámetros analíticos en el momento del diagnóstico se muestran en la tabla II.

El 100% de los pacientes tenía niveles de AC_TGt positivos al diagnóstico. El 70,8% de ellos presentaba cifras diez veces superiores a las normales. El 70,1% de los pacientes tuvo anti-DGP IgA positivos y el 79,2% de los pacientes, anti-DGP IgG positivos (> 10 mg/dl). En los seis pacientes en los que se estudiaron los EMA, estos fueron positivos.

El 95,4% de los niños presentó al menos un alelo que codificaba HLA-DQ2 y en un paciente se encontró la genética HLA-DQ 8 (4,7%). El 28,6% eran HLA-DQ2 homocigotos.

Tabla I. Variables antropométricos al diagnóstico de enfermedad celiaca. Muestra total y distribución por sexos

Variables	Niños (n = 12)	Niñas (n = 12)	Total (n = 24)
Peso (kg)	33,0 ± 10,1	21,7 ± 8,37	27,4 ± 11
Talla (cm)	139,5 ± 13,5	118,2 ± 19,5	128,9±20
IMC (kg/m^2)	16,5 ± 2	14,9 ± 1,2	15,7± 1,8
ZS_Peso	- 0,3 ± 0,7	- 1 ± 0,48	- 0,7 ± 0,7
ZS_Talla	- 0,2 ± 1,1	- 1,1 ± 0,88	- 0,6 ± 1,1
ZS_IMC	- 0,4 ± 0,6	- 0,8 ± 0,48	- 0,6 ± 0,6

IMC: índice de masa corporal; ZS: z-score.

Tabla II. Variables analíticas al diagnóstico de enfermedad celiaca. Muestra total y distribución por sexos

Variables	Niños (n = 12)	Niñas (n = 12)	Total (n = 24)
Hb (g/dl)	14 ± 1,3	13 ± 0,73	14 ± 1,1
Fe (mcg/dl)	78 ± 28	80 ± 29,9	79 ± 28
Ferritina (ng/ml)	37 ± 28	26 ± 14,2	31 ± 22
Ca (mg/dl)	9,6 ± 0,5	9,8 ± 0,57	9,7 ± 0,5
P (mg/dl)	4,8 ± 0,4	5,1 ± 0,31	5 ± 0,4
FA (U/l)	482 ± 159	376 ± 124	429 ± 148

Hb: hemoglonina; Fe: hierro; Ca: calcio; P: fósforo; FA: fosfatasa alcalina.

El 41,7% del total de los pacientes tenían en la biopsia duodenal un grado IIIC de atrofia vellositaria según la clasificación de Marsh modificada. En cinco pacientes no se realizó biopsia duodenal porque cumplieron los nuevos criterios de la ESPGHAN para el diagnóstico de EC.

HALLAZGOS DEL ESTUDIO CON DXA

Los distintos parámetros de la DXA en el momento del diagnóstico y tras la realización de una dieta sin gluten se muestran en la tabla III. Los niños incluidos en el estudio presentaron niveles similares en dichos parámetros antes y después del tratamiento. Todos los pacientes tenían una mineralización ósea normal en los dos momentos del estudio.

CORRELACIÓN ENTRE VARIABLES CUANTITATIVAS

Las siguientes variables cuantitativas fueron correlacionadas entre sí: meses de evolución clínica antes del diagnóstico, peso, talla, IMC, z-scores de los mismos, parámetros analíticos del metabolismo del hiero y calcio/fósforo, niveles de AC_TGt, anti-DGP IgA, anti-DGP IgG, TBLH_DMO, TBLH_Z y L1-L4_Z Total_fem. Los resultados se muestran en la tabla IV.

Destaca que el tiempo de evolución hasta el diagnóstico se correlacionó de forma negativa (r = -0,523) con las cifras de calcio (p = 0,031).

COMPARACIÓN DE PARÁMETROS DE LA DXA EN FUNCIÓN DE ALGUNAS CARACTERÍSTICAS CLÍNICAS Y DE LOS RESULTADOS DE ALGUNOS EXÁMENES COMPLEMENTARIOS

La comparación de los resultados de la DXA entre los grupos obtenidos al dividir la muestra de acuerdo a los parámetros clíni-

Tabla III. Variables de la DXA al diagnóstico de enfermedad celiaca (M1) y tras realización de una dieta sin gluten (M2). Muestra total y distribución por sexos

	Niños (n = 12)		Niñas (n = 12)		Total (n = 24)	
Variables	**M1**	**M2**	**M1**	**M2**	**M1**	**M2**
TBLH_DMO	0,8 ± 0,1	0,837 ± 0,1	0,7 ± 0,13	0,692 ± 0,14	0,7 ± 0,1	0,746 ± 0,2
TBLH_Z	0,1 ± 0,8	0,516 ± 0,9	- 0,6 ± 1	- 0,47± 0,92	- 0,1 ± 0,9	- 0,99 ± 1
L1-L4_Z	- 0,5 ± 1	- 0,08 ± 0,9	- 0,6 ± 0,91	- 0,68 ± 0,99	- 0,5 ± 0,9	- 0,44 ± 1
Total_fem	0,8 ± 0,2	0,917 ± 0,2	0,7 ± 0,14	0,712 ± 0,15	0,8 ± 0,2	0,788 ± 0,2

TBLH_DMO: densidad mineral ósea corporal total exceptuando el cráneo (g/cm^2); TBLH_Z: z-score de TBLH; L1-L4_Z: z-score de densidad mineral ósea de la región lumbar L1-L4; Total_fem: densidad mineral ósea total del fémur (g/cm^2).

Tabla IV. Correlación (valor r) entre variables clínicas, analíticas, serológicas y parámetros de DXA, obtenidos al diagnóstico de la enfermedad celiaca

Var	T. evol	ZS_IMC	Anti-DPG IgA	Anti-DPG IgG	AC_TG	TBLH_DMO	TBLH_Z	L1-L4_Z	Total_fem
Hb	0,191	0,313	0,146	-0,088	-0,325	0,579†	0,570*	0,179	0,417*
Fe	0,074	0,471*	- 0,462*	-0,377	-0,265	0,061	-0,212	-0,246	-0,038
Fer	0,022	-0,023	-0,104	- 0,505*	-0,513*	0,542†	0,281	0,066	0,496*
Ca	- 0,523*	-0,274	0,034	-0,016	-0,238	-0,331	-0,074	-0,336	-0,412
P	-0,449	-0,029	0,025	0,409	-0,318	-0,47	-0,464	-0,692*	-0,623*
FA	0,455	0,199	0,017	-0,029	0,052	0,474	0,582*	0,336	0,407

*Hb: hemoglobina (g/dl); Fe: hierro (mcg/dl); Fer: ferritina: (ng/ml); Ca: calcio (mg/dl); P: fósforo (mg/dl); FA: fosfatasa alcalina (U/L); T. evol: tiempo de evolución de la clínica hasta M1; anti-DPG IgA: anticuerpos antigliadina deaminada IgA; anti-DPG IgG: anticuerpos antigliadina deaminada IgG; AC_TG: anticuerpos antitransglutaminasa; TBLH_DMO: densidad mineral ósea corporal total exceptuando el cráneo (g/cm2); TBLH_Z: Z-score de TBLH; L1-L4_Z: Z-score de densidad mineral ósea de la región lumbar L1-L4; Total_fem: densidad mineral ósea total del fémur (g/cm^2). *p < 0,05; †p < 0,01.*

cos y dependientes de los exámenes complementarios que implicaban supuestamente mayor gravedad se muestran en la tabla V.

Los pacientes que tuvieron síntomas en el momento del diagnóstico tuvieron niveles significativamente más bajos en el L1-L4_Z y en la DMO total del fémur con respecto a los que estaban asintomáticos. No se encontraron diferencias estadísticamente significativas en los parámetros de la DXA para el resto de grupos de pacientes.

DISCUSIÓN

La EC es una enfermedad sistémica inmunomediada, desencadenada por el consumo de gluten en individuos genéticamente predispuestos (1). En niños se caracteriza por la presencia de clínica típica de malabsorción, pérdida de masa muscular, falta de apetito, distensión, diarrea, esteatorrea y fallo de medro. Sin embargo, como ocurre entre los pacientes adultos, en los que destacan las formas clínicas oligosintomáticas con menor repercusión serológica e histológica que la descrita clásicamente en la infancia (11), es cada vez más frecuente el diagnóstico de niños con formas no clásicas u oligosintomáticas de EC (4). Uno de los síntomas extradigestivos característicos es la disminución de la densidad mineral ósea. Más del 70% de pacientes con EC tienen una pérdida de masa ósea en la edad adulta (5). En el estado de salud ósea juega un papel importante la ingesta de calcio. Los aportes recomendados de dicho mineral no se alcanzan en el 75% de niños y adultos de la población española (12). A su vez, en la enfermedad celiaca existe una disminución de la absorción de calcio. Ambos factores implican una situación de riesgo para la salud del hueso del niño celiaco, que es un hueso en formación y desarrollo (13).

Nuestro estudio fue planteado para conocer el estado de la densidad mineral ósea de los niños celiacos cuando son diagnosticados y observar qué modificaciones se producían en ella tras el tratamiento con una DSG. Además, se describieron diversas características de los pacientes, con el fin de conocer si alguno de los subgrupos con mayor gravedad teórica clínica-analítica-anatomopatológica tenía menor DMO, de forma que fuera posible realizar recomendaciones sobre la indicación de estudio con DXA en niños con EC.

La densitometría ósea mediante absorciometría dual de rayos X (DXA) es la técnica de elección para la detección de la densidad mineral ósea (DMO) y, por lo tanto, para determinar su afectación (14). Recientemente, se han cambiado los términos osteoporosis y osteopenia en pediatría por el de "baja densidad mineral ósea" (LBMD) cuando la puntuación z sea menor a -2 DS (14). Existen otros procedimientos utilizados para evaluar la DMO

Tabla V. Comparación de las distintas variables con perfil de mayor gravedad con las variables de la DXA

	L1-L4_Z		TBLH_Z		Total_fem	
	Media ± DS	Media ± DS	Media ± DS	Media ± DS	Media ± DS	Media ± DS
Variables	Sí	No	Sí	No	Sí	No
Clínica	-0,95 ± 0,95	0,22 ± 0,47* (p = 0,03)	-0,27 ± 1,03	0,32 ± 0,19 (p = 0,055)	0,73 ± 0,17	0,88 ± 0,12* (p = 0,036)
Diarrea	-0,63 ± 1,21	-0,76 ± 0,91	0,78 ± 1,30	-0,29 ± 0,75	0,76 ± 0,26	0,76 ± 0,14
Evol clínica ≤ 12 m	-0,5 ± 0,85	-1,10 ± 1,08	0,4 ± 0,58	-0,30 ± 1,23	0,74 ± 0,15	0,79 ± 0,20
IMC ZS < -1	-1,25 ± 0,83	-0,59 ± 0,97	-1,25 ± 0,83	-1,25 ± 0,83	0,63 ± 0,12	0,79 ± 0,16
Ferritina ≤ 15 ng/ml	- 1,02 ±1,14	- 0,67 ± 0,94	-0,51 ± 0,98	-0,06 ± 0,92	0,68 ± 0,16	0,79 ± 0,17
ACTG > 10 VN	-0,65 ± 0,93	- 0,9 ± 1,10	-0,20 ± 1,10	0,08 ± 0,35	0,76 ± 0,18	0,76 ± 0,15
DQ2 homocigoto	-0,57 ± 0,79	-0,78 ±1,09	-0,36 ± 1,28	0,02 ± 0,89	0,72 ± 0,14	0,77 ± 0,19
Bx Marsh IIIC	-0,93 ± 1,06	-0,22 ± 0,91	-0,10 ± 0,58	0,42 ± 0,82	0,75 ± 0,12	0,83 ± 0,21

*L1-L4_Z: z-score de densidad mineral ósea de la región lumbar L1-L4; TBLH_Z: z-score de densidad mineral ósea corporal total con exclusión de la cabeza; Total_fem: densidad mineral ósea total del fémur (g/cm2); IMC ZS < -1: z-score de IMC < -1; ACTG > 10 VN: cifras de anticuerpos antitransglutaminasa tisular > a diez veces los valores normales; Bx: biopsia duodenal. *p ≤ 0,05.*

como la radiografía convencional, la radiogrametría, la absorciometría radiográfica simple (SXA), la tomografía computarizada cuantitativa espinal y periférica (QCT/pQCT), el ultrasonido cuantitativo (QUS) y la resonancia magnética. Estas técnicas difieren en su precisión, exactitud y capacidad discriminatoria y en su metodología, disponibilidad y utilidad en la práctica clínica (15). La DXA es la que ha demostrado mejor correlación entre los hallazgos en la DMO y el riesgo de fractura. Asimismo, es la que posee más tablas de referencias en población pediátrica. Las QCT aportan mucha información así como radiación, por lo que su uso no está indicado en la infancia. Así bien, recientemente se han establecido unas recomendaciones generales y unos protocolos para minimizar la exposición a la radiación, lo que se consigue realizando una correcta calibración y análisis de los resultados con el *software* apropiado para niños (16). La ultrasonografía (QUS) es una técnica fácil, rápida, barata e inocua y algunos autores como Alonso Franch y cols. abogan por la realización como *screening* de LBMD (17).

La International Society for Clinical Densitometry (ISCD) indica que la DXA es el método preferido para la evaluación de la densidad mineral ósea, seleccionando la columna vertebral y el análisis corporal total con exclusión de la cabeza como las mejores zonas para el estudio. El intervalo mínimo para realizar seguimiento densitométrico es de 6-12 meses. Existen bases de datos con valores de normalidad en distintas situaciones de edad, sexo, raza y programas informáticos pediátricos que analizan estos resultados (14). La DXA puede ser útil en la evaluación del estado óseo en diferentes enfermedades crónicas y es recomendable su realización en aquellas patologías que cursan con disminución de la DMO por distintos mecanismos y en las que el riesgo de fractura sea alto. La evaluación ósea y el diagnóstico de LBMD es útil para el inicio de un tratamiento precoz y la prevención de fracturas en la edad adulta.

En nuestro estudio, los niños con enfermedad celiaca tenían una densidad mineral ósea normal en el momento en el que fueron diagnosticados de dicha enfermedad.

Hay numerosos estudios en pacientes adultos celiacos que evalúan el estado del hueso y el riesgo de fracturas al diagnóstico de la enfermedad (5), pero no son tantos los realizados en población pediátrica (18-21).

En el año 1993, Mora y cols. ya se empezaron a preocupar por el estado de salud ósea de los niños celiacos y evaluaron la DMO radial de 33 niños en el momento del diagnóstico y después de que consumieran una dieta sin gluten, observando cifras más bajas de DMO en los celiacos que en los pacientes control al diagnóstico y cómo con el tratamiento mejoraba más su DMO que la de los controles (18). En 2001, el mismo autor estudió a 19 niños celiacos con un diseño similar y observó la mejoría de la DMO con la DSG. Además, valoró la FA y el telopéptido N-terminal del colágeno tipo I, de los cuales detectó cifras más bajas en los celiacos (19). En otro estudio más reciente fue valorada la DMO de 54 niños celiacos a la vez que se estudiaron los niveles de vitaminas K y D, y se observaron LBMD en el 10-20% de los pacientes al diagnóstico, independientemente de los síntomas que presentaban, y deficiencias en las vitaminas liposolubles, con mejoría de las vitaminas tras la DSG (20). En el estudio de Kuloğlu Z y cols., realizado en 109 niños celiacos, se detectó una baja DMO en aproximadamente un 25% del total (21).

El hecho de encontrar en la literatura evidencias de LBMD en enfermos celiacos en el momento del diagnóstico en una proporción variable, aunque no desdeñable, podría alentarnos a añadir dentro de la batería de pruebas complementarias indicadas al diagnóstico de la enfermedad celiaca la realización de una DXA a todos estos niños, como recomendaban Pietzak en 2005 o la International Society for Clinical Densitometry (ISCD) en 2007 (22,23). El presente estudio, sin embargo, demuestra que en

nuestro medio los niños con enfermedad celiaca tienen una densidad mineral ósea normal en el momento en el que son diagnosticados. El tipo de pacientes y el medio geográfico y económico en que son diagnosticados parecen jugar un papel importante en las características de su mineralización ósea. Es imprescindible, por tanto, tener en cuenta el perfil de los pacientes incluidos en los estudios. Así, por ejemplo, en el estudio de Kuloğlu Z y cols. presentaban retraso de las variables antropométricas cerca del 40% de los niños y alteraciones del perfil férrico incluso hasta el 80% de los pacientes (21). No es exagerado pensar que los datos de la densitometría podrían estar influidos por la gravedad de la clínica de los pacientes expuestos. En pacientes con características clínicas, analíticas, serológicas y anatomopatológicas similares a las de los pacientes de nuestro estudio no parece necesario realizar valoración de su DMO en el momento del diagnóstico, puesto que resulta improbable que se encuentre alterada.

La DMO de los pacientes de nuestra muestra no sufrió modificaciones significativas tras 6-12 meses de exclusión del gluten de la dieta. Esto es acorde con lo expuesto en 2001 por Kalayci y cols., los cuales observaron mejoría de la DMO pero sin que la LBMD se resolviera tras un año de DSG, especialmente en los pacientes sin manifestaciones gastrointestinales (24).

Por el contrario, en la literatura se describen numerosos estudios en los que se observa una recuperación de la salud del hueso tras un año de tratamiento. En un estudio realizado por Mora y cols., analizaron a 44 pacientes celiacos e hicieron un control tras un año de DSG a 25 de ellos y a controles sanos. Detectaron menor DMO en los pacientes celiacos en el momento del diagnóstico y observaron cómo tras un año de tratamiento ya no había diferencias significativas entre los grupos (25). Otro estudio posterior, realizado por el mismo grupo de trabajo, analizó a 22 pacientes y obtuvo resultados en la misma línea (26).

Es generalmente aceptado que una dieta libre de gluten parece promover un aumento de la DMO en niños celiacos con normalización progresiva de la mineralización ósea. Este hecho no pudo ser comprobado en el presente estudio puesto que nuestros pacientes no presentaban una DMO alterada al diagnóstico ni tras el tratamiento. En este hecho, parecen jugar, de nuevo, un papel muy importante las características particulares de cada paciente y el medio en el que están inmersos.

En nuestros pacientes se observó una correlación positiva entre los niveles de hemoglobina y FA con el TBLH_Z y negativa entre el Z_L1-L4 y la fosforemia. En ese mismo sentido, otros autores encontraron una correlación positiva entre el nivel de calcio y la DMO y el contenido mineral óseo (24). Asimismo, en un estudio italiano pudo observarse que las concentraciones plasmáticas de FA de los niños celiacos fueron significativamente inferiores a las de los sujetos control en el momento del diagnóstico, con un aumento de las cifras con el tratamiento (26).

Kavak y cols., en 2003, compararon a 34 niños celiacos no tratados y 28 que realizaban la DSG desde hacía un año, encontrando niveles más bajos de calcio y más altos de paratohormona en los pacientes no tratados (27). Estos hallazgos concuerdan con el hecho de que en nuestra serie también pudiera demostrarse una correlación negativa entre el tiempo de evolución y la calcemia, lo que sugiere quizás en su conjunto un mayor riesgo de afectación en la mineralización ósea en los paciente que llevaban un tiempo de evolución más prolongado antes del inicio de la dieta.

En los niños que presentaban un perfil clínico-analítico de mayor gravedad, como sería el compuesto por los pacientes con cifras más bajas de ferritina, con niveles de anticuerpos más elevados, genética con HLA-DQ2 homocigoto y con mayor atrofia vellositaria, tampoco se pudo observar que la DMO estuviera más afectada que en los que no tenían esas características. Solo se encontraron diferencias significativas en los pacientes que tuvieron síntomas en el momento del diagnóstico con respecto a los que estaban asintomáticos, teniendo los pacientes sintomáticos niveles más bajos de DMO en columna y fémur.

Vaquero y cols. encontraron una asociación entre la presencia de los alelos que codifican HLA-DQ2/8 en homocigosis y títulos más altos de anticuerpos y grados más avanzados de atrofia duodenal (28), al igual que otros autores que observaron una correlación entre el riego de tener EC y el presentar los genes de HLA-DQ2 en homocigosis, lo que podría ser útil con fines de seguimiento (29).

Hay estudios que observan cómo los pacientes con IMC más bajo y con daño histológico avanzado (Marsh IIIC) podían presentar mayor afectación ósea (30). Por el contrario, y coincidiendo con los resultados del presente estudio, Margoni D y cols. no pudieron encontrar ningún parámetro bioquímico con alto valor predictivo positivo para el desarrollo de LBMD (31).

Diversos estudios han detectado afectación de la DMO en los pacientes celiacos cuando son diagnosticados y han percibido mejoría en la evaluación tras un año de tratamiento (18-21,24-26). Por otro lado, otros autores refieren que tras dos años de DSG no está garantizada la normalización de la DMO y apuntan que no hay datos analíticos predictivos, por lo que indican la DXA a todos los niños celiacos (31). Finalmente, otros detectan que los pacientes que realizan mal la DSG (EMA positivos tras dos años del diagnóstico) pueden presentar LBMD (32) y se recomienda la DXA solo si la adherencia al tratamiento no fuera adecuada y después de un año del diagnóstico (5).

No parecen existir, por tanto, unas indicaciones claras de a qué pacientes y en qué momento debe realizarse este procedimiento diagnóstico. En las últimas recomendaciones de la ISCD (33), se reserva el uso de la DXA a situaciones en las que se sospeche que pueda haber fracturas y un beneficio para el paciente. Asimismo, se restringe su uso por aspectos de gestión. Concluyen que la DXA no está indicada de forma rutinaria para la valoración de niños celiacos y que únicamente se solicitará en aquellos que presenten una desnutrición grave, un importante estancamiento ponderoestatural y aquellos que no mejoren a pesar de una dieta estricta sin gluten. Nuestros hallazgos concuerdan en gran medida con estas recomendaciones puesto que de ellos se desprende que solo es previsible encontrar afectación en la DMO de los niños celiacos cuando las manifestaciones clínicas de la enfermedad están presentes y, probablemente, si el tiempo de evolución de estas manifestaciones es prolongado.

En cualquier caso, siguen siendo necesarios más estudios que aclaren definitivamente las características del paciente en el

que estaría indicado realizar la DXA, en cuánto tiempo realizar el seguimiento o conocer si estudiar la DMO sirve para conocer el pronóstico de padecer fracturas en la edad adulta.

CONCLUSIONES

En nuestro medio, los niños con enfermedad celiaca tienen una densidad mineral ósea normal al ser diagnosticados y esta no varía significativamente tras realizar una dieta sin gluten.

Cifras bajas de fosfatasa alcalina y altas de fósforo se correlacionan con menor DMO. Los niveles de calcio sérico son menores cuanto más larga haya sido la evolución clínica.

No parece necesario realizar valoración de la DMO en niños con características similares a las de los participantes de nuestro estudio. Únicamente podría estar indicada esta valoración en caso de que hayan presentado clínica de evolución prolongada antes del diagnóstico, ya que los niveles de calcio son menores cuanto más larga sea la evolución clínica.

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ARÁN

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Trabajo Original

Pediatría

Adolescents' eating behaviors and its relationship with family meals, body mass index and body weight perception

Comportamiento alimentario de los adolescentes y su relación con las comidas familiares, el índice de masa corporal y la percepción del peso corporal

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Abstract

Introduction: healthy diet is important because it affects wellbeing and health, and can reduce the risk of developing diseases or illnesses.

Objectives: this study aimed to analyze the relationship of eating behaviors with family meals, body mass index and body weight perception on adolescents.

Methods: data from 3,693 (1,723 boys) adolescents aged 14-17 years were collected. Adolescents were classified as realistic positive, realistic negative, overestimators, and underestimators, according to their eating habits and eating practices. Logistic regression models were used to analyze the data.

Results: having breakfast with family several times a week (OR = 1.42, $p < 0.001$) or everyday (OR = 1.64, $p < 0.001$), and having normal weight (OR = 1.74, $p < 0.001$) were associated with being realistic positive. On the contrary, realistic negatives were less likely to have breakfast with family several times a week (OR = 0.57, $p < 0.001$) or everyday (OR = 0.48, $p < 0.001$), and have normal weight (OR = 0.40, $p < 0.001$).

Conclusion: adolescents' eating behaviors are related to family meals, and body weight perception. Eating breakfast with family and having normal weight are positive factors in adolescents' awareness of good eating behaviors.

Key words:

Food. Eating behavior. Family. Breakfast.

Resumen

Introducción: una dieta saludable es importante porque afecta al bienestar y la salud y puede reducir el riesgo de desarrollo de enfermedades.

Objetivos: analizar la relación de los comportamientos alimentarios con las comidas familiares, el índice de masa corporal y la percepción del peso corporal de los adolescentes.

Métodos: se recogieron datos de 3.693 (1.723 niños) adolescentes de 14-17 años. Los adolescentes fueron clasificados como positivos realistas, negativos realistas, sobreestimadores y subestimadores, de acuerdo con sus hábitos alimenticios y prácticas alimentarias. Se utilizaron modelos de regresión logística para analizar los datos.

Resultados: desayunar con la familia varias veces a la semana (OR = 1,42, $p < 0,001$) o todos los días (OR = 1,64, $p < 0,001$) y tener un peso normal (OR = 1,74, $p < 0,001$) se ha asociado con ser positivo realista. Por el contrario, los negativos realistas eran menos propensos a desayunar con la familia varias veces a la semana (OR = 0,57, $p < 0,001$) o todos los días (OR = 0,48, $p < 0,001$) y tenían peso normal (OR = 0,40, $p < 0,001$).

Conclusión: los comportamientos alimentarios de los adolescentes están relacionados con las comidas familiares y con la percepción del peso corporal. Comer el desayuno con la familia y tener un peso normal son factores positivos en la conciencia de los adolescentes de buenos hábitos alimenticios.

Palabras clave:

Alimentos. Comportamiento alimentario. Familia. Desayuno.

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INTRODUCTION

During adolescence, a healthy diet is important because it affects wellbeing and health, and can reduce the risk of developing diseases or illnesses in adulthood; components such as these influence health related quality of life (1). Conversely, a poor diet quality or eating disturbances can contribute to an increased risk of obesity (2) and, consequently, can lead to risk factors such as heart disease and type 2 diabetes (3). An adolescent's eating behavior is the result of a myriad of influences (4). Multiple factors contribute to eating behaviors; these include family meals and dieting habits, weight status, and societal norms for thinness, which is related to body weight perceptions.

Adolescents are more likely to skip breakfast (5) and less likely to participate in family dinners (6,7), which may explain why adolescents are failing to meet dietary recommendations (8). The frequency of family meals has been associated with adolescents' health, including good nutritional intake (9) and promoting better outlook towards food and diet quality (10,11). On the other hand, the absence of family meals is related to a decreased diet quality, and unhealthy eating patterns (12).

Considering the existence of an eating transition from childhood to adolescence, which is characterized by changes in eating frequency, size portions, increased consumption of sugar sweetened beverages, calorie-dense, nutrient poor snacks and food away from home, it is expected that these eating behaviors have a relationship with weight status. A positive connection has been observed between eating and body mass index (BMI), as BMI predicted more restrained eating (13). Moreover, less frequent eating predicts gain in adiposity (14) and larger portion sizes of high-energy-dense foods are positively associated with BMI (15).

The body weight perception is a multidimensional concept that involves the self-perception of body size, feelings, beliefs and behaviors toward physical appearance (16). Because of the mass media influence and social and cultural norms, adolescents are constantly concerned about their body weight (17). The growing concern with body image has led many adolescents to change their eating habits, which can potentially be a serious threat on psychosocial development (18,19), nutritional status (17) and to the development of eating disturbances (20).

Therefore, this study aimed to analyze the connection between eating behaviors and family meals, body mass index and body weight perception on adolescents. Understanding the factors related to adolescents' eating behaviors is a valuable asset in matters of research, clinical practice and health promotion.

METHODS

PARTICIPANTS AND PROCEDURES

This is a cross-sectional study based on data from the Health Behavior in School-Aged Children (HBSC) Portuguese survey conducted in 2014 (21). HBSC is a World Health Organization collaborative study that is conducted every four years in nationally representative, school-based samples (22). Over 40 countries participate in the study. HBSC examines a number of health behaviors and lifestyles and their context in young people.

The Portuguese HBSC 2014 survey included a representative sample of 6,026 adolescents (2,872 boys) from 125 public schools, with weighted distributions reflecting the distribution of Portuguese students in grades 6, 8, and 10. For the present study, only students from grades 8 and 10 were selected, because they had better awareness of eating behaviors and body weight; therefore, students from grade 6 were excluded (n = 2,157). In addition, 71 adolescents did not report weight and/or height, 87 did not report their body weight perception, 19 did not report their eating habits, and were removed from the sample. The result was a final sample size of 3,693 adolescents (1,723 boys), aged 14-17 years (mean = 12.6 ± 1.1).

The survey consists of a self-administered questionnaire that is completed in public schools. The schools were randomly selected from a national list, which had been stratified by administrative regions. A detailed description of the methods and instrument can be found elsewhere (23,24). The administration of the surveys was conducted according to standard guidelines from the HBSC survey protocol (23,24) and was carried out by trained teachers during class time. All school administrators, legal guardians, and students gave their written consent. Adolescents' participation in the study was voluntary, anonymous, and there were no incentives for participation. Research was conducted in accordance with both the Ethical Committee of the Oporto Medical School and the National Data Protection System.

MEASURES

Adolescents' socio-demographic characteristics included sex, school grade, age, and parents' education (a proxy for socioeconomic status). Adolescents' eating habits were assessed by asking "describe your eating habits, do you eat well?". Response options were "never or almost never", "sometimes" and "always or almost always". The first two response options were combined as "sometimes or rarely" and the third option was named "almost always". For the second section, adolescents were asked to report their eating practices, measuring unhealthy food consumption by stating if they overate, ate very little, ate only what was available, and if it was difficult to stop eating. The response options were similar to the previous questions. A general eating practice score was created based on six possible eating habit responses. It was considered that adolescents who answered at least once "sometimes or rarely" did not have good eating practices and that the others did. Combining the adolescents' eating habits and their general eating practice score generated a new variable that was computed. This lead to the creation of four eating behavior profiles: a) realistic negative were those who did not have good eating practice and reported not having good eating habits; b) underestimators were those who had good eating practice, but reported not having good eating habits; c) overestimators were those who did not have good eating practice, but reported having

good eating habits; and d) realistic positive were those with good eating practice and reported having good eating habits.

The actual weight (to the nearest 0.5 kg) and height (to the nearest 0.5 cm) were also self-reported. Body mass index (BMI) was then calculated based on mass (kilograms) divided by height (m^2). Adolescents were placed into normal weight, overweight, and obese categories according to age- and sex-specific cut-off points proposed by the World Health Organization (25). The group of adolescents categorized as underweight was small, and that is the reason why this category was removed from the analysis and these adolescents were added into the normal weight category.

Body size perception was assessed by asking adolescents, "do you think your body is…?", with the response options "too thin", "a bit too thin", "about the right size", "a bit too fat", and "too fat", which were combined to be perceived as underweight ("too thin" and "a bit too thin"), normal weight and overweight ("a bit too fat", and "too fat"), respectively.

DATA ANALYSIS

Descriptive statistics are presented as means and standard deviation or percentages. Bivariate analysis between eating habits and eating practices were tested by Chi-squared or Fisher's exact test. The relationship between family meals, BMI categories and body weight perception with adolescents' profiles according to their eating habits and eating practices were tested by Chi-squared. Then, multiple binary logistic regressions were used to assess the extent to which factors were associated with each of the four adolescents' eating behaviors profile. Analyses were adjusted based on sex, age, and parents' education. Data analysis was performed using SPSS version 22, and the level of significance was set at 0.05.

Table I. Sample characteristics

	Total (n = 3,693)
Sex	
Boys	46.6
Girls	53.4
School grade (%)	
8 grade	61.2
10 grade	38.8
Age (M ± SD)	14.7 ± 1.1
Father's education (%)	
Low	55.9
Middle	26.7
High	17.4
Mother's education (%)	
Low	48.3
Middle	29.4
High	22.3
ZBMI (M ± SD)	0.00 ± 0.98
BMI category (%)	
Normal weight	78.0
Overweight	18.0
Obese	4.0
Body weight perception (%)	
Underweight	14.7
Normal weight	49.9
Overweight	35.4
I have good eating habits	
Sometimes or rarely	28.5
Almost always	71.5

BMI: body mass index. ZBMI: standarized BMI-score.

RESULTS

Adolescents' characteristics are presented in table I. Most adolescents had a normal weight (78%), but it is important to note that 22% were overweight or obese. However, only 49.9% classified themselves as normal weight. The majority of adolescents reported good eating habits as "almost always" (71.5%). Almost one quarter (24.4%) of adolescents misperceived their weight status (data not shown).

The relationship between eating habits and eating practices is represented in table II. Picking the response "almost always" concerning good eating habits was related to eating unhealthy food ($\chi^2[1] = 5.252$, $p = 0.022$) and eating very little ($\chi^2[1] = 47.347$, $p < 0.001$) less often.

The cross-tabulation between eating habits and eating practices was shown in table III. Those who "almost always" had good eating habits and good eating practices were classified as realistic positive (51.6%). In opposition, those who had good eating habits "sometimes or rarely" and did not have good eating practices were classified as realistic negative (9.6%). These two groups of adolescents were aware of their eating behaviors. On the other hand, 19.9% of the adolescents reported having good eating habits "almost always" but did not have good eating practices, and as such, they were classified as *overestimators.* Finally, there were 18.9% of adolescents classified as *underestimators*, who had good eating practices but stated that they had good eating habits only "sometimes or rarely".

The adolescents' eating behaviors profiles were related to family meals, BMI category and body weight perception. The results can be seen in table IV. Realistic positives and overestimators accounted for the higher proportion that had breakfast ($\chi^2[6] = 133.711$, $p < 0.001$) and dinner with their families ($\chi^2[6] = 53.230$, $p < 0.001$). The percentage of normal weight ($\chi^2[3] = 18.603$, $p < 0.001$) and perception of being normal weight ($\chi^2[6] = 152.624$, $p < 0.001$) were significantly higher among realistic positives and overestimators.

Results of the binary logistic regression analysis for the associations between adolescents' eating behaviors profile with family meals, BMI and body weight perception are shown in table V. Having breakfast with family several times a week (OR = 1.42, 95% CI: 1.20-1.68, $p < 0.001$) or every day (OR = 1.64, 95%

Table II. Relationship between self-report eating habits and eating practices

Eating practices	I have good eating habits		
	Sometimes or rarely	Almost always	p
I eat unhealthy food			0.022
Sometimes or rarely	91.8	93.9	
Almost always	8.2	6.1	
I overeat			0.470
Sometimes or rarely	88.4	89.2	
Almost always	11.6	10.8	
I eat very little			< 0.001
Sometimes or rarely	92.7	97.6	
Almost always	7.3	2.4	
I eat what is available			0.161
Sometimes or rarely	90.7	89.1	
Almost always	9.3	10.9	
I eat when food is available			0.153
Sometimes or rarely	91.6	93.0	
Almost always	8.4	7.0	
It is hard to stop eating			0.367
Sometimes or rarely	94.6	93.9	
Almost always	5,4	6.1	

Tested by Chi-squared or Fisher's exact test.

CI: 1.37-1.97, $p < 0.001$), and having a normal weight (OR = 1.74, 95% CI: 1.41-2.14, $p < 0.001$) were positively associated with being classified as realistic positive. On the contrary, realistic negatives were less likely to have breakfast with family several times a week (OR = 0.57, 95% CI: 0.43-0.75, $p < 0.001$) or every day (OR = 0.48, 95% CI: 0.34-0.67, $p < 0.001$), and have normal weight (OR = 0.40, 95% CI: 0.29-0.56, $p < 0.001$).

DISCUSSION

The purpose of this study was to analyze the relationship between perception of quality of eating behaviors, and family meals, body mass index and body weight perception on adolescents. There are several aspects of this study to highlight. First, having breakfast with family more often and being of normal weight were positively related with being classified as realistic positive (having good eating practices and being aware of them). On the other hand, having breakfast with family often and being of normal weight were negatively associated with being realistic negative (not having good eating practices and being aware of it). Second, adolescents classified as having good eating habits also reported eating unhealthy food and eating very little less often. Third, most adolescents were aware of their eating behaviors, but 38.8% misjudged their diet either positively or negatively.

The findings of this study confirm that family meals, essentially breakfast, are associated with adolescents' better eating behaviors, as previously observed in other studies (9,10). Findings are also consistent with research regarding the inverse relationship between family meal frequency and unhealthy eating patterns (12,26). This relationship might be due to the fact that family, mainly parents, influence their children's eating behavior by actively making food choices for the family (such as higher intake of fruit, whole grains, and fiber), serving as models for dietary choices and patterns, and using feeding practices to reinforce the development of healthy eating patterns and behaviors that they believe to be appropriate (9,27). Other than the benefits related with adolescents' dietary intake, breakfast consumption with family is also essential in obesity prevention, because those who have it are less likely to be overweight/obese (9,28,29). Therefore, breakfast consumption with family should be encouraged as a mean to promote adolescents' better eating behaviors, and prevent obesity. This is particularly important nowadays because adolescents are more likely to skip breakfast (5).

Dinner with family was not associated with adolescents' eating behaviors, as observed previously (9,30). However, these results were different from others in which eating dinner with the family was associated with healthy dietary intake patterns (6,31). More studies on how family dinner impact adolescents' eating behaviors should be done to better understand the discrepancy of these studies. Nonetheless, family dinners seem to be more than just a meal time: they promote better family connections and are a protective factor that may help reduce high-risk behaviors among youth (i.e., substance use, sexual activity, depression/suicide,

Table III. Adolescents eating behaviors profile

I have good eating habits	General eating practice*		Total
	Not so good	Good	
Sometimes or rarely	Realistic negative n = 369 (9.6%)	Underestimators n = 695 (18.9%)	n = 1,064 (28.5%)
Almost always	Overestimators n = 733 (19.9%)	Realistic positive n = 1,901 (51.6%)	n = 2,634 (71.5%)
Total	n = 1,102 (29.5%)	n = 2,596 (70.5%)	n = 3,698 (100.0%)

**General eating practice was calculated based on six items of self-report eating practices. Those who reported "sometimes or rarely" in all self-report eating practices were considered to have good eating practices.*

Table IV. Relationship between adolescents eating behaviors profile with family meals, body mass index and body weight perception

	Adolescents profiles (%)				
	Realistic negative	**Underestimators**	**Overestimators**	**Realistic positive**	**p**
Breakfast with family					
Never or rarely	55.9	45.3	35.3	31.4	< 0.001
Several times a week	27.2	35.1	30.6	34.1	
Every day	16.9	19.6	34.1	34.6	
Dinner with family					
Never or rarely	6.2	3.9	3.7	2.7	< 0.001
Several times a week	24.4	18.0	16.1	12.5	
Every day	69.4	78.1	80.1	84.7	
BMI category					
Normal weight	74.7	73.5	77.4	80.7	< 0.001
Overweight/obese	25.3	26.5	22.6	19.3	
Body weight perception					
Underweight	21.6	15.4	16.8	12.3	< 0.001
Normal weight	32.0	36.1	54.6	56.2	
Overweight	46.3	48.5	28.6	31.5	

BMI: body mass index. Tested by Chi-squared.

Table V. Binary logistic regression model of meals with family, body mass index, body weight perception and adolescents' eating behavior

	Adolescents' eating behavior profile OR (95% CI)			
	Realistic negative	**Underestimators**	**Overestimators**	**Realistic positive**
Breakfast with family				
Never or rarely	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Several times a week	0.57 (0.43-0.75)‡	0.90 (0.73-1.11)	0.93 (0.75-1.15)	1.42 (1.20-1.68)‡
Every day	0.48 (0.34-0.67)‡	0.52 (0.40-0.67)‡	1.16 (0.93-1.46)	1.64 (1.37-1.97)‡
Dinner with family				
Never or rarely	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Several times a week	1.27 (0.72-2.24)	1.34 (0.80-2.26)	0.91 (0.54-1.53)	0.81 (0.53-1.24)
Every day	0.69 (0.41-1.18)	1.14 (0.70-1.86)	0.88 (0.55-1.43)	1.20 (0.81-1.78)
BMI category				
Normal weight	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Overweight/obese	1.04 (0.76-1.42)	1.07 (0.84-1.35)	1.18 (0.93-1.50)	0.85 (0.70-1.03)
Body weight perception				
Underweight	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Normal weight	0.40 (0.29-0.56)‡	0.65 (0.49-0.85)†	1.01 (0.78-1.30)	1.74 (1.41-2.14)‡
Overweight	0.74 (0.52-1.05)	1.18 (0.88-1.57)	0.77 (0.57-1.04)	1.17 (0.92-1.48)

*OR: odds ratio; CI: confidence interval; BMI: body mass index. Analysis were adjusted for sex, age, and father and mother education. *p < 0.05, †p < 0.01, ‡p < 0.001.*

antisocial behaviors, violence, school problems, and excessive weight loss), especially if the family maintains good communication (32,33).

Although it was expected that eating behaviors would have a relationship with weight status (13-15), it was only verified in bivariate analysis. The proportion of normal weight among those who had healthy eating behaviors (realistic positive) was significantly higher than among those with unhealthy eating behaviors (realistic negative). In binary logistic regressions the analysis did not show any link between the two variables. Once body weight perception was related to adolescents' eating behavior in bivariate analysis and in binary logistic regressions analysis, even when adjusted for potential confounders (sex, age, and father and mother education), it appears that perceptions are very important to

predict behavior. Studies indicated that body weight perception influences eating behaviors, such as food restriction, and the use of pharmaceutical drugs that promote weight loss (20,34). This indicated that adolescents are very concerned about body image (17) and that they establish a link between body weight perception and eating behaviors (19,20,34). Thus, this explained why adolescents that had a better eating behavior were more likely to perceive themselves as having a normal weight and, on the contrary, those who had worse eating behaviors or even those who perceive having good eating habits only sometimes or rarely (underestimators) were less likely of being normal weight. These findings made it possible to conclude that awareness and perception of not having good eating behavior is related to body weight perception (35).

Although it was not directly related with this study's aims, it is noteworthy that 38.8% of the teenagers were not aware of their eating behaviors. This leads to the topic of food literacy. This is a relatively new concept that is described as the capacity of an individual to understand basic information about nutrition and food as well as the competence to use that information in order to make appropriate health decisions (36). Food literacy seems to influence adolescents' eating behaviors, as adolescents with greater food knowledge are shown to have healthier practices (37-39). As a result, it is essential that public health promotion and interventions should focus on health and food literacy during adolescence.

Some limitations and strengths should be noted. First, the cross-sectional design of the study precludes any inference about causality. Second, self-report eating habits and practices might introduce recall bias. However, self-report is appropriate for population-based studies or those with epidemiological characteristics, since they are easy to use and inexpensive. Third, height and weight were self-reported and are subject to bias. Nevertheless, self-reporting weight and height is considered as a valid tool for BMI estimates in epidemiological studies (40). Furthermore, the eating information did not contain nutrition information. The strengths of the study include the representative sample of adolescents, which allows generalization of the Portuguese adolescent population, and the fact that the study follows a rigorous methodological procedure in line with the demands of a large scale cross-European recognized study.

Adolescents' eating behaviors are related to family meals, and body weight perception. Having breakfast with family more often and being normal weight were positively related to adolescents' awareness of good eating behaviors. An understanding of the factors that influence eating behaviors during adolescence is needed to improve the dietary patterns and health status of this age group, mainly due to the higher prevalence of overweight and obesity among adolescents (41,42).

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Pediatría

Índice de masa corporal, motivos de práctica deportiva extraescolar y modelos familiares en alumnado de 6.º de Educación Primaria

Body mass index, motives for extracurricular sport practice and family type in grade 6 Primary Education children

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Resumen

Introducción: la obesidad infantil tiene muchas aristas, por eso se desarrollaron tres estudios complementarios.

Objetivos: el objetivo del estudio 1 fue determinar el índice de masa corporal (IMC) de toda la población de estudiantes de 6.º de Primaria de una ciudad española de tamaño medio y conocer sus hábitos de práctica deportiva extraescolar, el del estudio 2 fue conocer los motivos de práctica de los que realizan deporte extraescolar y el del estudio 3, conocer el papel que juega la familia sobre la práctica deportiva extraescolar.

Métodos: enfoque mixto, diseño ex-post-facto transversal. Estudio 1: 377 estudiantes de 6.º de Primaria. Instrumentos: tallímetro, báscula, cuestionario *ad hoc*. Estudio 2: 275 estudiantes de 6.º de Primaria. Instrumentos: cuestionarios (BREQ-3; MPAM-R). Estudio 3: 228 progenitores. Instrumento: Cuestionario de Percepción de las Familias.

Resultados: estudio 1: IMC: 20,73 ± 4,12 kg/m^2, 38,7% sobrepeso, 10,1% obesidad, 73% hace deporte; IMC: no existen diferencias significativas entre practicantes y no-practicantes, sí en base al nivel socioeconómico. Estudio 2: alta motivación intrínseca; motivo de participación: *diversión*. Estudio 3: los progenitores valoran la *importancia de hacer actividad física*; diferencias significativas a favor de los que tienen hijos haciendo deporte y nivel socioeconómico medio-alto. Padres cuyos hijos hacen deporte: *bueno para su salud/desarrollo*, *le gusta/lo eligió*, *socializarse* y *valores*; padres cuyos hijos no hacen: *falta de tiempo de los hijos*, *no le gusta/no encuentra un deporte que le guste* y *falta de tiempo de los padres*.

Conclusiones: IMC cercano al sobrepeso; la práctica de deporte extraescolar no marca diferencias en el IMC, el nivel socieconómico sí (estudio 1). Practicantes motivados intrínsicamente, lo hacen por diversión (estudio 2). La familia como modelo para hacer deporte (estudio 3).

Palabras clave:

Índice de masa corporal. Educación Primaria. Obesidad. Deporte. Motivación.

Abstract

Introduction: obesity has many edges. Therefore, three complementary studies were conducted.

Objectives: study 1: determining body mass index (BMI) of the whole population of grade 6 students of a middle-size city and assessing their extracurricular sport habits. Study 2: assessing the motives for sport practice. Study 3: examining the role that family plays in extracurricular sport practice.

Methods: mixed focus, ex-post-facto transversal design. Study 1: 377 grade 6 students. Instruments: measuring rod, scale and questionnaire. Study 2: 275 grade 6 students. Instruments: questionnaire (BREQ-3; MPAM-R). Study 3: 228 parents. Instrument: Families' Perception Questionnaire.

Results: study 1: BMI: 20.73 ± 4.12 kg/m^2, 38.7% overweight, 10.1% obesity, 73% practice sport. BMI: no significant differences between those who practice sports and those who do not; significant differences based on socioeconomic status. Study 2: high intrinsic motivation; motive to participate: enjoyment. Study 3: parents value the importance of doing physical activity; significant differences favor those whose children play sports and have medium-high socioeconomic status. Parents whose children play sport: good for their health/development, he/she likes/choses it, socialization and values; parents whose children do not play sport: children's lack of time, he/she does not like it (can't find a sport he/she likes), parent's lack of time.

Conclusions: BMI close to overweight; extracurricular sports do not make a difference in BMI, socioeconomic status does (study 1). Sport participants intrinsically motivated, playing sports for enjoyment (study 2). Family: a model for sport practice (study 3).

Key words:

Body mass index. Primary Education. Obesity. Sport. Motivation.

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INTRODUCCIÓN

Asistimos a un problema social de una relevancia notable a nivel global, una cuestión de salud pública que numerosos autores y autoridades a nivel internacional como la Organización Mundial de la Salud (OMS) no han dudado en calificar de epidemia. Nos referimos al sobrepeso y a la obesidad, dos enfermedades caracterizadas por un exceso de grasa corporal. Este carácter epidémico tiene su constatación directa a través de estudios de prevalencia: cerca de un 25% de niños en edad escolar de los países de la Unión Europea padecen sobrepeso, con una subida aproximada de 400.000 casos por año (1). España presenta una de las tasas más elevadas de sobrepeso y obesidad, siendo en población infantil (5-14 años) del 20% y 9% respectivamente (2). Es importante destacar que el problema no solo atañe a países desarrollados, sino que ambas están aumentando en los países de ingresos bajos y medianos, especialmente en las zonas urbanas (3). Probada su presencia a nivel planetario, resulta pertinente indagar en las causas que han propiciado esta situación y cuáles son las consecuencias que subyacen a la misma. Empezando por su origen, la obesidad es una enfermedad metabólica multifactorial, influida por elementos genéticos y contextuales (4). Aunque el primer apartado permita explicar un porcentaje de casos, las causas en la mayoría de situaciones se deben a variables de tipo ambiental. En cualquier caso, todas ellas se articulan en el denominado "entorno obesogénico" (8), un entramado de variables que explican las causas del sobrepeso y la obesidad (genética, sedentarismo, hábitos alimentarios, etc.). La obesidad durante la niñez tiene consecuencias médicas relevantes a corto y largo plazo y entre sus efectos se incluyen un mayor riesgo de padecer fracturas y problemas articulares, hipertensión, afecciones respiratorias y diabetes tipo II (6). También a nivel psicológico es frecuente que los sujetos posean una baja autoestima (7).

Por desgracia, el sistema educativo español no cubre la cantidad de actividad física que requieren los niños y adolescentes, reduciendo progresivamente el tiempo asignado al área de Educación Física en el currículo (8). Esta circunstancia, ligada al sedentarismo en las horas extracurriculares, provoca que los jóvenes no realicen la suficiente actividad física diaria. Teniendo en cuenta la importancia que esta tiene en el estatus corporal, las denominadas actividades extraescolares se han abierto paso como una correcta receta para compensar el déficit aludido. Son todas aquellas actividades físicas-deportivas realizadas por niños/jóvenes en edad escolar, dentro y fuera del centro educativo, las cuales propician el perfeccionamiento motor y la generación de hábitos saludables (9). Por otro lado, cabe preguntarse cuáles son los motivos que dificultan o favorecen la inclinación de los estudiantes a realizarlas en su tiempo libre. Estos, son las disposiciones que inducen a una persona a practicar ciertas actividades, las cuales se activan bajo determinadas condiciones (10).

La motivación juega un gran papel. Se trata de un constructo complejo afectado por aspectos biológicos, emocionales, cognitivos y sociales, el cual se infiere de la conducta que manifiesta el sujeto (11). La mayor parte de las investigaciones de la psicología motivacional realizadas en el ámbito deportivo se circunscriben dentro de la perspectiva cognitiva-social, la cual se basa en la relevancia que tienen las expectativas y valores que los individuos asignan a diferentes metas y actividades de ejecución (12). Bajo su paraguas, se ha ido perfilando en las últimas décadas una teoría con una amplia base científica capaz de explicar la motivación humana en diversos ámbitos, incluido el deportivo: la teoría de la autodeterminación (13). Dicha teoría presenta un *continuum* motivacional que abarca desde la desmotivación, pasando por la motivación extrínseca, hasta la motivación intrínseca o autodeterminada. La desmotivación supone una falta completa de motivación hacia una tarea. La motivación extrínseca es aquella en la que el individuo posee una visión instrumental de la tarea. Dentro de este grupo, los autores de la teoría señalan cuatro subregulaciones; desde la menos a la más autodeterminada serían: externa, introyectada, identificada e integrada. Finalmente, la motivación intrínseca se manifiesta cuando el individuo percibe la actividad como fuente de satisfacción y diversión.

Por otro lado, conocer los motivos de práctica deportiva implica tener en cuenta variables que trascienden la barrera del propio individuo, tales como las situacionales y las sociales. En este sentido, la familia constituye el primer y más poderoso agente socializador en la niñez, transmitiendo valores, comportamientos y normas de actuación (14), entre las que se incluye el deporte. Existe evidencia científica sobre el papel de modelado de la familia en la infancia tanto a nivel internacional (15) como nacional (16). Por último, no se debe olvidar la importancia del estatus socioeconómico familiar como variable predictora de aspectos como el IMC de los hijos, tal y como ha evidenciado una investigación precedente (17).

En base a todo lo anterior, el presente proyecto de investigación se desarrolló a lo largo de tres estudios complementarios.

- Estudio 1: el objetivo fue determinar el IMC de toda la población de estudiantes de 6º de Primaria de una ciudad española de tamaño medio y conocer sus hábitos de práctica deportiva extraescolar.
- Estudio 2: el objetivo fue conocer los motivos de práctica de aquellos que realizaban deporte extraescolar.
- Estudio 3: el objetivo fue conocer el papel que juega la familia sobre la práctica deportiva extraescolar y el estatus de IMC de los hijos.

MATERIAL Y MÉTODOS

Diseño estudio 1: cuantitativo *ex-post-facto* de tipo transversal. *Participantes estudio 1*: la totalidad de estudiantes de 6.º de Educación Primaria de centros públicos de la ciudad de Avilés: n = 377; 213 varones, 164 mujeres; 11,53 ± 0,84 años. *Instrumentos estudio 1*: para la talla se utilizó un tallímetro de pared de tipo escuadra Soehnle 5002 (rango 0-220 cm, grado de precisión 1 mm). Para la masa corporal se empleó una báscula profesional portable Tanita BC-587 (soporte máximo 200 kg, precisión de lecturas 100 g). El cálculo del IMC se obtuvo dividiendo el peso en kilogramos por el cuadrado de la altura en metros. Paralelamente a la toma de datos antropométricos, se entregó a cada niño un

cuestionario en el que debían indicar los datos de sexo, edad, n.º de clase y si practicaba o no deporte extraescolar reglado. Si este último caso era afirmativo, había una sección del cuestionario donde se preguntaba si estaba o no federado, la titularidad del organizador de la actividad (colegio o club) y el número de horas de práctica semanales. Se entrevistó a los equipos directivos de cada centro educativo para clasificarlos en función del nivel socioeconómico predominante. *Procedimiento estudio 1:* solicitada y aprobada la petición para llevar a cabo la investigación a la Consejería de Educación y Cultura del Principado de Asturias y al Comité de Ética de la universidad de los investigadores, se estableció contacto con los colegios participantes a fin de realizar la recogida de información, pactándose los horarios de conveniencia con cada uno de los centros. Previamente se informó mediante carta a las familias para que otorgaran su consentimiento al respecto. La investigación se desarrolló cumpliendo fielmente los estándares de la Declaración de Helsinki. *Análisis estudio 1:* se utilizó el programa estadístico de IBM SPSS v.24 para Windows. Se utilizaron procedimientos de estadística descriptiva, paramétrica e inferencial. Los cortes empleados para las categorías de IMC han sido para niños de 11,5 años (18,19).

Diseño estudio 2: cuantitativo ex-post-facto de tipo transversal. *Participantes estudio 2*: todo el alumnado de 6.º de Educación Primaria de colegios púbicos avilesinos que realizaban actividad física extraescolar (n = 275: 162 hombres, 113 mujeres). *Instrumentos estudio 2*:

1. BREQ-3 (Behavioral Regulation in Exercise Questionnaire) (25). Se ha empleado la versión validada del mismo en castellano (26), en la cual se obtuvieron propiedades psicométricas satisfactorias. El alpha de Cronbach arrojó los resultados que se indican a continuación: *desmotivación* (0,70), *regulación externa* (0,78), *regulación introyectada* (0,72), *regulación identificada* (0,66), *regulación integrada* (0,87) y *regulación intrínseca* (0,87). El cuestionario integra como factores los distintos grados de motivación de la teoría de la autodeterminación de Deci & Ryan (15): *desmotivación* (i.e.: "No veo por qué tengo que hacerlo"), *regulación externa* (i.e.: "Porque los demás me dicen que debo hacerlo"), regulación introyectada (i.e.: "Porque me siento culpable cuando no lo practico"), *regulación identificada* (i.e.: "Porque valoro los beneficios que tiene el ejercicio físico"), *regulación integrada* (i.e.: "Porque está de acuerdo con mi forma de ser"), *regulación intrínseca* (i.e.: "Porque creo que el ejercicio es divertido"). Consta de 23 preguntas con una escala Likert (1 = totalmente en desacuerdo, 5 = totalmente de acuerdo).
2. MPAM-R (Motives for Physical Activity Measure-Revised) (27). Se ha empleado la versión validada al castellano (28), en la cual se obtuvieron propiedades psicométricas aceptables. El alpha de Cronbach arrojó los siguientes resultados: *fitness/salud* (0,80), *social* (0,81), *apariencia* (0,87), *disfrute* (0,84) y *competencia* (0,85). Se emplearon solo cuatro de sus cinco factores por resultar la *competencia* no relevante para la presente investigación: *fitness/salud* (i.e.: "Porque quiero estar en buena forma física"), *apariencia* (i.e.: "Porque quiero resultar atractivo a los demás"), *social* (i.e.: "Porque me gusta estar con mis amigos") y *disfrute* (i.e.: "Porque me gusta hacer esta actividad"). Emplea una escala de respuesta Likert de 1 a 7 puntos que va desde "totalmente en desacuerdo" a "totalmente de acuerdo" respectivamente.

Procedimiento estudio 2: se pactó de nuevo con los colegios un horario para la segunda fase de recogida de información. Ya en el centro educativo, el alumnado que realizaba deporte extraescolar organizado acudía en presencia del investigador a la sala de ordenadores para contestar a los dos cuestionarios señalados (en formato *Google*). Previamente, se explicaban con detalle a los estudiantes las instrucciones y se atendían las posibles dudas durante el proceso. *Análisis estudio 2*: se utilizó el programa estadístico de IBM SPSS v.24 para Windows, así como procedimientos de estadística descriptiva, correlacional, paramétrica e inferencial.

Diseño estudio 3: enfoque mixto bajo un diseño ex-post-facto de tipo transversal. *Participantes estudio 3*: 228 progenitores de todos los estudiantes de 6º de Primaria de la ciudad de Avilés. *Instrumentos estudio 3: Cuestionario de Percepción de las Familias* (32). Este instrumento fue diseñado por un grupo multidisciplinar de cinco expertos concernientes a las áreas de Educación Física, Psicología y Sociología. Posteriormente fue sometido a una prueba piloto, seguida de una reelaboración llevada a cabo por el mismo grupo de expertos con las correcciones oportunas. El instrumento consta de 12 preguntas con una escala Likert de 1 a 5 (totalmente en desacuerdo, totalmente de acuerdo, respectivamente) agrupadas en tres factores: *importancia de la educación física* (i.e.: "La educación física tiene una gran importancia en la formación de mi hijo/a"), *importancia de hacer actividad física o deporte* (i.e.: "Practico ejercicio físico o deporte habitualmente") e *importancia de hacer actividad física o deporte con los hijos/as* (i.e.: "Intento hacer actividad física o deporte con mis hijos/as"). A este cuestionario se le añadieron dos preguntas adicionales: en la primera se les solicitaba responder si su hijo/a realizaba o no deporte extraescolar, mientras que en la segunda, de respuesta abierta, se les instaba a describir en varias líneas cuáles eran los motivos de la anterior respuesta. *Procedimiento estudio 3*: aprovechando la notificación de consentimiento para participar en la investigación se añadió en cada sobre el citado cuestionario, el cual era recogido por el investigador en la sesión del "estudio 2". Cada estudiante fue el encargado de entregar a su familia su correspondiente sobre (numerado por orden de lista) y de traerlo de vuelta al aula. *Análisis estudio 3*: se utilizó el programa estadístico de IBM SPSS v.24 para Windows, así como procedimientos de estadística descriptiva, correlacional, paramétrica e inferencial. Para el tratamiento cualitativo de los datos se utilizó el programa MAXqda v.10. Se emplearon métodos de comparaciones constantes (33) y de inducción analítica (34) con la finalidad de identificar y extraer categorías, así como patrones de respuesta comunes. En primer lugar, se transcribieron las respuestas y estas fueron leídas y releídas por los dos investigadores. A continuación, ambos determinaron por separado las categorías a partir del análisis y agrupamiento de las distintas respuestas. Identificadas las categorías de análisis, estas se compararon y contrastaron. Por último, los datos fueron reanalizados con el objetivo de encontrar discrepancias o interpretaciones erróneas (35).

RESULTADOS

ESTUDIO 1

El 2,4% de los casos representó bajo peso; el 59%, normopeso; y 38,6%, sobrepeso (10,1% obesidad). La media global del IMC fue de 20,73 ± 4,12 kg/m^2, valores cercanos al sobrepeso (≥ 21,04 kg/m^2). El valor mínimo fue de 13,55 kg/m^2 y el máximo, de 43,30 kg/m^2. No se encontraron diferencias estadísticamente significativas por sexo respecto al IMC, ni en los datos globales, ni por categorías. Tampoco se encontraron diferencias estadísticamente significativas entre hacer o no deporte extraescolar, independientemente del género. Finalmente, el IMC varió en función del entorno socioeconómico, presentando diferencias estadísticamente significativas entre el nivel medio-alto y el medio ($p = 0,025$), así como entre el medio-alto y el medio-bajo ($p = 0,021$). La prevalencia global de actividad física extraescolar fue del 73% (77% varones, 69% mujeres). De entre los que practican, la tasa de federados fue del 72% (72% varones, 28% mujeres) y la de práctica fuera del colegio, del 81% (62,8% varones, 37,2% mujeres). La media de horas de práctica deportiva semanal fue de dos horas y 45 minutos: tres horas y 15 minutos en los clubes y dos horas y 15 minutos en los colegios.

ESTUDIO 2

De mayor a menor puntuación, el perfil motivacional fue: *regulación intrínseca* (4,56 ± 0,53), *regulación identificada* (4,47 ± 0,59), *regulación integrada* (4,1 ± 0,84) y desmotivación (1,4 ± 0,59). Por otro lado, los motivos de participación deportiva extraescolar fueron, de mayor a menor: *disfrute* (6,16 ± 0,78), *fitness* (5,91 ± 0,84), *social* (5,21 ± 1,01) y *apariencia* (4,15 ± 1,48). En función del género se observó el mismo patrón tanto en la motivación como en los motivos. Un análisis más exhaustivo a través de la t de Student mostró diferencias estadísticamente significativas ($p \leq 0,05$) a favor de los varones en: *regulación intrínseca* (dif. de $x = 0,14$, $p = 0,44$), *regulación integrada* (dif. de $x = 0,28$, $p = 0,01$), *regulación introyectada* (dif. de $x = 0,25$, $p = 0,42$), *desmotivación* (dif. de $x = 0,16$, $p = 0,33$), *social* (dif. de $x = 0,31$, $p = 0,17$), *fitness* (dif. de $x = 0,23$, $p = 0,31$) y *apariencia* (dif. de $x = 0,61$, $p = 0,001$). Finalmente, el análisis correlacional de Pearson entre los factores de ambos cuestionarios mostró que la *desmotivación* correlaciona inversamente con el *disfrute* de forma muy significativa ($p \leq 0,01$) y con el *fitness* de manera significativa ($p \leq 0,05$), mientras que lo hacía positivamente de forma muy significativa con la *apariencia*.

ESTUDIO 3

Las puntuaciones del cuestionario pueden considerarse medias-altas: *importancia de hacer actividad física o deporte* (3,82 ± 0,95), *importancia de hacer actividad física o deporte con los hijos/as* (3,77 ± 0,83), *importancia de la educación física* (3,62 ± 0,81). El análisis de t de Student con la variable dicotómica extraescolar indicó diferencias estadísticamente muy significativas ($p \leq 0,01$) en el factor *importancia de hacer actividad física o deporte* para los padres cuyos hijos hacían deporte extraescolar. El post-hoc de Bonferroni entre colegios de diferente contexto socioeconómico mostró diferencias estadísticamente muy significativas ($p = 0,002$) en el factor *importancia de hacer actividad física o deporte* entre los colegios de estatus medio-alto y medio-bajo, a favor de los primeros. Finalmente, el análisis correlacional de Pearson mostró una relación estadísticamente significativa y positiva (en el nivel 0,05) entre la variable *disfrute* de los hijos y la *importancia de la educación física* otorgada por los padres.

Respecto al análisis cualitativo, en las respuestas de aquellas familias cuyos hijos practicaban actividades extraescolares se encontraron cuatro temas/categorías. A continuación, se presenta cada una con el número de extractos de texto en los que aparece y un ejemplo: *es bueno para su salud/desarrollo* (113 extractos), "hacer ejercicio físico es fundamental para el buen funcionamiento motor y mental" (Ana); *le gusta/lo eligió* (62 extractos), "le encanta, le gusta mucho entrenar" (Javier); *socializarse* (47 extractos), "es muy bueno para hacer amigos" (Luis); *valores* (31 extractos), "por los valores que el deporte inculca, tales como el esfuerzo, la autodisciplina, la tolerancia, el trabajo en equipo…" (Nuria).

En los hogares en los que el hijo/a no hacía deporte extraescolar se encontraron tres temas/categorías: *falta de tiempo de los hijos* (19 extractos), "porque va a varias clases particulares" (Toñi); *no le gusta/no encuentra un deporte que le guste* (13 extractos), "se cansa de todos, aunque siempre le digo que una actividad física tiene que hacer" (Emilio); *falta de tiempo de los padres* (seis extractos), "porque trabajo y mis horarios no me lo permiten; además, no tengo quien la lleve y la traiga a los torneos" (Antonio).

DISCUSIÓN

ESTUDIO 1

El objetivo fue determinar el IMC de toda la población de estudiantes de 6º de Primaria de una ciudad española de tamaño medio y conocer sus hábitos de práctica deportiva extraescolar. Los resultados han mostrado que el valor medio del IMC fue de 20,73 kg/m^2, con un 38,7% de sujetos con sobrepeso (10,1% de obesidad); la prevalencia de práctica deportiva extraescolar fue del 73%, con una gran parte realizada fuera del colegio (81%); y no se encontraron diferencias estadísticas en el IMC entre practicantes y no practicantes, aunque sí en función del nivel socioeconómico.

Respecto al IMC, los datos globales obtenidos son parecidos, aunque ligeramente superiores (0,3), a los encontrados en otro estudio (20) con sujetos de edad similar. Por otro lado, en la presente investigación la heterogeneidad de la muestra en cuanto al IMC ha sido mayor, lo que puede ser debido a particularidades contextuales. Por otra parte, en el anterior estudio citado la

comparación por categorías no es pertinente, ya que el criterio de agrupación fue el nivel de actividad física de los individuos (sedentarios, activos y deportistas). En este sentido, el estudio de Pérez-Soto (21) sí incluye los mismos puntos de corte de IMC que los empleados en la presente investigación; además, la edad de los sujetos es la misma. Sus resultados por categorías son más saludables que los de la investigación aquí tratada (normopeso 59% < 67,1%; sobrepeso 28,6% > 26,3%; obesidad 10,1% > 6,6%). En los estudios citados tampoco se han encontrado diferencias estadísticamente significativas en función del sexo. Por último, se confirma que aquellos niños inmersos en ambientes socioeconómicos deprimidos tienen un mayor riesgo de padecer sobrepeso y obesidad. Esta circunstancia ha quedado patente en otros estudios (17).

Respecto a las actividades extraescolares, se ha obtenido una alta tasa de participación (73%), con una ligera predominancia de los varones, resultados que coinciden con los de otros estudios (22). La tasa de inscritos en clubs es sustancialmente elevada (59% del total de la muestra) en comparación con otro estudio similar (23) donde se obtuvo solo un 18%. La amplia red de clubes deportivos en la ciudad parece haber provocado este hecho. Finalmente, la hegemonía de varones federados ha sido confirmada en otras ocasiones (24). Parece ser que aún permanecen vigentes estructuras que no favorecen la participación de las mujeres en el deporte de competición.

Finalmente, no se han observado diferencias estadísticamente significativas entre el IMC de practicantes y no practicantes de deporte extraescolar. No se han encontrado estudios que investiguen la relación entre actividad física extraescolar organizada y el IMC en población de 11 a 12 años, lo que limita las comparaciones de los resultados. Sí existen respecto a la actividad física en general fuera del horario escolar, incluida la organizada. Martínez-Castañeda (20) sí encontró diferencias estadísticamente significativas entre individuos sedentarios y aquellos activos o muy activos. Si bien es cierto que en el presente estudio la asociación entre deporte extraescolar e IMC no ha alcanzado significación estadística, sí se ha observado una tendencia hacia la misma, de manera que los estudiantes que realizan deporte extraescolar presentaron valores medios inferiores que aquellos que no lo hacen. Del mismo modo, se ha observado que los estudiantes que entrenan en un club tienen valores medios de IMC inferiores, aunque no llegan a ser estadísticamente significativos. Este hecho tiene sentido en la medida que estos practican de media una hora semanal más de actividad física. Además, los estudiantes apuntados a un club están federados, y por ende compiten los fines de semana, lo que no siempre ocurre en el caso de las actividades organizadas por los centros educativos.

ESTUDIO 2

El objetivo fue conocer los motivos de práctica del alumnado de 6.º de Primaria que realizaba deporte extraescolar. Los resultados mostraron que estos individuos estaban intrínsecamente motivados y su principal motivo para realizarlo era el disfrute.

Respecto a los motivos para realizar actividad física extraescolar, los participantes han señalado el *disfrute*, seguido del *fitness*, lo *social* y la *apariencia.* En la totalidad de estudios encontrados, el alumnado preadolescente opta por la *diversión* y la misma jerarquía de motivos (29). Por lo tanto, parece importante que los responsables del deporte extraescolar se aseguren de que este sea fuente de diversión y disfrute, porque de este modo querrán seguir practicándolo.

En cuanto a los perfiles motivacionales, los resultados muestran una alta motivación intrínseca en el alumnado objeto de estudio. De acuerdo a los postulados de la TAD (15) y a investigaciones recientes (30), existe una relación significativa entre la *regulación intrínseca* y la cantidad de ejercicio físico extraescolar en estudiantes de 10-12 años, lo que explicaría la alta tasa de actividad encontrada en el presente estudio. En relación a la mayor puntuación de los hombres en las regulaciones motivacionales, parece ser algo recurrente (31), lo que hace pensar que estos, al igual que con los motivos, presentan una polaridad comportamental más marcada que las mujeres.

Respecto al análisis correlacional, concuerda con el contenido de la TAD (15) en tanto que la *desmotivación* es un factor que correlaciona positivamente con motivos de práctica deportiva eminentemente extrínsecos como la *apariencia*. Por el contrario, se comporta de manera inversamente proporcional con aquellos de carácter intrínseco como el *disfrute*.

ESTUDIO 3

El objetivo fue conocer el papel que juega la familia sobre la práctica deportiva extraescolar de los hijos. Los resultados han mostrado que los progenitores valoran la *importancia de hacer actividad física o deporte*, aunque existen diferencias significativas entre los padres cuyos hijos hacen actividad deportiva extraescolar y los que no, así como en función del nivel socioeconómico. Las respuestas de los padres cuyos hijos hacen deporte extraescolar reflejaron cuatro temas/categorías positivas (*es bueno para su salud/desarrollo*, *le gusta/lo eligió*, *socializarse* y *valores*), mientras que las de aquellos cuyos hijos no hacen deporte extraescolar reflejaron tres temas/categorías negativas (*falta de tiempo de los hijos*, *no le gusta/no encuentra un deporte que le guste* y *falta de tiempo de los padres*).

La relación observada entre el factor *importancia de hacer actividad física o deporte* y la práctica de actividad física extraescolar del hijo indica el efecto como modelo deportivo de la familia, en la medida en que dicho factor mide la realización de actividad física de los progenitores. El papel de la familia como modelo deportivo ha sido evidenciado en la etapa prepuberal también en otros estudios (15). Acorde con este argumento, el análisis correlacional ha indicado que los niños cuyos padres dan más importancia a hacer deporte disfrutan más del deporte extraescolar que realizan, lo que es muy significativo.

Se ha observado la importancia que tiene el nivel socioeconómico familiar como predictor de la adherencia al deporte, en la medida en que, en situaciones desfavorecidas, el modelado es

escaso o inexistente. También se ha encontrado que el nivel de estudios de los padres influye en la cantidad de actividad física de los hijos (36).

En lo relativo a los resultados cualitativos, las familias cuyos hijos hacen deporte extraescolar han señalado mayoritariamente que es *bueno para su salud/desarrollo*, ubicando en segunda posición *le gusta/lo eligió*, resultados coincidentes con otras investigaciones (37). En tercer lugar, la *socialización* parece ser un valor añadido de los padres para este tipo de actividades. También a destacar en cuarta posición es la idea equivocada que parece prevalecer todavía en la sociedad en lo que se refiere a la transmisión innata de valores positivos por parte del deporte (38). Por otra parte, las familias cuyos hijos no hacen deporte extraescolar aluden prioritariamente a la *falta de tiempo de su hijo*. Este argumento bien podría rebatirse preguntándoles si en realidad los estudiantes de 6.º de Primaria tienen una carga horaria excesiva de tareas y actividades en el tiempo de ocio, o por el contrario es un problema de motivación hacia la actividad física. En segundo lugar, el factor *no le gusta/no encuentra un deporte que le guste* es una llamada de atención a todas las personas que imparten actividad física (profesores, técnicos deportivos, etc.), así como a las encargadas de su promoción y desarrollo (políticos, expertos en deporte, etc.). En tercer lugar, la *falta de tiempo de los padres* es, a diferencia del primer caso, un motivo más objetivo y justificado en tanto que existen condicionantes de fuerza mayor como el trabajo que interfieren con la práctica deportiva extraescolar de los niños.

Como conclusiones, cabe señalar que la práctica de deporte extraescolar no marca diferencias en el IMC de estudiantes de 6.º de Primaria, mientras que el nivel socieconómico sí que lo hace (estudio 1); los practicantes de deporte extraescolar están motivados intrínsicamente y su principal motivo para realizarlo es la diversión (estudio 2); existe una relación fuerte entre la importancia que los padres otorgan a realizar actividad física y la práctica y disfrute de deporte extraescolar de sus hijos. Los padres cuyos hijos hacen deporte extraescolar valoran más la *importancia de hacer actividad física o deporte*, así como los de nivel socioeconómico más elevado. Los padres cuyos hijos no hacen deporte extraescolar señalan como motivos la *falta de tiempo de los hijos*, que *no le gusta/no encuentra un deporte que le guste* y la *falta de tiempo de los padres* (estudio 3). Queda pendiente la tarea de adaptar la oferta deportiva extraescolar a la realidad social circundante, ofreciendo alternativas realistas desde un enfoque multidisciplinar en el que se impliquen conjuntamente educadores, médicos, técnicos deportivos, políticos y familias.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Nutrición en el anciano

Nutritional evaluation of geriatric patients with Alzheimer's disease in Southern Brazil: case-control study

Evaluación nutricional de pacientes geriátricos con enfermedad de Alzheimer en el Sur del Brasil: estudio de controles de caso

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Abstract

Introduction: elderly's malnutrition is linked, among other factors, to chronic-degenerative diseases, requiring an improvement in the clinical evaluation of nutritional status of this population. Studies have tried to find out new tools to assess aged-people nutritional status. One of most used scales to investigate nutritional status on geriatric patients is the Mini Nutritional Assessment (MNA).

Objective: the present study aims to evaluate nutritional status of Alzheimer's disease (AD) patients, by comparison with a control group, via Mini Nutritional Assessment.

Methods: a cross-sectional study, which includes 35 alzheimer's old-people and 43 control old-people, was performed evaluating nutritional status with MNA.

Results: total score of MNA in the alzheimer group shows that 71.42% were in malnutrition risk, 14.28% were malnourished and 14.25% presented normal nutritional status. In addition, in the control group 79.06% of patients (n = 34) were classified as having normal nutritional status and 20.93% (n = 9), as being at risk of malnutrition.

Conclusion: results reinforce the purpose that MNA can be used as a proper instrument to evaluate nutritional status in elderly, mainly in AD, because measuring risk and nutritional status of this population is indispensable.

Key words:

Nutritional status. Alzheimer's disease. Elderly. Malnutrition.

Resumen

Introducción: la malnutrición en ancianos está vinculada, entre otros factores, con patologías crónicas degenerativas, por lo que es necesaria una mejora en la evaluación clínica del estado nutricional de esta población en particular. Algunos estudios han intentado hallar nuevas herramientas para evaluar el estado nutricional de los ancianos. Una de las escalas más utilizadas para la investigación del estado nutricional en pacientes geriátricos es el test Mini Nutritional Assessment (MNA).

Objetivo: el objetivo del presente estudio es evaluar el estado nutricional de pacientes con enfermedad de Alzheimer mediante la comparación con un grupo control, vía Mini Nutritional Assessment.

Métodos: se realizó un estudio transversal que incluyó a 35 ancianos con alzhéimer y 43 ancianos control para evaluar el estado nutricional con MNA.

Resultados: la puntuación total del MNA en el grupo con alzhéimer muestra que el 71,42% de los pacientes estaba en riesgo de malnutrición, el 14,28% estaba desnutrido y el 14,25% presentaba un estado de nutrición normal. Además, en el grupo control, el 79,06% (n = 42) presentó un estado de nutrición normal y el 20,93% (n = 9) mostró riesgo de malnutrición.

Conclusión: los resultados refuerzan la idea de que el MNA puede ser utilizado como un instrumento apropiado para evaluar el estado nutricional en ancianos, principalmente en caso de alzhéimer, porque la medida del riesgo y del estado nutricional de esa población es indispensable.

Palabras clave:

Estado nutricional. Enfermedad de Alzheimer. Ancianos. Malnutrición.

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INTRODUCTION

The elderly is the population segment that increases faster, with an estimated boost of more than 4.0% per year, between 2012 and 2020. This tendency has a significant impact on population projection, which, in 2060, should totalize about 73.5 million elderlies (1). With this demographic transition comes an epidemiological one, and the main feature is an increase of chronic-degenerative diseases incidence, among them even Alzheimer's disease (AD) (2).

In the elderly, malnutrition is commonly linked to chronic-degenerative diseases. In this condition, evaluating nutritional status becomes very important and that is why some studies have tried to find reliable tools to assess elderly nutritional status (3). In this sense, one of the most used scales to measure nutritional status on geriatric patients is the Mini Nutritional Assessment (MNA). Even though MNA is a simple test, it is considered as effective and efficient in detecting malnutrition (1,3).

Nutritional status can be strongly altered in AD patients and this can be possibly due to an inability to accept, chew, swallow or assimilate food. When AD progresses, weight loss increases, which is considered to be a determinant mortality factor (2). Higher energetic demand or a dysfunction in body weight regulation, low caloric intake, loss in eating independency (caused by cognitive decline), depression, altered taste and smell, atrophy of cortex, as well as associated diseases (5), are possible reasons of weight loss in AD patients.

The aim of the present research was analyzing nutritional status in AD' people compared to elderly with similar age without AD by using the Mini Nutritional Assessment, since studies show that nutrition is very altered in AD, leading to progressive worsening of health status (2,3). Evaluating this condition may help interventions and improve quality of life for this population.

METHODS

The project was previously approved by the Ethics Committee from the Midwest State University (Universidade Estadual do Centro-Oeste - UNICENTRO), number 026/2011. All patients and caregivers were informed about objectives, methods, risks and benefits prior to signing the informed consent form (ICF). Patients who had any nutritional alteration were forwarded to the Nutrition's Clinic School – UNICENTRO for subsequent monitoring.

The present research is a cross-sectional study, counting 35 elderlies with AD and 43 elderlies in a control group. People previously diagnosed clinically with AD, attended by the Unified Health System (hereby SUS) and assisted by the Association of Studies, Research and Assistance to People with Alzheimer's (In Brazil: Associação de Estudos, Pesquisas e Auxílio à Pessoas com Alzheimer, AEPAPA) from Guarapuava, Paraná (Brazil), were included in the study. The control group included only healthy people, assessed by the Secretariat of Social Assistance from Guarapuava.

Some exclusion criteria were applied: patients not founded for three attempts by visit, those who died, patients who lived in the countryside or moved to a different city, people who rejected to participate in the research after the first visit or those who disagreed with the conditions of the ICF.

Data collection was performed between August 2013 and June 2014. The initial population was composed by 55 patients with AD. However, some people was not found at home, had death record or gave up during the study (Fig. 1). The control group comprehended 43 elderlies, who agreed voluntarily to participate in the study; initially this group included 50 people, however, seven gave up.

Via questionnaires applied to patients or caregivers, we reported socio-demographic data (age, gender, education level, average income, age, marital status, smoking habits and physical activity), comorbidities and medication. In this context, associations between AD and clinical indicators such as high cholesterol, diabetes, and high blood pressure were also reported. According to the Brazilian guidelines, reference values to LDL cholesterol are: 130-159 mg/dl (limit values), 160-189 mg/dl (high values) and ≥ 190 mg/dl (very high values) (6). For diabetes, when fasting, glucose levels are classified as follows: normal (< 100 mg/dl), tolerance (≥ 100 to < 126 mg/dl) and diabetes (≥ 126 mg/dl) (7). In addition, high blood pressure values are: normotensive (≤ 120/80 mmHg), pre-hypertension (121-139/81-89 mmHg) and hypertension (140-159/90-99 mmHg) (8).

Nutritional status was evaluated via Mini Nutritional Assessment (MNA). This tool consists in a questionnaire, divided in four parts: a) anthropometric evaluation, arm and calf circumference and body mass index (BMI: weight [kg]/height [m²]), evaluated according to the classification of the Pan-American Health Organization; b) global evaluation; c) dietetic evaluation; and d) self-evaluation. MNA scores describe nutritional status, beside the risks. The scores were classified as follows: good nutritional status (≥ 24 points), malnutrition risk (17-23.5 points) and malnutrition

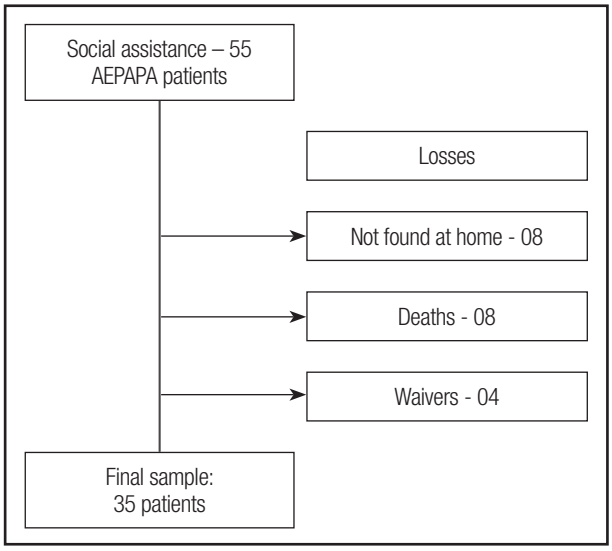

Figure 1.
Recruitment flowchart of the study population.

(< 17 points) according to the classification or values proposed by Cavalcante (9).

When, due to health conditions, weight and height were unmeasurable, they were estimated using formulas with arm and calf circumference' measures, knee height and subscapular skinfold. To obtain weight (kg) in old-age patients, the following formulas were used: a) men's weight = ([1.73 x arm circumference {cm}] + [0.98 x calf circumference {cm}] + [0.37 subscapular skinfold {mm}] + [1.16 x knee height {cm}] – 81.69); and b) women's weight = ([0.98 x arm circumference {cm}] + [1.27 x calf circumference {cm}] + [0.4 x subscapular skinfold {mm}] + [0.87 x knee height {cm}] – 62.35) (24). To estimate elderly's height, the following formulas were used: a) man's height = (64.19 – [0.04 x old-age {in years}] + [2.02 x knee height {cm}]); and b) women's height = (84.88 – [0.24 x old-age {in years}] + [1.83 x knee height {cm}]) (5).

To classify AD patients according to the stage of the disease, the Clinical Dementia Rating (CDR) scale was used, consisting in a questionnaire divided in categories (memory, orientation, judgment and problems solving, community relations, home and hobbies and personal cares) to evaluate patients according to an interview with the caregiver. Each category is classified resulting in total scores corresponding to healthy (CDR 0), questionable (CDR 0.5), mild (CDR 1), moderate (CDR 2) or severe dementia (CDR 3) (10). The CDR scale was applied and evaluated by a trained health professional.

Data were presented as average and standard deviation or absolute and relative frequency. Numeric variables were checked for distribution of the data and homogeneity of variance errors through the Shapiro-Wilk and Levene tests, respectively. The Chi-squared, continuity correction, Chi-squared for tendency and Fisher's correction tests were used to examine possible associations between behavior and the characteristics of subjects with and without AD. In addition, the MANCOVA test, considering sex and group as factors, followed by the Bonferroni test for multiple comparisons, were used to test differences between the control and AD groups, separated by sex. CDR was compared using the MANCOVA test one way. Age was used as co-variable due to the differences observed between the control and AD groups. Therefore, results shown are regardless of age effect. A significance value of $p < 0.05$ had been used and analyses were made using the SPSS 20.0 statistical program.

RESULTS

According to the MNA score, as shown in table I, the majority of Alzheimer's patients had malnutrition risk (71.42% [n = 25]) and 14.28% (n = 5) were malnourished. Also, most of the participants in the control group had normal nutritional status (79.06% [n = 34]), 20.93% (n = 9) had malnutrition risk and no patients were malnourished. Age, gender and average income are also described in table I.

Classifications for AD staging were compared considering age as a co-variable in table II. The CDR 3 group shows lower BMI (23.97 ± 1.13 F: 3.475; p = 0.043) and MNA total score (19.10 ± 0.84 F: 4.290; p = 0.023) than CDR 2 (IMC 28.20 ± 1.24) and CDR 1 (MAN 23.12 ± 1.25) groups, respectively. No significant differences were observed regarding weight and height values between CDR groups.

In table III, there is a comparison between the control and AD groups divided by sex and adjusted to age. Among women, height (1.56 ± 0.01, p = 0.034) and MNA (24.78 ± 0.61, p < 0.001) in the control group are significantly higher than in the AD group (height = 1.52 ± 0.01; MNA = 20.82 ± 0.67). Among men, the control group had only MNA (26.08 ± 0.81, p < 0.01) significantly higher than the AD group. No significant differences were observed regarding other variables.

Table IV reports associations of AD with social and clinical indicators such as civil status, high cholesterol, diabetes, Parkinson's disease and high blood pressure paired by gender, but there were no statistically significant associations. In addition, a significant difference was observed in AD diagnosis and nutritional status using MNA in women (p < 0.001) and men (p < 0.002).

DISCUSSION

Aging implies several alterations in nutritional status as a decrease in odor perception and taste buds' atrophy, which contrib-

Table I. Profile of patients with Alzheimer's disease attended by the AEPAPA and control group

	Alzheimer (n = 35)	Control group (n = 43)
Age (years)	78.90 ± 8.72	68.35 ± 5.69
Gender	62.85% (n = 22) female	67.44% (n = 29) female
Average income (Brazilian real)	R$ 1,031.13 ± 67.29	R$ 904 ± 8.99
MNA Normal nutritional status	14.25% (n = 5)	79.06% (n = 34)
Malnutrition risk	71.42% (n = 25)	20.93% (n = 9)
Malnutrition	14.28% (n = 5)	

Data presented by average ± standard deviation.

Table II. Comparison of nutritional status according to the Clinical Dementia Rating (CDR)

	CDR 1 (n = 7)		CDR 2 (n = 13)		CDR 3 (n = 15)		F	p
Weight (kg)	69.15	4.79	68.54	3.53	58.30	3.22	2.990	0.065
Height (m)	1.58	0.03	1.56	0.02	1.55	0.02	0.253	0.778
BMI (kg/m²)	27.32	1.68	*28.20**	*1.24*	*23.97**	*1.13*	3.475	*0.043**
MNA total score	*23.12**	*1.25*	21.69	0.92	*19.10**	*0.84*	4.290	*0.023**

*CDR 1: mild dementia; CDR 2: moderate dementia; CDR 3: severe dementia; BMI: body mass index; MNA: Mini Nutritional Assessment. Data presented as average ± standard deviation; *p < 0.05 showing statistical difference. Comparison was made using ANCOVA one way, followed by Bonferroni test for multiple comparisons. Age as covariable = 78.371.*

Table III. Comparison of nutritional status in relation to gender and Alzheimer's disease

	Women					Men				
	Control (n = 29)		Alzheimer (n = 23)		p	Control (n = 14)		Alzheimer (n = 16)		p
Weight (kg)	69.17	2.60	61.30	2.84	0.060	71.53	3.47	73.76	3.38	0.658
Height (m)	*1.56*	*0.01*	*1.52*	*0.01*	*0.034**	1.67	0.02	1.66	0.02	0.471
BMI (kg/m²)	28.56	1.06	26.46	1.15	0.213	25.51	1.41	27.03	1.37	0.458
MNA total score	*24.78*	*0.61*	*20.82*	*0.67*	*< 0.001**	*26.08*	*0.81*	*21.27*	*0.79*	*< 0.001**

*BMI: body mass index; MNA: Mini Nutritional Assessment. Data presented as average ± standard deviation; *p < 0.05 showing statistical difference. Comparison between groups was made with MANCOVA and Bonferroni test for multiple comparisons, considering the groups as fixed factor and age as covariable = 73.268.*

ute to downfall in dietary intake and lead to nutrient and muscular depletion as well as foods malabsorption (11). Elderly with AD show higher difficulties in mobility, more atrophy and bad motor cordination, which reduce the range of nutritional daily needs (12- 14). This is in line with data found in our research, where 71.42% of AD elderly presented malnutrition risk, since elderly people with dementia present loss of appetite, chewing and swallowing difficulties, and indifference and lack of awareness about the importance of power (15,16); by contrast, 79.06% of participants in the control group show normal nutritional status after MNA analysis.

According to Silva (2017) (16), after analyzing AD patients, from 58.3% (n = 14) men, 85.7% (n = 12) are malnourished and, from 41.7% (n = 10) women, all of them are malnourished. This results are similar to those of our research, where women show significant differences in height and MNA scores when compared to the control group. Some explanations were proposed to elucidate women prevalence regarding AD. In average, women have longer life expectancy than men; in other words, they have a higher chance to reach up to 65 years, which is a high risk age to AD (12). In the elderly, gender imbalance is accentuated: 57% are women and 43% are men, against 52% and 48%, respectively, in the non-elderly, and this is due to lower mortality among the female gender (11).

The study by Sturmer et al. (2011) (17) analyzes the nutritional status in AD patients, and 83.3% of the patients under study showed malnutrition risk. Nobre (18) presented a higher percentage of malnutrition risk in the AD group, whereas the control group showed more well-nourished individuals, using the MNA.

In spite of the differences observed between CDR groups, in this study BMI is, on average, at normal levels in the elderly population. However, there is a strong trend to malnutrition as the disease becomes more severe. These results can be observed in table II. There was a lower BMI and a lower result for MNA total score in the elderly group classified as CDR 3, when compared to the other groups. Our results are compatible with those of Goes (18), who found that CDR 3 presented higher weight loss and more malnourished patients. In a study by Goulart et al. (2017) (20), CDR 0.5 and CDR 1 patients show malnutrition risk (65.4%) and in CDR 2 and CDR 3, 65.4% of patients show malnutrition through MNA.

Protein-energy malnutrition is frequent in AD and progresses as diseases severity increases. In mild and moderate stage, malnutrition is around 3%, whereas in severe stage it may be around 50% (14). Furthermore, people with dementia usually present decline in power's abilities and exhibit conducts of low intake. These behaviors are normally linked to dementias and include restrictive nutritional habits as well as refusing swallowing, spitting the food out and keeping the mouth open (18). Low appetite may arise through depression, difficulty in reporting needs, lack of activity, pain, oral problems, medication side-effects or constipation, among others (21).

Malnutrition has been presented as an imbalance between food intake and food requirements, which results in metabolism changes. Disabilities in the ingestion of vitamins may induce changes in cognitive functions (14), harming up elderly's health. Associations between nutritional status and severity from cognitive status prove that, with dementia, nutritional status deteriorates significantly.

Table IV. Association between Alzheimer's presence and social and clinical indicators

	Women					Men				
	Control (n = 29)		Alzheimer (n = 23)		p	Control (n = 14)		Alzheimer (n = 16)		p
	n	%	n	%		n	%	n	%	
Civil status					0.427					0.453
Single	3	3.7%	2	2.4%		0	0.0%	1	1.2%	
Married	10	12.2%	5	6.1%		13	15.9%	11	13.4%	
Widower	14	17.1%	17	20.7%		1	1.2%	3	3.7%	
Cohabiting	1	1.2%	0	0.0%		0	0.0%	1	1.2%	
High cholesterol					1.000					0.378
No	18	22.0%	15	18.3%		10	12.2%	14	17.1%	
Yes	8	9.8%	8	9.8%		4	4.9%	2	2.4%	
Unknown	2	2.4%	1	1.2%		0	0.0%	0	0.0%	
Diabetes					0.910					0.552
No	19	23.2%	15	18.3%		13	15.9%	14	17.1%	
Yes	9	11.0%	9	11.0%		1	1.2%	2	2.4%	
Parkinson's disease					0.092					0.228
No	28	34.1%	21	25.6%		14	17.1%	13	15.9%	
Yes	0	0.0%	3	3.7%		0	0.0%	3	3.7%	
High blood pressure					0.496					0.260
No	11	13.4%	8	9.8%		11	13.4%	9	11.0%	
Yes	15	18.3%	16	19.5%		3	3.7%	7	8.5%	
Unknown	2	2.4%	0	0.0%		0	0.0%	0	0.0%	
Nutritional status					*< 0.001*					0.002
Malnutrition	0	0.0%	5	6.2%		0	0.0%	4	4.9%	
Malnutrion risk	12	14.8%	16	19.8%		5	6.2%	10	12.3%	
Normal	16	19.8%	2	2.5%		9	11.1%	2	2.5%	

**p < 0.05 showing statistical difference. Comparison between groups were made using Pearson's, Chi-squared and Fisher's exact tests.*

Elderly with dementia develop dietary needs, requiring a global support to maintain or reestablish weight (22). In addition, weight loss and malnutrition generate complications and lead to infections, respiratory failure and health failure and decrease protein synthesis, increasing mortality. A proper nutrition has a fundamental role in this disease, because it is able to prevent higher vulnerability and provide a better quality of life, delaying symptoms and progressiveness of AD (19).

Due to physiological and psychological alterations, feeding can be really difficult in AD patients. When both disease and age progress, autonomy loss may occur, which has a negative impact in food intake and nutrition. Therefore, AD people meals should be nutritionally rich as well as sensory appealing (colors, consistency, aroma); in other words, they must stimulate the desire to consume foods (24).

It is important to analyze that malnutrition compromises substantially limited populations, as elderly with AD. Nutritional problems, like thinness and loss of lean body mass are associated to morbidity and mortality increase, with a negative impact in quality of life, mainly in advanced ages (18). Alzheimer progressively makes patients unable to make daily activities, such as eating, independently, causing nutritional problems, weight loss and inadequate nutrients intake. All these things are observed in AD patients, and for this reason, a precocious nutritional assessment is really important (16).

A study limitation was the small sample and the difference in age between groups; however, this was statistically corrected. A review and meta-analysis by Prince et al. showed a significant increase of dementia associated to age, with higher prevalence in women and men in all age groups (10). A major risk factor to AD is age increase, because one in four people aged 85 years and over has dementia (22).

Therefore, nutritional assessment in AD has shown to be of great importance to perform effective interventions aiming to preserve or recover nutritional status in third-age, reducing medical interventions due to fractures and diseases caused by poor nu-

trition and reduced nutrient absorption, which may be corrected through vitamin and food supplements (20,21).

CONCLUSION

The results of the present study reinforce the hypotheses that MNA can be used as a proper instrument to evaluate nutritional status in the elderly, identifying malnutrition risk before clinical manifestations happen. It is important to measure risk and nutritional status of AD' people to monitor this condition.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Green tea supplementation promotes leukocyte telomere length elongation in obese women

La suplementación con té verde promueve la elongación de los telómeros de leucocitos en mujeres obesas

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Abstract

Introduction: inflammation and oxidative stress are factors that may play a substantial role in telomere attrition. In line of this, obesity is associated with telomere shortening. Green tea had anti-inflammatory and antioxidant effects and may alter telomere length (TL).

Objectives: we evaluated the effect of decaffeinated green tea supplementation in obese women on TL.

Methods: we conducted a cross-sectional interventional study with ten obese (body mass index [BMI] > 40 kg/m²) and eight normal weight (BMI > 18.5 and < 24.9 kg/m²) women (age between 27 and 48 years). The supplementation was carried out with capsules (each contained 450.7 mg of epigallocatechin-3-gallate) during eight weeks. Anthropometric and dietary intake assessment, and blood collection (for biochemical and TL analysis by quantitative PCR) were performed before and after supplementation. Normal weight patients were evaluated at a single moment.

Results: we observed a significant increase on TL after supplementation (1.57 ± 1.1 to 3.2 ± 2.1 T/Sratio; $p < 0.05$). Moreover, we found shorter TL in obese patients (day 0) when compared to normal weight individuals (3.2 ± 1.9 T/Sratio; $p < 0.05$) and an inverse association between TL and BMI, even after age adjustment (beta = -0.527; $r^2 = 0.286$; IC = -0.129, -0.009).

Conclusion: obesity is related to shorter telomeres. Green tea supplementation during eight weeks promotes telomere elongation in obese women.

Key words:

Obesity. Epigallocatechin-3-gallate. Green tea. Telomere length. Supplementation.

Resumen

Introducción: la inflamación y el estrés oxidativo son factores que pueden jugar un papel importante en el desgaste de los telómeros. En línea con esto, la obesidad está asociada con el acortamiento de los telómeros. El té verde tiene efectos antiinflamatorios y antioxidantes y puede alterar la longitud de los telómeros (LT).

Objetivos: evaluamos el efecto de la suplementación de té verde descafeinado en la LT en mujeres obesas.

Métodos: realizamos un estudio intervencionista de corte transversal con 10 mujeres obesas (IMC > 40 kg/m²) y 8 con peso normal (IMC > 18,5 y < 24,9 kg/m²) (edad entre 27 y 48 años). La suplementación se llevó a cabo con cápsulas (cada una contenía 450,7 mg de epigalocatequina-3-galato) durante 8 semanas. La evaluación de la ingesta antropométrica y dietética y la recolección de sangre (para análisis bioquímicos y LT por PCR cuantitativa) se realizaron antes y después de la administración de suplementos. Los pacientes de peso normal fueron evaluados en un solo momento.

Resultados: observamos un aumento significativo en LT después de la suplementación (1,57 ± 1,1 a 3,2 ± 2,1 T/S ratio; $p < 0,05$). Además, encontramos LT más corta en pacientes obesos (día 0) en comparación con individuos de peso normal (3,2 ± 1,9 T/S ratio; $p < 0,05$) y una asociación inversa entre LT e IMC, incluso después del ajuste de edad (beta = -0,527; $r^2 = 0,286$; IC = -0,129, -0,009).

Conclusión: la obesidad está relacionada con los telómeros más cortos. La administración de suplementos de té verde durante 8 semanas promueve la elongación de los telómeros en mujeres obesas.

Palabras clave:

Obesidad. Epigalocatequina-3-galato. Té verde. Telómero. Suplementación.

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INTRODUCTION

Telomeres consist of long stretches of 5'-TTAGGG-3' repeats associated with specific proteins and are located at the end of chromosomes in eukaryotic cells (1,2), promoting chromosomal stability (2) by preventing attrition, end-to-end fusions and chromosomal rearrangements (3). In this context, it is well established that telomere length (TL) of leukocytes is a reliable marker of biological aging (4).

Inflammation and oxidative stress are factors that may play a substantial role in telomere attrition (5). Given that lifestyle factors affect oxidative stress and inflammation pathways, recent studies have showed that they might relate to telomere biology (6). On the other hand, telomere shortening, which is sensitive to the level of oxidative stress, has been associated with chronic diseases such as hypertension, insulin resistance and, mainly, obesity (7). However, the relationship between TL and obesity is still controversial in literature (8,9). Shorter TL was associated with obesity by some authors (10), but other studies showed no association (11,12). Moreover, recently, weight loss has been associated with telomere lengthening (13).

In line with this, recent studies showed a correlation between TL and energy intake (inverse correlation) (14) and dietary antioxidant intake, particularly β-carotene (direct correlation) (15). Supporting the evidence that antioxidant nutrients are related to longer TL, several studies have reported that the intake of antioxidant-rich foods, such as nuts and coffee, is positively related to TL (16).

Emerging evidences have demonstrated that green tea and its most abundant catechin (polyphenol epigallocatechin-3-gallate, EGCG) have anti-inflammatory (17) and antioxidant (18) effects. Thus, considering the association between telomere and oxidative status, green tea components may alter TL. The aim of this study was to evaluate the effect of decaffeinated green tea supplementation in obese women on TL and aid the knowledge of molecular mechanisms of EGCG to improve the treatment of obesity.

MATERIAL AND METHODS

PATIENTS

We conducted a cross-sectional interventional study in which ten obese (body mass index [BMI] > 40 kg/m²) and eight normal weight (BMI > 18.5 and < 24.9 kg/m²) women aged between 27 and 48 years were recruited. Patients were recruited from a previous study of our research group (data not published) that occurred between February 2015 and November 2015. Patients with alterations in liver biomarkers (glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, gamma-glutamyl transpeptidase and alkaline phosphatase) were not included. Patients with a history of metabolic diseases such as diabetes, Cushing syndrome, hypo or hyperthyroidism and dyslipidemias, smokers and patients in use of medications such as antidepressants, antiobesity or hormone therapy, were excluded.

The present study was approved by the Research Ethics Committee of the Clinical Hospital of Ribeirão Preto Medical School, University of São Paulo, SP, Brazil (CAAE: 30247414.6.0000.5440) and conducted according to the Declaration of Helsinki. All participants provided a written informed consent.

GREEN TEA SUPPLEMENTATION PROTOCOL

The decaffeinated green tea supplementation was carried out with capsules. Each capsule contained 1,009.6 mg of green tea extract and 450.7 mg of EGCG. Other adjuvants included in the capsule were vegetable celluloses, magnesium stearate and silica. All capsules were purchased from the company Solaray®, USA (single lot). Patients were instructed to use two capsules per day in the morning for eight weeks.

The patients were attended at the Metabolic Unit of the University Hospital at Ribeirão Preto Medical School, São Paulo University, in three different moments: baseline (day 0), after four weeks (day 28) and after eight weeks (day 56). At day 0, the patients received 56 green tea capsules and the first assessment was performed. At day 28, they returned to the hospital to attend a conference on the capsules and received 56 capsules more. At day 56, they came to the final assessment and another capsules conference was performed. Indeed, patients were contacted weekly by telephone as a form of control of the capsules ingestion.

To ensure the green tea effect and control possible bias, patients were instructed not to change their dietary pattern and physical activity habits.

DATA COLLECTION

For obese patients supplemented with green tea, data collection occurred on day 0 and day 56. Normal weight patients were evaluated at a single moment. In all the stages, anthropometric and dietary intake assessment and blood collection (for biochemical analysis and the TL) were performed.

ANTHROPOMETRIC EVALUATION

After emptying the bladder, weight was measured with a Filizola® digital scale type platform with 300 kg capacity and 0.2 kg precision, with the participant barefoot and wearing light clothing. Height was measured with a vertical rod with 0.5 cm graduations.

DIETARY INTAKE ASSESSMENT

Dietary intake was evaluated by a 24-h recall (two were applied on weekdays and one on the weekend). A specific nutrition (NutWin-CIS Program of Nutrition Support) was used to calculate the amount of dietary calories, carbohydrate, protein and lipid intake.

BIOCHEMICAL ASSESSMENT

After 12 hours of fasting, a trained professional collected patients' peripheral blood. Total cholesterol (TC), low-density lipoprotein (LDL cholesterol), high-density lipoprotein (HDL cholesterol), and triglycerides (TG) levels were determined by automated colorimetric, and plasma level of glucose was determined by an enzymatic method.

QUANTIFICATION OF TELOMERE LENGTH BY QUANTITATIVE REAL-TIME PCR

The DNA was automatically extracted using the Maxwell® MDx (Promega Corporation, Madison, WI) instrument and the Maxwell® 16 Blood DNA Purification kit, which uses paramagnetic bead separation method. The methodology was modified from original protocol. Blood samples were collected in EDTA tubes, centrifuged at 2,000 x g for ten minutes and 300 ul of buffy coat was used for the DNA purification.

TL was measured according to the protocol described by Cawthon in 2002 (19) by quantifying the relative average of the telomeres by qPCR. The thermal cycler used was the 7500 Fast Real Time PCR System (Applied Biosystems®). For the reaction, the SYBR® Green PCR Mastermix kit (Qiagen) was used in a final volume of 20 ul. The set of primers used is described in table I. The concentration of primers and sample were modified from the original protocol: 700 nM of each primer and 20 nM DNA were used (these values were selected from the stander curve). The specificity was confirmed through the melting curve in all reactions. The assays were conducted in triplicate. The relative quantification of TL was determined using the telomere to single copy gene ratio (T/S) by calculating the $\Delta C_t(C_t^{(telomeres)}/C_t^{(single\ gene)})$. The ratio of T/S for each sample was calculated from the following formula: $2^{-\Delta Ct(telomere) - \Delta Ct(Single\ gener)} = 2^{-\Delta\Delta Ct}$, following the parameters of Phillip Scheinberg et al. (2010). In this assay, the 36B4 (ribosomal protein large PO) gene was used as a reference for the single copy gene. For the calculation of $2^{-\Delta\Delta Ct}$ in this assay, each sample was normalized to the average T/S ratio of a reference sample, using the stander curve and validation sample as reference.

STATISTICAL ANALYSIS

As a preliminary analysis, the Shapiro-Wilk test was used to assess the normality of the data. Paired t test was used to compare variables at day 0 and day 56. The independent t test was used to compare variables between groups. The Pearson correlation between all the variables and TL, and multiple regression analysis with the TL as dependent variable and the other continuous variables (weight, BMI, age, biochemical variables) as the independent ones were performed. The significance level used for the tests was set at $p < 0.05$. All analyses were performed by using SPSS Statistics 21.0 (SPSS Inc.).

Table I. Primers designed for telomere quantification

Primer	Sequence
Tel 1	5'-GGTTTTTGAGGGTGAGGGTGAGGGTGAGGGTGAGGGT-3'
Tel 2	5'-TCCCGACTATCCCTATCCCTATCCCTATCCCTATCCCTA-3'
36B4u	5'-CCCATTCTATCATCAACGGGTACAA-3'
36B4d	5'-CAGCAAGTGGGAAGGTGTAATCC-3'

RESULTS

Table II summarizes the general features of the patients at baseline and after eight weeks of supplementation. There are no significant weight losses or BMI changes with the intervention. However, significant reductions in cholesterol total and LDL cholesterol levels were observed. All biochemical variables were within the normal range already at baseline.

As expected, there was no change in energy and macronutrients intake during supplementation.

As shown in figure 1, TL was markedly increased after green tea supplementation. Indeed, we found shorter TL in obese patients (day 0) when compared to normal weight individual. There was an inverse correlation between TL and BMI (Fig. 2); however, TL was not correlated with biochemical variables (data not shown). The linear regression analysis confirms the influence of BMI on TL, even after age adjustment (beta = -0.527; $r^2 = 0.286$; IC = -0.129, -0.009).

DISCUSSION

In our study, a significant increase in TL in obese patients after eight weeks of green tea supplementation was observed. Furthermore, our study is the first to evaluate the TL after this type of intervention. Interestingly, our results showed that BMI influences TL and obese patients have shorter telomeres.

It is still unclear whether telomere shortening is a cause or a consequence of obesity. The oxidative stress and chronic inflammation associated to the obesity condition play an important role on telomere loss (20) and may accelerate telomere attrition (5,21). Elevated reactive oxygen species (ROS) levels may attack G triplets in telomeres, leading to DNA cleavage and, consequently, to telomere shortening and cellular dysfunction (20,22). However, while most of the studies reported a significant association with obesity and shorter TL (9,23,24), a few did not observe any correlation (25-27). In addition, Muezzinler et al. (2014) (24) suggest that there is a biologically plausible inverse association between BMI and leukocyte TL.

Our data are consistent with previously published studies that show telomere lengthening after different strategies to control obesity (13,28,29). In this context, it has been shown that the Mediterranean diet promotes weight loss and longevity, changing TL (28,29). In addition, Carulli et al. (2016) (13) evidenced telomere elongation after six months of bioenteric intragastric balloon.

Table II. General characteristics of obese patients at baseline and after green tea supplementation and normal weight individuals

	Obese patients (n = 10)			Normal weight patients (n = 8)	p value†
	Day 0	Day 56	p value*		
Weight (kg)	119.7 ± 17.8‡	120 ± 18	0.772	55.2 ± 5.6	*0.000*
BMI (kg/m²)	45.3 ± 4.7	45.4 ± 5	0.695	21.5 ± 2	*0.000*
Glycemia (g/dl)	92.2 ± 6.9	92.4 ± 8.5	0.932	84.6 ± 10.6	0.116
Total cholesterol (g/dl)	192.8 ± 33.2	182.4 ± 31.2	*0.017*§	154.6 ± 10.6	0.065
HDL cholesterol (g/dl)	45.2 ± 7.7	42.7 ± 4.2	0.184	47 ± 9.7	0.711
LDL cholesterol (g/dl)	128.2 ± 20.8	120.2 ± 20.1	*0.002*	94.4 ± 31.8	0.024
Triglycerides (g/dl)	114.4 ± 46.2	116.3 ± 60.3	0.837	65.6 ± 25.5	0.049
AST (U/l)	17.1 ± 2.7	16.1 ± 2.3	0.162	24.4 ± 7.4	*0.013*
ALT (U/l)	19.7 ± 6	17.6 ± 4.8	0.060	26.4 ± 19.9	0.335
GGT (U/l)	31.1 ± 10.3	26.7 ± 8.2	*0.009*	33.8 ± 18.1	0.715
Alkaline phosphatase (U/l)	167.4 ± 33.7	174.3 ± 29	0.410	140.2 ± 39.6	0.187
Energy intake (kcal)	2,438 ± 344	2,309.4 ± 155.7	0.302	1,701.7 ± 628.6	*0.008*
Protein intake (g)	96.9 ± 19.9	102.2 ± 27.3	0.640	60.7 ± 17.4	*0.002*
Carbohydrate intake (g)	320 ± 68.6	260 ± 60.6	0.060	221.7 ± 85.8	*0.036*
Lipid intake (g)	87.3 ± 25.4	93.4 ± 1.4	0.391	71.5 ± 39.7	0.254

*BMI: body mass index; HDL: high density lipoprotein; LDL: low density lipoprotein; AST: aspartate transaminase; ALT: alanine transaminase; GGT: gamma-glutamyl transferase. *Paired t test for comparison between day 0 and day 56 (before and after eight weeks of green tea supplementation). †Independent t test for comparison between groups (obese at day 0 and normal weight patients). ‡Mean ± standard deviation (SD). §Bold values indicate p < 0.05.*

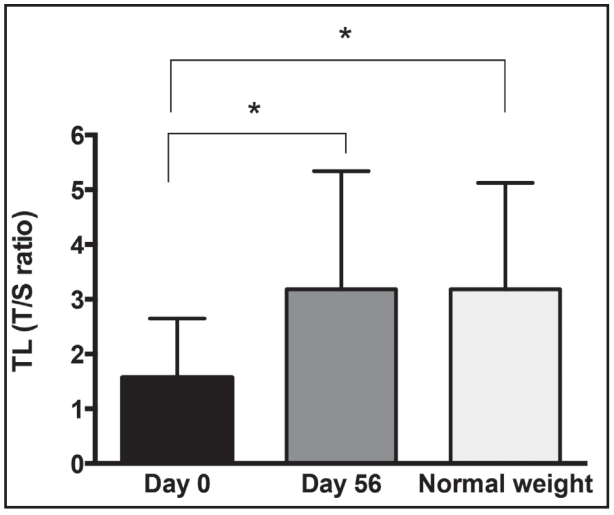

Figure 1.

TL in obese patients before (day 0) and after (day 56) green tea supplementation and in normal weight patients. *p < 0.05. TL: telomere length.

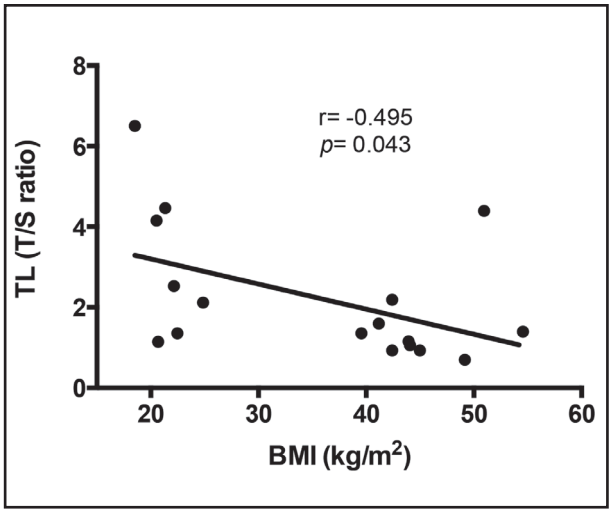

Figure 2.

Inverse correlation between TL and BMI. TL: telomere length; BMI: body mass index.

In spite of the association between weight loss and TL changes in the literature, it is noteworthy that green tea supplementation for eight weeks was not enough to modify weight; however, it modified TL, showing that this changes may be due to tea's compounds.

Green tea flavonoids are an important source of catechins, which are strong antioxidants (30), and epigallocatechin-3-gallate (EGCG) has been attributed to decrease oxidative stress development (31). The antioxidant properties of green tea, especially of its major compound, EGCG, are directly connected to the number and

the position of the hydroxyl (-OH) groups distribute on aromatic ring in the molecule (32). It has been shown that the hydroxyl group contributed to antioxidant activity. This effects was attribute by the electron-donating hydroxyl groups location, the presence of -OH in the position 5- and 7- in the A ring, and the presence of the catechol group (3,4-dihydroxyl) in B ring was directly associated with the antioxidant activity. Another effect that can strongly modulate the potential as free radical scavengers of the catechins is the presence of the gallate group linked in the ring C (33,34).

The relationship between TL and nutrients, foods, and dietary patterns is well documented in the literature. Thus, we know that dietary intake during the period of supplementation may be a factor that interferes with TL. However, there were no changes in energy and macronutrients intake during the intervention period. Moreover, no correlation was found between food intake and TL. Therefore, we assume that the changes found in TL were due to green tea supplementation.

A potential limitation of the present study needs to be considered and is represented by the relatively limited sample size due to the peculiar intervention design of the study.

In summary, the results from this study show that obesity is related to shorter telomeres and, in obese women, green tea supplementation during eight weeks promotes telomere elongation. This indicates that obesity may accelerate the aging process and supports the evidence that the intake of antioxidant-rich foods and beverages affect longevity and health.

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ETHICAL APPROVAL

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the Declaration of Helsinki of 1964 and its later amendments or comparable ethical standards.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Visceral adiposity increases the risk of breast cancer: a case-control study

La adiposidad visceral aumenta el riesgo de cáncer de mama: un estudio de casos y controles

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Abstract

Introduction: in recent decades, lifestyle changes in women involving physical inactivity, insulin resistance and body fat distribution have been associated with an increase in breast cancer.

Objective: to assess whether insulin resistance, lipid profile, and visceral adiposity are associated with increased risk of breast cancer.

Methods: a hospital-based case control study was conducted with 116 women newly diagnosed with breast cancer and 226 controls. Body mass index, waist circumference, total cholesterol, high-density lipoproteins (HDL), low-density lipoproteins (LDL), very-low-density lipoproteins (VLDL), triglycerides, glycated hemoglobin, HOMA-IR, HOMA-β, lipid accumulation product (LAP), and visceral adiposity index (VAI) were assessed. Logistic regression was adjusted for body mass index and age to quantify the association between breast cancer risk and insulin resistance, dyslipidemias, and visceral adiposity.

Results: the case group had higher insulin resistance ($p < 0.001$), LAP ($p = 0.012$), and VAI ($p = 0.004$), and lower concentrations of HDL ($p = 0.024$) and HOMA-β ($p = 0.010$) compared to the control. Insulin resistance (OR = 3.00, 95% CI: 1.75-5.17, $p < 0.001$) and higher VAI (OR = 1.91, 95% CI: 1.17-3.13, $p = 0.01$) were associated with breast cancer, whereas the highest concentration of HDL reduces the chances of cancer by 53% (95% CI: 0.32-0.86, $p = 0.026$). In the multivariate analysis, only LAP and VAI were associated to breast cancer.

Conclusions: visceral fat accumulation increases the risk of breast cancer.

Key words:

Breast cancer. Insulin resistance. Visceral adiposity. Lipid profile.

Resumen

Introducción: en las últimas décadas, los cambios de estilo de vida en las mujeres relacionados con la actividad física, la resistencia a la insulina y la distribución de la grasa corporal se han asociado con el aumento de cáncer de mama.

Objetivo: evaluar si la resistencia a la insulina, el perfil lipídico y la adiposidad visceral están asociados con un mayor riesgo de padecer cáncer de mama.

Métodos: se realizó un estudio de casos y controles en hospitales en el que participaron 116 mujeres recién diagnosticadas con cáncer de mama y 226 controles. Fueron evaluados índice de masa corporal, circunferencia de la cintura, colesterol total, lipoproteínas de alta densidad (HDL), lipoproteínas de baja intensidad (LDL), lipoproteínas de muy baja densidad (VLDL), triglicéridos, hemoglobina glicosilada, HOMA-IR, HOMA-β, el producto de acumulación de líquidos (LAP) y el índice de adiposidad visceral (VAI). La regresión logística se adaptó al índice de masa corporal y a la edad para cuantificar la asociación entre el riesgo de cáncer de mama y la resistencia a la insulina, dislipidemias y adiposidad visceral.

Resultados: el grupo de casos presentó mayor resistencia a la insulina ($p < 0,001$), LAP ($p = 0,012$) y VAI ($p = 0,004$) y menores concentraciones de HDL ($p = 0,024$) y HOMA-β ($p = 0,010$) frente al grupo de control. La resistencia a la insulina (OR = 3,00, IC 95%: 1,75-5,17, $p < 0,001$) y mayor VAI (OR = 1,91, IC 95%: 1,17-3,13, $p = 0,01$) fueron asociadas al cáncer de mama, mientras que la mayor concentración de HDL reduce las probabilidades de cáncer al 53% (IC 95%: 0,32-0,86, $p = 0,026$). En el análisis multivariado, solo LAP y VAI se asociaron al cáncer de mama.

Conclusión: la acumulación de grasa visceral aumenta el riesgo de cáncer de mama.

Palabras clave:

Cáncer de mama. Resistencia a la insulina. Adiposidad visceral. Perfil lipídico.

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Informed consent: The study was approved by the Human Research Ethics Committee of the Federal University of Goiás (reference number 751.387/2014). Participants were informed of the risks and purposes of the study before written consent was obtained. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Author´s contributions: JCM Godinho-Mota conceived the study and performed the statistical analysis. JCM Godinho-Mota, KA Martins and R Freitas-Junior participated in the study design and coordination. JCM Godinho-Mota, L Vaz-Gonçalves, JF Mota and LR Soares conducted the research. All authors were involved in writing the paper and had final approval of the submitted and published versions.

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INTRODUCTION

In Brazil, breast cancer is one of the most common types of cancer and the leading cause of cancer mortality in women (1). According to estimates from the American Institute for Cancer Research (AICR), in the next 14 years the prevalence of breast cancer in Brazilian women is expected to increase by 1.8 times, with an estimated 104,617 new cases in 2030 (2).

In recent decades, several factors of modifiable or potentially modifiable risks have been associated with mammary carcinogenesis, such as physical inactivity, body adiposity, and body fat distribution (3,4). However, there is no consensus on the link between adiposity and breast cancer, since there is no differentiation between the total body fat mass and its distribution in some of these studies (3,4-9).

Insulin resistance and lipid abnormalities resulting from the accumulation of body fat are risk factors for well-established cardiovascular disease (7,8). However, the combination of these changes with breast cancer remains unknown and, recently, some studies have suggested an association among increased triglyceride (TG) concentrations, low density lipoproteins (LDL), and decreased high density lipoprotein (HDL) concentrations in the pathogenesis of some types of cancer, especially breast cancer (9,10).

Insulin sensitivity seems to have a key role in the risk of breast cancer, since obese women without insulin resistance have significantly less risk (11). This raises the hypothesis that the concentration of fat in the abdominal region as well as lipid levels and insulin resistance may increase the risk of breast cancer.

MATERIALS AND METHODS

STUDY DESIGN

This is a case-control study conducted in a university hospital of reference for diagnosis and treatment of breast cancer, with the data collected in the period between August 2014 and June 2016.

PARTICIPANTS AND CALCULATION OF THE SAMPLE

The study included women aged between 30 and 80 years. In the case group, those with a recent breast cancer diagnosis (incident case), immediately after diagnostic confirmation by biopsy and before the start of any treatment were considered as eligible, and those who had metastasis, recurrence, or history of another cancer were excluded. The control group included women without a history of breast cancer or other anatomical sites who recently underwent mammography and physical examination of the breasts without changes.

Exclusion criteria included the presence of any cognitive or psychiatric impairment that prevented the understanding of the work and the collection of necessary information. The carriers of clinical conditions that compromised nutritional status and/or damage to physical activities, such as diabetes mellitus, hypothyroidism, metabolic syndrome, morbid obesity, hypercholesterolemia, and hypertriglyceridemia were also excluded (12). The two groups were matched for age (five years) and nutritional status, which was initially classified using the body mass index (BMI).

To calculate the sample size, an expected prevalence of insulin resistance measured by HOMA-IR of 34.0% was considered in women without cancer and 52.6% for those newly diagnosed with breast cancer (13). A significance level of 5.0% was admitted, considering a two-tailed test, a rejection power of the null hypothesis of 90.0%, and a composition of two controls for each case. The estimated minimum necessary sample was 110 cases and 220 controls, totaling 330 women in the study.

ANTHROPOMETRIC AND BIOCHEMICAL PARAMETERS

We conducted a pilot study for the adequacy, accuracy, and precision of anthropometric measurements and body composition using as a reference the anthropometry standardization technique recommended by Habicht (1974) (14).

We used a digital anthropometric scale, with an accuracy of 0.1 kg and a 150 kg capacity, for the evaluation of body weight (kg), and a stadiometer, with an accuracy of 0.1 cm, to obtain height. Both were performed with the procedures described by Heyward and Stolarczyk (2000) (15). BMI was calculated by the ratio of weight (kg) by the square of height (m). We used the cut-off points recommended by the World Health Organization (WHO) (1997) (16). Waist circumference (WC) was measured in triplicate with inextensible and inelastic millimeter tape with accuracy of 0.1 cm at the midpoint between the anterior superior iliac crest and the last rib (17).

To evaluate the glycemic and lipid profile, peripheral vein blood samples were collected in the morning after 12 hours of fasting, 24 hours in the absence of strenuous effort, and 72 hours without drinking alcohol. The plasma samples were separated from the whole blood by centrifugation at 3,500 rpm for ten minutes at 4 °C (Combate, C.E.L.M).

The total cholesterol (TC), HDL, TG, and fasting plasma glucose (FPG) were determined by enzymatic colorimetric method using an automatic analyzer System Vitros® Chemistry 950 Xrl (Johnson & Johnson). The concentration of LDL was calculated using the Friedewald formula for TG values up to 400 mg/dl, where LDL = CT-HDL-TG/5 (18). The determination of glycated hemoglobin was performed by automated equipment turbidimetric method A-25 Biosystems®. The insulin was determined using Insulin AccuBind ELISA kits (Monobind Inc.©). The CV% of the assay corresponding to insulin was CV% = 5.1 intra-assay and 7.2 inter-assay. HOMA-IR and HOMA-β were calculated to evaluate the insulin resistance and functional capacity of pancreatic beta cells, respectively (19). Patients who had values greater than 2.7 were classified as insulin-resistant (20).

The visceral adiposity index (VAI) and the lipid accumulation product (LAP) were obtained by the respective formulas:

VAI = WC/(36.58 + 1.89 x BMI) x (TG/0.81) x (1.52/HDL) (6); LAP = (WC [cm] - 58 x TG concentration [mmol/l]) (5).

In order to ensure good reliability of the results obtained in the measurement of visceral adiposity, patients who had TG levels higher than 279 mg/dl, morbid obesity (BMI 39.99 kg/m²), and pendulous abdomen were excluded from these analyses (6). The VAI, LAP, and HOMA-β values were categorized according to the distribution of the total sample in less than or equal to the 50th percentile and above the 50th percentile. This distribution was adopted because there are no validated cut-off points for these indexes in a sample diagnosed with breast cancer.

STATISTICS

The database was entered in duplicate in the Epi-Info™ (version 7.1.5) and data analysis in Stata software for Windows (version 12.0), considering diagnosis of breast cancer as the outcome variable. We used the Kolmogorov-Smirnov test to verify the normal distribution of continuous variables. To compare continuous variables between groups, the Mann-Whitney U test was applied (non-parametric distribution). Posteriorly, a binary logistic regression adjusted by age and BMI, respectively, was performed in order to get the odds ratio (OR) and 95% confidence interval (95% CI). The coefficient of determination (R^2) was evaluated for diagnosis by the regression model. In addition, collinearity between the variables was tested by correlation test and none returned significant values ($r > 0.90$) that excluded them from the logistic regression analysis. Variables whose significance level was less than 0.05 ($a < 5.0\%$) were considered to be associated with breast cancer outcome. Backward stepwise regression was used to determine independent covariates contributing to the final model on multivariate analysis.

RESULTS

The study included 342 women, 116 newly diagnosed with breast cancer and 226 healthy, with a mean age of 52.36 ± 11.05 years. The majority (61.11%) was in post-menopause, and the average age of menopause did not differ between groups (cases: 46.82 ± 6.41 years; controls: 47.61 ± 6.52 years; p = 0.400). There was a prevalence of overweight patients (67.84%, n = 232) in both groups, with an average BMI of 27.26 ± 4.87 kg/m² and 26.68 ± 5.06 kg/m² between cases and controls, respectively (p = 0.929).

Among the glycemic profile variables, only glycated hemoglobin showed no mean differences between groups. Additionally, women newly diagnosed with breast cancer had higher VAI and LAP and lower HDL when compared to controls (Table I).

It was observed that there was a higher prevalence of women in the case group with fasting insulin above the 50th percentile when compared to healthy women (OR = 2.87, 95% CI: 1.70-4.85). Similar results were found for the categories of glucose intolerance, as measured by fasting glucose (OR = 2.11, 95% CI: 1.21-3.69) and insulin resistance (OR = 3.00, 95% CI: 1.75-5.17). VAI and LAP above the 50th percentile increased by 91% and 74% the chances of having breast cancer (OR = 1.91, 95% CI: 1.17-3.13 and OR = 1.74, 95% CI: 1.06-2.85), respectively. In contrast, HDL above 50 mg/dl reduced the chances for breast cancer by 53% (Table II). On multivariate analysis using (Table III), we found that VAI and LAP were associated with breast cancer.

Table I. Differences in glycemic and lipid profile and markers of abdominal fat between cases and controls

Variables	Controls (n = 226)		Cases (n = 116)		p*
	Median	Interquartile	Median	Interquartile	
Fasting glucose (mg/dl)	89.0	83.0-95.0	93.0	86.0-101.0	*0.004*
Hemoglobin A1C (%)	6.0	5.3-6.9	5.9	5.4-6.9	0.652
Insulin (uU/ml)	7.7	5.5-10.9	9.9	7.0-14.2	*< 0.001*
HOMA-IR	1.8	1.2-2.6	2.3	1.6-3.6	*< 0.001*
HOMA-β	106.8	79.6-153.6	122.4	92.0-190.9	*0.010*
Total cholesterol (mg/dl)	193.0	166.0-217.0	196.0	170.0-216.0	0.750
HDL (mg/dl)	56.0	48.0-66.0	52.0	44.0-61.0	*0.024*
LDL (mg/dl)	113.5	88.5-133.0	115.0	90.0-137.5	0.383
VLDL (mg/dl)	21.0	15.0-31.0	23.0	17.5-30.5	0.106
Triglycerides (mg/dl)	106.0	77.0-154.0	118.0	90.0-153.0	0.123
Visceral adiposity index	1.6	1.0-2.5	1.95	1.3-2.8	*0.004*
Lipid accumulation product	23.1	17.1-32.7	27.2	18.5-38.0	*0.012*

**Mann-Whitney U test. HDL: high density lipoprotein; LDL: low density lipoprotein; VLDL: very low density lipoprotein.*

Table II. Association of insulin resistance, lipid profile, markers of abdominal fat and breast cancer risk in women

Variables	Controls (n = 226)		Cases (n = 116)		β (constant)	OR (95% CI)	p*
	n	%	n	%			
Fasting glucose (mg/dl)							
< 100	183	82.4	75	70.8	0.70 (-0.56)	1.00	*0.009*
100-125	39	17.6	31	29.2		2.11 (1.21-3.69)	
Hemoglobin A1C							
< 6.50	141	64.0	68	64.8	-0.03	1.00	*0.906*
≥ 6.50	79	35.1	37	35.2	(-0.91)	0.97 (0.59-1.58)	
Insulin (uU/ml)							
< 8.51	122	57.3	37	35.9	0.94	1.00	*< 0.001*
≥ 8.51	91	42.7	66	64.1	(0.73)	2.87 (1.70-4.85)	
Homa-IR							
< 2.71	166	77.9	60	58.2	1.01	1.00	*< 0.001*
≥ 2.71	47	22.1	43	41.8	(-0.39)	3.00 (1.75-5.17)	
Homa-β							
< 113.16	112	52.6	46	44.7	0.31	1.00	*0.112*
≥ 113.16	101	47.4	57	55.3	(-1.18)	1.49 (0.91-2.44)	
Total cholesterol (mg/dl)							
< 200	128	56.9	68	60.2	-0.14	1.00	*0.492*
≥ 200	97	43.1	45	39.8	(-1.00)	0.85 (0.53-1.36)	
HDL (mg/dl)							
< 51	68	30.2	48	42.5	-0.55	1.00	*0.011*
≥ 51	157	69.8	65	57.5	(0.31)	0.53 (0.32-0.86)	
LDL (mg/dl)							
< 130	160	71.4	73	65.2	0.30	1.00	*0.256*
≥ 130	64	28.6	39	34.8	(-1.02)	1.33 (0.81-2.19)	
VLDL (mg/dl)							
< 23	125	56.0	52	46.4	0.38	1.00	*0.066*
≥ 23	98	44.0	60	53.6	(-1.02)	1.55 (0.97-2.49)	
Triglycerides (mg/dl)							
< 150	164	72.9	82	72.6	-0.01	1.00	*0.840*
≥ 150	61	27.1	31	27.4	(-1.02)	1.05 (0.63-1.76)	
Visceral adiposity index							
< 1.72	120	55.3	44	41.5	0.59	1.00	*0.010*
≥ 1.72	97	44.7	62	58.5	(-6.98)	1.91 (1.17-3.13)	
Lipid accumulation product							
< 24.39	117	53.9	45	42.4	0.49	1.00	*0.027*
≥ 24.39	100	46.1	61	57.5	(-0.82)	1.74 (1.06-2.85)	

**Logistic regression adjusted for age and BMI. β: beta coefficients; HDL: high density lipoprotein; LDL: low density lipoprotein; VLDL: very low density lipoprotein; OR: odds ratio.*

DISCUSSION

The main finding in this study was the association of the visceral adiposity to the outcome. Furthermore, values above 50 mg/dl HDL were inversely related to breast cancer in the univariate analysis. It is noteworthy that the VAI and the LAP are representative indicators of a higher risk for the development of and mortality from heart disease, diabetes, and hypertension in different pop-

Table III. Multivariate regression analysis of risk factors for breast cancer

Variables	β	OR (95% CI)	p*
Visceral adiposity index			
< 1.72		1.00	
≥ 1.72	0.72	1.98 (1.19-3.29)	0.008
Lipid accumulation product			
< 24.39		1.00	
≥ 24.39	0.64	1.80 (1.09-3.01)	0.023

*Constant: -1.30. *Backward logistic regression. β: beta coefficients; HDL: high density lipoprotein; LDL: low density lipoprotein; VLDL: very low density lipoprotein; OR: odds ratio.*

ulations (5-8). However, we did not identify other studies investigating their association with breast cancer.

Adipose tissue is an endocrine organ composed mainly of subcutaneous adipose tissue (SAT), located in the hypodermis, and visceral adipose tissue (VAT), which is in the deepest layer of the abdomen, around the organs. There has been observed an increase in VAT in sedentary people, as well as in the aging process, especially after menopause, due to hormonal changes (21). Adipose tissue is directly related to an increased risk of cardiovascular and metabolic diseases; however, its association with the pathophysiology of breast cancer is still uncertain (5-8,21-23).

In the current study, there was a positive association between breast cancer and the VAI and LAP indexes for the assessment of VAT. This association may be due to chronic systemic inflammation due to increased production of pro-inflammatory cytokines, such as C-reactive protein, tumor necrosis factor (TNF-α), and interleukin-6 (IL-6) via toll-like receptor 4 (TLR4) activation and the production of reactive oxygen species (21-26). Moreover, visceral adiposity may result in adipocyte hypertrophy, increased lipolytic activity, and insulin resistance, which results in compensatory hyperinsulinemia (9-11).

Adipocytes in the android region increase the availability of free estrogen through androgen hormone conversion by the enzyme aromatase (9). Thus, it is an important risk factor for breast cancer for possessing an anti-apoptotic and pro-angiogenic effect and an inducer of cell proliferation by binding to the estrogen receptor (ER) in breast cells (10). Some studies have noted increased local secretion of cortisol and pro-inflammatory adipokines, which may also be a cause for increased risk of proliferative diseases such as breast cancer (9-11,21-26).

These mechanisms may explain the association between breast cancer and higher VAI values. The use of this index in clinical practice may help to identify patients at higher risk of developing breast cancer and be useful in the monitoring of women with a previous diagnosis without increasing the costs to health, since they are derived from tests and routine measures that are usually used in the care of women on an outpatient basis.

The association between abnormal glucose and insulin resistance and mammary carcinogenesis remains unclear. However, several studies have found results similar to those observed in this study (9-11,24,27,28), mainly related to insulin resistance.

Insulin resistance reduces the action of insulin in peripheral tissues, competing with the hyperglycemia framework with consequent compensatory hyperinsulinemia. Even with its low hypoglycemic action, this hormone is described to act in specific gene transcription and modulation of cell growth and differentiation, which can be overexpressed, such as in cases of breast cancer (26,27).

The increase in free serum insulin also reduces the production of binding proteins, insulin-like growth factor-binding protein 1 (IGFB-1), and insulin-like growth factor-binding protein 2 (IGFB-2), which may increase the availability of insulin-like growth factor (IGF-1) free bioactive, resulting in concomitant changes in the cellular environment that favor the formation of tumors (24,27,28). The bioactive free IGF-1 can bind to its receptor and the insulin receptor, stimulating DNA synthesis and mitosis of preneoplastic and neoplastic mammary cells (28,29). Thus, both the growth factor similar to the insulin receptor and the insulin receptor are frequently overexpressed in neoplastic mammary cells and are also associated with the tumor size and mortality of the disease (27).

Another reason for the association between breast cancer and insulin metabolism involves the hormonal etiology of this disease (10,13). The high serum concentration of insulin and IGF-1 in women with insulin resistance inhibits the synthesis of sex hormone binding globulin (SHBG). This low serum concentration of SHBG can result in increased availability of free bioactive estrogen, which is able to increase the stimulation and density of breast parenchyma (10,24,27).

In a case-control study that included 124 newly diagnosed Mexican women with breast cancer and 197 healthy controls in order to identify the effect of insulin resistance (HOMA-IR > 3.5) in the development of breast cancer, an association between HOMA-IR and the outcome was not observed, regardless of the menopausal status (13). In the current study, there was a significant association between these variables in a univariate analysis, although a HOMA-IR value greater than 2.7 has been considered as a reference. Thus, a reassessment of the reference values of HOMA-IR is suggested, which could add new information about the association between breast cancer and resistance to insulin action.

The hyperglycemia that precedes diagnosis of diabetes was also associated with the diagnosis of breast cancer and can be explained by the "Warburg effect", which is the ability of tumor cells to alter glucose metabolism, giving priority to rapid cell proliferation and uncontrolled tumor growth (27,29).

The association between the lipid profile and breast cancer has been investigated in different population groups (30-33). In the present study, we observed a higher prevalence of low HDL among women newly diagnosed with breast cancer ($p = 0.011$). This lipoprotein fraction may present anti-inflammatory and antioxidant properties and the ability to inhibit cell proliferation (33). In addition, elevated levels of endogenous estrogens are inversely associated with HDL (31). It is noteworthy that the carcinogenesis process can alter the lipid profile, which may start years before the diagnosis of cancer. It is difficult to establish whether chang-

es in HDL concentrations precede or are a consequence of the disease (34). Thus, prospective and larger sample size studies should be conducted to define the relevance of the lipid profile in the tumor biology of breast cancer, as well as the evaluation of serum estrogens.

Among the limitations of the case-control studies, there is the bias of memory and selection. However, the main variables in research were measured. Furthermore, recruitment of patients in both groups involved the same population to ensure similarity between them, especially with regard to age and BMI.

To the best of our knowledge, this is the first study to evaluate the association of the VAI and LAP indicators of breast cancer. In this context, the homogenization of the case and control groups reduced the influence of age and body composition variables in the research. However, prospective studies are needed to establish a better relationship and the impact of these indicators on the development and monitoring of breast cancer.

The results of this study suggest that women with greater deposition of visceral fat have a higher chance of developing breast cancer. Thus, this study highlights the importance of analyzing the body compartments rather than a partial analysis of total body weight.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Incremento en el consumo de fibra dietética complementario al tratamiento del síndrome metabólico

Increasing consumption of dietary fiber complementary to the treatment of metabolic syndrome

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Resumen

Introducción: la fibra ingerida por la población en Latinoamérica es inferior (10-20 g/d) a lo recomendado por la Organización Mundial de la Salud (OMS) (25-35 g/d). Su consumo se debe promover para pacientes con síndrome metabólico (SM), ya que reduce el riesgo cardiovascular y previene la obesidad y alteraciones asociadas.

Objetivo: evaluar si el incremento del consumo de fibra dietética como coadyuvante para el tratamiento de SM en sujetos del Centro de Salud de San Martín Mexicapam "La Joya", Oaxaca (México), mejora los parámetros clínicos y laboratoriales de los mismos.

Métodos: se trató de un estudio analítico-longitudinal llevado a cabo desde enero hasta abril de 2017, en el cual se evaluó el estado nutricional antes y después de la intervención con fibra dietética y se midieron los niveles de colesterol, triglicéridos y glucosa en sangre en ayuno. Se indicó un incremento de 15 g de fibra (frutas-verduras y/o salvado de avena y/o salvado de trigo) a la dieta habitual por un lapso continuo de ocho semanas.

Resultados: la muestra fue de 30 participantes del Grupo de Ayuda Mutua diagnosticados con SM, cuya media de edad fue de 37,26 años y con un índice de masa corporal (IMC) al inicio de 30,75 kg/cm^2, glucemia de ayuno de 153,87 mg/dl, triglicéridos de 209,67 mg/dl y colesterol de 213,81 mg/dl. Al finalizar la intervención se obtuvo una diferencia estadísticamente significativa ($p < 0,05$): IMC de 29,7 kg/cm^2, glucemia de ayuno de 127,77 mg/dl, triglicéridos de 179,71 mg/dl y colesterol de 207,13 mg/dl.

Conclusión: el incremento del consumo de fibra dietética (salvado de avena) funciona como complemento al tratamiento del SM para disminuir los parámetros clínicos y laboratoriales de los sujetos de estudio. Sin embargo, se requiere de más estudios para generar recomendaciones más claras.

Palabras clave:

Estado nutricional.
Fibra dietética.
Síndrome metabólico.
IMC.

Abstract

Introduction: the amount of fiber ingested in Latin American countries is lower (10-20 g/d) than recommended (35 g/d). An increase is recommended for patients with metabolic syndrome (MS) to reduce cardiovascular risk, as well as to prevent obesity and other complications.

Objective: to evaluate whether increased dietary fiber consumption complements MS treatment and improves clinical and laboratory parameters in subjects at the San Martín Mexicapam "La Joya" Health Center, Oaxaca (Mexico).

Methods: an analytical-longitudinal study was carried out from January to April 2017, to evaluate nutritional status before and after intervention with dietary fiber and to measure cholesterol levels, triglycerides and fasting blood glucose. An increase of 15 g of fiber (fruits-vegetables and/or oat bran and/or wheat bran) was indicated in the usual diet over eight weeks.

Results: the sample consisted of 30 participants from the Mutual Aid Group diagnosed with MS, with an average age of 37.26 years, starting from a body mass index (BMI) of 30.75 kg/cm^2 and levels of fasting glycemia at 153.87 mg/dl, triglycerides at 209.67 mg/dl, and cholesterol at 213.81 mg/dl. Following the intervention, a statistically significant difference ($p < 0.05$) was obtained with a BMI of 29.7 kg/cm^2, fasting glycemia at 127.77 mg/dl, triglycerides at 179.71 mg/dl and cholesterol at 207.13 mg/dl.

Conclusion: a reduction in the results for the parameters tested in patients of MS is improved by a greater consumption of dietary fiber, such as oat bran. However, additional studies are required to generate clearer recommendations.

Key words:

Nutritional status.
Dietary fiber.
Metabolic syndrome.
BMI.

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Este manuscrito es de un artículo original con respecto a una propuesta de incremento de 15 g en el consumo de fibra dietética para sujetos diagnosticados con síndrome metabólico.

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INTRODUCCIÓN

El síndrome metabólico (SM) y la obesidad (Ob) han experimentado un aumento sin precedentes y su velocidad de incremento ha sido de las más altas en el ámbito mundial. En Latinoamérica, según la Organización Mundial de la Salud (OMS), más de 1.900 millones de adultos de 18 o más años tenían sobrepeso, de los cuales 600 millones presentaban obesidad. De acuerdo a datos obtenidos del ENSANUT 2012, siete de cada diez adultos mexicanos de las distintas regiones, localidades y nivel socioeconómico presentaron Ob o SM (1). El exceso de tejido adiposo se encuentra asociado con una serie de desajustes metabólicos. Las características más importantes de este síndrome son la obesidad abdominal, la dislipidemia aterogénica, la hipertensión, la resistencia a la insulina y la situación protombótica-proinflamatoria. De acuerdo al panel de expertos en la detección, evaluación y tratamiento de los niveles altos de colesterol en los adultos (ATP III) (2), en la evaluación del estado de nutrición se emplean técnicas de medición y recolección de datos con la finalidad de conocer la situación en la que se encuentra el individuo en ese momento, diagnosticando así su estado nutricional y las modificaciones a realizar en su estilo de vida y alimentación (3-6). Gibson, en 1990, propuso para la evaluación del estado nutricional la toma de los indicadores antropométricos (4-6), clínicos (2), bioquímicos (7) y dietéticos (2,3), además de la comparación de datos obtenidos con parámetros de referencia con la finalidad de realizar un diagnóstico más efectivo (1). Esta evaluación da la pauta para brindar un diagnóstico de la situación en la que se encuentra la alimentación del individuo. Además de cuantificar las calorías así como los nutrimentos que esté consumiendo el individuo, nos permite modificar su alimentación y mejorar así su estado de salud.

La diabetes mellitus (DM) está caracterizada por hiperglucemia, derivada de un defecto en la alteración de la secreción de insulina, o bien por acción de la insulina o por ambas a la vez (8). Es una enfermedad crónica que requiere asistencia médica continua y una educación no solo dirigida al paciente, sino también a su familia para comprender mejor dicha enfermedad, con el fin de responsabilizarse para alcanzar las metas de tratamiento y prevenir o retardar el desarrollo de complicaciones agudas y crónicas (8,9). El SM se caracteriza por una serie de desórdenes o anormalidades metabólicas que en conjunto son considerados factor de riesgo para desarrollar diabetes y enfermedad cardiovascular. Su aparición puede ser simultánea o secuencial, asociada a la presencia de resistencia a la insulina y depósitos de adipocitos en vísceras (10,11). Se considera SM si el individuo presenta tres de los cinco factores según los criterios diagnósticos del Adult Treatment Panel III 2014 (ATP III). Estos son los siguientes:

- Circunferencia de cintura: > 102 cm en hombres y > 88 cm en mujeres.
- Presión arterial: > 130/85 mmHg.
- Glicemia elevada en ayuno: ≥ 100 mg/dl.
- Lipoproteína de alta densidad: < 40 mg/dl en hombres y > 50 mg/dl en mujeres.
- Hipertrigliceridemia: triglicéridos plasmáticos ≥ 150 mg/d (12).

Las dislipidemias son enfermedades asintomáticas que se manifiestan por una elevación en la concentración plasmática de triglicéridos, colesterol o lipoproteínas. Las dislipidemias se relacionan con factores de riesgo como la edad (hombres de 40 o más años, mujeres de 50 o más años), tabaquismo, alcoholismo, DM, hipertensión arterial (HTA), antecedentes heredo-familiares de enfermedades cardiovasculares, sobrepeso y obesidad (13,14). Las causas más frecuentes de dislipidemias son la mala alimentación y el sedentarismo; debido a falta de actividad física se propicia la acumulación de grasa corporal y esto, unido al consumo de una alimentación rica en grasa saturada y baja en fibra, incrementa los factores de riesgo ya antes mencionados.

La fibra dietética se considera un elemento importante para una nutrición sana, además de ser la parte comestible de las plantas o hidratos de carbono análogos que son resistentes a la digestión y absorción en el intestino delgado. Con fermentación completa o parcial en el intestino grueso, se incluyen polisacáridos, oligosacáridos, lignina y sustancias asociadas de la planta (15,16). Las fibras dietéticas promueven efectos benéficos fisiológicos como el laxante y disminuyen los niveles de colesterol en sangre así como los niveles de glucosa en sangre (17). La fibra se clasifica en función de su comportamiento en contacto con el agua como fibra soluble e insoluble. En base a su fermentabilidad, se clasifica en fibras no fermentables, fibras parcialmente fermentables y fibras fermentables. Según su estructura, se divide en carbohidratos de cadena larga o de cadena corta (18). Dentro de las fibras solubles, se encuentran las viscosas (*Psyllium*, betaglucanos, goma guar, salvado de avena) y las no viscosas (inulina, maltodextrina, goma guar parcialmente hidrolizada) (19).

Los grupos de ayuda mutua surgen a partir de los años 30 en forma paralela a la creación de Alcohólicos Anónimos, con la finalidad de brindar herramientas y apoyo a los individuos pertenecientes al mismo y conformando así una red social en donde se comparten problemáticas comunes. Estos grupos han surgido en diversos ámbitos como la salud física y mental, el comportamiento de adicciones y las crisis que se pueden tener en la vida, así como en torno a diversas problemáticas sociales. Se basan en la interacción social y la responsabilidad de los mismos ya que sin su participación los grupos de ayuda mutua no funcionan adecuadamente. El tipo de ayuda que ofrecen es principalmente emocional y se crean para intercambiar información, sentimientos y actividades recreativas que sirven para salir de la rutina y dejar de pensar en los padecimientos que aquejan a sus integrantes. Pertenecer a un Grupo de Ayuda Mutua permite encontrar la compresión con personas que se encuentran en una situación similar, brindando apoyo a quienes lo necesitan, aclarando dudas y saliendo del aislamiento en el que se encuentra el individuo en ese momento (20). El Grupo de Ayuda Mutua del Centro de Salud de San Martín Mexicapam "La Joya", Oaxaca, es un grupo de individuos cuya característica común es el diagnóstico de SM (diabetes mellitus tipo 2, dislipidemias, hipertensión, obesidad abdominal, IMC > 30 kg/cm^2 y la presencia de *Acantosis nigricans*). En base a lo anterior, se decidió aumentar 15 g/d de fibra dietética sobre el consumo habitual estipulado en la normativa mexicana (35 g/d).

Los participantes de este estudio eran miembros del Grupo de Ayuda Mutua del Centro de Salud de San Martín Mexicapam "La Joya", Oaxaca, México, y en él se evaluó la respuesta al incremento del consumo de fibra dietética como complemento para el tratamiento del SM.

MATERIALES Y MÉTODOS

DISEÑO

Se realizó un estudio analítico-longitudinal con una duración de ocho semanas, que incluyó a los integrantes del Grupo de Ayuda Mutua del Centro de Salud de San Martín Mexicapam "La Joya", Oaxaca, cuya asistencia fuera superior al 80% del total de sus citas-talleres programadas, todo ello previa autorización bajo la firma del consentimiento informado.

La población objetivo fue de 30 integrantes que conforman el Grupo de Ayuda Mutua. A dicha población se le evaluó el estado nutricional mediante la aplicación de la historia clínica, toma de medidas antropométricas, análisis bioquímicos y la historia dietética correspondiente. Dicha evaluación fue personalizada y sirvió para identificar el estado de nutrición de los integrantes y presentar así un panorama general de la situación del grupo. La historia dietética aplicada constó de frecuencia de consumos de alimentos, recordatorio de 24 horas y un diario de consumo de alimentos y bebidas.

PROCEDIMIENTO

Las pruebas bioquímicas empleadas abarcaron la toma de glucosa en ayuno, colesterol total y triglicéridos totales. En cuanto a los datos clínicos, se determinó la presión arterial de las participantes, actividad física, antecedentes heredo-familiares y patologías presentes. Y en cuanto a antropometría, los datos a valorar fueron: peso (báscula Tanita® modelo OMROM HBF-514C), talla (estadímetro Seca® modelo Met 211), IMC (Norma Oficial Mexicana: NOM-043-SSA2-2012) y circunferencia de cintura (Flexómetro Vitamex® modelo ANTTQ). Todos los datos mencionados anteriormente fueron valorados a través de cada consulta-taller programada, además de intervenir nutricionalmente con un aumento de 15 g/d en la ingesta de fibra (salvado de avena, salvado de trigo y alimentos variados) ya que las normas oficiales mexicanas 043 (NOM-043-SSA2-2012) y 008 (NOM-008-SSA3-2010) establecen un consumo de 35 g/d de fibra dietética al día para el tratamiento de dichas patologías. Se propuso este incremento de fibra hasta llegar a un consumo total de 50 g/d de fibra dietética en cada sujeto de estudio, tomando en cuenta que cada uno de los participantes cubrió de manera inicial sus 35 g/d a través de la inclusión de alimentos ricos en fibra. Esto se llevó a cabo mediante el uso del Sistema Mexicano de Alimentos Equivalentes. Para el primer grupo se alcanzaron los 15 g restantes de fibra dietética a través del consumo de frutas y vegetales distribuidos durante sus cinco tiempos de comida; para los sujetos del segundo y tercer grupo, cuyo incremento se presentó a través del consumo de salvado, el salvado se brindó a través de una mezcla de 5 g de fibra en un volumen de 250 ml de agua, tres veces al día. Para verificar su consumo durante cada consulta-taller se realizó la frecuencia de alimentos y para ello, los grupos se subdividieron en tres subgrupos diferentes: A) alimentos variados; B) salvado de avena; y C) salvado de trigo. Los alimentos con contenido de fibra del subgrupo A fueron seleccionados del Sistema Mexicano de Alimentos Equivalentes incluyéndose en el plan de alimentación individual y ajustado al contenido calórico, índice glucémico y carga glucémica para cada uno de los sujetos. En cuanto a los 15 g de fibra a través de salvado de avena o bien de salvado de trigo, estos fueron pesados y dosificados para consumir 5 g de fibra antes de cada tiempo de comida (desayuno, comida y cena). Para la obtención de salvados se empleó una descascaradora centrífuga (FKS-560). Además, los subgrupos siguieron un cronograma de actividades y una planeación temática. En cuanto a los estudios laboratoriales estos fueron realizados por el laboratorio del mismo centro de salud empleando métodos de química seca. El procesamiento de los datos obtenidos se realizó a través de Excel®. El análisis descriptivo para las variables cuantitativas incluyó medidas de tendencia central como media, mediana y moda y como medida de dispersión, la desviación estándar. Para las variables cualitativas se utilizaron frecuencias absolutas y porcentajes, así como un análisis estadístico a través de la prueba t de Student con un nivel de confianza del 95% y 5% de error ($p < 0,05$).

RESULTADOS

Para el estudio participaron los 30 sujetos que conforman el Grupo de Ayuda Mutua, con una edad promedio de 37,26 años. Todos los participantes manifestaron tener nula actividad física al iniciar el estudio y presentaron diabetes mellitus tipo 2 controlados con metformina® (500 mg) o bien metformina/glibenclamida® de (500 mg/5 mg). En cuanto al IMC se encontró una media inicial de 30,75 kg/m^2 (Fig. 1). Se identificó a través de la historia dietética que el consumo más frecuente en los sujetos era el de alimentos ricos en grasas saturadas así como un consumo excesivo de hidratos de carbono simples (Tabla I), iniciando con una media de glucosa capilar de 153,87 mg/dl, colesterol total de 213,81 mg/dl y de triglicéridos 209,67 mg/dl. La media de la presión arterial fue de 122/72 mmHg.

Se brindó un total de citas citas-talleres (una cada 15 días hasta completar los dos meses) para cada subgrupo, con la finalidad de proporcionar orientación alimentaria a los participantes. Los planes de alimentación que recibieron los subgrupos fueron individualizados y estuvieron distribuidos en porciones adecuadas al Sistema Mexicano de Alimentos Equivalentes, tal como se muestra en la tabla II. La intervención nutricional consistió en aumentar un 15 g/d el consumo de fibra dietética en los sujetos de estudio, por lo que se subdividieron en grupos de diez sujetos (A, B y C). Durante las sesiones de cita-taller se realizaron frecuencias de alimentos para estimar la adherencia a la intervención establecida. Para el grupo A, se aumentó a través de un consumo mayor

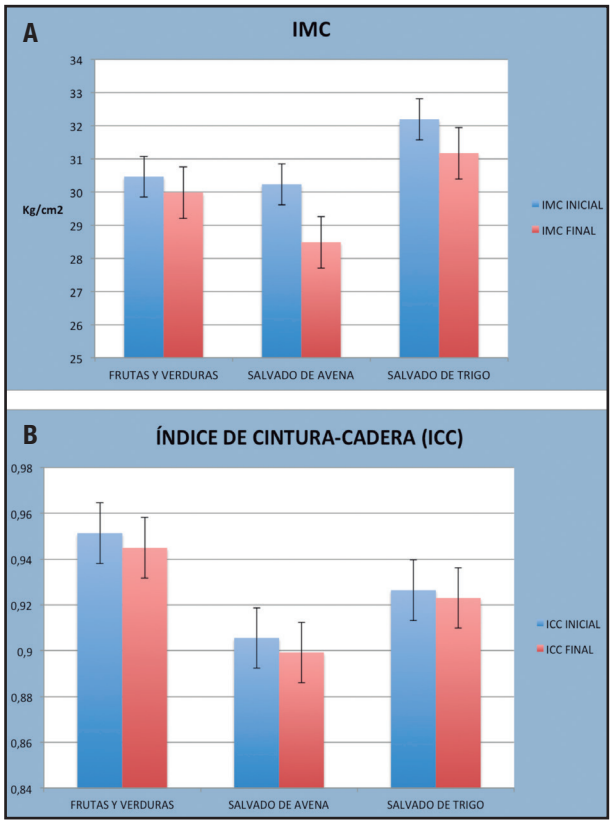

Figura 1.

A. Media inicial y final del índice de masa corporal (IMC) en la población de estudio. B. Media de índice cintura-cadera (ICC) en la población de estudio. En ambas mediciones se observa que hay diferencias estadísticamente significativas entre ellas ($p < 0,05$).

en cantidad de fibra proveniente de diversos alimentos tales como frutas y vegetales, mientras que en el grupo B se incrementó a través de salvado de avena y en el grupo C se otorgó a través de salvado de trigo. En la tabla III se presenta la comparación de los datos bioquímicos obtenidos antes y después de la intervención nutricional para los tres grupos. En ella se observa una disminución en cuanto a los niveles plasmáticos de glucosa, triglicéridos y colesterol. Cuando se compararon los resultados iniciales y finales a la intervención, tanto en los estudios laboratoriales como en datos antropométricos, se encontró que existen diferencias estadísticamente significativas entre los subgrupos ($p < 0,05$). Esto se determinó a través de un análisis mediante la prueba t de Student. Cabe mencionar que los sujetos de estudio manifestaron tener una nula actividad física.

Tabla III. Datos bioquímicos obtenidos antes y después de la intervención nutricional

Grupo	Glucosa (mg/dl)	Triglicéridos (mg/dl)	Colesterol (mg/dl)
A	A. I: 167,27 D. I: 147,63	A. I: 216,09 D. I: 214,54	A. I: 215 D. I: 212,24
B	A. I: 145,7 D. I: 107,2	A. I: 183,2 D. I: 155,9	A. I: 212,6 D. I: 194,1
C	A. I: 147,3 D. I: 126,5	A. I: 229 D. I: 212	A. I: 213,7 D. I: 212

A. I: antes de la intervención nutricional. D. I: después de la intervención nutricional.

Tabla I. Evaluación dietética previa a la intervención nutricional en la población de estudio

Grupo	Hidratos de carbono simples (%)	Hidratos de carbono complejos (%)	Grasas saturadas (%)	Proteína (%)
A	13,34	50,83	9,34	13,6
B	13,21	48,37	6,52	12,96
C	9,74	49,78	10,61	14,73

Tabla II. Distribución general de alimentos con fibra dietética (35 g/d) brindada a los sujetos participantes durante la intervención nutricional

Grupo	*Equivalentes							
	Verdura	Fruta	Cereales s/grasa	Leguminosas	Alimentos de origen animal	Aceites y grasas con proteína	Aceites y grasas sin proteínas	Leche semidescremada
A, B y C	3,5	2,5	7	1,3	2	4	3	0,5

**Basado en el Sistema Mexicano de Alimentos Equivalentes.*

DISCUSIÓN

Los sujetos de estudio en este trabajo presentaron en general una disminución en los niveles de glucosa capilar que fue más notoria en aquellos que consumieron salvado de avena (grupo B). Cabe mencionar que el tipo de fibra que se tiene en el salvado pueden ser celulosas, β-glucanos y hemicelulosas (14). En cuanto a la reducción de glucemia en ayuno, se coincide con lo reportado por Anderson en 2009, el cual determinó que el consumo de fibra dietética está asociado con una disminución significativa en la prevalencia de diabetes tipo 2, siendo la fibra de cereales la que ha presentado un efecto protector en el desarrollo de esta patología.

También se observó una disminución en las medidas antropométricas de estos sujetos, con una disminución de peso corporal y con ello, un descenso en el IMC, sobresaliendo la fibra de salvado de avena con una media de pérdida en el peso promedio de 3,87 kg y disminución en el perímetro de cintura con un promedio de 5 cm. Cabe mencionar que los sujetos de estudio manifestaron bajo entrevista no haber adicionado actividad física durante el estudio.

Muchos estudios prospectivos han demostrado una asociación inversa significativa entre la ingesta de fibra dietética, cereales, vegetales y frutas *versus* diversas variables antropométricas (peso corporal, IMC, perímetro de cintura) (20-22). Por ello la ingesta tanto de cereal entero como de fibra de cereal puede presentar una asociación similar entre las variables ya mencionadas (23). Por otro lado, el estudio multicéntrico sobre prevención primaria de enfermedades cardiovasculares con dieta mediterránea (PREDIMED) en personas de alto riesgo cardiovascular, que se llevó a cabo durante tres meses, corroboró un descenso significativo en el peso y en el perímetro de cintura al comparar entre todos los quintiles de ingesta de fibra dietética ($p \leq 0,001$) (24), así como una disminución significativa de los niveles plasmáticos de colesterol-LDL, concluyendo que el consumo de fibra puede ser un método preventivo para este tipo de patologías. En cuestión de triglicéridos también se presentó una reducción en los sujetos de estudio, siendo la fibra de salvado de avena la más eficiente. Cabe mencionar el metaanálisis de Threapleton y cols. (25,26), publicado en 2013, donde se estableció la relación entre el consumo de fibra y los eventos coronarios, fatales y no fatales y se concluyó que un consumo de fibra elevado (fibra total, fibra insoluble y fibra proveniente de cereales y vegetales) se asocia con un riesgo más bajo de enfermedad cardiovascular y eventos coronarios. Además, un consumo elevado de cereales integrales, fruta y vegetales se ha asociado con una reducción de la prevalencia de ictus isquémicos (27). En cuestión de niveles de colesterol plasmáticos, hubo una reducción de aproximadamente el 9% a través del consumo de fibra de salvado de avena. Esto podría deberse a la participación activa de la fibra sobre la HMG-CoA reductasa, ya que se tienen antecedentes de que la fibra participa activamente en la disminución de los niveles plasmáticos de colesterol (28). Brown y cols. (29) publicaron un metaanálisis en el cual analizaron el efecto hipolipemiante de la fibra y donde concluyeron que las dietas con alto contenido en fibra soluble (2-10 g/d), independientemente del tipo (*Psyllium*, avena, pectina, betaglucano o goma guar), disminuyen el colesterol total y el LDL-colesterol sin que esto afecte significativamente los niveles de HDL-colesterol ni de triglicéridos. La utilización de fibra insoluble también ha sido evaluada, demostrándose una disminución en las cifras de colesterol total tras la administración de salvado de trigo en el desayuno (30). Para cada una de las variables solo se compararon las medias entre grupos a través de la t de Student.

CONSIDERACIONES FINALES

Los hallazgos de este estudio exponen lo siguiente: los individuos del Grupo de Ayuda Mutua del Centro de Salud de San Martín Mexicapam "La Joya", Oaxaca, distribuidos en tres grupos A, B y C (fruta-verdura, avena y trigo, respectivamente), presentaban antes de la intervención un consumo excesivo de hidratos de carbono complejos, hidratos de carbono simples y grasas saturadas (Tabla I). Además, se determinó previamente el estado de nutrición de los individuos del Grupo de Ayuda Mutua del Centro de Salud de San Martín Mexicapam "La Joya", Oaxaca mediante el A, B, C, D (evaluaciones antropométricas, bioquímicas, clínicas y dietéticas). Durante la intervención se les brindó plan de alimentación individualizado, además de proporcionar un incremento de 15 g/d sobre lo recomendado, que son 35 g/d de fibra, en un periodo de ocho semanas, pudiendo mejorar la salud digestiva en el individuo, teorizando que se puede retrasar el vaciado gástrico, favoreciendo la saciedad, acelerando el tránsito intestinal e incrementando en un momento determinado la masa fecal. Por otro lado se presentó una disminución significativa en los valores de estudios de laboratorio, lo que demuestra que la fibra del salvado de avena reduce los niveles de glucosa, triglicéridos y colesterol sérico y puede ser una opción coadyuvante en el tratamiento nutricional del síndrome metabólico. Los sujetos que participaron en este estudio seguirán siendo monitoreados constantemente a pesar de haber salido parcialmente de las condicionantes para el diagnóstico de síndrome metabólico. Esto no solo depende del tratamiento farmacológico que reciben ni de la intervención nutricional otorgada, sino que es necesario modificar hábitos de alimentación y agregar actividad física a su rutina cotidiana. Sin embargo, se requieren más estudios para otorgar recomendaciones específicas para este tipo de patologías. Además, los grupos de ayuda mutua día a día se posicionan como una estrategia en la línea educativa para mejorar el control de las enfermedades. La organización y participación activa de sus integrantes favorece que las intervenciones sean mucho más efectivas y provechosas, al tiempo que son factor de cambio del estilo de vida y de alimentación dentro de sus familias. Es necesario ampliar los estudios en este grupo de ayuda mutua con la finalidad de incorporar un mayor número de personas con estas patologías y que se pueda predecir y corregir la patología, según las correcciones en su dieta.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Effects of modified banana *(Musa cavendish)* starch on glycemic control and blood pressure in rats with high sucrose diet

Efectos del almidón modificado de banano (Musa cavendish AAA) *sobre el control glucémico y la presión arterial en ratas con dieta alta en sacarosa*

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Abstract

Introduction: insulin resistance (IR) is the preliminary stage of diseases such as diabetes and hypertension. These diseases can be controlled through medication, yet the consumption of functional foods (FF) may be one complementary treatment option. Ingredients for these FF could be the pyrodextrin and enzymatically resistant maltodextrin (ERM) obtained from the native starch (NS) of *M. cavendish* in this study.

Objective: to evaluate the effects of modified banana starch on glycemic control and blood pressure in rats with high sucrose diet (HSD).

Methods: we utilized 25 male Wistar rats 20 of which received a HSD and five were fed a normal diet and purified water (PW) for 12 weeks. At the end of week 8, the rats fed a HSD were divided into four groups: positive control (PC), native starch (NS), pyrodextrin (PI), and enzymatically resistant maltodextrin (ERM). The negative control (NC) comprised the five rats fed PW. We evaluated the glucose tolerance test, blood pressure (BP), insulin levels, total cholesterol (TC), high-density lipoproteins (HDL), and triglycerides.

Results: differential scanning calorimetry and scanning electron microscopy of the modified starches demonstrated that the pyroconversion treatment did not visibly affect the NS granules, while ERM was modified by the action of α-amylase. Starch treatments reduced glucose, insulin, HOMA-IR, and BP in comparison with PC ($p < 0.05$). Glucose AUC (0-120 min) was also decreased after starch treatments with respect to PC ($p < 0.05$).

Conclusion: NS and its modified products exerted beneficial effects on glycemic control, lipid metabolism, and BP in obese rats fed a HSD. Although the modified starches presented lower resistance to digestion than NS, their expected properties were maintained.

Key words:

Blood glucose. Enzymatically resistant maltodextrin. High sucrose diet. Pyrodextrinization. Resistant starch.

Resumen

Introducción: la resistencia a la insulina es la etapa preliminar de enfermedades como hipertensión y diabetes. Estas pueden controlarse a través de fármacos; sin embargo, el consumo de alimentos funcionales (AF) puede ser una opción de tratamiento complementario. Ingredientes para estos AF podrían ser la pirodextrina y la maltodextrina enzimáticamente resistente (MER), las cuales se obtuvieron a partir de la modificación al almidón nativo (AN) de *M. cavendish* para este estudio.

Objetivo: evaluar los efectos del almidón modificado de banano sobre el control glucémico y la presión arterial en ratas con dieta alta en sacarosa.

Métodos: se utilizaron 25 ratas macho cepa Wistar, de las cuales 20 fueron alimentadas con dieta alta en sacarosa (DAS) y cinco consumieron dieta normal con agua purificada (AP) durante 12 semanas. Al finalizar la octava semana, las ratas que consumieron DAS fueron divididas en cuatro grupos: control positivo (CP), almidón nativo (AN), pirodextrina (PI) y maltodextrina enzimáticamente resistente (MER). El control negativo (CN) fueron las cinco ratas que consumieron AP. Se evaluaron tolerancia a la glucosa, presión arterial (PA), niveles de insulina, colesterol total, lipoproteínas de alta densidad (HDL) y triglicéridos.

Resultados: la calorimetría diferencial y la microscopía electrónica de barrido demostraron que el tratamiento de piroconversión no afectó visiblemente a los gránulos de AN, mientras que la MER fue modificada por acción de la α-amilasa. Los tratamientos de los almidones redujeron glucosa, insulina, índice de HOMA-IR y presión arterial en comparación con CP ($p < 0,05$). El área bajo la curva de la prueba de tolerancia a la glucosa (0-120 minutos) fue también disminuida posterior al consumo de los almidones con respecto a CP ($p < 0,05$).

Conclusión: el AN y sus productos modificados tienen efectos benéficos sobre el control glucémico, el metabolismo lipídico y la presión arterial en ratas obesas que consumieron una dieta alta en sacarosa. Aunque los almidones modificados presentaron menos almidón resistente que el AN, sus propiedades esperadas fueron mantenidas.

Palabras clave:

Almidón resistente. Dieta alta en sacarosa. Glucosa en sangre. Maltodextrina enzimáticamente resistente. Pirodextrinización.

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INTRODUCTION

Environmental and genetic factors are implicated in the development of obesity and metabolic disorders, which can cause dyslipidemia, insulin resistance, and arterial hypertension (AHT), which it is considered will affect approximately 1.56 billion persons in the world by 2025 (1). Furthermore, these conditions increase the risk of developing cancer, cardiovascular diseases and diabetes (2). Insulin resistance (IR) is involved in the development of AHT, highlighting the importance of further exploring the effects of glycemic tolerance and IR on health and its possible treatments (3). The aforementioned disorders are controllable through pharmaceutical drugs, yet represent a high cost to health services worldwide. Currently, distinct research studies have focused on formulating food ingredients with therapeutic benefits for human health (4). In this respect, certain studies demonstrate that slowly digestible starch (SDS) and resistant starch (RS) offer beneficial physiological effects (5,6). For instance, SDS is not completely digestible in the small intestine and provides sustained and prolonged release of glucose. Meanwhile, RS is a starch fraction that is not digested in the small intestine; therefore, it acts as a dietary fiber, aids in the reduction of body weight and caloric intake, improves energy balance, and decreases levels of serum lipids. In addition, RS can decrease insulin secretion and postprandial glucose control, preventing the development of diabetes (7), and is partially fermented in the colon, leading to the production of short-chain fatty acids (SCFA) (8). Native starch (NS) can present limitations for industrial use resulting from its retrogradation, syneresis, instability at an acidic pH, and unstable textures, among others (9). For this reason, the modification of NS has received attention as one means of creating functional ingredients for use in the food industry.

One modification of starch is enzymatically resistant maltodextrin (ERM), which is obtained by sequentially performing pyroconversion and enzymatic hydrolysis. ERM are low-molecular-weight compounds that reduce to sugars and that contain the α-1,4 and α-1,6 linkages and the β-1,2 and β-1,3 linkages of NS, enabling them to be partially digested (10). These compounds have low viscosity and high solubility; thus, they are used as additives in milk, juice, soups, enteral formulas, and sports and carbonated drinks (11). In addition, they act as soluble fiber, slowing the absorption of carbohydrates, as observed in postprandial glucose (12), cholesterol, and triglyceride (TG) levels in blood following intake (13). Supplementation with resistant dextrins in patients with type 2 diabetes was shown to improve IR and to reduce oxidative stress and inflammatory biomarkers. Therefore, modified starches could potentially be utilized as supplements in the food industry and as substitutes for sugar and fat (14).

Dietary supplementation with native *Musa cavendish* starch has demonstrated beneficial effects in rats through decreasing glycemia and dyslipidemia (15). In subjects with type 2 diabetes and obesity, this product induced body weight reduction and improved insulin response (16). Acute supplementation improved the mean blood glucose (MBG) and total glucose area under the curve (AUC) over a 48-h period in both subjects with obesity and in those with normal weight (17).

Food-industry applications require starches with certain functional and nutritional properties that meet specific needs. Unmodified NS often does not meet these needs, therefore requiring modification through chemical, physical, and biochemical methods.

The objective of the present study was to evaluate the effects of modified banana starch produced by pyroconversion and enzymatic hydrolysis on glycemic response and blood pressure (BP) in obese rats.

MATERIALS AND METHODS

CHEMICALS

Green bananas were purchased in Teapa, Tabasco, Mexico. The chemical reagents employed were of analytical grade (J. T. Baker; Phillipsburg, NJ, USA), and the enzymes were obtained from Sigma Chemical Co. (St. Louis, MO. USA). Megazyme (K-RSTAR 05/2008 Megazyme© International Ireland Ltd. 2008) was also used, in addition to a glucometer and reactive strips for glucose testing from Roche (Mannheim, Germany) and rat/mouse insulin Enzyme-Linked ImmunoSorbent Assay (ELISA) kits from Millipore TM (Cat. # EZRMI-13K).

STARCH ISOLATION

Bananas without peels were ground, washed (water at 40 °C with 0.3% citric acid) and sieved (no. 100 mesh). Sediments were separated and dried in an air furnace at 50 °C under atmospheric pressure for 24 h. The resulting starch was sieved (no. 100 mesh) and stored (18).

MODIFIED STARCH: PYRODEXTRINIZATION AND ENZYMATIC HYDROLYSIS

Both starch modifications were previously described (19). To modify starches, a proportion of 160:1 (w/v) starch:acid (2.2 M HCl) was used. The acid was dispersed following its reaction with starches for 16 h at ambient temperature (HAT), and the products were subsequently placed in a convection oven for one hour at 90 °C. Color was analyzed using a Chroma-meter photoelectric colorimeter and the Hunter classification system (20).

For enzymatic hydrolysis, the pyrodextrin was hydrolyzed employing the thermostable α-amylase EC. 3.2.1.1 (Sigma A-3306). The pyrodextrin was suspended in water at 30% (w/v), and the pH was adjusted to 6. The mixture was heated to 95 °C in a water bath under constant agitation. Then, 0.01% α-amylase (4,000 activity units/mL) was added based on the weight of the pyrodextrin, and the mixture was allowed to react for ten minutes. Dextrose equivalents (DE) were measured according to the Lane-Eynon method and expressed as a percentage of total starch content on a dry basis (21). The RS (pyrodextrin and maltodextrin) content was determined using a test kit (Megazyme© International,

Ireland), following AOAC International (2002.02) and AACC International (32-40.01) guidelines.

SCANNING ELECTRON MICROSCOPY

Images of the starches were examined under a JEOL electron microscope model JSM-7610F (FESEM, USA), with 1 nm resolution, 500x magnification, a micrograph of 10.3 mm, a voltage accelerator of 5 kV, and a probe current of up to 200 nA (22).

DIFFERENTIAL SCANNING CALORIMETRY

The gelatinization temperature was determined utilizing a differential scanning calorimeter (DSC6, Perkin Elmer™), with a heating rate of 10 °C min-1 for NS and 5 °C min-1 for the pyrodextrin and maltodextrin selected; heat flow ranged from 30 to 120 °C (23).

CRYSTALLINITY

The x-ray diffraction of starches was performed with a diffractometer (Bruker D8-Advance, USA) equipped with a copper source producing CuKα radiation (λ = 1.5418 Å) and operated at 40 kV and 30 mA. Measurements were taken at an angular range (2-θ) of 3° to 60°, and scan speed was 0.02° s-1. The crystallinity of the starches was determined and directly measured by plotting a curve that connected the peak baselines of the diffractograms. The ratio of the AUC was taken as the degree of crystallinity according to the following equation (24):

$$\% \text{ Crystallinity} = \frac{Ac}{Ac + Aa} \quad (100)$$

Where AC = crystalline area under the x-ray diffractogram
Aa = amorphous area under the x-ray diffractogram

ANIMAL ASSAY

All experimental protocols were approved by the Institutional Animal Care and Use Committee of the School of Medicine of the Autonomous University of the State of Morelos (UAEM) (approval number: 006/2015) and comply with the applicable Mexican Official Norm (NOM-062-ZOO-1999), "Technical Specifications for the Care and Use of Laboratory Animals," and with all applicable federal and institutional regulations. Twenty-five male Wistar rats were used. The production, management, and care of the rats was performed in the Animal Production, Care, and Experimental Unit (UPCEA) located in the Health Sciences Academic Department (DACS) of the Autonomous Juarez University of Tabasco (UJAT). The rats weighing 250-280 g were placed under controlled conditions of temperature (21 ± 1 °C), relative humidity (55%), and 12-h light/darkness, with free access to purified water (PW) and food, and were fed on demand a commercial 18% protein rodent diet (Harlan Teklad) throughout the experimental phase.

EXPERIMENTAL DEVELOPMENT

The experimental phase comprised two periods: a period of induction of obesity with a high sucrose diet (HSD) (for eight weeks), and a period of treatments with NS and its modified products (for four weeks). Twenty-five male Wistar rats were individually housed in cages. Following one week of adaptation, five rats received Harlan Teklad diet *ad libitum* and PW (negative control [NC]), and 20 rats were offered the same diet *ad libitum* and had 20% sucrose solution in PW (HSD) throughout the experimental period (2). After finishing the first phase (eight weeks), the 20 rats that consumed HSD were randomly divided into four groups of five animals each and were randomly assigned to one of the following experimental groups: positive control (PC), native starch (NS), pyrodextrin (PI), and enzymatically resistant maltodextrin (ERM). Rats under starch treatments (NS, PI, and ERM) were administered a corresponding dose of 0.43 g/kg of body weight, based on the dietary fiber recommendation (14 g/1,000 kcal, 20-38 g/day) for humans by gavage for four weeks (25). Both controls, that is, the NC and PC groups received only PW as placebo by the same route during this period. All of the animals received the Harlan-Teklad diet mentioned previously and the respective PW (NC) or 20% sucrose solution (PC, NS, PI, and ERM) during the last four weeks. Weight gain was monitored weekly and the water and feed consumption, daily.

PHYSIOLOGICAL TESTS

At the end of weeks 8 and 12, an oral glucose tolerance test (GTT) was performed on the rats, and their BP was measured.

For the GTT, rats were fasted for 12 h. Then, the animals were intragastrically (i.g.) administered a dose of 1 g glucose/kg body weight using a feeding needle, and blood samples were then drawn from the animal's tail at time intervals of 0, 15, 30, 60, 90, and 120 minutes. Glucose levels were determined using a glucometer. The glucose AUC curve was calculated using the trapezoidal rule, according to the following formula:

$$AUC_G = (G_0 + G_{15}/2)15 + (G_{15} + G_{30}/2)15 + (G_{30} + G_{60}/2)30 + (G_{60} + G_{120}/2)60$$

Where:
ABC_G = AUC of the oral glucose tolerance test;
G_0, G_{15}, G_{30}, G_{60} and G_{120} are the measured glucose levels.

To measure BP, a pressure sensor connected to a non-invasive blood pressure monitor (CODA™ Monitor, Kent Scientific Co., Torrington, CT, USA) was placed at the base of the tail. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were obtained in mmHg (26).

BLOOD SERUM ANALYSIS

At the end of the experimental treatments, the rats were anesthetized (ketamine [50 mg/kg] + xylazine [10 mg/kg], injected intraperitoneally [i.p.]) following 12 h of fasting. A cardiac puncture was performed to collect blood, and the insulin levels of the blood sera were determined using a rat/mouse kit (Millipore™). Total cholesterol (TC), high-density lipoproteins (HDL), and TG were determined with a clinical chemistry system (Advia® 1200 Chemistry Analyzer, Bayer).

The homeostatic model assessment (HOMA) was used to quantify IR according to the following formula (27):

$$\text{HOMA-IR} = \frac{\text{fasting insulin } \left(\frac{\mu IU}{mL}\right) \text{ x fasting glucose (mmol)}}{22.5}$$

STATISTICAL ANALYSIS OF THE RESULTS

The resulting data for the HOMA index, BP, TC, HDL, and TG were analyzed in the Statgraphics plus ver. 5.1 statistical software package. The results were expressed as arithmetic means ± standard errors of the mean. The *in vivo* study was based on a randomized block design, wherein the blocks were the weights and the treatments were the diets. A one-way analysis of variance (ANOVA) was conducted for this model at a significance level of $p < 0.05$, and a Duncan test was applied to determine the significant differences among the treatment averages.

RESULTS

PYRODEXTRINIZATION AND ENZYMATIC HYDROLYSIS OF *M. CAVENDISH* STARCH

The NS yield of *M. cavendish* was 5.5% and the resulting RS content was 70.51%. The pyrodextrin yielded 63.84% RS and showed a minimal color difference ($\Delta E = 7.66$) with respect to NS. The ERM presented 11.04% RS and 8.90% DE.

SCANNING ELECTRON MICROSCOPY

The NS granules (Fig. 1A) were irregular in form, elongated and, in some cases, spheroidal, with a size of 11-71 µm. Figure 1B depicts the pyrodextrin: some granules were resistant to pyrodextrinization, yet the size of the granules did not change. Figure 1C reveals the loss of granular structures in ERM resulting from enzymatic treatment with α-amylase.

DIFFERENTIAL SCANNING CALORIMETRY AND CRYSTALLINITY

The thermograms of NS after pyrodextrinization and its modification into ERM are illustrated in figure 2. The recorded gelatinization enthalpy was 12.67 J/g, while the initial, peak, and final gelatinization temperatures for native *M. cavendish* starch were 67.84, 73.58, and 81.59 °C, respectively. Initial (68.49 °C), peak (72.38 °C), and final (76.21 °C) temperatures slightly changed after the pyrodextrinization treatment. Following the α-amylase treatment, the ERM obtained did not demonstrate an endothermic peak identifying the gelatinization transition. This indicates a loss of granular and crystalline structure, as observed in the scanning electron microscopy (SEM) image. Crystallinity for NS was 29.12%, for pyrodextrin this was 14.72%, and for ERM, crystallinity was 8.12%.

EXPERIMENTAL MODEL

No differences were observed in food and water consumption between the HSD and NC groups during the 8-week period; however, the HSD induced higher blood glucose levels in rats in comparison with NC ($p < 0.05$). Glucose AUC (0-120 min) value was higher in the HSD group in comparison with the NC group ($p < 0.05$) (787.1 ± 1.11 vs 583.7 ± 1.5). The 2-h postload glucose value was higher in the HSD group in comparison

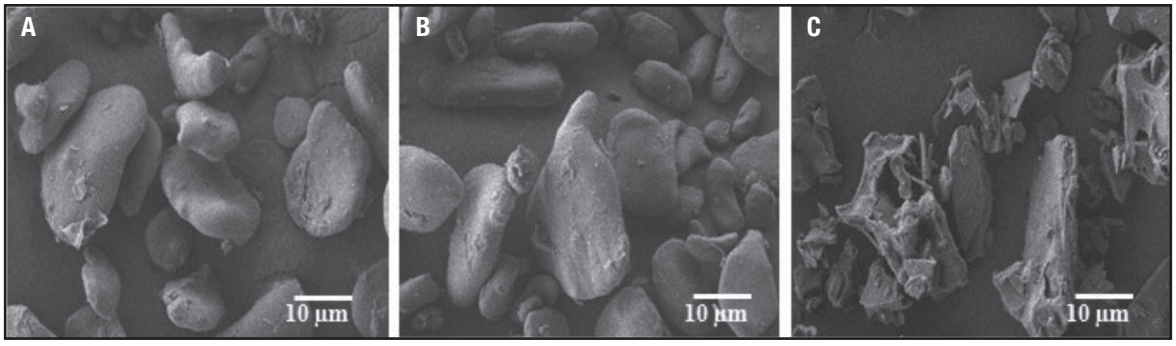

Figure 1.

Micrograft of *Musa cavendish* starch: native (A), pyrodextrin (B) and ERM (C) (ERM: enzymatically resistant maltodextrin).

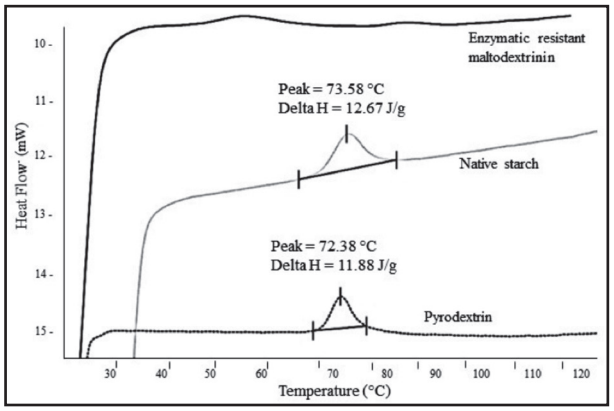

Figure 2.

Thermograms of native starch, pyrodextrin and enzymatically resistant maltodextrin obtained from *Musa cavendish* starch.

with NC group (118.66 ± 2.84 mg/dl vs 91.0 ± 1.23 mg/dl; $p < 0.05$). Also, SBP and DBP values were increased in the HSD group ($p < 0.05$) compared to the NC.

EFFECT OF TREATMENTS ON BLOOD SERUM PARAMETERS

Table I presents the effects of the different treatments on biochemical parameters related to glycemic and lipidic metabolism. The three starch treatments led to a decrease in the HOMA-IR index ($p < 0.05$) with respect to the PC, with the values of the PI and ERM groups similar to those of the NC ($p > 0.05$). All treatments decreased fasting glucose and insulin concentrations in comparison with PC ($p < 0.05$); in particular, the ERM treatment led to a glucose level comparable to that of the NC. Fasting glucose concentrations decreased by 10.0% following ingestion of PI and by 19.80% following ingestion of ERM.

The results obtained for lipid concentrations are also detailed in table I. With respect to TC and HDL, differences were not observed between treatments ($p > 0.05$). However, in the TG serum level, a decrease ($p < 0.05$) was observed in the three starch treatments with respect to the PC and NC treatments ($p < 0.05$). In particular, the ERM group presented a lower TG concentration ($p < 0.05$) in comparison with the NS and PI groups.

The results of the GTT performed at the end of the experimental period are shown in figure 3. Over the course of the tested interval, the glucose excursions of the starch-treatment groups estimated as AUC were reduced in comparison with the PC ($p < 0.05$). The glucose AUC (0-120 min) value in the ERM group was similar to that of the NC ($p > 0.05$).

EFFECT OF THE TREATMENTS ON BLOOD PRESSURE

The starch treatments led to lower DBP and SBP ($p < 0.05$) with respect to the PC (Table II). SBP decreased 61.40% in the ERM group, 60.40% in the NS group, and 59.60% in the PI group. DBP decreased 59.40% in the NS group, 50.60% in the PI group, and 42.20% in the ERM group.

Table I. Effect of native, pyrodextrinized and enzymatic hydrolyzed *M. cavendish* starch on biochemical parameters in serum of rats with high-sucrose diet

Parameters	NC	PC	NS	PI	ERM
HOMA IR	2.02 ± 0.01*	7.02 ± 0.01†	4.59 ± 0.04‡	2.55 ± 0.03*	2.43 ± 0.01*
Glucose (mg/dl)	99.2 ± 1.76*	115.4 ± 2.07†	102.8 ± 0.86‡	105.4 ± 1.77‡	95.6 ± 1.22*
Insulin (µg/mL)	0.29 ± 0.08*	1.25 ± 0.05†	0.63 ± 0.18*	0.33 ± 0.11*	0.36 ± 0.04*
TC (mg/dl)	75.33 ± 1.17*	87.33 ± 3.23*	85.67 ± 1.45*	73.67 ± 0.33*	81.67 ± 1.04*
HDL-C (mg/dl)	52.67 ± 2.79*	42.33 ± 1.89*	51.13 ± 1.38*	46.73 ± 0.87*	49.07 ± 2.70*
TG (mg/dl)	145.0 ± 0.57*	159.33 ± 5.95†	113.0 ± 1.0‡	126.67 ± 1.80‡	75.67 ± 3.84§

*Data are mean ± standard error (n = 5). *,†,‡,§Different symbols mean statistical difference ($p < 0.05$). NC: negative control; PC: positive control; NS: native starch; PI: pyrodextrin; ERM: enzimatically resistant maltodextrin; AUC: area under the curve; TC = total cholesterol; HDL-C: high-density lipoprotein-cholesterol; TG: triglycerides.*

Table II. Effect of native, pyrodextrinized and enzymatic hydrolyzed *Musa cavendish* starch on the blood pressure of rats with high-sucrose diet

Parameters	NC	PC	NS	PI	ERM
SBP (mmHg)	111.6 ± 1.20*	197.4 ± 2.99†	137.0 ± 3.14*	137.8 ± 1.40*	136.0 ± 3.57*
DBP (mmHg)	88.8 ± 5.72*	150.6 ± 2.94†	91.2 ± 1.58*	100.0 ± 4.91*	108.4 ± 1.46*

*Data are mean ± standard error (n = 5). *,†Different symbols in the same rows mean statistical difference ($p < 0.05$). NC: negative control; PC: positive control; NS: native starch, PI: pyrodextrin; ERM: enzymatically resistant maltodextrin; SBP: systolic blood pressure; DBP: diastolic blood pressure.*

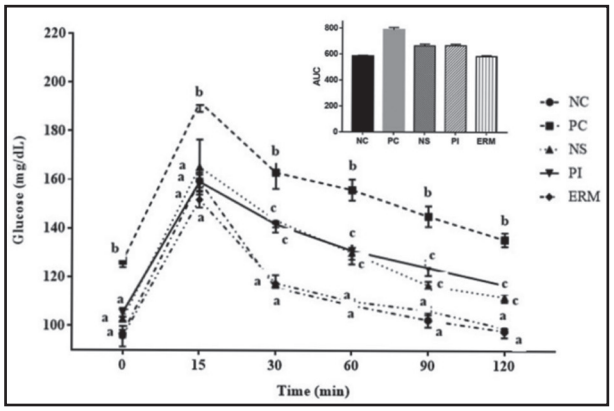

Figure 3.

Effect of native, pyrodextrinized and enzymatically hydrolyzed *Musa cavendish* starch on glucose tolerance test in rats with high-sucrose diet. Data are mean ± standard error (n = 5). A-C. Different letters mean statistical difference ($p < 0.05$). NC: negative control; PC: positive control; NS: native starch; PI: pyrodextrin; ERM: enzymatically resistant maltodextrin; AUC: area under the curve.

DISCUSSION

Several studies have shown that native *Musa cavendish* starch consumption favors a decrease in glucose and lipid levels in animals and humans (15-17). These effects can be due to the quantity of the RS present. Even so, the use of NS in industrial and food applications presents limitations. Therefore, the modification of NS is recommendable in order to maintain the properties of its RS and for its use in practical applications (9). For these reasons, the NS of *M. cavendish* was pyrodextrinized and enzymatically hydrolyzed in this study to evaluate its effects on glycemia and BP in rats fed with a HSD. High sucrose intake is related to the accumulation of body fat and the development of obesity, AHT and diabetes (28). In the present study, the HSD produced an increase in DBP, SDP, and glycemia levels in rats. Similar behavior was observed in another study wherein rats undergoing the same dose and periodic administration of HSD developed IR and experienced an increase in SBP (2).

Although the pyroconversion of starch represents a promising strategy for increasing the RS fraction (29), the pyrodextrin and the ERM produced in the present study did not increase the RS content. Contrariwise, this value decreased. In this line, on employing the same conditions of the present study, 48.76% RS was reported for a pyrodextrin of *Musa esculenta* starch (19). In another study, native banana starch (*Musa cavendish*) treated with HCl (2.2 M) was reported to be resistant to acid hydrolysis. Even so, a loss of granular structure was observed, and the residues formed could have contained amorphous material, rendering the starch enzymatically hydrolyze and possibly increasing the digestion time of starch through increasing the amount of SDS. Concretely, the proportion of RS was reduced more than 70%, and the SDS increased more than 30% (30). In the present study, the amount of SDS could have similarly increased, explaining the decrease in RS. The pyrodextrinization treatment weakened the granule, although hydrolysis might not have occurred completely at the molecular level. In contrast, a granular structure did not exist in the ERM, as observed in the SEM images (Fig. 1) and thermograms (Fig. 2). Native green banana starch has a smooth and dense surface, which might partially explain its resistance to digestion. The thick outer layer of the granule likely limits enzymatic action and reduces the rate of hydrolysis, as indicated by electron transmission microscopy (ETM) studies (31). In this regard, the crystallinity of starch granules influences the RS fraction (32). A reduction in the crystallinity of modified starches indicates a loss of structural organization in a lateral direction to the semicrystalline lamellae via dextrinization. In dextrins of native maize starch, crystallinity has been found reduced, although the crystalline region of the starch was not completely destroyed; instead, the crystallites became smaller during dextrinization (33). The same effect could be taking place in the present study, as the crystallinity of the modified starches was reduced. The ERM did not exhibit an endothermic peak identifying the gelatinization transition, therefore indicating a loss of granular and crystalline structure, as observed in the SEM results. The same behavior was found for potato starch treated with diluted acids and heat (50 °C) (21).

The experimental starch treatments in rats fed a HSD led to a decrease in the HOMA-IR index. In another study in male Wistar rats fed a high-fat diet during nine weeks, the use of RS (Hi Maize® 260) as a carbohydrate substitute in the diet (41.6%) led to a decrease in the HOMA-IR index of treated rats with respect to the control group (34). To the contrary, the ingestion of different doses of RS type II (16% daily) in male Sprague-Dawley rats along with a moderate-fat diet (for four weeks) did not lead to changes in the HOMA-IR index. These differences may partially be explained by the different structure and administered doses of RS. In the present study, NS and its modified products decreased the hyperglycemic effect of the HSD, and the consumption of ERM even led to glucose levels similar to the NC. An exact explanation for these findings was not found; however, the dextrinization process may have produced a molecular reorganization and these indigestible polymers (maltodextrins) could have functioned as inhibitors of α-glucosidase enzymes (35). The mechanisms of how RS works remain unclear. The effect of dietary fiber in reducing energy intake and glycemic load is thought to be achieved by energy dilution and food expansion through traditional mechanisms. Energy dilution reduces the energy density of the food intake, and food expansion prevents further food intake (36). However, there are some evidences indicating that the mechanism of regulation of the blood glucose level by RS is likely related to RS fermentation in the large intestine and the production of short-chain fatty acids (SCFA). SCFA have been shown to stimulate enteroendocrine L-cells and to enhance the secretion of the anorectic hormone peptide YY (PYY, also denominated peptide tyrosine tyrosine) and the incretin glucagon-like peptide 1 (GLP-1) (37). Thus, gastrointestinal peptides are currently attracting increasing attention in terms of being the possible interpretation of the effect of RS in reducing the blood glucose level (36). The reduction in RS in the present study following pyrodextrinization and ERM formation can be attributed to the increase of SDS in the modified starches,

as previously reported following the hydrolysis of native *Musa cavendish* with HCl (2.2 M) (30). SDS is totally absorbed in the intestine but is released slowly. At the same time, the atypical links that formed in this process might have been those that resisted enzymatic hydrolysis during the elaboration of the ERM.

A decrease in serum lipids following ingestion of RS has been reported in a previous study (38). In the present study, an increase in TG was observed following the administration of an HSD. Hypertriglyceridemia has been observed to inhibit the utilization and oxidation of glucose as a result of insulin action in peripheral tissue. The increase in TG is due to the increasing reesterification of fatty acids as a consequence of the hepatic metabolism of sucrose (39). In the present study, TG levels were reduced after the starch treatments, and those of the ERM group were even lower than those of the NC group, probably due to the atypical links formed.

In another study, the effects of ingesting native indica rice starch, as well as two physically and enzymatically modified starches, on the effects of blood glucose and TG serum levels were evaluated. In this case, the NS was hydrolyzed with α-amylase, resulting in a product with 15.3% RS and 20.2% crystallinity. The starch treatments were evaluated in streptozotocin-induced diabetic rats and were administered daily through a stomach tube at a dose of 2 g. The modified starches led to a greater hypoglycemic effect in comparison with the same proportion of NS, and the TG concentration of the group treated with RS was similar to that of the control (40). Similarly, in male Wistar rats fed non-digestible dextrin (35 g/kg of body weight) on demand during 28 days, decreases in TG serum ($p < 0.05$) and HDL ($p < 0.001$) concentrations were observed. The TG values reported in blood serum were lower than those of the present study, which may be due to the RS type and the higher administered dose (41). Thus, a relationship can be confirmed between the elevation of BP and the elevation of TC, TG and glucose levels, among others, in blood serum (42). Consequently, a decrease in these latter parameters occurred in the present study as a result of the dietary treatments, coinciding with the effects of decreasing BP.

In conclusion, the native banana starch and its modified products (pyrodextrin and enzymatically resistant maltodextrin) had beneficial effects on glycemic metabolism, insulin resistance, and blood pressure in obese rats fed a high sucrose diet. Although the modified starches presented lower resistance to digestion than the native starch, their expected properties were maintained. This is relevant because native starch must first be modified before being incorporated into foods during their processing. The changes in the structural reorganization of starch during its modification likely increase the proportion of slow digestible starch, which has favorable physiological effects. Thus, the incorporation of modified starches as ingredients in foods is a promising source of non-conventional fiber for use in special dietary regimes.

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ARÁN

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Trabajo Original

Valoración nutricional

Dietary intake of pregnant adolescents cared for in primary health care units of a Brazilian urban municipality

Consumo dietético de adolescentes embarazadas atendidas en unidades de atención primaria de salud de un municipio urbano brasileño

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Abstract

Objective: to evaluate the adequacy of dietary intake and the anthropometric nutritional status of pregnant adolescents in the city of Niterói, Rio de Janeiro, Brazil.

Materials and methods: forty-two adolescents (13-19 years of age), with single-fetus gestation, assisted in the public prenatal health care units between 2008-2014, participated in the study. Body mass index (BMI) was used to assess the nutritional status. Dietary intake was assessed by 24h dietary recalls on two days during a week and one during weekend. Basal metabolic rate was measured by indirect calorimetry and used to determine the energy requirements. Mixed effects models were used to assess dietary intake over the gestational weeks (random effect) and BMI.

Results: mean age (SD) of the pregnant women was 16.5 (1.5) years and the majority received allowance from a cash transfer federal program. Overall, 30.3% were overweight/obese pre-pregnancy and 16.7%, during pregnancy. Energy and protein intake adequacies decreased with increasing BMI and gestational week. There was adequate dietary intake of energy, protein, vitamin A and zinc and insufficient intakes of iron and calcium. There was excessive intake of sodium.

Conclusions: pregnant adolescents living in underprivileged socio-economic environments assisted for prenatal care in primary health care units have adequate intakes of energy, protein, vitamin A and zinc. Pre-pregnancy overweight and high sodium intake are causes of concern due to the future implications for their health. The official Brazilian recommended criterion for anthropometric assessment in pregnancy of adolescents proved to be inadequate.

Key words:

Pregnancy.
Adolescent.
Nutritional status.
Dietary intake.

Resumen

Objetivo: evaluar la adecuación de la ingesta dietética y el estado nutricional antropométrico de adolescentes embarazadas en Niterói, Río de Janeiro, Brasil.

Materiales y métodos: participaron en el estudio 42 adolescentes de 13-19 años, con gestación de feto único, asistidas en las unidades públicas de atención prenatal entre 2008 y 2014. El índice de masa corporal (IMC) se utilizó para evaluar el estado nutricional. La ingesta dietética fue evaluada por recuerdos diarios de 24h dos días durante una semana y uno durante el fin de semana. La tasa metabólica basal se midió mediante calorimetría indirecta y se utilizó para determinar los requerimientos energéticos. Se emplearon modelos de efectos mixtos para evaluar la ingesta alimentaria durante las semanas de gestación (SG, efecto aleatorio) y el IMC.

Resultados: la mayoría de las mujeres embarazadas recibían subsidios de un programa federal de transferencia de efectivo. En general, el 30,3% tenía sobrepeso/obesidad antes del embarazo y el 16,7%, durante el embarazo. La cantidad de energía y la ingesta de proteínas disminuyeron con el aumento del IMC y la SG. Había una ingesta dietética adecuada de energía, proteínas, vitamina A y una ingesta insuficiente de hierro y calcio.

Conclusiones: las adolescentes embarazadas tienen un consumo adecuado de energía, proteínas y vitamina A. El sobrepeso previo y el alto consumo de sodio son causas de preocupación debido a las implicaciones futuras para su salud. El criterio oficial brasileño recomendado para la evaluación antropométrica en el embarazo de los adolescentes demostró ser inadecuado.

Palabras clave:

Gestación.
Adolescente. Estado nutricional. Ingesta dietética.

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Ethical standards disclosure: This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the Institutional Review Committee of the Universidade Federal Fluminense (CAAE 0983.0.000.258-08). Written informed consent was obtained from all subjects/patients.

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Authors' contributions: EOF Sally, LA Anjos and V Wahrlich planned the research. EOF Sally, V Wahrlich, LA Anjos and BAM Silva collected and analyzed the data. EG Ramos and VM Fonseca helped in the interpretation of the results. EOF Sally and LA Anjos wrote the first draft of the paper, which was revised and approved by all authors.

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INTRODUCTION

Physiological changes in pregnant women lead to an increase in energy requirements (ER) in order to cover the cost of tissue synthesis, lipid and protein deposits, and increase in basal metabolic rate (BMR), which is the major component of energy expenditure during pregnancy (1). This makes ER during pregnancy an important piece of information to be considered for appropriate dietary advice that contemplates the regulation and control of body mass during pregnancy. Positive energy balance (EB) (energy intake [EI] > energy requirement [ER]) during this period allows for the accumulation of energy reserves to meet the demands of childbirth and the beginning of lactation (1). In excess, it may predispose the pregnant woman to obesity and the fetus to macrosomia (2). If insufficient, it can lead to low gestational body mass gain and restriction of fetal growth (3). In this sense, pre-conception and gestation are considered as critical periods for coping, at a contextual level, with the obesity epidemic in childhood and adolescence (4). In Brazil, the estimated prevalence of overweight and obesity in adolescents is 20.5% and 4.9%, respectively (5). In a probability sample of adolescents attending public schools in the city of Niterói in 2013, 17.9% of the girls were overweight and 8.5% were obese (6).

Micronutrient requirements also increase during pregnancy to meet the need of accelerated fetal growth and intense cell differentiation and may require adaptations in dietary intake, especially in scenarios of habitual marginal intake to promote maternal and fetal health and the prevention of unfavorable outcomes (7). Thus, the assessment of dietary intake and anthropometric nutritional status in pregnancy should be included in the list of actions of prenatal care to subsidize health education practices, directed to nutritional disorders, for a healthy pregnancy (8).

Adolescence, the period between 10 and 19 years of age according to the World Health Organization (WHO) (9), is a social construction and takes on different forms according to its historical conditioners. The behavior of adolescents is influenced by the social, economic and cultural characteristics of their reference context (10). In Brazil, adolescents living in social contexts of social and economic inequality and precarious material conditions of life are more likely to be pregnant (11). Despite the decline of 23% in the fertility rate of the Brazilian women from 15 to 19 years observed between 2004 and 2014 (12), pregnancy during adolescence is still a major challenge for the society as a whole and the health system in particular (13). Dietary inadequacies and malnutrition have been reported as frequent phenomena in pregnant adolescents derived from the social context in which they live (7,14), representing a public health issue both in developed and developing countries. There are scarce data on the characteristics of dietary intake of pregnant adolescents in Brazil. Among those from low socioeconomic classes, it is assumed that the dietary intake is not balanced and does not cover the nutritional requirements and, therefore, need be evaluated. Considering the current scenario of growing prevalence of obesity in all segments of the Brazilian population (5), the present study aimed to assess the anthropometric and dietary intake (energy, macro and micronutrients) of pregnant adolescents recruited from primary health care units of a municipality located in the tropical region of Brazil.

MATERIALS AND METHODS

Between February 2008 and March 2014, all pregnant adolescents who sought prenatal medical care in basic health care units in the municipality of Niterói, RJ, Brazil, regardless of their gestational week, were contacted by researchers who provided oral and written information about the research project. At this time, identification data and obstetric history of the adolescents interested in participating in the study were collected from the Prenatal Card and a visit to the Nutritional and Functional Assessment Laboratory at the University was scheduled for anthropometric, dietary intake and BMR measurements.

Sixty eight pregnant adolescents agreed to participate in the study and came to the laboratory early in the morning accompanied by their adult legally responsible companion. All research procedures were explained one more time and the voluntary agreement to participate in the study was confirmed by all participants and their adult legally responsible companion upon signing the informed consent form. The inclusion criteria were gestation of a single and primigravida pregnancy, and maternal age below 20 years at the estimated time of delivery. The exclusion criteria included the presence of chronic diseases prior or during pregnancy.

Prior to measuring BMR, the adherence to the protocol (absence of fever, alcohol or cigarette consumption and avoidance of heavy physical activity on the day before and on the day of measurement, ten hours of fasting and eight hours of sleep) was checked. BMR was measured in a quiet room with low luminosity and noise level and controlled ambient temperature. After a 15-minute rest period in the supine position, a mask was fixed on the adolescent's face and connected to a validated (15) indirect calorimeter (VO2000 Portable Metabolic Testing System; MedGraphics, St. Paul, MN, USA), which measured oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) for 25 minutes with the pregnant adolescent lying down motionless. Minute BMR was obtained using the equation described by Weir (16) with gas exchange data of the final 20 minutes and expressed in kcal/day. ER was calculated as the product of measured BMR and the physical activity level (PAL) with the addition of the energy cost of pregnancy according to the trimester as recommended by FAO/WHO/UNU (1). Light PAL was assumed for all pregnant adolescents.

Anthropometric measures were obtained with the pregnant women wearing standard clothing and barefoot following standardization described in Lohman et al. (17). Stature was measured twice in a wooden stadiometer with precision of 0.1 cm. The measurement was carried out at the end of an expiration and the average of the two measurements provided the final value. Body mass (BM) was obtained in an electronic scale (TANITA® BC-418) with precision of 0.1 kg. Body mass index (BMI) was calculated as the division of BM by squared stature. Pre-pregnancy BMI was calculated with the self-reported pre-pregnancy BM but

when not available, the BM measurement obtained before the 13th gestational week was used. Pre-pregnancy nutritional status assessment was available for 33 of the pregnant adolescents and it was determined by the WHO BMI for age cut-off recommendations (18) for nonpregnant adolescents. Gestational nutritional status was determined with BMI for pregnancy age cut-off points (19) as suggested by the Brazilian Ministry of Health (8). For both instances, nutritional status was classified as underweight, adequate and overweight + obesity.

After these measurements, the pregnant adolescents were scheduled to respond 24-hour dietary recalls (R24h) during telephone interviews on three non-consecutive days, including one weekend day within the following week. All of these procedures (anthropometry, BMR and dietary intake) were planned to be repeated every four weeks thereafter.

Of the 68 pregnant adolescents who agreed to participate in the study, 21 did not respond at least two R24h and five either had infectious or contagious disease, had some discomfort with the facemask or BMR was not measured or pregnancy was not confirmed. Thus, the final sample was composed of 42 pregnant adolescents with dietary, anthropometric and BMR data. Eighteen pregnant women were assessed on two or more occasions, resulting in R24h data of 208 days.

During the R24h, ingested portion sizes were estimated with the help of an album containing photographs of foods and preparations given to participants on the day of the visit to the laboratory. The reported foods were converted to energy, macro and micronutrients according to the Brazilian Food Composition Table (20). When the food item was not available in TACO, the American food composition table (21) was used.

Protein recommendation was based on the safe level of protein intake and the additional protein for the adolescent's pregnancy trimester (22). The macronutrient and sodium intake adequacies were based on the intake goals for the prevention of chronic diseases (23). The percentage of energy, macro and micronutrient (calcium, iron, zinc and vitamin A) intake adequacies was calculated for each category of nutritional status. EI was considered to be excessive when it was over 100% of the individually-determined ER.

The economic class of the adolescents was based on the possession of goods in households and on the education level of the head of the household according to the economic classification in Brazil (24). Schooling was measured in number of full years of school attendance. Information on the occupation of the head of household was available for only 36 of the pregnant adolescents.

The project and its procedures were approved by the Ethics Committee of the Universidade Federal Fluminense. All statistical analyses were carried out in the software SAS for microcomputer version 9.2. Descriptive statistics (means, standard deviations, medians, 95% confidence intervals, coefficients of variation and percentage of distribution or adequacy) were calculated. The results were expressed in relation to both pre-pregnancy and gestational nutritional status because the diagnosis of altered nutritional status may be useful clinically in nutritional care. The association of the percentage of adequacy of energy, macro and micronutrient intakes with variables related to body size (gestational BMI), gestational week (GW) and day of the week (coded as 1 for Sunday, 2 for Monday, etc.) was assessed by mixed linear models. In these linear models, the random effects were included in the intercept, subject and GW to take into consideration the inter and intra-subject variability of the repeated dietary intake measurements during pregnancy. The models were adjusted using the restricted maximum likelihood (REML) method. The significance level was defined as $\alpha < 5\%$ for all analyses.

RESULTS

Two-thirds of the pregnant adolescents had completed between five to eight years of schooling and 57.1% were attending school. Among the adolescents who had interrupted their studies, the most often alleged motives were moving to a different house and the lack of willingness to study. All pregnant adolescents maintained some form of relationship with the baby's father but the minority (38.1%) lived with them as an extended family or as a nuclear family. Only two pregnant adolescents were smokers. Most belonged to the low economic class (C1 and C2 = 73.8%) and 62.0% received benefits from the *Bolsa Família* (Family Allowance Cash Transfer Federal Program). The average schooling of the head of the household was low and equal to the pregnant adolescent's (7.3 ± 3.3 years) and 73.2% of them worked, while 14.6% were unemployed.

The average GW of the adolescents was 23.3 (SD = 8.0) and most of them had adequate nutritional status prior to pregnancy (Table I).

Table II presents the physical and physiological characteristics of the pregnant adolescents according to the pre-pregnancy and gestational nutritional status. Independently of stages, there was a tendency of BMR to increase with increasing BMI. Energy intake decreased with increasing BMI and lipid intake remained approximately around 30% of EI in both pre-pregnancy and gestational nutritional status (Tables III and IV). Dietary intake of sodium, vitamin A and zinc were higher than required except for pre-pregnancy underweight but they were insufficient for iron and calcium in both analyses (Tables V and VI).

The mixed linear models were only significant for the percentage of energy and protein adequacy (Table VII). In both models the coefficients for GW, BMI and day of the week were negative.

DISCUSSION

The situation of social vulnerability of the present sample of pregnant adolescents is confirmed by the fact that most of them were registered in the *Bolsa Família*, a federal cash transfer program. This is in agreement with Vieira et al. (13), who reported that the situation of social and economic inequality does not appear as a direct consequence of adolescent pregnancy, but reflects the context of inequality in which the adolescents live. In the present study, favorably, just a few of the adolescents smoked but many maintained high bond with the baby's father, although most did not live together with their partner.

Table I. Physical, physiological and nutritional status characteristics of the 42 pregnant adolescents in Niterói, RJ

Variables	Mean (SD)	Min	Max
Age (years)	16.5 (1.5)	13.6	19.6
Gestational age (weeks)	23.3 (8.0)	8.5	36.3
Stature (cm)	162.0 (0.1)	150.0	173.0
Pre-pregnancy body mass (kg)	57.8 (11.0)	40.0	83.8
Gestational body mass (kg)	63.5 (12.5)	42.6	102.8
Pre-pregnancy BMI (kg/m^2)	22.2 (3.7)	14.1	30.7
Gestational BMI (kg/m^2)	24.0 (4.1)	16.9	37.2
Basal metabolic rate (kcal/day)	1,301.3 (219.1)	941.9	1,849.3
	n	**%**	
Gestational age (trimester)			
1st	12	28.5	
2nd	23	54.8	
3rd	7	16.7	
Pre-pregnancy nutritional status			
Underweight	4	12.1	
Adequate	19	57.6	
Overweight	10	30.3	
*Gestational nutritional status**			
Underweight	15	35.7	
Adequate	20	47.6	
Overweight + obesity	7	16.7	

*Data are from the first visit to the laboratory. SD: standard deviation; BMI: body mass index; BMR: basal metabolic rate. *Based on body mass index for gestational week (19).*

Pre-pregnancy overweight/obesity was more frequent than underweight but the opposite was observed for the gestational nutritional status. The pre-pregnancy results are consistent with the changes in the nutritional profile of the Brazilian female population in the last decades, characterized by an increase in the prevalence of obesity and a decrease in malnutrition (5). The high prevalence of underweight observed during pregnancy suggests that the Atalah's curve (19) used to classify the nutritional status of adolescents is inadequate. This method is adopted in the gestational weight policy in three other American countries (25), and in Brazilian adolescents it has been shown to overestimate the low gestational weight (26). The Brazilian Ministry of Health (8) recommends that the interpretation of the results obtained using this method be flexible for this specific group due to the possibility of many adolescents being classified as having low gestational weight. Thus, pregnant adolescents should be viewed as having some nutritional risk but careful attention must be given not to induce excessive weight gain. It is well documented that gestational obesity increases the chances of complications in the course of pregnancy (27) and has negative effects on the growth of the child in the short, medium and long terms (28).

Bianchi et al. (29) simulated the effects of pregnancy on the nutritional adequacy of the diet of women at childbearing age in the United States and France. Various nutrients (vitamins A and zinc) had reduced probability of adequacy induced by pregnancy. Calcium was not affected because their intake by women of childbearing age was already deficient. Further, the increase in EI by approximately 150 kcal daily did not imply improvement in the nutritional adequacy of the diet, except when the additional energy was provided by dietary sources based on fruit and dairy foods.

The diet of the present sample of pregnant adolescents was inadequate, characterized by excessive intakes of energy, protein and sodium and insufficient intakes of iron and calcium. Comparing the intake estimates obtained in this study with those in the literature, one can speculate that it is not difficult for the pregnant adolescents of low-income urban areas to meet the ER. Lee et al. (7) also observed positive energy balance (EB) in adult and adolescent pregnant women from Latin American countries of low and medium income including Brazil. On the other hand, in an area with a high concentration of social inequalities in the UK, the energy intake (2,148.0 ± 623.6 kcal/day) of 290 sedentary pregnant adolescents who were late in pregnancy was slightly

Table II. Physical and physiological characteristics according to pre-pregnancy nutritional status of the 42 pregnant adolescents in Niterói, RJ

	Pre-pregnancy nutritional status*								
	Underweight (n = 4)			Adequate (n = 19)			Overweight + obesity (n = 10)		
	Mean	Std	Median	Mean	Std	Median	Mean	Std	Median
	IC 95%			IC 95%			IC 95%		
Age (years)	15.4	1.4	15.2	16.7	1.2	16.7	16.1	1.6	16.6
	13.2; 17.6			16.1; 17.3			15.0; 17.2		
Body mass (kg)	49.8	7	50.2	57.6	6.7	56.8	73.4	11.4	70.6
	38.5; 61.0			54.4; 60.9			65.2; 81.5		
Body mass index (kg/m^2)	20.0	3.3	19.2	21.5	1.9	20.7	28.0	3.5	27.2
	14.7; 25.3			20.6; 22.4			25.5; 30.5		
Basal metabolic rate (kcal/day)	1,164.5	184.2	1,157.8	1,293.8	188.9	1,300.7	1,542.1	174.8	1,521.2
	871.5; 1,457.6			1,202.7; 1,384.8			1,417.0; 1,667.1		
	Gestational nutritional status†								
	Underweight (n = 15)			Adequate (n = 20)			Overweight + obesity (n = 7)		
	Mean	Std	Median	Mean	Std	Median	Mean	Std	Median
	IC 95%			IC 95%			IC 95%		
Age (years)	16.4	1.7	16.5	16.7	1.4	16.8	16.7	1.3	17.0
	15.5; 17.3			16.1; 17.4			15.4; 17.9		
Body mass (kg)	51.9	6.5	51.0	61.5	6.2	61.1	78.0	10.1	78.2
	48.3; 55.5			58.6; 64.3			68.7; 87.3		
Body mass index (kg/m^2)	19.4	1.5	19.3	23.8	2.0	23.8	29.4	2.9	30.5
	18.6; 20.2			22.9; 24.7			26.6; 32.1		
Basal metabolic rate (kcal/day)	1,230.5	181.7	1,269.6	1,307.8	209.5	1,358.3	1,546.2	199.0	1,509.8
	1,129.9; 1,331.1			1,209.8; 1,405.8			1,362.1; 1,730.2		

*Data are from the first visit to the laboratory. *Based on body mass index for age (18). †Based on body mass index for gestational week (19).*

lower (3%) than the recommendation (26). Since a third of them were overweight + obese, they may have been oriented to restrict the EI (30). Aspects inherent to the methods of assessment limit the comparability of results between studies.

The inadequacy of the micronutrient intake observed here confirms what was observed among the adolescent population in Brazil (31). On the other hand, the results of the present study contrast with the findings of Campos et al. (2013) (32), who investigated 139 pregnant adolescents attending prenatal care at a public maternity hospital in Rio de Janeiro. Estimates of calcium and vitamin A intakes, although inadequate, outweigh the values found in the present study. Low sodium intake, lower than the required, and less variability in nutrient intake, especially vitamin A, were also observed. This contrast may reflect aspects related to the use of a food frequency questionnaire, used in that study, which consisted of a list of only 20 food items.

In the present sample of pregnant adolescents, GW and BMI were inversely related to the percentage of adequacy of EI. One possible explanation is the reduction in dietary intake in order to control the gain of body mass after some inadequate high accumulation in the early stages of pregnancy. The presence of negative EB (percentage of adequacy of EI < 100%) observed in the overweight/obese adolescents is in agreement with data in nonpregnant individuals (33). This finding may have been due to underreporting of dietary intake, caused in part by the characteristics of the method of obtaining dietary intakes and by the inadequacy of the calculation of the ER. To our knowledge, this is the first study in which the ER of pregnant adolescents was estimated using measured BMR values. The lack of studies on energy metabolism of adolescents does not allow the development of specific procedures and methods for ER determination in this population, a gap recognized by the international agencies that establish the nutritional requirements (1). The use of measured BMR data in this study made it possible to obtain closer estimates of ER for the pregnant adolescents, since this is the metabolic component that contributes the most to total daily energy expenditure.

Table III. Dietary intake of energy and macronutrients according to pre-pregnancy nutritional status of the 33 pregnant adolescents in Niterói, RJ

	Pre-pregnancy nutritional status*								
	Underweight			Adequate			Overweight + obesity		
	Mean	Std	Median	Mean	Std	Median	Mean	Std	Median
	IC 95%			IC 95%			IC 95%		
n	15			101			53		
Energy (kcal/day)	2,575.9	978.5	2,432.3	2,350.6	920.4	2,358.4	2,430.9	934.8	2,211.3
	2,355.2; 2,796.5			2,155.6; 2,545.7			2,139.6; 2,722.2		
Energy (% of daily requirement)	116.4	48.3	109.9	104.4	46.3	98.7	95.1	40.0	83.6
	105.5; 127.3			94.6; 114.2			82.6; 107.6		
Protein (g/day)	102.8	45.7	99.5	84.6	40.9	76.0	104.9	41.5	98.4
	92.5; 113.1			75.9; 93.2			92.0; 117.9		
Protein (% of daily requirement)	174.0	88.0	160.3	133.7	77.6	110.8	127.1	56.5	114.6
	154.1; 193.8			117.2; 150.1			109.5; 144.7		
Carbohydrate (g/day)	349.8	144.9	323.2	313.2	121.8	301.5	311.1	128.7	300.5
	317.1; 382.4			287.4; 339.1			271.0; 351.2		
Carbohydrate (% of energy)	54.5	9.7	56.1	54.3	10.0	54.3	51.3	8.2	52.1
	52.4; 56.7			52.1; 56.4			48.7; 53.8		
Lipids (g/day)	86.0	43.3	82.9	85.3	47.7	72.5	85.8	45.6	75.6
	76.2; 95.8			75.2; 95.4			71.6; 100.0		
Lipids (% of energy)	29.5	7.3	28.6	31.4	8.4	31.5	30.6	6.6	30.9
	27.9; 31.2			29.7; 33.2			28.6; 32.7		

*Data are from the repeated 24h dietary recalls. *Based on body mass index for age (18).*

Table IV. Dietary intake of energy and macronutrients according to gestational nutritional status of the 42 pregnant adolescents in Niterói, RJ

	Gestational nutritional status*								
	Underweight			Adequate			Overweight + obesity		
	Mean	Std	Median	Mean	Std	Median	Mean	Std	Median
	IC 95%			IC 95%			IC 95%		
n	78			88			42		
Energy (kcal/day)	2,313.8	1,019.1	1,923.1	2,506.5	927	2,574.1	2,381.6	915.3	2,194.2
	1,749.5; 2,878.2			2,323.4; 2,689.5			2,129.4; 2,633.9		
Energy (% of daily requirement)	113.4	55.0	106	109.2	45.4	109.2	93.8	39.3	83.3
	82.9; 143.8			100.3; 118.2			82.9; 104.6		
Protein (g/day)	83.7	30.6	80.8	100.1	49.4	91.7	97.7	41.1	86.7
	66.8; 100.7			90.4; 109.9			86.4; 109.1		
Protein (% of daily requirement)	152.5	87.1	128.1	163.1	93.1	145.1	124.6	55.6	112.6
	104.3; 200.7			144.8; 181.5			109.3; 139.9		
Carbohydrate (g/day)	321.7	147.8	256.8	333.3	128.3	315.4	313	128.5	301.4
	239.8; 403.5			308.0; 358.6			277.6; 348.4		
Carbohydrate (% of energy)	55.8	7.4	54.5	54.1	10.9	54.6	52.6	8.1	53.6
	51.7; 59.9			52.0; 56.3			50.4; 54.9		
Lipids (g/day)	78.3	45.9	57.2	86.3	45.5	81.5	82.9	43.3	72
	52.9; 103.7			77.3; 95.3			71.0; 94.8		
Lipids (% of energy)	29.5	7.6	27.9	30.1	8.3	30.1	30.4	6.2	30.3
	25.3; 33.8			28.5; 31.7			28.7; 32.1		

*Data are from the repeated 24h dietary recalls. *Based on body mass index for gestational week (19).*

Table V. Dietary intake of micronutrients according to pre-pregnancy nutritional status of the 33 pregnant adolescents in Niterói, RJ

	Pre-pregnancy nutritional status*								
	Underweight			Adequate			Overweight + obesity		
	Mean	Std	Median	Mean	Std	Median	Mean	Std	Median
	IC 95%			IC 95%			IC 95%		
n	15			101			53		
Iron (mg/day)	10.8	5.2	10.2	12.2	7.8	10.9	11.1	5.4	
	8.0; 13.7			10.7; 13.8			9.6; 12.6		
Iron (% of daily requirement)	47.0	22.5	44.4	53.2	33.9	47.4	48.1	23.7	
	34.6; 59.5			46.5; 59.9			41.5; 54.6		
Calcium (mg/day)	643.6	282.9	711.8	567.8	384.6	469.2	490.2	310.9	
	486.9; 800.2			491.8; 643.7			404.5; 575.9		
Calcium (% of daily requirement)	64.4	28.3	71.2	56.8	38.5	46.9	49.0	31.1	
	48.7; 80.0			49.2; 64.4			40.5; 57.6		
Sodium (mg/day)	3,958.7	2,490.0	3,240.4	4,570.3	2,809.8	3,936.8	3,882.2	1,972.1	
	2,579.8; 5,337.6			4,015.6; 5,125.0			3,338.7; 4,425.8		
Sodium (% of daily requirement)	197.9	124.5	162.0	228.5	140.5	196.8	194.1	98.6	
	129.0; 266.9			200.8; 256.3			166.9; 221.3		
Vit A (µg/day)	368.6	262.4	412.9	2,397.7	7,861.9	258.1	832.6	3,951	
	223.3; 513.9			845.7; 3,949.8			-256.4; 1,921.7		
Vit A (% of daily requirement)	69.6	49.5	77.9	452.4	1,483.4	48.7	157.1	745.5	
	42.1; 97.0			159.6; 745.2			-48.4; 362.6		
Zinc (mg/day)	10.2	5.0	10.0	13.5	7.5	12.2	12.6	7.3	
	7.5; 13.0			12.0; 15.0			10.6; 14.7		
Zinc (% of daily requirement)	97.6	47.9	95.2	128.7	71.7	116.2	120.4	69.7	
	71.1; 124.1			114.6; 142.9			101.2; 139.6		

*Data are from the repeated 24h dietary recalls. *Based on body mass index for age (18).*

Usually, studies evaluate the dietary adequacy of pregnant adolescents using either individual dietary pattern or BMR estimated by equations as suggested by international health/nutrition agencies (1). In addition, there is no specific anthropometric method for the nutritional assessment of pregnant adolescents. To this end, the positive EB observed in the adolescents with adequate nutritional status of the present investigation, even though small, considering both pre-pregnancy and gestational nutritional status, is of concern within the context of the obesity epidemic and requires doubled attention in health surveillance actions with the use of appropriate methods for its determination.

Unlike energy and macronutrients, minerals and vitamins are nutrients whose adequacy seems harder to achieve during pregnancy. Except for sodium, these nutrients are scarce in the diet when the dietary patterns are characterized by industrial products with low quantity and little variation in natural vegetable sources and, on the contrary, with high energy density (29). This may explain the inadequate intakes of iron and calcium observed in the present pregnant adolescents, as well as among other Latin American pregnant (7) women, for whom the intake of zinc, iron and calcium was also inadequate. In the present study, the higher protein intake may have led to adequate zinc intake since the main sources of this mineral are foods, such as bovine, chicken, fish and beans, among others.

Regarding calcium, only a third of the pregnant adolescent reached the recommendation. Inadequacy was observed in the three categories of pre-pregnancy and gestational nutritional status and may be related to insufficient intake of milk and dairy products, since these foods, the main sources of calcium, are one of the groups less consumed by the Brazilian adolescent population, presenting an estimated inadequacy in more than 90% of the population (31). Calcium has a preventive role for some chronic diseases, including arterial hypertension, whose presence during pregnancy puts at risk maternal and fetal health (27).

The iron requirement during pregnancy increases almost three-fold and is difficult to achieve by dietary intake. The prevalence of inadequacy among pregnant adolescents was critical, similar to what was found in English adolescents (30). According to a national dietary survey conducted in Brazil in 2008, the diet of adolescents between 14 and 18 years of age presented 21.7% of inadequacy, twice that observed in the 10-13 year age range (31).

The high variability observed in vitamin A intake was relevant, especially among pregnant women with adequate nutritional status.

Table VI. Dietary intake of micronutrients according to gestational nutritional status of the 42 pregnant adolescents in Niterói, RJ

	Gestational nutritional status*								
	Underweight			Adequate			Overweight + obesity		
	Mean	Std	Median	Mean	Std	Median	Mean	Std	Median
	IC 95%			IC 95%			IC 95%		
n	78			88			42		
Iron (mg/day)	12.5	7.7	11.2	10.6	5.6	9.8	11.7	5.8	9.9
	10.8; 14.2			9.4; 11.8			9.9; 13.5		
Iron (% of daily requirement)	54.4	33.6	48.7	46.2	24.1	42.6	50.9	25.4	42.8
	46.8; 61.9			41.1; 51.3			43.0; 58.8		
Calcium (mg/day)	564.3	404.7	453.5	600.5	395.0	526.0	479.7	308.3	378.8
	473.1; 655.5			516.9; 684.2			383.6; 575.8		
Calcium (% of daily requirement)	56.4	40.5	45.4	60.1	39.5	52.6	48.0	30.8	37.9
	47.3; 65.6			51.7; 68.4			38.4; 57.6		
Sodium (mg/day)	4,663.3	2,656.7	3,909.2	3,969.0	2,478.7	3,435.2	3,850.7	1,750.4	3,522.1
	4,064.3; 5,262.2			3,443.8; 4,494.2			3,305.2; 4,396.2		
Sodium (% of daily requirement)	233.2	132.8	195.5	198.5	123.9	171.8	192.5	87.5	176.1
	203.2; 263.1			172.2; 224.7			165.3; 219.8		
Vit A (µg/day)	998.5	3,858.7	205.6	2,283.4	7,866.4	306.7	959.0	4,439.0	169.6
	128.5; 1,868.5			616.7; 3,950.2			-424.3; 2,342.3		
Vit A (% of daily requirement)	188.4	728.1	38.8	430.8	1,484.2	57.9	180.9	837.6	32.0
	24.2; 352.6			116.4; 745.3			-80.1; 441.9		
Zinc (mg/day)	13.3	6.6	12.3	11.9	7.1	10.7	13.3	7.7	11.1
	11.8; 14.8			10.4; 13.4			10.9; 15.7		
Zinc (% of daily requirement)	126.4	62.5	116.7	113.7	67.2	101.9	126.8	73.4	105.2
	112.3; 140.5			99.5; 128.0			103.9; 149.7		

*Data are from the repeated 24h dietary recalls. *Based on body mass index for gestational week (19).*

Table VII. Summary results of mixed linear models of % energy and protein daily requirement of the 42 pregnant adolescents in Niterói, RJ

Variables in the model	Estimates				
	β	Std error	95% CI	t-value	p-value
Energy (% of daily requirement)					
Intercept	206.16	27.119	151.39; 260.93	7.60	< 0.0001
Gestational week	-1.059	0.433	-1.9325; -0.185	-2.45	0.0188
Body mass index	-2.743	1.247	-5.2123; -0.274	-2.20	0.0298
Day of the week	-2.812	1.396	-5.5764;-0.0485	-2.01	0.0462
Protein (% of daily requirement)					
Intercept	320.07	45.109	228.97; 411.17	7.10	< 0.0001
Gestational week	-2.968	0.714	4.411; -1.525	-4.15	0.0002
Body mass index	-4.177	2.079	8.293; -0.061	-2.01	0.0467
Day of the week	-1.828	2.293	6.367; 2.711	-0.80	0.4269

This high variability can be explained by the ingestion of certain foods with a high concentration of the vitamin, such as viscera; their intake may not be regular but is encouraged in dietary counseling during prenatal care (8).

Sodium is an important marker of food quality and high intake of this mineral may be related to the ingestion of ultra-processed foods such as snacks, processed meats, snack foods, biscuits and soda, among others. The median sodium intake by the pregnant adolescents exceeded the estimates of the adolescent female population in the southeastern Brazilian region (2,815.0 mg for the 10-13 year age group and 2,774.0 mg for the 14-18 year old age group) (31).

This study can contribute to a better understanding of relevant aspects of nutrition and health of pregnant adolescents cared for in primary health care units. An important aspect of the study was the possibility of measuring BMR in the pregnant adolescents, making it possible to calculate the ER as accurate as possible. The number of R24h obtained in the present study covered a wide period of time, as well as a variety of foods and preparations, despite the small sample size. Nutritional anthropometric assessment during gestation proved to be a critical issue given the limitations of the criteria recommended and adopted. One of the possible limitations of this study is the presence of information bias. The effects of socioeconomic level and nutritional status on self-reported IE were observed in pregnant and adult pregnant women from developed countries (34) where EI underreporting was positively associated with socioeconomic status and excessive BM gain. In the present study, this effect may have been neutralized or minimized due to the low socioeconomic class to which they all belonged.

It is expected that the knowledge generated herein may be of practical importance for professionals involved in nutritional care of pregnant women, who must consider the specificities of adolescence pregnancy, without losing sight of the dimension that the nutrition/food has in the life of the subjects. At the local level, educational actions must be made in light of the dietary counseling based on the approach through dialogue with the adolescents, to understand the reality of their life, considering their beliefs, cultural values, material conditions of access and, especially, their relative autonomy (35). The situations of excessive intake should also be worked under a more comprehensive understanding of food, although the need for dietary restriction is pressing.

CONCLUSION

This study found that adolescents seen during prenatal care in primary care units living in disadvantageous socioeconomic settings have excessive intake of energy, protein and sodium. The dietary intake was insufficient for some important micronutrients such as iron and calcium. There is a negative association between the adequacy of energy and protein intakes with GW and BMI when considering inter and intra-subject variability. The pre-pregnancy overweight and obesity levels as well as the high intake of sodium are reasons for concern due to future implications to the health of the adolescents. The official Brazilian recommended criterion for anthropometric assessment in pregnancy of adolescents may not be adequate for pregnant adolescents.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Mejora de la situación nutricional y la calidad de vida de los pacientes oncológicos mediante protocolo de evaluación y de intervención nutricional

Improvement of the nutritional status and quality of life of cancer patients through a protocol of evaluation and nutritional intervention

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Resumen

Objetivo: aplicar un protocolo que facilite la detección de malnutrición en los pacientes oncológicos durante su tratamiento de radioterapia o quimioterapia, seleccionando los que se podrían beneficiar de una intervención nutricional específica.

Metodología: se determinó la presencia de riesgo de desnutrición con el método de cribado Malnutrition Screening Tool (MST). A los sujetos con riesgo se les aplicó el cuestionario Valoración Global Subjetiva Generada por el Paciente (VGS-GP) y en un subgrupo de la muestra estudiada también se midió la calidad de vida (CV) mediante el cuestionario EORTC QLQ-C30.

Resultados: de un total de 222 pacientes se observó riesgo de desnutrición en 126 (56,7%). La VGS-GP muestra una prevalencia inicial de desnutrición del 69,2% (61,7% desnutrición moderada y 7,5% desnutrición severa) y una media de pérdida de peso de -10,27 kg. En la última valoración (+12 meses), el porcentaje de desnutrición o riesgo se redujo de forma significativa a un 23,5% y la media de pérdida de peso disminuyó a -7,1kg. Durante el seguimiento, mejoraron las puntuaciones del cuestionario EORTC QLQ-C30, en especial a los tres meses la escala diarrea ($p = 0,037$), a los seis meses la escala dolor ($p = 0,009$) y a los 12 meses las escalas dolor ($p = 0,026$), náusea y vómito ($p = 0,002$), disnea ($p = 0,016$), pérdida de apetito ($p = 0,002$) y estreñimiento ($p = 0,05$).

Conclusión: el protocolo ha resultado eficaz y ha mejorado la situación nutricional y la calidad de vida de los pacientes oncológicos, con recuperación parcial del peso perdido.

Palabras clave:

Valoración Global Subjetiva Generada por el Paciente (VGS-GP). Cáncer. Desnutrición. Calidad de vida. EORTC QLQ-C30.

Abstract

Objective: to apply a protocol that facilitates the detection of malnutrition in cancer patients during their treatment of radiotherapy or chemotherapy, selecting those that could benefit from a specific nutritional intervention.

Methodology: malnutrition was assessed with the Malnutrition Screening Tool (MST). Patients at malnutrition risk were evaluated with patient generated subjective-global assessment (PG-SGA) and a subgroup of the sample studied was also assessed with a quality of life (CV) using the EORTC QLQ-C30 questionnaire.

Results: from 222 patients, risk of malnutrition was observed in 126 (56.7%). The PG-SGA shows an initial prevalence of malnutrition of 69.2% (61.7% moderately malnourished and 7.5% severe malnutrition) and a mean weight loss of -10.27 kg. In the last evaluation (+12 months), the percentage of malnutrition or risk was significantly reduced to 23.5% and the mean weight loss decreased to -7.1 kg. During follow-up, the scores of the EORTC QLQ-C30 questionnaire improved, especially at three months on the diarrhea scale ($p = 0.037$), at six months on the pain scale ($p = 0.009$), and at 12 months on the pain ($p = 0.026$), nausea and vomiting ($p = 0.002$), dyspnea ($p = 0.016$), loss of appetite ($p = 0.002$) and constipation ($p = 0.05$) scales.

Conclusion: the protocol has been effective in improving the nutritional status and quality of life of cancer patients with partial recovery of lost weight.

Key words:

Patient-generated subjective global assessment. Cancer. Malnutrition. Quality of life. Nutritional assessment. EORTC QLQ-C30.

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INTRODUCCIÓN

Los trastornos de la nutrición son muy frecuentes en el enfermo con cáncer (1,2). Es bien sabido que los pacientes con cáncer pueden llegar a presentar desnutrición tanto al inicio de la enfermedad (15-20%) como en los estadios más avanzados o terminales de su proceso (80-90%) (3). En el estudio PREDyCES, que valoraba la desnutrición en pacientes hospitalizados en el territorio español, se realizó un subanálisis de un total de 401 pacientes oncológicos, que objetivó que el 33,9% se encontraba en riesgo nutricional al ingreso y la prevalencia aumentaba hasta el 36,4% al alta (4).

La prevalencia de desnutrición es muy variable y existen varios factores que están relacionados con su aparición, como pueden ser: la localización y el estadio tumoral y los tratamientos oncológicos instaurados, el tipo de cirugía, la quimioterapia y/o la radioterapia. Todo esto repercutirá en distintos aspectos, como son la evolución de la enfermedad (morbimortalidad) y su tolerancia, el cumplimiento terapéutico, la calidad de vida y la esfera psicosocial (5,6). Los pacientes sin desnutrición tienen una mayor capacidad para solventar las complicaciones derivadas de la cirugía, la radioterapia y la quimioterapia (7).

Si el estado nutricional está alterado o existe riesgo de desnutrición, la instauración de un soporte nutricional debe ser inmediata. Toda intervención nutricional debe empezar por una valoración nutricional apropiada del paciente realizada, a poder ser, en el momento del diagnóstico de cáncer y a intervalos regulares durante su enfermedad por nutricionistas capacitados (8,9). Una vez conocida la situación nutricional del paciente, en función del tipo y la extensión tumoral, de la clínica inicial y del tratamiento antineoplásico al que se va a someter, se indicará la actuación nutricional más adecuada como arma terapéutica más involucrada en el tratamiento oncológico activo (10-12).

Esta estrategia de intervención nutricional se respalda en las nuevas guías de práctica clínica de la Sociedad Europea de Nutrición Enteral y Parenteral (ESPEN) de 2016 (13) así como por otras sociedades internaciones (14-16).

MATERIAL Y MÉTODOS

Se trata de un estudio descriptivo, observacional, prospectivo realizado en la Unidad de Hospital de Día del Hospital Mateu Orfila de Menorca. Entre marzo de 2014 y marzo de 2016, el protocolo se puso en marcha en 222 pacientes mayores de 18 años de ambos sexos, que inician tratamiento con radioterapia o quimioterapia en las consultas externas de Oncología Médica.

VARIABLES RECOGIDAS

Las variables de estudio durante el seguimiento fueron: valores antropométricos (peso, talla, índice de masa corporal [IMC] y porcentaje de pérdida de peso a seis meses); variables bioquímicas e inmunológicas (albúmina, proteínas totales, colesterol total y linfocitos); edad, sexo, diagnóstico tumoral y estadio, riesgo nutricional según el test Malnutrition Screening Tool (MST), diagnóstico nutricional con la escala VSG-GP y calidad de vida según las puntuaciones de las escalas del cuestionario EORTC QLQ-C30.

Se analizaron las puntuaciones medias de la escala EORTC QLQ-C30 con el programa informático SPSS v12.0, realizando una comparación de medias con t de Student para variables continuas relacionadas y Chi-cuadrado para variables categóricas.

FASES DEL PROTOCOLO

- Aplicar el cribado MST a todos los pacientes ambulatorios con cáncer en la primera visita a radioterapia o quimioterapia para detectar los que están en riesgo y prevenir, mediante la intervención adecuada, el inicio o la progresión de la desnutrición.
- Resultado del MST negativo (< 2): se ha repetido en cada visita de revisión del tratamiento.
- Resultado del MST positivo (≥ 2): se ha procedido a realizar una valoración nutricional completa a través del cuestionario Valoración Global Subjetiva Generada por el Paciente (VGS-GP) junto con el cuestionario de calidad de vida EORTC QLQ-C30 a un subgrupo de la población estudiada.

RESULTADOS

Se estudiaron un total de 222 pacientes (52,15% hombres y 47,85% mujeres) con una edad media de 63,92 años (Tabla I). La localización del tumor (Tabla II) fue principalmente colorrectal en el 21% de los casos, mama en el 19,3% y pulmón en el 19,3%. En relación al cribado MST, se observa riesgo de desnutrición en 126 pacientes (56,7%). De estos 126 pacientes se ha realizado seguimiento a 111 pacientes, con un total de 397 valoraciones.

Tabla I. Principales características de la muestra estudiada (n = 222)

Parámetros	Resultados (n = 222)
Edad	63,92 años
Hombre/mujer	52,15/47,85%

Tabla II. Principales diagnósticos tumorales

Localización	Resultados
Neocolorrectal	21%
Pulmón	19,3%
Mama	19,3%
Esófago	6%
Estómago	4,7%
Otros	29,7%

En relación a la clasificación inicial por el método VGS-GP (Tabla III), el 30,8% correspondió al grupo A; un 61,7%, al grupo B; y un 7,5%, al C. En las valoraciones posteriores (tres, seis y 12 meses), el porcentaje de desnutrición o riesgo se redujo de forma notable a un 33,3%, 30,3% y 23,5%, respectivamente. Asimismo, el porcentaje de pacientes con desnutrición severa se redujo a 7,2% en la revaloración a tres meses y no hubo ningún caso en las revaloraciones posteriores (seis y 12 meses). En cambio, la mejora del diagnóstico nutricional se hizo evidente con el paso del periodo de estudio. Del 30,8% inicial con criterios de buen estado nutricional, pasó a un 59,5% a los tres meses, 69,7% a los seis meses y 76,5% de los pacientes al llegar al año de seguimiento.

Respecto al riesgo nutricional del tratamiento oncológico atendiendo al tipo de terapia (Tabla IV), se observa que 18 (16,2%) pacientes fueron sometidos a tratamiento de bajo riesgo nutricional; 63 (56,8%), a tratamiento de moderado riesgo; y 28 (25,2%), a tratamiento de elevado riesgo.

Cabe destacar que del total de 111 pacientes con seguimiento nutricional, un 77,5% recibió algún tipo de intervención dietética-nutricional por parte del dietista-nutricionista, que incluyó recomendaciones dietéticas generales, recomendaciones para el control de síntomas y soporte nutricional especializado, especialmente suplementos nutricionales orales. De las principales variables analizadas (Tabla V), destaca que la población estudiada presentaba una recuperación parcial del peso perdido. De media, los 111 pacientes con seguimiento presentaban una considerable pérdida de peso de -10,27 kg en la visita inicial. Transcurridos 12 meses, se ha observado una recuperación parcial del peso y la diferencia entre la media del peso actual y el habitual se reducía a -7,1 kg, lo cual es significativo clínicamente. Asimismo, el IMC pasaba del 23,52 inicial de media al 24,46 a los 12 meses de seguimiento.

En cuanto a las variables bioquímicas e inmunológicas, tras tres meses se halló aumento significativo de los valores de linfocitos (23,88% a 29,03%) y tras seis meses, de proteínas totales (6,51 g/dl a 6,76 g/dl) y linfocitos (23,88% a 28,58%).

Se ha analizado el impacto de esta valoración e intervención nutricional en la CV del paciente oncológico en un subgrupo de la población estudiada (Tabla VI).

Prácticamente todas las puntuaciones de las escalas del test EORTC QLQ-C30 mejoraron proporcionalmente con el paso del tiempo. En el medio plazo (tres y seis meses), únicamente las escalas diarrea ($p = 0,037$) y dolor ($p = 0,009$) mejoraron de forma significativa con respecto al inicio. En cambio, en la última valoración a los 12 meses hubo una mejora significativa en el dolor ($p = 0,026$), náuseas y vómitos ($p = 0,002$), disnea ($p = 0,016$), pérdida de apetito ($p = 0,002$) y estreñimiento ($p = 0,05$).

Tabla IV. Riesgo nutricional del tratamiento oncológico (n = 111)

Terapia de bajo riesgo	Terapia de riesgo moderado	Terapia de alto riesgo
18 (16,2%)	63 (56,8%)	28 (25,2%)

Tabla III. Diagnóstico nutricional VSG-GP (n = 111)

	A Buen estado nutricional	B Desnutrición moderada o elevado riesgo	C Desnutrición severa
Inicio	30,8%	61,7%	7,5%
+3 meses*	59,5%	33,3%	7,2%
+6 meses*	69,7%	30,3%	-
+12 meses*	76,5%	23,5%	-

**Prueba Chi-cuadrado, valor p < 0,05.*

Tabla V. Principales variables estudiadas (n = 111)

	1.ª valoración (inicio)	2.ª valoración (+3 meses)*	3.ª valoración (+6 meses)*	4.ª valoración (+12 meses)*
Colesterol (mg/dl)	173,93	183,37	186,09	191,42
Linfocitos (%)	23,88	29,03 **	28,58 **	35,23
Proteínas totales (g/dl)	6,51	6,59	6,76	6,71
Albúmina (g/dl)	3,57	3,31	3,63	3,94
Prealbúmina (mg/dl)	18,57	19,50	24,0	28,0
Peso actual (kg)	64,23	63,85	64,80	66,08
Peso habitual (kg)	74,5	73,30	72,78	73,18
IMC	23,52	23,49	24,08	24,46

**Análisis t de Student de comparativa de medias entre 2.ª valoración, 3.ª valoración y 4.ª valoración. ** = p ≤ 0,05*

Tabla VI. Escalas del cuestionario EORTC QLQ-C30 (n = 53)

	1.ª valoración inicial	2.ª valoración 3 meses*	3.ª valoración 6 meses*	4.ª valoración 12 meses*
Estado global de salud/calidad de vida	65 ± 26	73 ± 23	73 ± 16	77 ± 12
Escalas funcionales				
Función física	74 ± 36	80 ± 19	80 ± 24	91 ± 11
Función de rol	61 ± 36	74 ± 35	71 ± 37	75 ± 46
Función emocional	70 ± 25	72 ± 30	77 ± 26	81 ± 17
Función cognitiva	85 ± 25	85 ± 22	82 ± 25	85 ± 19
Función social	64 ± 29	78 ± 22	63 ± 33	75 ± 36
Escala de síntomas				
Fatiga	36 ± 32	30 ± 29	33 ± 27	32 ± 37
Náusea y vómito	4 ± 9	3 ± 12	3 ± 8	0 **
Dolor	18 ± 27	13 ± 25	11 ± 16 **	12 ± 12 **
Disnea	8 ± 21	10 ± 25	12 ± 23	0 **
Insomnio	24 ± 32	28 ± 35	19 ± 26	17 ± 25
Pérdida de apetito	36 ± 37	26 ± 37	14 ± 28	4 ± 12 **
Estreñimiento	16 ± 28	15 ± 24	19 ± 34	0 **
Diarrea	7 ± 19	14 ± 26 **	11 ± 16	12 ± 18
Dificultades económicas	28 ± 35	19 ± 28	32 ± 36	29 ± 38

**Análisis t de Student de comparativa de medias entre 2.ª valoración, 3.ª valoración y 4.ª valoración. ** = p ≤ 0,05.*

DISCUSIÓN

La aplicación del test MST ha permitido incluir un cribado nutricional sistemático a todos los pacientes oncológicos que inician tratamiento con radio o quimioterapia y ha facilitado la detección de riesgo de desnutrición al 56,7% de los pacientes. Isenring y cols., en 51 pacientes ambulatorios tratados con quimioterapia, comparan el MST con una valoración nutricional completa medida mediante VGS-GP y demuestran que tiene una sensibilidad del 100% y una especificidad del 92% (17).

En el estudio de Bauer y cols., realizado en 72 pacientes, se comparan la sensibilidad y la especificidad entre la VGS-GP con puntuación y la simple VGS y se documenta que este primer método tiene una sensibilidad del 98% y una especificidad del 82% para predecir la clasificación de la VGS. En dicho estudio, se documentó una prevalencia de desnutrición del 75%, el 59% de los pacientes estaban moderadamente desnutridos y el 17%, severamente desnutridos (18). En nuestro estudio, un 69,2% de los pacientes fueron diagnosticados de desnutrición al aplicar la VGS-GP, el 61,7% presentaba desnutrición moderada o riesgo de desnutrición y el 7,5%, desnutrición severa.

En cuanto a cuál es el mejor momento para hacer la valoración nutricional, Fearon y cols. (19) y Muscaritoli y cols. (20) señalaron que la valoración nutricional debe realizarse cuando los pacientes todavía no están severamente desnutridos usando herramientas de cribado nutricional, con el fin de identificar rápidamente a los individuos que están en riesgo nutricional. Al analizar nuestros datos, la población evaluada está constituida exclusivamente por pacientes ambulatorios con cáncer que visitan por primera vez la consulta específica de Oncología Médica previo al inicio del tratamiento de radioterapia o quimioterapia, lo cual concuerda con la recomendación mencionada.

Una vez realizada la valoración, y tal y como evidenciaron varios autores en sus trabajos, los objetivos de una intervención nutricional en oncología son mejorar la tolerancia al tratamiento oncológico específico, disminuir la incidencia de complicaciones, aumentar el control tumoral y, ante todo, mejorar la CV del paciente (7,21,22).

Dos metaanálisis recientes (23,24) han demostrado la eficacia de la intervención nutricional en el paciente oncológico. Halfdanarson y cols. publicaron cinco ensayos clínicos aleatorios con un total de 488 pacientes y observaron una mejora en la puntuación de CV entre los que recibieron asesoramiento nutricional *vs.* ningún asesoramiento nutricional (IC 95%, p = 0,06). Esto sugiere que el asesoramiento nutricional puede justificarse en pacientes con una ingesta oral disminuida y pérdida de peso. Por su parte, la revisión sistemática de Baldwin y cols. examinaba la eficacia de combinar consejo dietético personalizado y/o suplementos nutricionales orales en pacientes oncológicos desnutridos o con riesgo de desnutrición. La revisión incluyó 13 ensayos controlados aleatorios con un total de 1.414 pacientes. No hubo diferencia en la supervivencia (p = 0,43). En cambio, la calidad de vida mejoraba de forma significativa en los pacientes que recibieron radioterapia adyuvante y las intervenciones se asociaron con mejoras estadísticamente significativas en el peso corporal (diferencia media de peso 1,86 kg, IC 95%, p = 0,02). Estos datos concuerdan con los

obtenidos en otro trabajo de Bourdel-Marchasson y cols., que en un estudio aleatorio de dos años demostraron que una intervención nutricional mejoraba el peso corporal y la ingesta oral de pacientes oncológicos desnutridos tratados con quimioterapia (25).

Ravasco y cols. investigaron el impacto del asesoramiento dietético o de los suplementos nutricionales en la CV de 111 pacientes con cáncer colorrectal durante la radioterapia y tres meses después. Los pacientes (n = 37) que recibieron asesoramiento dietético individualizado presentaban una recuperación ponderal de 4 kg en el seguimiento a tres meses. Además, al final del tratamiento, todas las puntuaciones de las escalas del test de CV EORTC-QLQ C30 mejoraron significativamente ($p \leq 0,002$) asociado con la mejora del estado nutricional de los pacientes ($p \leq 0,05$). En el seguimiento de tres meses, y en comparación con el final de la radioterapia, todos los pacientes que recibían atención nutricional mantuvieron o mejoraron su CV total ($p \leq 0,02$). Las puntuaciones de las escalas funcionales también mejoraron o se mantuvieron ($p \leq 0,04$) y las escalas de síntomas o ítems individuales fueron similares a las puntuaciones basales (7).

Al comparar nuestros resultados con los de esos trabajos, en nuestro estudio también se observa una mejora en la CV de los pacientes que recibieron atención nutricional individualizada, en especial, con una mejora significativa a los tres meses de seguimiento de la escala diarrea ($p = 0,037$), a los seis meses de la escala dolor ($p = 0,009$) y a los 12 meses de las escalas de síntomas dolor ($p = 0,026$), náuseas y vómitos ($p = 0,002$), disnea ($p = 0,016$), pérdida de apetito ($p = 0,002$) y estreñimiento ($p = 0,0$). Asimismo, transcurridos 12 meses, se ha observado una recuperación parcial del peso corporal (diferencia media de peso 1,85 kg). A lo largo de todo el periodo de nuestro estudio, incluidas la valoración y la intervención, se ha observado una mejora significativa del diagnóstico nutricional con el paso del periodo de estudio. Del 30,8% inicial con criterios de buen estado nutricional, pasó a un 76,5% de los pacientes al llegar al año de seguimiento. Estos resultados coinciden con los de Ravasco y cols., que observaron deterioro nutricional únicamente en un 18% de los pacientes con asesoramiento dietético. En cambio, los pacientes que no recibían atención nutricional durante el tratamiento presentaban deterioro de su estado nutricional en más del 90% de los pacientes (7). En el estudio de Isenring y cols., con una muestra de 60 pacientes con cáncer gastrointestinal (GI), cabeza y cuello y tratamiento de radioterapia, el grupo de pacientes que recibieron consejo dietético regular e intensivo por un dietista-nutricionista durante 12 semanas, incluyendo la pauta de suplementos nutricionales en caso necesario, tuvieron una recuperación más rápida de la CV según la puntuación global del test EORTC en comparación con el grupo control ($p = 0,009$) (26).

Varios autores demostraron que el asesoramiento nutricional individualizado realizado por un profesional capacitado, en comparación con no recibir consejo, puede mejorar la ingesta oral, el peso corporal y la CV, sin que sea necesario suspender o discontinuar el tratamiento de radioterapia (7,21,26-28). Asimismo, diferentes autores sugieren que un asesoramiento nutricional junto con la prescripción de suplementos nutricionales orales puede mejorar la ingesta oral y la CV y estabilizar el peso corporal, aunque no observaron mejora de la intervención nutricional en la respuesta al tratamiento o en la supervivencia (23). También se deber tener en cuenta que esta mejora en la CV puede ser debido a que durante las primeras semanas los pacientes estaban en tratamiento de quimioterapia y/o radioterapia y la CV puede estar influenciada negativamente por los efectos secundarios que experimentan los pacientes.

En conclusión, la desnutrición es un diagnóstico muy prevalente en pacientes oncológicos. Teniendo en cuenta las importantes repercusiones a nivel de morbimortalidad, CV y coste sanitarios, es importante integrar la valoración nutricional como parte de la evaluación global inicial de los pacientes con cáncer e instaurar, cuando sea necesario, la terapia nutricional de la forma más precoz posible. En nuestro trabajo, la valoración e intervención nutricional no ha resultado ser una mejora estadísticamente significativa en la CV global en pacientes con cáncer. No obstante, sí se observan mejoras en otros ámbitos (dolor, pérdida de apetito…) de forma que nuestro estudio sugiere el beneficio de una mayor atención nutricional, especialmente si los pacientes presentan una ingesta oral disminuida y pérdida de peso.

LIMITACIONES

1. Existen pocos estudios que incorporan datos sobre el impacto de una intervención nutricional en la CV.
2. El número limitado de pacientes hace que nuestros resultados no sean directamente extrapolables. Se necesita aumentar el tamaño de la muestra para obtener resultados más fiables y certeros.
3. Además, cabe consignar como limitación del estudio la heterogeneidad en los diagnósticos tumorales de la población estudiada, no fácilmente comparables.
4. Falta una comparativa con un grupo control (sin valoración ni intervención nutricional).

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Trabajo Original

Valoración nutricional

Hydration habits before, during and after training and competition days among amateur basketball players

Hábitos de hidratación antes, durante y tras el ejercicio y la competición en jugadores de baloncesto amateurs

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Abstract

Background: fluid intake before, during and after exercise is the most important way to replace water lost during exercise and avoid dehydration.

Aim: to assess fluid intake habits before, during and after exercise in amateur basketball players on both training and competition days.

Methods: one hundred and eighty-three amateur basketball players (87 women and 96 men, 19-29 years old) were interviewed. Data was obtained from a drinking habits questionnaire.

Results: overall, 20.8%, 5.5% and 2.7% of subjects did not drink before, during and after exercise on training days, respectively; 17.5% of subjects did not drink before exercise on competition days. Water was the preferred beverage before, during and after exercise on both training and competition days, with fruit juice being the second most consumed beverage before exercise. All subjects also drank fizzy drinks and other beverages during exercise on competition days. According to the recommendations, good hydration habits were found in 54.6%, 74.2% and 76.5% of subjects before, during and after training days, respectively.

Conclusions: most amateur basketball players drink before, during and after exercise on both training and competition days, but not all of them complied with the hydration recommendations.

Key words:

Adults. Liquid intake. Survey. Hydration recommendations.

Resumen

Introducción: la ingesta de líquidos antes, durante y tras el ejercicio es la forma más importante de recuperar el agua perdida durante el ejercicio y de evitar la deshidratación.

Objetivo: analizar los hábitos de ingesta de líquidos, durante y tras el ejercicio en jugadores de baloncesto amateurs tanto durante el entrenamiento como durante la competición.

Métodos: fueron entrevistados 183 jugadores de baloncesto amateurs (87 mujeres y 96 hombres, de 19-29 años de edad). Los datos se obtuvieron por aplicación de un cuestionario de hábitos de bebida.

Resultados: globalmente, el 20,8%, 5,5% y 2,7% de los sujetos no bebieron antes, durante y tras el entrenamiento, respectivamente; el 17,5% de los sujetos no bebieron antes de la competición. El agua fue la bebida preferida antes, durante y tras el ejercicio, tanto durante el entrenamiento como durante la competición, en tanto que los zumos de frutas fueron la segunda bebida consumida antes del ejercicio. Todos los sujetos tomaron bebidas gaseosas y de otro tipo durante la competición. De acuerdo con las recomendaciones, se encontraron buenos hábitos de hidratación en el 54,6%, 74,2% y 76,5% de los sujetos antes, durante y tras el entrenamiento, respectivamente.

Conclusiones: la mayoría de los jugadores de baloncesto amateurs beben antes, durante y tras el ejercicio, tanto durante el entrenamiento como durante la competición, pero no todos ellos cumplen con las recomendaciones de hidratación.

Palabras clave:

Adultos. Ingesta líquida. Entrevista. Recomendaciones de hidratación.

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INTRODUCTION

A balanced diet and appropriate hydration are fundamental to sport performance, but specific needs will depend on several factors, such as individual physiological conditions, intensive physical activity, time of the season and training or competition period (4,5). An average daily water intake of 2.2 to 2.6 ml/d in men and 1.9 to 2.4 ml/d in women meets the needs of most adult people (1). However, strenuous physical exercise and heat stress can greatly increase daily water needs, and individual variability between athletes can be substantial (6).

Dehydration can negatively affect different physiological systems including the nervous system (7,8), cardiovascular, thermoregulation and endocrine systems or metabolism (3), which may have negative consequences on health (9), affect athletic performance (10-12) and increase the risk of exertional heat injury (13) in both anaerobic and aerobic sports (14). Physical and mental performance during physical exercise and sport practice is impaired in the under-hydrated individual (15) and to avoid this, as well as the negative effects on physical performance, the athlete must drink enough fluids before (16-18), during (19-21) and after practicing physical exercise, maintaining proper hydration throughout the day (3). Furthermore, not only the amount of beverage is important, but also the type of beverage to be drunk.

Currently, many people practice some kind of recreational intensive activity sport, such as basketball, for more than one hour a day (4), but there are few studies evaluating whether drinking habits are in line with the recommendations made by national and international sports institutions. Basketball is an aerobic-anaerobic sport, characterized by high-intensity intermittent exercise (22) and mainly played indoors, so dehydration may also be affected by high temperature and humidity. Health and disease prevention do not only depend on physical activity practice (23), but also on eating and hydration habits (20). Therefore, the aim of this work was to assess the drinking habits of amateur basketball players before, during and after exercise on both training and competition days.

METHODS

STUDY DESIGN

The study was a population-based cross-sectional study carried out in the city of Barcelona between October 2011 and February 2012.

SELECTION OF PARTICIPANTS, RECRUITMENT AND APPROVAL

Barcelona city's basketball clubs (n = 50) were contacted by e-mail and phone and all players registered as senior category (1st, 2nd and 3rd) in the Catalan Federation of Basketball (CFB) and aged between 19 to 29 years were invited to participate in the study. One hundred and eighty-three players (96 men and 87 women), from 45 clubs, performing intensive physical activity 2-3 times per week, accounting for 60 to 120 min/d, agreed to participate.

ETHICS

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and the URL's Committee of Ethics in Research (CER-URL, Barcelona, Spain, ref. 2010_05) approved all procedures involving human subjects. Written informed consent was obtained from all subjects.

ANTHROPOMETRIC MEASUREMENTS

Anthropometric characteristics are part of the biological variables related to sport performance. Anthropometric characterization of subjects was included in table I. All anthropometric variables were measured according to the protocol recommended by the

Table I. Anthropometric characteristics of the amateur basketball players

	Women (n = 87)	Men (n = 96)	p‡
Missing (n)	1	4	
Age (years)*	22.4 (20.1-24.6)	21.7 (20.4-25.3)	0.883
Body mass (kg)*	61.7 (56.7-67.1)	78.7 (71.4-83.9)	< 0.001
Height (m)*	169.0 (164.8-173.0)	184.5 (178.0-190.0)	< 0.001
BMI (kg/m^2)*	21.9 (20.2-23.4)	23.0 (21.6-24.6)	< 0.001
WHtR*	0.42 (0.41-0.45)	0.44 (0.42-0.47)	< 0.001
Somatotype components			
Endomorphic†	4.33 ± 1.07	3.06 ± 0.90	< 0.001
Mesomorphic†	2.84 ± 1.54	4.02 ± 1.16	< 0.001
Ectomorphic†	2.68 ± 1.22	2.92 ± 1.09	0.182

*BMI: body mass index; WHtR: waist-to-height ratio. Values are the *median (1st quartile-3rd quartile) and †mean ± standard deviation. ‡Statistical significant differences between genders were assessed by means of unpaired Student t test or Mann-Whitney U test.*

International Society for the Advancement of Kinanthropometry (ISAK) (24). All the anthropometric measurements were objectively obtained by trained personnel. Height was determined using a mobile anthropometer (Seca 217®, Hamburg, Germany), to the nearest millimeter, with the subject's head in the Frankfurt plane. Body mass was determined to the nearest 100 g using a digital scale (Seca 874®, Hamburg, Germany). The subjects were weighed in bare feet and light underwear. Height and weight measures were used to calculate the body mass index (BMI, kg/m^2). Waist circumference (WC) was also measured. Height and WC measures were used to calculate the waist-to-height ratio (WHtR).

The three somatotype components (endomorphy, mesomorphy and ectomorphy) were calculated according to the Carter and Heath anthropometric somatotyping method (25). The ten variables used to calculate the anthropometric somatotype were height, mass, four skinfolds (triceps, subscapular, supraspinale, medial calf), biepicondylar breadth of humerus and femur, and arm (flexed and tensed) and calf circumferences. Skinfold thicknesses were measured using a skinfold caliper (Holtain®, Crosswell, UK), to the nearest 0.2 mm. Circumferences were measured using a non-stretch measuring tape (Lufkin Executive® w606pm, Lufkin, USA) to the nearest 1 mm. Bone widths were measured with a small sliding bone caliper (Holtain® Ltd., Crosswell, UK) to the nearest 1 mm. The subjects were asked to stand erect in a relaxed position with both feet together on a flat surface. The median was used for statistical analysis if the measurements had to be taken three times, while the mean was used if the first two measurements were within the acceptable range (26).

ASSESSMENT OF BEVERAGE CONSUMPTION

A drinking habits questionnaire based on a previously published questionnaire (27) was self-administered by computer. This questionnaire included the following questions about beverage intake before, during and after exercise on both training and competition days:

1. Type of beverage, which was categorized into five groups: fruit juice (i.e., natural fruit juice and fruit juice sweetened with sugar), water (i.e., tap, bottled and spring water), energy drinks (i.e., cola and *guarana* drinks), soda (i.e., carbonated soft drinks) and others (i.e., carrot juice, alcohol-free beer, chocolate, vanilla and strawberry milkshakes and diet milkshakes, soya milk, rice milk, oat milk, fermented milk drinks with sugar, fermented milk drinks, kefir and sweetened iced tea).
2. The amount of fluid drunk, which was categorized into three groups: < 250, 250-500, and ≥ 500 ml.
3. The beverage time, which was categorized into four groups before and after the exercise: < 10, 10-20, 20-30, and > 30 min; and into three groups during the exercise: 1-3, 4-6 and > 6 times. Fluid intake was only considered if it occurred within four hours before starting or after finishing physical exercise.

According to the drinking habits recommendations published by the American College of Sport Medicine (ACSM) (28,29) and the Spanish Federation of Sports Medicine (FEMEDE) (4), the following criteria were established to assess healthy hydration habits:

1. Before exercise: less than one glass (< 250 ml) between 10-30 minutes beforehand, or more (≥ 250 ml), 30 minutes before exercise.
2. During exercise: less than one glass (< 250 ml) more than six times; between one to two glasses (250 to 500 ml) 4-6 times; or more than two glasses (≥ 500 ml) regardless of the frequency.
3. After exercise: more than one glass (≥ 250 ml) within 30 minutes after exercise ended.

STATISTICS

Analyses were performed with the Statistical Package for the Social Sciences version 24.0 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp USA). All tests were stratified by gender. Categorical variables were presented as frequencies and/or proportions. Significant differences in prevalence were calculated by means of χ^2 or Fisher's exact test. Normality of data was assessed using Kolmogorov-Smirnov test. Continuous variables were expressed as follows: mean (standard deviation [SD]) for normally distributed data (somatotype components: endomorphy, mesomorphy, ectomorphy), and median (1st-3rd quartile) for non-normally distributed data (age, weight, height, BMI, and WHtR). For normally distributed data, the unpaired Student's t-test was used to compare the mean of two independent groups. For non-normally distributed data, the Mann-Whitney U test was used to compare the median of two independent groups. The level of significance was established for p values at < 0.05.

RESULTS

Table II shows the type of beverage consumed before, during and after exercise on both training and competition days. Overall, 20.8%, 5.5% and 2.7% of the subjects reported that they did not drink before, during and after exercise on training days, respectively. More women than men reported that they did not drink before exercise (27.6% *vs* 14.6%, $p < 0.05$) while more men than women did not drink during exercise (9.4% *vs* 1.2%, $p < 0.05$). No statistically significant difference in the prevalence of non-drinkers was found between men and women after exercise (2.1% and 3.4%, respectively). In competition days, 17.5% of subjects reported that they did not drink before exercise, with a higher prevalence among women than in men (25.3% *vs* 10.4%, $p < 0.01$). Almost none of them reported that they did not drink during or after exercise on competition days.

Water was the preferred beverage before, during, and after exercise on both training and competition days. In fact, 64.5% of the subjects reported that they drank water before exercise on training days, followed by fruit juice (21.3%), soda (10.9%), energy drinks (6.0%) and other beverages (4.9%). Overall, a

Table II. Type of beverages consumed before, during and after the exercise in training and competition days among amateur basketball players

		Training day			Competition day		
	n	Before	During	After	Before	During	After
Nothing							
All	183	38 (20.8)	10 (5.5)	5 (2.7)	32 (17.5)	0 (0.0)	2 (1.1)
Women	87	24 (27.6)	1 (1.2)	3 (3.4)	22 (25.3)	0 (0.0)	1 (1.1)
Men	96	14 (14.6)	9 (9.4)	2 (2.1)	10 (10.4)	0 (0.0)	1 (1.0)
p		0.030	0.020	0.670	0.008	1.000	1.000
Fruit juice							
All	183	39 (21.3)	1 (0.5)	11 (6.0)	25 (13.7)	3 (1.6)	14 (7.7)
Women	87	19 (21.8)	1 (1.1)	4 (4.6)	10 (11.5)	1 (1.1)	6 (6.9)
Men	96	20 (20.8)	0 (0.0)	7 (7.3)	15 (15.6)	2 (2.1)	8 (8.3)
p		0.868	0.475	0.444	0.416	1.000	0.715
Water							
All	183	118 (64.5)	172 (94.0)	149 (81.4)	126 (68.9)	180 (98.4)	142 (77.6)
Women	87	51 (58.6)	85 (97.7)	75 (86.2)	54 (62.1)	86 (98.9)	68 (78.2)
Men	96	67 (69.8)	87 (90.6)	74 (77.1)	72 (75.0)	94 (97.9)	74 (77.1)
p		0.115	0.044	0.113	0.059	1.000	0.861
Energetic drinks							
All	183	11 (6.0)	2 (1.1)	21 (11.5)	15 (8.2)	8 (4.4)	25 (13.7)
Women	87	3 (3.4)	1 (1.1)	5 (5.7)	3 (3.4)	3 (3.4)	4 (4.6)
Men	96	8 (8.3)	1 (1.0)	16 (16.7)	12 (12.5)	5 (5.2)	21 (21.9)
p		0.165	1.000	0.021	0.026	0.723	0.001
Soda							
All	183	20 (10.9)	0 (0.0)	33 (18.0)	10 (5.5)	183 (100.0)	45 (24.6)
Women	87	10 (11.5)	0 (0.0)	11 (12.6)	6 (6.9)	87 (100.0)	25 (28.7)
Men	96	10 (10.4)	0 (0.0)	22 (22.9)	4 (4.2)	96 (100.0)	20 (20.8)
p		0.816	1.000	0.071	0.522	1.000	0.215
Others							
All	183	9 (4.9)	0 (0.0)	8 (4.4)	13 (7.1)	183 (100.0)	3 (1.6)
Women	87	6 (6.9)	0 (0.0)	2 (2.3)	10 (11.5)	87 (100.0)	2 (2.3)
Men	96	3 (3.1)	0 (0.0)	6 (6.3)	3 (3.1)	96 (100.0)	1 (1.0)
p		0.313	1.000	0.283	0.028	1.000	0.605
≥ 2 type of beverages							
All	183	48 (26.2)	2 (1.1)	39 (21.3)	35 (19.1)	8 (4.4)	45 (24.6)
Women	87	24 (27.6)	1 (1.1)	12 (13.8)	17 (19.5)	3 (3.4)	18 (20.7)
Men	96	24 (25.0)	1 (1.0)	27 (28.1)	18 (18.8)	5 (5.2)	27 (28.1)
p		0.691	1.000	0.018	0.892	0.723	0.243

Values are: n (%). Statistical significant differences between genders were assessed by χ^2 or Fisher's exact test.

quarter of the subjects reported more than one type of beverage before exercise on training days. On competition days, 68.9% of the subjects also reported that they drank water before exercise, followed by fruit juice (13.7%), energy drinks (8.2%), other beverages (7.1%) and soda (5.5%). However, men were more likely to show a preference for energy drinks than women. Almost all of

the subjects reported that they only drank water during exercise on training days. However, all the subjects reported that they also drank soda and other beverages during exercise on competition days. Despite the fact that the preferred beverage after exercise on both training and competition days included water (81.4% and 77.6%, respectively), some subjects reported that they also drank soda (18.0% and 24.6%), energy drinks (11.5% and 13.7%), fruit juice (6.0% and 7.7%) and/or other beverages (4.4% and 1.6%). After exercise, men were also more likely to prefer energy drinks than women were.

The overall amount of beverage intake before, during and after exercise on both training and competition days is shown in figure 1. Overall, 1.4%, 41.4% and 57.2% of the subjects reported that they drank < 250, 250-500, and ≥ 500 ml, respectively, before exercise on training days, with no statistically significant differences between genders (p = 0.265). On competition days, 62.3% of subjects reported that they drank ≥ 500 ml before exercise. On the other hand, statistically significant differences in the distribution of the sample according to the amount of beverage intake during exercise were obtained on both training (p = 0.006) and competition (p = 0.042) days, with men more likely to drink ≥ 500 ml than women were. After exercise, around 70% of the subjects reported that they drank ≥ 500 ml.

Figure 2 shows the time of fluid intake for those subjects who reported drinking some beverage before (A), during (B) and after (C) exercise on both training and competition days. Most of the subjects reported that they drank < 10 or > 30 minutes before exercise on both training and competition days. During exercise, most subjects (89.0%) reported that they drank 1-3 times on training days, while only 52.1% of men and 28.7% of women did

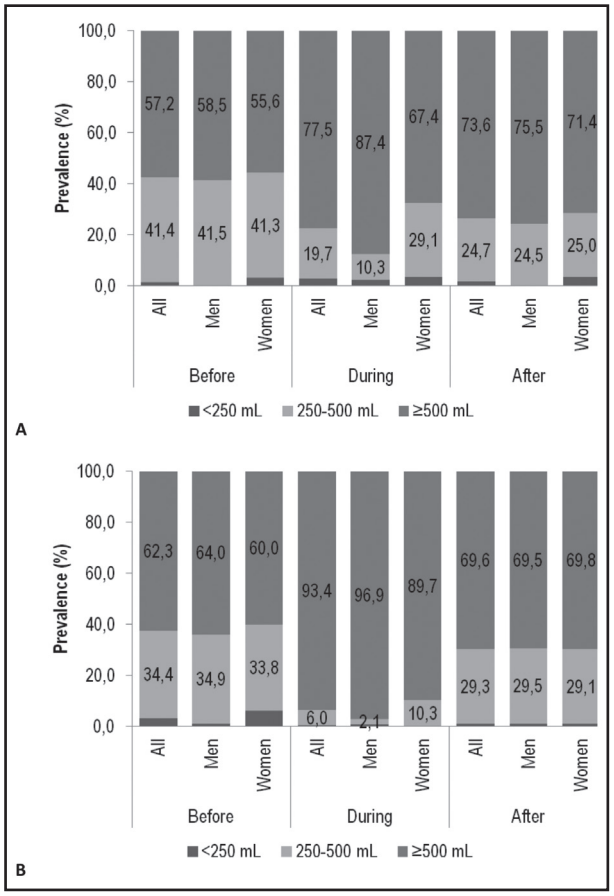

Figure 1.

Amount of beverage consumed before, during and after exercise in training (A) and competition (B) days among amateur basketball players.

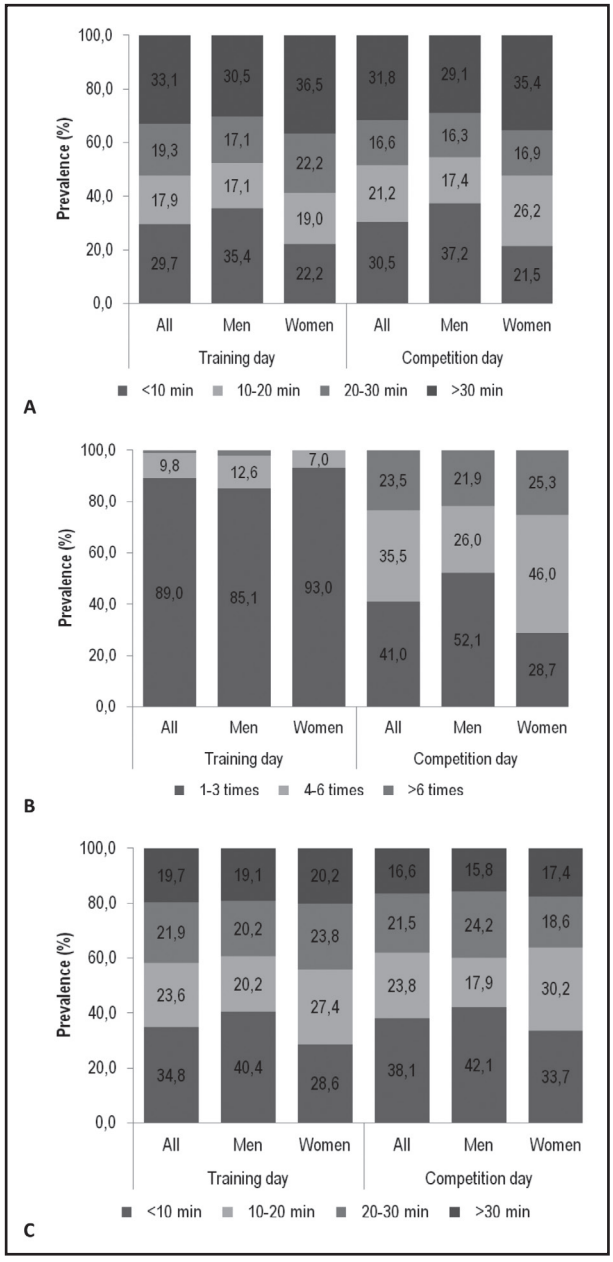

Figure 2.

Time of the fluid intake among amateur basketball players who reported to drink several beverages before (A), during (B) and/or after (C) the exercise in training and competition days.

so 1-3 times on competition days. Furthermore, 21.9% of men and 25.3% of women reported that they drank > 6 times during exercise on competition days. Overall, 80.3% and 83.4% of the subjects reported that they drank < 30 minutes after exercise on training and competition days, respectively.

Table III shows the prevalence of good hydration habits before, during and after exercise on training days according to the recommendations released by the ACSM and FEMEDE. Good hydration habits were found in 54.6%, 74.2% and 76.5% of the subjects, respectively.

DISCUSSION

The first main finding of this study was that 20.8%, 5.5% and 2.7% of amateur basketball players reported that they did not drink before, during and after exercise on training days, respectively. Furthermore, 17.5% of the subjects reported that they did not drink before exercise on competition days, with a higher prevalence among women than in men. To our knowledge, there is little previous data regarding the drinking habits of amateur sportspeople. Previously, Alarcon et al. (27) assessed the drinking habits of 35 basketball players (14-32 years) from the Polaris World basketball Club (Murcia, Spain) on a competition day. In this study, 94.3% of the participants drank some fluid before exercise against the 82.5% from this study.

In agreement with the research by Alarcon et al. (27), water was the preferred beverage before, during, and after exercise on both training and competition days. Moreover, fruit juice was the second most-consumed beverage on both training and competition days prior to exercise. However, in contrast to the study by Alarcon et al. (27), all the subjects in our work reported that they also drank soda and other beverages during exercise on competition days. Finally, beverage intake in the Alarcon et al. study (27) included water (40%), fruit juice (22.8%), soda (20%) and energy drinks (17.1%) after exercise. Likewise, in this study participants also reported that they drank water, soda, energy drinks, fruit juice and other beverages after exercise on both training and competition days. Finally, 31.8% of the subjects in our study reported that they drank some type of beverage 30 minutes before exercise on competition days, against the 8.6% seen in the Alarcon et al. study (27). Furthermore, 16.6% of the subjects in this study reported that they drank some type of beverage 30 minutes after exercise on competition days, against the 22.8% observed in the study by Alarcon et al. (27).

The National Athletic Trainers Association (NATA) (13) proposed that, to ensure proper pre-exercise hydration, athletes should consume approximately 500-600 ml of water or sport drinks 2-3 hours before exercise. If hydration levels are low, athletes should drink 200-300 ml of water or sport drinks 10-20 minutes before exercise. In this study, most subjects reported drinking at least 250 ml before exercise; however, only 26 subjects reported that they drank it 10-20 minutes before exercise. The NATA (13) recommended that, during exercise, fluid replacement generally requires 200-300 ml of water or sports drinks every 10-20 minutes and proposed that post-exercise hydration should aim, within two hours afterwards, to correct fluid losses accumulated during the practice or event and that, ideally, rehydration should contain water to restore hydration levels.

A review by Rowland (17) pointed out that the amount of liquid intake could be calculated as a fluid intake of

Table III. Hydration habits according to the recommendations released by the American College of Sports Medicine (ACSM) and the Spanish Federation of Sports Medicine (FEMEDE) among amateur basketball players in a training day

	Training day		
	All (n = 183)	**Women (n = 87)**	**Men (n = 96)**
Before the exercise			
≥ 250 ml; 10-30 min before the exercise	54 (29.5)	26 (29.9)	28 (29.2)
250-500 ml; > 30 min before the exercise	19 (10.4)	9 (10.3)	10 (10.4)
≥ 500 ml; > 30 min before the exercise	27 (14.8)	12 (13.8)	15 (15.6)
Total	100 (54.6)	47 (54.0)	53 (55.2)
During the exercise			
< 250 ml; > 6 times	1 (0.5)	0 (0.0)	1 (1.0)
250-500 ml; 4-6 times	1 (0.5)	1 (1.1)	0 (0.0)
≥ 500 ml; independently of times	134 (73.2)	58 (66.7)	76 (79.2)
Total	136 (74.2)	59 (67.8)	77 (80.2)
After the exercise			
≥ 250 ml within 30 min	140 (76.5)	64 (73.6)	76 (79.2)

Values are: n (%).

13 ml/kg body weight/h. According to the ACSM (28,29) and FEMEDE (4), prior to exercise individuals should drink beverages at least four hours before exercise and around 5-7 ml/kg body weight (300-600 ml) or 3-5 ml/kg body weight approximately two hours before exercise. In the present study, about 60% of the subjects reported that they drank at least 500 ml before exercise. However, post-exercise fluid intake is equally important to avoid commencing subsequent bouts of exercise in a dehydrated state (4,17,26). In fact, the ACSM (29) and FEMEDE (4) also pointed out that, 30 minutes after exercise starts, it is necessary to compensate fluid loss, and after one hour it is essential to drink 400-500 ml/h or 150-200 ml/20 min. Moreover, post-exercise hydration should aim to restore fluid losses accumulated during the practice or event within two hours. In this study, around 70% of the subjects reported that they drank at least 500 ml after exercise, but around 80% of basketball players rehydrated by drinking water and 25% drank also soda. Ideal rehydration should contain water to restore hydration levels. Finally, good hydration habits were found in 54.6%, 74.2% and 76.5% amateur basketball players before, during and after exercise on training days, respectively.

STRENGTHS AND LIMITATIONS

The main strength of this study is that there are many studies regarding the relationship between hydration and health and performance in the field of elite sport, but few studies have been conducted on adults in the field of recreational sports. However, this study has also several limitations. Firstly, good hydration habits should consider the intake of liquid throughout the day to learn about the level of hydration before starting exercise in order to determine the amount of liquid that each subject should drink after completing the exercise. This should be 150% (4) of the amount of weight lost during exercise. Secondly, the evaluation of good hydration was only carried out on a training day, because not all subjects played for more than one hour on a competition day.

CONCLUSIONS

Good hydration habits were found in 54.6%, 74.2% and 76.5% of subjects before, during and after the training day, respectively. It is difficult to instil hydration habits into all sportsmen, and even more so in non-professional categories and in the lower divisions. Because good hydration substantially contributes to the improvement of physical performance, and drinking water *ad lib* is not enough, hydration patterns should be an important part of training (30). These results should be taken into account to establish recommendations by sports organizations in relation to the amount and quality of liquid to drink before, during and after exercise, taking into account the type of sport, duration and climate.

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ARÁN

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Depression and food consumption in Mexican college students

Depresión y consumo de alimentos en estudiantes universitarios mexicanos

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Abstract

Introduction: depression is frequently accompanied by overeating and a preference for certain foods that may consequently lead to weight gain.

Objectives: a) to determine the prevalence of depression and the consumption of unhealthy food in first-year college students; and b) to analyze the association between depression score and food consumption frequency.

Methods: a cross-sectional study was carried out in 1,104 freshman students, 40.3% men and 59.7% women, at a public university in Mexico City. The 20-item depression scale (CES-D) and Food Frequency Questionnaire were applied to measure depressive symptoms and food consumption. Logistic regression analysis was carried out for food consumption frequency and CES-D depression score grouped in quartiles.

Results: the prevalence of depression symptoms was 18.2% in men and 27.5% in women ($p < 0.001$). A considerable proportion of the students reported poor eating habits: consumption of fried food (30.3%), sweetened drinks (49.0%) and sugary food (51.8%) 2-7 times/week; and less than half the students practiced vigorous physical activity (39.7%). In women, a higher depression score was associated with a higher frequency of consumption of fast food (OR = 2.08, p = 0.018), fried food (OR = 1.92, p = 0.01) and sugary food (OR = 2.16, p = 0.001), and a lower frequency of physical exercise (< 75 min/week; OR = 1.80, p = 0.017). In men, no association was observed between depression score and food consumption variables. An association was observed between depression and low exercise frequency (OR = 2.22, p = 0.006).

Conclusions: women vulnerable to depression may use food to cope with negative mood states. Therefore, institutional health promotion and nutritional education programs should include adequate emotion and stress management.

Key words:

Depression. Food intake. College students.

Resumen

Introducción: la depresión se asocia frecuentemente con comer en exceso y con una preferencia por ciertos alimentos, lo cual puede llevar, consecuentemente, al aumento de peso.

Objetivos: a) determinar la prevalencia de depresión y de consumo de alimentos no saludables en estudiantes universitarios de nuevo ingreso; y b) analizar la asociación entre depresión y consumo de alimentos.

Métodos: se llevó a cabo un estudio trasversal con 1.104 estudiantes de nuevo ingreso, 40,3% hombres y 59,7% mujeres, en una universidad pública de la Ciudad de México. Se aplicaron la escala de depresión de 20 items (CES-D) y el Cuestionario de Frecuencia de Consumo de Alimentos para identificar síntomas depresivos y el consumo de alimentos. Se llevó a cabo un análisis de regresión logística para estudiar la asociación entre la frecuencia de consumo de alimentos y el puntaje de depresión CES-D agrupado en cuartiles.

Resultados: la prevalencia de depresión fue del 18,2% en hombres y el 27,5% en mujeres ($p < 0,001$). Una proporción considerable de estudiantes presentó malos hábitos alimentarios: consumo de frituras (30,3%), bebidas azucaradas (49,0%) y alimentos azucarados (51,8%) 2-7 veces/semana; menos de la mitad de los estudiantes realizó ejercicio vigoroso (39,7%). En las mujeres, la depresión se asoció con una mayor frecuencia de consumo de comida rápida (OR = 2,08, p = 0,018), frituras (OR = 1,92, p = 0,01), alimentos con alto contenido de azúcar (OR = 2,16, p = 0,001) y baja frecuencia de ejercicio (< 75 min/semana; OR = 1,80, p = 0,017). En hombres, no se observó asociación entre depresión y las variables de consumo de alimentos; se detectó asociación entre depresión y baja frecuencia de ejercicio (OR = 2,22, p = 0,006).

Conclusiones: mujeres vulnerables a la depresión pueden usar los alimentos para mejorar los estados del ánimo negativos. Por lo tanto, los programas institucionales de promoción de la salud y de educación nutricional deben incluir un manejo adecuado de las emociones y el estrés.

Palabras clave:

Depresión. Consumo de alimentos. Estudiantes universitarios.

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INTRODUCTION

In recent years, a number of behavioral studies have tried to explain the relationship between nutrition and depressive disorders, taking into consideration overeating, frequency of eating, and preferences for certain foods (1-3). Depression is frequently accompanied by appetite changes, which may take the form of either decreased appetite (melancholic depression) or increased appetite (depression with atypical features) (3,4).

According to affective theories, people with depression may use food not only for nourisment, but also to cope with negative emotions; therefore, food intake can be considered as an inadequate coping mechanism in response to stress and tension that can be part of the causal link for developing overweight or obesity (5,6). Other theoretical frameworks have focused on neurobiological data such as brain-environment interaction referred to as midbrain dopamine system (3). Food represents a potent natural reward and gratification related to dopamine production that influences nutrition choice regarding higher fat and sugary foods ("comfort foods") (7). As part of a broader framework, reduced affective self-control (impulsive food choices), particularly for "comfort foods", and a desire to achieve immediate reward may be a shared cognitive mechanism contributing to the high prevalence of co-morbid mood disorders and weight gain (8). Additionally, increasingly greater food availability over recent decades may be another factor that contributes to the relationship between nutrition and depressive symptoms (3).

Studies on food cravings have mostly focused on carbohydrates consumption and, especially, mildly dysphoric mood. It is commonly assumed that carbohydrate craving is related to serotonin deficit (9); therefore, some people tend to overeat sugary food (carbohydrate beverages, pastries, sweets and chocolate, cakes and biscuits) to improve negative mood states (10,11).

Consistent with this theory, recent data suggests that there is an association between a preference for sweet taste and a higher depression score in patients with severe obesity (12). Other studies have shown that intake of "comfort foods", sweet foods, and a Western-type diet had an effect on physiological and psychological wellbeing and was associated with a higher depression score and obesity in the general population, especially in women (13-21).

Regarding college students and their eating habits, in studies performed in Germany (22), the USA (23) and the United Arab Emirates (24), it has been reported that young adults tend to overeat and consume unhealthy food in response to stressful situations. In the USA, Moorevile et al. (2) have shown that in non-treatment-seeking youths, aged 8-17 years, depressive symptoms were associated with significantly greater consumption of total energy and energy from sweet snack foods, which could lead to weight gain over time.

However, there are contradictory findings with respect to negative mood and food intake. In spite of the fact that in scientific literature food choice was considered as a deliberate strategy to modify temperament and mood, some researchers have found no consistent differences in dietary composition in comparing the periods of high and low life stress or depression. In addition, to this day it remains unclear whether the food consumption improves negative moods or whether the intake of certain foods can have an effect on human behavior (25).

In the study by Mikolajczyk et al. (26), conducted in three countries (Germany, Poland and Bulgaria) among first-year college students, a positive association has been found between food consumption (i.e., fast-food, cakes, snacks, sweets) and stress, but not between food consumption and depressive symptoms among female students; however, these patterns were not found among male students.

Additionally, Fulkerson and Nancy (27), in the study on depressive symptoms and eating behavior in adolescents, have shown that total caloric intake and snaking frequency were not significantly associated with depressed mood.

In Latin America, depression represents a growing problem among young adults. A high prevalence of depressive symptomatology has been reported among college students, from 11.8% to 30%, which can rise to 50% during stressful situations (28,29). Additionally, in Mexico overweight and obesity have a high and increasing prevalence, 36.3% in adolescents from 12 to 19 years old and 72.5% in individuals over 20 years old (30). Therefore, it is important to study eating habits and their relationship to mood disorders in young population groups. When students experience the transition to university life they are frequently exposed to stress, fatigue, and time restraints. Poor eating habits acquired at this age generally continue into adulthood and may lead to weight gain. An understanding of the influence of negative emotions on eating behavior, along with nutritional education, may be essential in preventing overweight/obesity in adulthood.

The aim of the present study was to investigate a possible association between perceived depression and unhealthy food consumption in college students in Mexico City, and to test the hypothesis that college students with a higher level of depression would have higher consumption of carbohydrate-rich and/or energy-rich food. Therefore, the objectives of this study were: a) to determine the prevalence of depression and unhealthy food consumption in first-year students, both men and women; and b) to analyze the possible association between depression score and unhealthy food consumption.

MATERIAL AND METHODS

SAMPLE

A cross-sectional study was performed at the Autonomous Metropolitan University in Mexico City with first-year students (n = 1,131), who participated in an on-line survey from a total population of 1,364 freshman students enrolled at the university in the autumn of 2016. The response rate was 82.9%.

The questionnaire section of this study was part of the online health survey for freshman students applied during the first week of classes in computer rooms.

ETHICS

The questionnaire was completed anonymously, and the participants were assured of data confidentiality. The students participated on a voluntary basis, and they acknowledged informed consent on-line. The University Review Board approved the project, where ethical aspects were considered.

INSTRUMENTS

A Spanish-language version of the 20-item depression scale created by the Center for Epidemiologic Studies (CES-D) was used to identify depressive symptoms.

This instrument has been validated and utilized in various studies with non-clinical Mexican populations (31). Twenty Likert-type items assessed the frequency of depressive symptomatology in the previous week, including depressed mood, feelings of guilt and worthlessness, psychomotor retardation, and sleep difficulties. This scale had shown a good internal consistency in Mexico's student population, with Cronbach's alpha 0.87. The maximum score of the instrument is 60, indicating severe depression, and the minimum score is 0, indicating absence of depressive symptoms. In this study, a cut-off point of 16 was used to recognize the presence of depressive symptomatology.

The assessment of food intake was performed using the Food Frequency Questionnaire, which consists of 69 items and encompasses all groups of foods (32). The carbohydrate-rich and/or energy-rich foods (unhealthy foods) were selected from this list and categorized into five groups: cereals (white bread was selected from white wheat cereals), fried food (such as potato chips, corn chips and tortilla chips, French fries, greaves and fried bananas), sweet food (cakes, cookies, pastries, sweets, chocolate, cakes, biscuits, sweet bread), and sweetened beverages (sugary soft drinks, natural and industial jucies). The fast food group (such as hamburgers, fried chicken, pizza, or sausages) was added to the questionnaire. Food intake frequency was measured as the consumption of respective food choices over a number of days of the week with the corresponding answers: almost never, once a week, two or three times per week, four or more times per week. A frequency of consumption of 2-3 times or more per week was considered as unhealthy behavior (33). Physical activity was assessed with the question "How many times per week do you exercise for at least one hour?" Less than 75 minutes of vigorous physical activity per week was considered as unhealthy behavior in line with the World Health Organization criteria and the recommendations of the American College Health Association (34,35).

Self-reported weight and height were recorded and BMI was calculated. According to the World Health Organization (WHO) criteria (36), the cutoff point for being overweight was BMI $\geq$ 25 kg/m^2; for being obese, $\geq$ 30 kg/m^2; and for being underweight, $<$ 18.5 kg/m^2.

DATA ANALYSIS

The main characteristics of the study group are presented as means and standard deviations for continuous variables and percentage for categorical variables. To study the associations between food consumption frequency and depression, 78 students with low BMI (BMI $<$ 18.5) were excluded from this analysis. A logistic regression analysis was carried out for food consumption frequency and CES-D depression score was divided by quartiles. The observations in the 1st quartile (non or few depression symptoms) were used as the reference group. The models were constructed by sex and adjusted for age and BMI. Odds ratios and 95% confidence intervals (CI) were obtained. Statistical significance was set at p-value $<$ 0.05. The statistical package STATA V12 (College Station TX. StataCorp LLC) was used for data analysis.

RESULTS

A total of 1,104 students were evaluated; 445 (40.3%) of them were men and 659 (59.7%) were women. The mean age of participants was 19.6 $\pm$ 2.4. Descriptive characteristics of the participants are presented in table I.

About 19% of the students revealed that they had prior psychological treatment (16.2% men and 21.1% women, p = 0.041). Additionally, 268 students (23.8%) presented depressive symptoms (cutoff point of 16), more women (27.5%) than men (18.2%), p $<$ 0.001.

Considering BMI, 228 participants (20.6%) were overweight and 57 (5.2%) were obese. Mean BMI was higher in men than in women (23.6 $\pm$ 3.6 and 23.0 $\pm$ 3.4, p = 0.006). Students with higher depression score demonstrated a higher BMI (β = 0.04, p = 0.002).

In terms of eating habits, college students frequently do not make healthy food choices and their diet was high in fried food (in 30.3% of the participants), soft drinks (in 49.0% of the participants) and, especially, sugary food (in 51.8%); less than a half of the students (39.7%) practice vigorous physical activity. Men consumed more fast food (p = 0.007), sweetened soft drinks (p $<$ 0.001) and white bread (p $<$ 0.001) than women; however, women exercised less than men (p $<$ 0.001). Frequency of unhealthy eating habits and physical exercise is shown in table II.

Bivariate and multivariate logistic regression models to analyze the relationship of depressive symptoms with food consumption and physical exercise are shown in table III.

In women, according to bivariate analysis, the frequent consumption of fast food (OR = 2.07, 95% CI 1.13-3.78, p = 0.018), fried food (OR = 1.85, 95% CI 1.13-3.03, p = 0.014) and sugary food (OR = 2.17, 95% CI 1.37-3.42, p $<$ 0.001), as well as exercising less than 75 min/week (OR = 1.80, 95% CI 1.11-2.91, p = 0.016) were associated with higher depression score. No association was observed between depression score and food variables in men. However, an association was found between the 4th quartile of depression

Table I. Descriptive characteristics of the study group (n = 1,104)

Characteristics	Total 1,104 (100%)	Men 445 (40.3%)	Women 659 (59.7%)	p-value
Age (mean ± SD)	19.6 (± 2.4)	20.0 (± 2.6)	19 (± 2.3)	< 0.001
Students who study and work				
Yes	314 (28.4%)	154 (34.6%)	160 (24.3%)	0.002
No	790 (71.6%)	291 (65.4%)	499 (75.7%)	
Prior psychological treatment				
Yes	211 (19.1%)	72 (16.2%)	139 (21.1%)	0.041
No	893 (80.9%)	373 (83.8%)	520 (78.9%)	
Depressive symptoms				
CES-D < 16	842 (76.2%)	364 (81.8%)	478 (72.5%)	0.001
CES-D 16-23	163 (14.8%)	55 (12.4%)	108 (16.4%)	
CES-D ≥ 24	99 (9.0%)	26 (5.8%)	73 (11.1%)	
Body mass index (mean ± SD)	23.2 (± 3.5)	23.6 (± 3.6)	23.0 (± 3.4)	0.006
Body mass index (BMI kg/m^2)				
BMI < 18.5	77 (7.0%)	33 (7.4%)	44 (6.7%)	0.002
BMI 18.5-24.9	742 (67.2%)	272 (61.1%)	470 (71.3%)	
BMI 25-29.9	228 (20.6%)	116 (26.1%)	112 (17.0%)	
BMI ≥ 30	57 (5.2%)	24 (5.4%)	33 (5.0%)	

Table II. Eating habits and physical exercice in Mexican college students

Variables	Total* 1,027 (100%)	Men 412 (40.1%)	Women 615 (59.9%)	p-value
Fast food (≥ 2 times/week)	214 (20.8%)	103 (25.0%)	111 (18.0%)	0.007
Fried food (≥ 2 times/week)	311 (30.3%)	123 (29.8%)	188 (30.6%)	0.807
Sweetened drinks (≥ 2 times/week)	503 (49.0%)	228 (55.3%)	275 (44.7%)	< 0.001
Sugary food (≥ 2 times/week)	532 (51.8%)	219 (53.2%)	313 (50.9%)	0.478
White bread (≥ 2 times/week)	396 (38.6%)	197 (47.8%)	199 (32.4%)	< 0.001
Physical exercise (≥ 75 min/week)	408 (39.7%)	208 (50.5%)	200 (32.5%)	< 0.001

**Students with BMI < 18.5 were excluded from this table*

score and low physical activity compared with the 1st quartile of depression score in men (OR = 2.22, 95% CI 1.26-3.91, p = 0.006).

In women, according to the multivariate logistic analysis, significant associations were observed between the 4th quartile of depression score and the frequent consumption of fast food (OR = 2.08, 95% CI 1.14 -3.82, p = 0.018), fried food (OR = 1.92, 95% CI 1.17-3.15, p = 0.010), sugary food (OR = 2.16, 95% CI 1.37-3.43, p < 0.001) and low frequency of exercise (OR = 1.80, 95% CI 1.11-2.91, p = 0.017) (Table III).

DISCUSSION

The present study examined the association of depression symptoms with unhealthy food consumption and exercise in first-year college students. Our findings support the hypothesis that higher depression score is related to unhealthy behavior (poor eating habits and low exercise frequency). According to the results, the prevalence of depression was high among participants, especially in women (27.5%), similar to other studies performed in student populations that have shown an onset of depression from a young age, its elevated prevalence among young adults, and a higher prevalence in females than in males (28,29).

A considerable number of the participants reported the consumption of unhealthy food more than two times per week, i.e., fast food (20.8%), fried food (30.3%), sugary drinks (49.0%), sweet foods (51.8%) and white bread (38.6%). Approximately one third of women (32.5%) and half of men (50.5%) performed rigorous physical activity at least 75 minutes per week. These data are consistent with previous findings that have shown low levels

Table III. Odd ratios from the logistic regression models for food consumption variables and depression score in female college students (n = 615)

Variable	Crude OR 95% CI	p-value	Adjusted OR*	p-value
Fast food (≥ 2 times a week)				
Depression score				
2nd quartile	1.41 (0.77-2.58)	0.273	1.42 (0.77-2.61)	0.260
3rd quartile	1.65 (0.87-3.13)	0.126	1.69 (0.89-3.21)	0.112
4th quartile	2.07 (1.13-3.78)	0.018	2.08 (1.14-3.82)	0.018
Fried food (≥ 2 times/week)				
Depression score				
2nd quartile	1.36 (0.84-2.20)	0.218	1.34 (0.82-2.17)	0.240
3rd quartile	1.36 (0.81-2.30)	0.250	1.38 (0.81-2.34)	0.232
4th quartile	1.85 (1.13-3.03)	0.014	1.92 (1.17-3.15)	0.010
Sweetened drinks (≥ 2 times/week)				
Depression score				
2nd quartile	0.71 (0.46-1.09)	0.117	0.71 (0.46-1.09)	0.117
3rd quartile	1.02 (0.64-1.63)	0.941	1.03 (0.64-1.65)	0.907
4th quartile	1.44 (0.92-2.26)	0.111	1.46 (0.93-2.29)	0.103
White bread (≥ 2 times/week)				
Depression score				
2nd quartile	1.11 (0.70-1.74)	0.669	1.11 (0.70-1.74)	0.667
3rd quartile	0.80 (0.48-1.33)	0.389	0.81 (0.48-1.35)	0.411
4th quartile	1.13 (0.70-1.81)	0.628	1.13 (0.70-1.83)	0.606
Sugary food (≥ 2 times/week)				
Depression score				
2nd quartile	1.13 (0.73-1.73)	0.592	1.12 (0.73-1.72)	0.616
3rd quartile	1.60 (1.00-2.57)	0.049	1.58 (0.98-2.53)	0.059
4th quartile	2.17 (1.37-3.42)	0.001	2.16 (1.37-3.43)	0.001
Physical exercise (less than 75 min/week)				
Depression score				
2nd quartile	1.37 (0.88-2.13)	0.169	1.37 (0.88-2.14)	0.168
3rd quartile	1.73 (1.05-2.86)	0.032	1.73 (1.05-2.87)	0.032
4th quartile	1.80 (1.11-2.91)	0.016	1.80 (1.11-2.91)	0.017

*Reference depression score 1st quartile. *OR adjusted for age and BMI.*

of physical activity and unhealthy habits such as the frequent consumption of sugary foods and a high intake of fast food in Mexican student groups (37,38). Regarding differences by sex, we found that some unhealthy eating (sweetened beverages and white bread) was significantly more frequent in men than in women, whereas women had less frequency of exercise than men had.

In women in the present study, depression symptoms were significantly associated with consumption of fast food, fried food, and sweet foods, as well as with lower exercise frequency. It is important to note that these unhealthy behaviors acquired at a young age can consequently lead to weight gain. In a systematic review and meta-analysis, it has been reported that considerable weight and adiposity gains occur throughout college life, with a mean change in weight of 1.55 kg and 1.17% in body fat mainly due to decreased physical activity and food consumption away from home (39). Obesity, unhealthy dietary practices, and physical inactivity are risk factors for the development of metabolic syndrome from early adulthood (40). In the follow-up study, performed in the USA among young adults, it has been reported that the risk of metabolic syndrome increases on average 23% per 4.5 kg of weight gained, whereas regular physical activity over time *versus* low activity was considered to be a protective factor (41).

Our data were similar to the results of previous studies performed in the USA, UK, Australia, and China that have shown an

association between a higher depression score and intake of a Western-type diet such as processed food, fried foods, refined grains, and sugary products in the general population (13-16), as well as with obesity (17), particularly in women (18-21). According to Dubé et al. (13), intake of "comfort foods" was associated with physiological and psychological wellbeing in women: high-calorie foods (high sugar and fat content) were more efficient in alleviating negative affects whereas low-calorie foods were more efficient in increasing positive emotions. In the study by Kampov-Polevoy et al. (14), it has been shown that hedonic response to sweet taste is associated with elevated sensitivity to mood altering effects and impaired control of eating sweet foods. Consistent with our data, Jeffery et al. (15) have found that in middle-aged U.S. women, depressive symptoms were positively associated with the consumption of sweet foods and negatively associated with the consumption of non-sweet foods.

In the present study, a significant association was found between depressive symptoms and BMI. This finding corroborates the hypothesis that people with higher depression score frequently use "comfort foods" to make them feel better. It is worth mentioning that a growing number of studies have shown a reciprocal relationship between depression and higher BMI (42); therefore, it is important to take into consideration the influence of negative mood on eating behavior in overweight prevention and treatment strategies. "Comfort foods" have become increasingly available in an "obesogenic" environment over the last half-century, and individuals with depression symptoms can seek out "comfort food" in order to improve their psychological wellbeing (3). A rational coping style (i.e., planning to solve a problem or thinking of an alternative way to solve it), is generally more effective than an emotional eating style, and these skills must be learned from an early age. The transition to university life is a stressful experience for many students; therefore, time management, stress and problem coping skills should be taught for those susceptible to depression.

However, we did not find any association between sweetened drink consumption and depression score, nor has an association between unhealthy eating behavior and depression score been found in men. The above suggests that these eating behaviors are more typical for women, and men may have other ways of managing their negative emotions and stressful situations (13-21).

Additionally, non-consistent results reported in this domain may be explained by the fact that depressive symptoms or emotional stress can lead to either increased or decreased appetite. Effects of emotions on eating have been studied extensively. Surveys have shown that most people experience changes of appetite and eating behaviors in response to emotional stress: 11% to 55% eat more, while 32% to 70% eat less (43). Therefore, due to individual variability it remains difficult to predict how negative emotions may affects eating habits in a given person.

However, due to the high and increasing prevalence of overweight/obesity worldwide and the fact that individuals with elevated depressive symptoms may be prone to overeating and exibit a preference for high-energy foods, an integral approach aimed at stress and emotion management and nutrition education may contribute to the development of healthy eating behavior (44).

Most countries have experienced nutrition transition, which is characterized by marked socio-economic transformation over recent decades. Such a transition has led to profound changes in food consumption and lifestyle patterns (45). The intake of fast food and sugar-sweetened beverages has increased drastically and the intake of milk, fruit, vegetables, and high fiber foods has decreased. Additionally, the level of physical activity has decreased and sedentary behavior has risen. This may contribute to the incidence of obesity and associated chronic diseases (46,47).

Finally, it is important to underline that information on the dietary and lifestyle patterns of young people is needed to prevent weight gain and to promote healthy food habits among the young population.

Among the limitations of the study, it should be noted that it was carried out with a specific non-clinical population (freshman students with a mean age of 19 years) and it is difficult to extrapolate the results to other population groups.

The self-reported questionnaire applied in the study for assessing depression only identifies symptoms or vulnerability to depression and does not diagnose a clinical condition. Additionally, a self-reported questionnaire may overestimate or underestimate food consumption frequency; weight and height were also self-reported. Despite this limitation, the study was carried out on a large sample of the student population, and associations were found between depression score and variables of food consumption in women, as well as between depression score and BMI. Further research with more precise techniques is required to assess the consistency of this data. Finally, longitudinal studies are needed to evaluate the long-term effect of depression on food consumption and body weight.

CONCLUSIONS

Freshman students presented a high prevalence of depression symptoms, and their diet was high in fried food, sweetened drinks and sugary food. Consumption of fast food, fried food and sweet food, as well as low exercise frequency were associated with higher depression score.

Individuals vulnerable to depression may use food for psychological comfort; therefore, an integral approach should be included in nutrition education. The efficiency of institutional programs, promotion of physical activities, and thematic workshops aimed at stress and emotion management may contribute to the development of healthy eating behaviors.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Serum zinc and copper concentrations and ratios in cirrhotic patients: correlation with severity index

Concentraciones séricas de zinc, cobre y sus cocientes correspondientes en pacientes cirróticos: correlación con el índice de severidad

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Abstract

Introduction: zinc (Zn) and copper (Cu) are essential elements that play an important role in the whole-body metabolism and seems to have a role in the pathogenesis of the liver cirrhosis (LC).

Objective: the aim of this study is to evaluate the influence on serum Zn and Cu concentrations and Cu/Zn ratios of different factors like cirrhosis, severity index, age, sex, death, and disease complications.

Methods: ninety-three patients with LC were included. The severity index was measured by the Child-Pugh index (CPI).

Results: mean serum Cu concentration and Cu/Zn ratio were significantly higher in patients than in healthy controls ($p \leq 0.001$). Serum Zn concentrations were reduced with higher cirrhosis severity (specifically low *vs* medium severity CPI, $p < 0.05$). Mean serum Cu concentration was significantly higher in the oldest (> 50 years) *versus* youngest (< 30 years) age group. Serum Zn concentrations were lower and Cu/Zn ratios were higher ($p < 0.05$) in patients that died. Among complications, significantly higher serum Zn concentrations were found in cirrhotic patients with ascites than in those with bacteremia-sepsis.

Conclusions: levels of Zn, Cu and Cu/Zn ratio are affected by the presence of hepatic cirrhosis. Serum Zn concentrations are lower with higher severity of cirrhosis, while those for Cu are increased in cirrhotic patients. We can observe that the presence of elevated Cu/Zn ratios in these patients might be useful in the evaluation of suspected liver cirrhosis.

Key words:

Serum Zn and Cu levels. Cu/Zn ratios. Severity index score. Liver cirrhosis.

Resumen

Introducción: el zinc (Zn) y el cobre (Cu) son elementos esenciales ya que juegan un papel fundamental en el metabolismo en general y parecen tener implicación en la patogénesis de la cirrosis hepática (CH).

Objetivos: el objetivo del presente estudio es evaluar la influencia sobre los niveles séricos de Zn y Cu, y sobre los cocientes entre los niveles de Cu y Zn de diferentes factores como la cirrosis, el índice de severidad, la edad, el sexo, la mortalidad y las complicaciones de la enfermedad.

Metodología: noventa y tres pacientes con CH fueron incluidos en el estudio y el grado de severidad se midió utilizando el índice Child-Pugh (ICP).

Resultados: las concentraciones séricas de Cu y los cocientes entre los niveles de Cu y Zn se encontraron significativamente aumentados en los pacientes con respecto a los controles sanos ($p \leq 0.001$). A mayor grado de severidad cirrótica, se obtuvieron valores medios de Zn significativamente disminuidos (concretamente en los enfermos con ICP bajo frente a los que tenían un ICP medio, $p < 0.05$). La media de las concentraciones séricas de Cu fue significativamente superior en el grupo de sujetos de mayor edad (> 50 años) con respecto al grupo más joven (< 30 años). En aquellos pacientes que habían sufrido un deceso, las concentraciones séricas de Zn estaban significativamente disminuidas, mientras que los cocientes entre los niveles de Cu y Zn se encontraron elevadas ($p < 0.05$). En cuanto a las complicaciones de la enfermedad, obtuvimos valores séricos significativamente elevados de Zn en aquellos pacientes cirróticos que padecían ascitis respecto a los que presentaban bacteriemia-sepsis.

Conclusiones: los valores de Zn, Cu y los cocientes entre los niveles de Cu y Zn se encuentran afectados en la enfermedad cirrótica. Las concentraciones séricas de Zn son bajas cuando existe un mayor grado de severidad de la cirrosis hepática, mientras que los valores de Cu apararen incrementados en los pacientes con esta enfermedad. Podemos observar que la presencia de valores elevados de los cocientes entre los niveles de Cu y Zn podría ser de utilidad en la evaluación de la posible presencia de la enfermedad.

Palabras clave:

Niveles séricos de Zn y Cu. Cocientes entre los niveles de Cu y Zn. Índice de severidad. Cirrosis hepática.

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INTRODUCTION

Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury, and it can lead to portal hypertension and end-stage liver disease. Although the etiology of cirrhosis is variable, its main causes in developed countries are excessive alcohol consumption and hepatitis C (1). Liver disease is also related to numerous nutritional vitamin and mineral deficiencies (1-6) and to the impaired metabolism of carbohydrates, proteins, and lipids. Among minerals, zinc (Zn) and copper (Cu) are essential micronutrients whose role is widely studied for their implication in liver cirrhosis (7).

The liver is involved in the homeostatic regulation of Zn and its levels are decreased in liver cirrhosis since some functions like urinary excretion are altered (8). Some authors have suggested that Zn depletion is a cause of hepatic fibrosis (9). Immune function depression, an increased infection rate, diarrhea, alopecia, and mental disorders are symptoms frequently observed in patients with liver cirrhosis and have been attributed by some authors to Zn deficiency; this also contributes on the predisposition and perpetuation of liver damage (3,4,6,10-16). It is seems to have an important role in the appearance of liver fibrosis because Zn is the most effective inhibitor for prolyl hydroxylase, an enzyme which plays a key role in collagen synthesis (11). The antioxidant action of Zn may be related to the ability of metalloproteins to remove the excess collagen produced by hepatic stellate cells (11).

The impaired liver function as a result of liver damage in liver cirrhosis leads to lower ability to detoxify substances. The liver regulates homeostasis and Cu distribution to overall system, so prolonged exposure to Cu toxicity contributes to liver cirrhosis, damaging renal tubules and other organs (17). Others studies have found that the Cu reagent generated in a specific process participated directly or indirectly in liver damage produced by stimulation of Kupffer cells, which contributes in the progression of liver fibrosis (3,18,19). In addition, Cu is a cofactor of lysyl oxidase, which participates in collagen formation, while increased concentrations of Cu and its accumulation in the liver have been reported to promote also hepatic fibrosis (3,18).

Liver cirrhosis involves complications such as ascites, hepatorenal syndrome or hepatocellular carcinoma (20), and higher serum Cu/Zn ratios have been observed in patients undergoing hemodialysis (21,22) and in those with hepatocellular carcinoma (23). This ratio could be considered as an interesting tool used in the evaluation of liver cirrhosis in elderly people because Malavolta et al. (24) have described the Cu/Zn ratio as an important inflammatory/nutritional biomarker of all-cause mortality and it also has been correlated with reductions in bone density, physical performance, and overall health status in this group (25). The clinical relevance of the Cu/Zn ratio is considered greater than that of the concentration of each element (26).

The hypothesis of the study is that serum Zn and Cu concentrations as well Cu/Zn ratios impair in cirrhosis, and this impairment would enhance the disease severity measured by the Child-Pugh index score. Few data appear to be available on the relationship between liver disease severity and serum Zn or Cu concentrations or Cu/Zn ratios. Other objectives are to determine serum concentrations of these elements in cirrhotic patients and healthy controls, using flame atomic absorption spectrometry, and to examine the influence on these values of age, sex, death, and its complications.

MATERIALS AND METHODS

The design of the study was previously described in detail elsewhere (27). The initial study population comprised patients with liver cirrhosis under follow-up in the Department of Digestive Diseases of our reference hospital (27). The diagnosis of cirrhosis was based on clinical and ultrasound criteria. Healthy controls were enrolled from among blood donors in the same geographic area. All subjects were fully informed of the aim of the study, and an informed consent was obtained from each one before blood was drawn (27).

This cross-sectional study was conducted in patients with liver cirrhosis in the Department of Digestive Diseases of the Hospital Universitario Virgen de las Nieves in Granada (Southern Spain) and in healthy controls. Exclusion criteria for study participation were: the presence or history of non-insulin-dependent diabetes mellitus, wide bowel resection, gastrectomy, inflammatory bowel disease, cancer, chronic renal failure, active alcoholism, corticoid therapy, or hypercortisolism, the receipt of drugs or dietary supplements known to have antioxidant capacity or interfere with muscle function, and the failure to sign informed consent. The study, including the release of human serum samples, was approved by the Ethics Committee of the hospital and was conducted in accordance with the Declaration of Helsinki. The final study sample comprised 92 patients with liver cirrhosis (38 women and 54 men, with mean ± standard deviation [SD] age of 41.4 ± 16.5 y) and 30 healthy adults from among blood donors at the hospital (13 women and 17 men, with mean age of 40.7 ± 18.8 y).

The patients were divided into two groups according to their Child-Pugh index (CPI) score: 5-6 points = CPI-A (low severity, well-balanced; n = 45); 7-9 points = CPI-B (medium severity, significant functional impairment; n = 47); or 10-15 points = CPI-C (high severity; n = 1; therefore, this patient has been excluded, and this group has not been considered) (28). The CPI score is the sum of points assigned by the physician for degree of ascites, concentrations of plasma bilirubin and albumin, prothrombin time, and degree of encephalopathy. The original CPI was designed to stratify surgical risk in patients with blood imbalance (28) and was subsequently modified (29) by replacing the nutritional status parameter with prothrombin time (30). The present patients were also divided into three age groups (< 30, 31-50, and > 50 y). The present study patients were also divided into eight groups in relation to disease complications: four in the group of complications in the past (ascites, bacteremia-sepsis, varicose vein and encephalopathy), which included patients whose complications were diagnosed and medically followed by the physicians of the Department of Digestive Diseases of the Hospital Universitario Virgen de las Nieves in Granada along one year; and the same four

complications in the group with complications at admission in the hospital, which included patients with *de novo* complications that were diagnosed along the same year when they went in a critical status to the Urgency Service of the hospital.

Blood samples were drawn after overnight fasting from the antecubital vein of each participant while seated. Samples were left to spontaneously coagulate and were then centrifuged at 3,000 g to obtain serum separated by gelose. Aliquots (1 ml) of serum were frozen at -25 °C for transportation and storage in the laboratory of the Department of Nutrition and Food Sciences (University of Granada) until their analysis (31).

Shortly after their delivery, samples were thawed and homogenized for Zn and Cu determination, diluting 200 µl serum in Milli-Q® water (1:5) using Eppendorf Tubes® and following a previously optimized procedure (31).

All chemicals were analytical reagent grade or higher purity. Bidistilled deionized water with a specific resistivity of 18 MΩ cm^{-1} was obtained using the Milli-Q® system (Millipore, Milford, MA). Total Zn and Cu in samples were measured by flame atomic absorption spectrometry using a Perkin-Elmer® Model 1100B spectrometer (Perkin-Elmer, Norwalk, CT, USA). The absorbance was correlated with Zn and Cu concentrations by the linear calibration technique. The accuracy and precision of the method were tested on 0148 Serum metal control A level 1 reference material (Kaulson Laboratories Inc., West Caldwel, NJ, USA) and Certified Reference Human Serum Material (Chengdu Shuyang Pharmaceutical Factory, Chengdu, China), obtaining similar ($p > 0.05$) mean Zn and Cu concentrations (0.789 ± 0.042 and 0.916 ± 0.016 mg/l, respectively) to the certified values (0.800 ± 0.060 and 0.900 ± 0.075 mg/l, respectively).

SPSS version 17.0 (IBM, Chicago, IL) was used for data analyses. The Kolmogorov-Smirnov test was applied to examine the normal distribution of variables and the Levene's test, to study the homogeneity of variances. Cu, Zn, and Cu/Zn ratio values were expressed as arithmetic means ± SD and were compared using the Student's t-test for parametric variables and the Kruskal-Wallis test for nonparametric variables. One-way analysis of variance was conducted to determine the influence on serum Zn and Cu concentrations and Cu/Zn ratios of CPI score, age, sex, death and disease complications. $p < 0.05$ was considered as statistically significant in all tests.

RESULTS

Mean serum Zn concentrations did not significantly differ between cirrhotic patients and controls ($p = 0.196$), while mean serum Cu concentrations were significantly higher in cirrhotic patients ($p = 0.001$) than in controls (1.263 ± 0.3250 *vs* 1.078 ± 0.097 ppm, respectively, $p = 0.003$), as were mean Cu/Zn ratios (Table I).

Mean serum Zn concentration was significantly higher in the CPI-A group than in the CPI-B group ($p = 0.025$, Kruskall-Wallis test) (Table II), whereas these groups did not significantly differ in serum Cu concentration or Cu/Zn ratio ($p > 0.05$).

The mean serum Cu concentration was significantly higher in the oldest age group (> 50 y; 1.360 ± 0.320 mg/l) than in the youngest (< 30 y; 1.130 ± 0.220 mg/l; $p = 0.043$). No significant differences in serum Zn concentration or Cu/Zn ratio were found among the three age groups of cirrhotic patients ($p > 0.05$) (Table III).

No significant difference was found between female and male cirrhotic patients in mean serum Zn or Cu concentrations or Cu/Zn ratios ($p > 0.05$; Student's-t test), although there was a non-significant tendency towards a difference between the sexes in mean Cu concentration and Cu/Zn ratio ($p = 0.074$ and $p = 0.070$, respectively; Student's t-test).

The mean serum Zn concentration was significantly lower ($p = 0.02$) and Cu/Zn ratio was significantly higher ($p = 0.03$) in non-surviving patients than in survivors during the one-year sampling period, whereas they did not significantly differ ($p > 0.05$) in mean serum Cu concentration (Table III).

Table I. Mean serum Zn and Cu concentrations and Cu/Zn ratios in patients with cirrhosis versus healthy controls

Groups	Mean Zn ± SD, mg/l	Mean Cu ± SD, mg/l	Mean Cu/Zn ratios ± SD
Cirrhosis patients	0.879 ± 0.199	1.261 ± 0.326*	1.513 ± 0.544†
Control group	0.847 ± 0.125	1.078 ± 0.096*	1.299 ± 0.217†

**†The same superscript for values in the same column indicates a significant difference ($p < 0.05$).*

Table II. Mean serum Zn and Cu concentrations and Cu/Zn ratios in patients with cirrhosis by disease severity index measured by the Child-Pugh index (CPI) score

Child-Pugh group	Mean Zn ± SD, mg/l	Mean Cu ± SD, mg/l	Mean Cu/Zn ratios ± SD
CPI A	0.928 ± 0.230*	1.256 ± 0.302	1.448 ± 0.563
CPI B	0.828 ± 0.171*	1.262 ± 0.354	1.599 ± 0.563

**The same superscript for values in the same column indicates a significant difference ($p < 0.05$).*

Table III. Mean serum Zn and Cu concentrations and Cu/Zn ratios in patients with cirrhosis as a function of death during the sampling period

Element	n	Death from cirrhosis	Mean ± SD, mg/l
Zn	43	Yes	0.823 ± 0.171*
	48	No	0.955 ± 0.205*
Cu	43	Yes	1.275 ± 0.355
	48	No	1.274 ± 0.300
Cu/Zn ratio	43	Yes	1.628 ± 0.582†
	48	No	1.390 ± 0.436†

**,†The same superscript for values in the same column indicates a significant difference ($p < 0.05$).*

No differences were observed among the groups of complications recorded in patients ($p = 0.067$) (Table IV). When the two-tailed statistical test was applied, mean serum Zn values were significantly higher in patients with a previous history of ascites than in those with a history or presence at hospital admission of bacteremia-sepsis ($p = 0.005$ and $p = 0.008$, respectively) and in those with ascites at admission ($p = 0.01$). Higher mean Zn and Cu concentrations were observed in patients with a history of disease complications (considered together) than in those with their presence at hospital admission ($p = 0.023$ and $p = 0.022$, respectively) (Table V).

DISCUSSION

In the present study, serum Cu concentrations and Cu/Zn ratios were higher in cirrhotic patients, while serum Zn concentrations were lower with greater severity of the disease. The mean serum Zn concentration was not significantly different between cirrhotic patients and controls (Table I), in disagreement with previous reports of significantly reduced serum Zn concentrations in patients with cirrhosis (3,32,33) and alcohol-related or other liver diseases (3,32). These findings of Zn deficiency may be explained by the frequent administration of diuretics to cirrhotic patients and their poor intestinal absorption of Zn (4,13). Other proposed explanations include the loss of Zn bound to albumin in the blood in liver disease or damage to the intestinal mucosa (11). Low serum Zn concentrations have also been related to protein reluctance or losses due to diarrhea and/or increased urinary excretion (3). Nangliya et al. (4) observed a significant decrease in serum Zn concentrations with more severe liver disease. Accordingly, our discrepant results may be attributable to the early stage of cirrhosis in the majority of our patients.

The mean serum Cu concentration was significantly higher in the patients than in healthy controls, in agreement with previous reports in patients with cirrhosis (3,4,6,32), chronic hepatitis C (34), and chronic hepatocellular carcinoma (2,23), among other liver diseases. Elevated Cu values have also been associated with nutritional abnormalities, oxidative stress, inflammation and immune dysfunction (21). It has been reported that nutritional disorders can impair biliary Cu excretion and thereby increase serum and hepatic concentrations of free Cu, which may produce

Table IV. Mean serum Zn and Cu concentrations and Cu/Zn ratios in patients with cirrhosis as a function of disease complications

Disease complication	Mean Zn ± SD, mg/l		Mean Cu ± SD, mg/l		Mean Cu/Zn ratios ± SD	
	In the past*	At admission	In the past*	At admission	In the past*	At admission
Ascites	1.020 ± 0.182‡,§,I	0.796 ± 0.170§	1.351 ± 0.318	1.086 ± 0.311	1.359 ± 0.411	1.472 ± 0.677
Bacteriemia-sepsis	0.843 ± 0.096‡	0.749 ± 0.171I	1.435 ± 0.290	1.181 ± 0.108	1.730 ± 0.446	1.634 ± 0.312
Varicose vein	0.881 ± 0.169	0.775 ± 0.225	1.218 ± 0.328	1.244 ± 0.251	1.406 ± 0.474	1.738 ± 0.660
Encephalopathy	0.910 ± 0.168	0.796 ± 0.170	1.452 ± 0.476	1.259 ± 0.346	1.681 ± 0.678	1.347 ± 0.413

**In the past (in patient with complications previously diagnosed during the routine checking by the hospital physician). +At hospital admission (in patients with de novo complications who would need hospital admission). ‡,§,IThe same superscript for values in the same column/row indicates a significant difference ($p < 0.05$).*

Table V. Mean serum Zn and Cu concentrations and Cu/Zn ratios in patients with cirrhosis as a function of a previous history or presence at admission of disease complications

Disease complications (considered together)	Mean Zn ± SD, mg/l	Mean Cu ± SD, mg/l	Mean Cu/Zn ratios ± SD
Previous history (during the last year)	0.912 ± 0.165*	1.365 ± 0.358†	1.549 ± 0.520
At hospital admission (in patients with de novo complications)	0.818 ± 0.188*	1.886 ± 0.190†	1.545 ± 0.546

**,†The same superscript for values in the same column indicates a significant difference ($p < 0.05$).*

injury from the resulting rise in oxidative stress (21). Excess Cu in the human organism has also been implicated in cell damage and the development of hepatocellular carcinoma (2).

The mean Cu/Zn ratio was significantly higher in cirrhotic patients than in controls, consistent with previous reports in patients with cirrhosis (2,21) or a digestive system, breast, lung, or hematological cancer, besides liver malignancies (23). The Cu/Zn ratio has been proposed as a useful biomarker of cirrhosis complications and liver disorders, among other diseases (22,25).

A significant reduction in mean serum Zn concentration was found with greater cirrhosis severity as measured with the CPI ($p < 0.05$), in agreement with previous reports (35). It has been previously reported that Zn deficiency is highly prevalent in cirrhotic patients with CPI-B or -C and is correlated with the severity of their disease (4). Zn deficiency may also play a critical role in the development of heart failure, and dietary supplementation and/or medical prescription of Zn for cirrhotic patients should not be ruled out (36). The lack of association between mean serum Cu concentrations and severity index is consistent with previously published results and may be attributable to the role of Cu in redox process (3,4). Our finding that Cu/Zn ratios were not related to cirrhosis severity is in disagreement with the report by Elzeiny et al. (37), possibly because only one patient in our series had the highest severity level. An elevated Cu/Zn ratio has also been associated with higher cardiovascular risk (26).

The age of the patients of this sample did not influence serum Zn concentrations or Cu/Zn ratios, as was previously observed by some authors (14), while others found significantly higher serum Zn concentrations in patients over *versus* under 60 years old (38,39). Another study in elderly people (39) reported Zn deficiency as well as cell-mediated immune dysfunction. In our patients, serum Cu concentrations were higher in patients over 50 than in those under 30 years of age. It has been reported that Cu overload may worsen cirrhotic disease and may impair other extrahepatic tissues, increasing the mortality risk in older patients (3,38).

Serum mean Zn concentrations did not differ between the male and female patients, as previously observed (3,38), but there was a tendency to slightly higher serum Cu and Cu/Zn values in the females. Grungreiff et al. (34) found higher serum Cu concentrations in female *versus* male chronic hepatitis C patients. Some authors have proposed that cirrhosis and the male sex may be involved in the progression of hepatocellular carcinoma (1).

Mean serum Zn concentrations were lower and Cu/Zn ratios were higher in patients who died from their disease during the study period. Zn deficiency could exacerbate liver damage by impairing antioxidant defense mechanisms (12), increasing the mortality risk, but more analysis must be done. Lin et al. (2) also reported elevated mean Cu/Zn ratios in patients with hepatic cirrhosis as well as in those with hepatoma, associating their increase with a greater risk of death from cardiovascular disease (24).

Serum Zn concentrations were higher in patients with than without ascites, a common symptom in patients with decompensated cirrhosis (1). Ascites have been found to produce muscle loss and a catabolic state in cirrhotic patients, leading to Zn losses (16). The administration of branched-chain amino was reported to reduce ascites in patients with liver cirrhosis (40).

In our opinion the main weakness of this study is the number of studied cirrhotic patients; in fact, for the CPI C group only one patient was considered and therefore, corresponding data were not included. Although serum Cu levels and Cu/Zn ratios were not influenced by the severity index of the liver disease, future studies should be performed with a higher and more balanced number of cirrhotic patients for the CPI A, B and C groups to elucidate definitively the hypothesis of this study. Inversely, its main strength is that, with the results obtained, we could expect that the Cu/Zn ratios could be useful as a predictive biomarker for cirrhosis disease status together with other complementary analysis.

Further research is warranted to determine whether the imbalance in antioxidant minerals observed in cirrhotic patients (increased serum Cu concentrations and Cu/Zn ratios and reduced serum Se concentrations [27]) may be directly related to the development of cardiovascular and renal disorders among others, as well as analysis related with oxidative stress or inflammation.

CONCLUSION

Serum Cu concentrations and Cu/Zn ratios are increased in cirrhosis. Serum Zn concentrations are significantly higher in the CPI-A group than in the CPI-B group. Serum Zn concentrations were lower and Cu/Zn ratios were higher in cirrhotic patients who died from the disease during the sampling period. These trace elements are essential during the progression of the disease so it is important control them. In addition, to the best of our knowledge, with the results obtained we could expect that the Cu/Zn ratios could be useful as a predictive biomarker for cirrhosis disease status together with other complementary analysis.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Score of *"eat-ability"* as a predictor of malnutrition in patients with gastrointestinal tract cancer: a pilot study

Evaluación de la "capacidad alimentaria" como predictor de desnutrición en pacientes con cáncer del tracto gastrointestinal: un estudio piloto

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Abstract

Introduction: decreased food intake, loss of appetite, and dysphagia are relevant symptoms in patients with gastrointestinal tract (GIT) cancer. However, these symptoms have been isolated or indirectly assessed when comprising quality of life questionnaires or risk assessment tools.

Objective: to determine whether a combined assessment of dysphagia, appetite and food intake may be used as a parameter of *eat-ability* (food capacity) in patients with GIT cancer.

Methods: a cross-sectional pilot study on 41 patients with GIT cancer were evaluated using a score for *"eat-ability"* (SEA) as compared to the Patient Generated Subjective Global Assessment (PG-SGA), anthropometry and laboratory profile.

Results: eleven (27%) patients had full *eat-ability* (SEA 0), three (7%) had moderate (SEA 1) and 27 (66%) had poor (SEA ≥ 2) *eat-ability*, which were significantly different, between upper and lower GIT tumors ($p \leq 0.05$). By ROC curves, SEA 1 and ≥ 2 showed an 80% for both sensibility (95% CI: 0.48-0.95) and specificity (95% CI: 0.63-0.91) to PG-SGA (A and B), with an area under curve (AUC) of 0.79 (95% CI: 0.64-0.95) ($p = 0.006$). Patients with SEA ≥ 2 had a significant weight loss within three ($p = 0.001$) and six months ($p < 0.001$) when compared to patients with SEA 0 and 1. Mortality was also significantly higher ($p = 0.01$) among patients with critical food capacity by SEA (77%) in severely malnourished patients by PG-SGA (84%).

Conclusion: by combining food intake, dysphagia and appetite assessment altogether, a reliable score clearly demonstrated compromised eating capacity affecting nutritional status of patients with GIT tumors at a higher risk for death.

Key words:

Dysphagia. Food intake. Appetite. Malnourished. Gastrointestinal cancer. Weight loss.

Resumen

Introducción: la disminución de la ingesta alimentaria, la pérdida de apetito y la disfagia son síntomas impactantes en pacientes con cáncer del tracto gastrointestinal (TGI). Sin embargo, estos síntomas se han estudiado individualmente o indirectamente al formar parte de cuestionarios de calidad de vida o herramientas de riesgo nutricional.

Objetivo: determinar la significancia del análisis combinado de disfagia, apetito e ingesta alimentaria como parámetros de "capacidad" alimentaria en pacientes con cáncer del TGI por medio de una nueva escala.

Métodos: estudio piloto transversal en el cual fueron evaluados 41 pacientes con cáncer del TGI utilizando la valoración de "*eat-ability"* (SEA), que se comparó con la valoración global subjetiva generada por el paciente (VGS-GP), la antropometría y métodos de laboratorio.

Resultados: once (27%) pacientes tenían capacidad alimentaria completa (SEA = 0), tres (7%) presentaban capacidad moderada (SEA = 1) y 27 (66%), severa (SEA ≥ 2). Se observó una diferencia significativa entre la capacidad alimentaria, cuando se comparó el TGI superior con el inferior ($p = 0,05$). Las SEA con valoración 1 y ≥ 2 fueron analizadas mediante la curva ROC para obtener un poder discriminatorio con respecto a VGS-GP (B y C), respectivamente. La sensibilidad y especificidad fue del 80% para ambos, con IC 95%: 0,48-0,95 e IC 95%: 0,63-0,91 respectivamente y área bajo la curva (AUC) de 0,79 (IC 95%: 0,64-0,95) ($p = 0,006$). Los pacientes con SEA ≥ 2 presentaron un mayor porcentaje de pérdida ponderal a los tres ($p = 0,001$) y seis meses ($p < 0,001$) en comparación con los pacientes con SEA 0 y 1. La mortalidad también fue significativamente mayor ($p = 0,01$) entre los pacientes con SEA ≥ 2 (77%) y los pacientes gravemente desnutridos por VGS-GP (84%).

Conclusión: al combinar la ingesta alimentaria, la disfagia y la evaluación del apetito, se demostró claramente una capacidad alimentaria comprometida que afecta al estado nutricional de los pacientes con tumores en TGI con un mayor riesgo de muerte.

Palabras clave:

Disfagia. Ingesta alimentaria. Apetito. Desnutrición. Cáncer gastrointestinal. Pérdida de peso.

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INTRODUCTION

Decreased food intake is a symptom frequently observed in patients with cancer (1). This may be due to a series of metabolic changes originated by or as a consequence of the tumor (2-6), which induces inflammatory response and changes in hypothalamic function directly affecting appetite (7), thus modifying food intake. In addition, antitumor treatment with chemotherapy and/or radiotherapy can induce a series of side effects, further decreasing food intake (1).

In patients with esophageal or esophagogastric junction (OGJ) cancers, food intake impairment is often caused by dysphagia, which is the main symptom related to tumor location (8). Dysphagia is also related to a number of factors such as tumor resection and addition of chemoradiotherapy treatment (9). All these changes can cause relevant weight loss, leading to malnutrition and cancer cachexia as well (6), which may be quite remarkable when tumors affect the gastrointestinal tract (GIT) (10,11).

Between 48% and 80% of patients with GIT cancer report weight loss at the time of diagnosis (11). Unintentional loss of 10% or more independently of time has been considered as an indicator of malnutrition (12).

In addition, malnourished patients presented high risk to develop postoperative complications such as increased infection rate (13) and longer hospital staying, with higher morbidity and mortality (14,15). Earlier detection of the risk of malnutrition, as well as of the main symptoms that may interfere with food intake, allows nutritional interventions to be performed (1) to avoid such complications and to reduce cachexia effects.

Inflammatory markers such as C-reactive protein (CRP) are used to quantify systemic inflammation (1,16,17). Similarly, some scores based on systemic inflammation may be useful in identifying those patients who are at risk for developing cachexia as well as to be used as prognostic and predictive factors of treatment response (2), such as the modified Glasgow Prognostic Score (mGPS) (18) and the neutrophil/lymphocyte ratio (NLR) (2).

There is currently no consensus on the best method for assessing nutritional status in cancer patients (19). Thus, distinct parameters such as anthropometric measurements of weight, percentage of weight loss, body mass index (BMI), laboratory assessment methods such as serum albumin (1), along with tools such as nutrition risk screening (NRS-2002) (20), subjective global assessment (SGA) (21) and patient generated subjective global assessment (PG-SGA) (22) have been often used for this purpose.

Anorexia, defined as loss of appetite (7), can be assessed by numerous specific tools, such as the Functional Assessment of Anorexia/Cachexia Therapy-European Society for Clinical and Metabolism score (FAACT-ESPEN score) or the use of visual analogue scales (VAS) (23).

The VAS is a tool used to translate a subjective sensation into an objective quantitative measure. The VAS for appetite is a 100-mm line in which ends are anchored to "hunger" and "no hunger" (23) or by the phrases "I have no appetite at all" and "my appetite has been very good" (7). These tools are presented to patients who should self-assess their appetite.

The severity of dysphagia is commonly measured in degrees and the scale developed by Atkinson's et al. is the most widely used in patients with esophageal tumors. This scale is divided into five levels based on the possibility of swallowing different textures of food ranging from ability to eat normal foods to complete inability to swallow (24). The internationally well-known guidelines of the National Comprehensive Cancer Network (25) for esophageal and OGJ also recommends to evaluate dysphagia by a methodology similar to that of Atkinson's et al.

Changes in dietary intake, loss of appetite and dysphagia compromise the nutritional status of cancer patients (1). Although these symptoms are relevant to the magnitude of problems affecting GIT cancer, they have been isolated or indirectly assessed when comprising quality of life questionnaires, risk assessment tools or nutritional status.

To our knowledge, there are no other tools that have been particularly developed to assess "food capacity" *(eat-ability)* as a whole in cancer patients. In addition, many tools used abroad that evaluate appetite or anorexia have not been validated for the Brazilian population and therefore, it may not be possible to compare efficiency and effectiveness of in-country use of these tools.

A more comprehensive way of determining an individual's "eat-ability", i. e., the ability to eat in the broadest sense, remains to be established, considering that ingesting, swallowing and having appetite, if assessed altogether, may provide a tool for determining "food capacity" or "food performance". Therefore, by developing an instrument that allows assessment of "food capacity" particularly weighing each ability itself in patients with cancer of the GIT would be of help as an ancillary parameter in the assessment of the nutritional status, being at the same time, simple, costless and reliable to minor changes as well as feasible to be used by any trained healthcare professional.

MATERIAL AND METHODS

This was a cross-sectional, prospective, nested study to a broader research project aiming to determine different methods of nutritional assessment in outpatients with tumors of the upper gastrointestinal tract, approved by the Ethics Committee of the Hospital de Clínicas de Porto Alegre (HCPA) University Attached Hospital, Southern Brazil (IRB #13-0520), according to the criteria set by the Declaration of Helsinki. This study is based on a convenience sample selected in a consecutive manner and is part of the research line of the Southern Surgical Oncology Research Group (SSORG).

In this study, 41 patients (21 males, 20 females), over 40 years, with a mean age of 59 years, with malignant neoplasms of the upper (esophagus, stomach, pancreas, gallbladder and liver) or lower GIT (colon, rectum), treated at the Department of Surgery, HCPA University Attached Hospital, from October 2013 to June 2016, who consented in writing to participate in the study were included.

Patients with comorbidities such as severe renal failure, liver dysfunction and active infection were excluded. Demographics,

clinical and laboratory data were retrieved from electronic patient records at the first outpatient appointment. Serum albumin, C-reactive protein (CRP) and whole blood counts for neutrophil/lymphocyte ratio (NLR) analysis were considered out of normal range when values were lower than < 3.5 g/dl, > 10 mg/l and ≥ 5, respectively.

Anthropometric data, including current weight (kg) and height (m), percentage of unintentional weight loss (%WL) and body mass index (BMI; kg/m²) were also noted. Weight and height were checked using a previously calibrated platform-type Welmy® digital scale and measuring ruler. Adult and elderly tables proposed by the World Health Organization (WHO) (26) and Lipschitz (27) were used to classify BMI, respectively.

Adults (from 40 up to 60 years) with BMI ≥ 25 kg/m² and elder patients with BMI > 27 kg/m² were considered as overweight. Adult patients with BMI < 18.5 kg/m² and elder ones with BMI < 22 kg/m² were classified as malnourished. Usual weight (UW) as reported was used to determine the %WL in relation to the current weight (CW) and determined at one, three and six months according to Blackburn et al. (28).

A validated Portuguese version of the Ottery's PG-SGA (1996) was used to determine nutritional status specifically for oncology patients (22). PG-SGA results were classified as A (well nourished), B (moderately malnourished) and C levels (severely malnourished).

Cancer diagnosis, staging and neoadjuvant therapies such as chemo- or radiotherapy when applied were also obtained from patient electronic charts. The classification of the American Joint Committee on Cancer (AJCC) was used to evaluate clinical staging (29).

The evaluation of appetite, food intake and dysphagia was performed separately; later, in an attempt to better determine the role of appetite, ability to ingest and swallow food as a broader food parameter, these abilities were evaluated altogether, generating a weighed scale which was called score of "*eat-ability*" (SEA).

To assess appetite changes, a visual analogue scale (VAS), adapted from the pain VAS (30) and composed of faces and colors on backward positions to pain VAS, was used. In this scale, 0 to 2 scores were considered as appetite loss; 3 to 7, as moderate appetite; and from 8 to 10 points, as normal appetite.

To determine food intake, a questionnaire-based tool of the Nutrition Day Worldwide (31), consisting of illustrative pictures ranging empty plates and glasses through full plates and glasses, where the patient points out which range better refers to current intake (i. e., 100% for full intake, 75% or more than half, half or up to 50%, 25% or less than half and 0% for nil), was used. Ingestion less than 60% was considered as impaired or poor; between 60% and 75%, as moderate intake; and more than 75%, as normal intake.

The severity of dysphagia was classified according to the recommendations by the National Comprehensive Cancer Network (25) as being grade 0 for no swallowing problems, grade 1 for swallowing of small pieces of solid foods, grade 2 and 3 for swallowing semisolid foods or liquid foods only, respectively, and grade 4 for patients unable to swallow.

For food intake, appetite and dysphagia, 0, 1 or 2 points were given according to the severity of the symptoms presented. Zero was assumed to be regular appetite, regular food intake and grade 0 or 1 dysphagia; similarly, 1 point was assumed to be moderate appetite, moderate food intake and grade 2 dysphagia; and score 2 was used for inappetence, poor or impaired food intake and grade 3 or 4 dysphagia.

The sum of those assigned points was used then to define the levels of *eat-ability* (0 to 2) as the SEA, in order to define the need for specific nutritional and therapeutic intervention. SEA 0 was considered for full *eat-ability*, indicating no nutritional intervention required at the time of assessment, but re-assessment on a regular basis during treatment. SEA 1 was considered as moderate or impaired *eat-ability*, indicating a need of nutritional intervention, while SEA ≥ 2 was considered to be critical *eat-ability*, indicating that both, specific nutritional and therapeutic approaches are needed.

Deaths were noted from patient records or by telephone contact to family members.

Statistical analyses included Chi-squared and Pearson's tests, with continuity or Fisher's exact correction by Monte Carlo simulation for categorical variables, while the adjusted residue test was applied to test remaining correlations. For quantitative assessment, the Shapiro-Wilk test was used to verify data symmetry. In the case of normal distribution, Student's t test for independent variables or analysis of variance (ANOVA) corrected by Tukey test were used. In case of asymmetry, Mann-Whitney and Kruskal-Wallis tests were applied, respectively.

SEA cut-off level (up to 1 or more than 2) was determined by the receiver operating characteristic (ROC) curve to get discriminatory power to the PG-SGA (B and C nutritional status, respectively). Statistical Package Social Sciences for Windows version 21.0 was used to analyze data, considering a significance level of 5% ($p \leq 0.05$).

RESULTS

Of the 41 patients included, 30 (73%) had upper and eleven (27%) had lower GIT tumors. Among the most prevalent tumors, in 15 (37%) cases the primary tumor was located in the esophagus, eleven (27%) in the stomach and in the colon in eight (19%) cases. Most of the patients presented at advanced stages of disease, with 18 (64%) classified as stage IV and seven (25%), as stage IIIa or IIIb. The results of these analyses are described in table I.

According to the nutritional status (Table II), three fourths of the patients had some degree of malnutrition, 12 (29%) were moderately malnourished (PG-SGA B) with almost half of them (46%) severely malnourished (PG-SGA C), while BMI showed only 13 (32%) malnourished patients. Similarly, only six (17%) patients had decreased serum albumin levels. Increased weight loss at three and six months prior to the outpatient assessment was observed. However, detailed analyses of weight loss at one, three and six months were not significant (NS).

Regarding inflammatory markers (CRP and NLR), patients with increased CRP levels approximately duplicated the number of patients with altered NLR (74% *vs* 39%). This analysis is presented in table II.

Table I. Characteristics of the sample

Variables	Total sample (n = 41)	Upper GIT (n = 30)	Lower GIT (n = 11)	p
Age, mean (SD); years	58.9 (11.9)	60.4 (12.0)	54.8 (11.3)	0.191
Sex, n (%)				
Male	21 (51.2)	18 (60.0)	3 (27.3)	0.088
Female	20 (48.8)	12 (40.0)	8 (72.7)	
Race, n (%)				
White	36 (87.8)	25 (86.2)	10 (90.9)	1.000
Non white	5 (12.2)	4 (13.8)	1 (9.1)	
Tumor location, n (%)				
Esophagus	15 (36.6)	15 (50.0)	-	< 0.001
Stomach	11 (26.8)	11 (36.7)	-	
Liver	2 (4.9)	2 (6.7)	-	
Pancreas	1 (2.4)	1 (3.3)	-	
Gallbladder	1 (2.4)	1 (3.3)	-	
Colon	8 (19.5)	-	8 (72.7)	
Rectum	3 (7.3)	-	3 (27.3)	
Comorbidities, n (%)				
Nil	28 (68.3)	20 (66.7)	8 (72.7)	0.790
Hypertension	6 (14.6)	4 (13.3)	2 (18.2)	
Type 2 diabetes	3 (7.3)	2 (6.7)	1 (9.1)	
Multiple	3 (7.3)	3 (10.0)	0 (0.0)	
Dyslipidemia	1 (2.4)	1 (3.3)	0 (0.0)	
Clinical stage, n (%)				
IB	1 (3.6)	1 (5.6)	0 (0.0)	0.022
IIB	2 (7.1)	1 (5.6)	1 (10.0)	
IIIA	2 (7.1)	0 (0.0)	2 (20.0)*	
IIIB	5 (17.9)	1 (5.6)	4 (40.0)*	
IV	18 (64.3)	15 (83.3)*	3 (30.0)	
Neoadjuvant treatment, n (%)				
Chemotherapy	5 (12.8)	2 (7.1)	3 (27.3)	0.125
Radiotherapy	4 (10.5)	3 (11.1)	1 (9.1)	1.000
Hospital staying, length (days)†	17 (9.5-24)	17 (8.5-30)	14 (11-24)	0.783
Death, n (%)				
Yes	25 (61.0)	19 (63.3)	6 (54.5)	0.723
No	16 (39.0)	22 (36.7)	35 (45.5)	

*n (%): values are presented in number and percentage, unless otherwise shown. *Statistically significant association by the test of residuals adjusted to 5% of significance. †Described by median (25-75 percentiles). Staging was classified according to the American Joint Committee on Cancer (AJCC, 7th ed. 2010).*

By stratifying upper and lower GIT tumors, statistical significance values were found for BMI (Table II), indicating that patients with upper GIT tumors had decreased mean BMI values when compared to patients with lower GIT tumors (p = 0.001). Malnutrition was more prevalent in patients with malignant neoplasms of upper GIT (n = 12; 40%), while most patients with lower GIT malignancies were overweight (p = 0.003). When evaluated by PG-SGA, 57% of patients with upper GIT tumors were considered as severely malnourished (category C), while only 18% of patients with lower GIT tumors did (NS).

Isolate assessment of dysphagia, appetite or food intake failed to demonstrate *eat-ability* changes between groups (NS).

Table II. Anthropometric data and inflammatory markers

Variables	Total sample (n = 41)	Upper GIT (n = 30)	Lower GIT (n = 11)	p
Weight loss, mean % (SD)				
1 month	2.2 (5.4)	1.9 (5.4)	3.1 (5.6)	0.539
3 months	7.9 (9.0)	8.8 (9.4)	5.4 (8.2)	0.297
6 months	10.2 (8.7)	11.2 (8.8)	7.6 (8.1)	0.242
BMI (kg/m^2), Mean (SD)	23.8 (5.4)	22.1 (4.7)	28.3 (4.5)	0.001
Classification by BMI				
Malnutrition	13 (31.7)	12 (40.0)	1 (9.1)	0.003
Normal	12 (29.3)	11 (36.7)	1 (9.1)	
Overweight	16 (39.2)	7 (23.3)	9 (81.8)	
PG-SGA				
A	10 (24.4)	5 (16.7)	5 (45.5)	0.062
B	12 (29.3)	8 (26.7)	4 (36.4)	
C	19 (46.3)	17 (56.7)	2 (18.2)	
NLR (n = 36)				
< 5	22 (61.1)	16 (59.3)	6 (66.7)	1.000
≥ 5	14 (38.9)	11 (40.7)	3 (33.3)	
Albumin (g/dl) (n = 35)				
< 3.5	6 (17.1)	4 (16.7)	2 (18.2)	1.000
≥ 3.5	29 (82.9)	20 (83.3)	9 (81.8)	
CRP (mg/l) (n = 31)				
≤ 10	8 (25.8)	4 (19.0)	4 (40.0)	0.381
> 10	23 (74.2)	17 (81.0)	6 (60.0)	

n (%): values are presented in number (n) and percentage (%), unless otherwise shown. BMI: body mass index; PG-SGA: Patient Generated Subjective Global Assessment; NLR: neutrophil/lymphocyte ratio; CRP: C-reactive protein.

However, when ranked and analyzed altogether by the SEA, a statistically significant change in food capacity was demonstrated when comparing upper and lower GIT tumors ($p = 0.05$). This analysis is shown in table III.

SEA cut-off points of up to 1 or 2 or more, i. e., moderate and critical food capacity, respectively, were analyzed by the ROC curve to get discriminatory power regarding PG-SGA moderate (B) and severe (C) malnutrition, both, sensitivity and specificity by SEA reached 80% with a 95% CI of 0.48-0.95 and 0.63-0.91, respectively, and an AUC estimated at 0.79 (95% CI: 0.64-0.95; $p = 0.006$). This analysis is depicted in figure 1.

Patients with a SEA 2 or higher presented a significantly greater weight loss at three ($p = 0.001$) and six ($p < 0.001$) months as compared to patients with SEA 0 or 1. Also, all or lower GIT patients with full (SEA 0) and moderate (SEA 1) food capacity had a higher prevalence of overweight, as opposed to those with critical food capacity by the BMI (Table IV).

Some SEA 0 patients (54.5%) showed moderate malnutrition (PG-SGA B), while those with SEA 1 and SEA > 2 were either well nourished (PG-SGA A) or severely malnourished (PG-SGA C), respectively.

The incidence of deaths was significantly higher in severely malnourished (PG-SGA C) patients and in SEA ≥ 2 (both $p = 0.01$) as well, as shown in figure 2.

DISCUSSION

Different parameters have been used to evaluate nutritional status in cancer patients (10). The Consensus of the North American Society of Surgeons and the European Society for Clinical Nutrition and Metabolism suggested serum albumin for assessing nutritional risk in the preoperative period (14,32). However, proper determination of such measure is often difficult because non-nutritional factors involved, such as inflammation (33) and hydration (10), prevent its use as a marker of risk and nutritional status.

Similarly, considering BMI as the only standard pattern to define nutritional status seems unsuitable, since BMI does not take body composition into account, expressing body weight that may lead to misdiagnosing malnutrition (19).

Several tools can be used for risk assessment and nutritional status in clinical practice (19). Although there is no agreement yet (19),

Table III. Data on food capacity and the score of "eat-ability"

Variables	Total sample (n = 41)	Upper GIT (n = 30)	Lower GIT (n = 11)	p
Dysphagia				
Grade 0/1	21 (51.2)	14 (46.7)	7 (63.6)	0.210
Grade 2	7 (17.1)	7 (23.3)	0 (0.0)	
Grade 3/4	13 (31.7)	9 (30.0)	4 (36.4)	
Appetite				
8-10	17 (41.5)	11 (36.7)	6 (54.5)	0.476
3-7	16 (39.0)	12 (40.0)	4 (36.4)	
0-2	8 (19.5)	7 (23.3)	1 (9.1)	
Food intake				
> 75%	19 (47.5)	12 (41.4)	7 (63.6)	0.289
60-75%	4 (10.0)	4 (13.8)	0 (0.0)	
< 60%	18 (43.9)	14 (46.7)	4 (36.4)	
Points of "eat-ability"*	3 (0-4)	3 (1.5-4)	1 (0-4)	0.294
Score of "eat-ability"				
0	11 (26.8)	6 (20.7)	5 (45.5)	0.050
1	3 (7.3)	1 (3.3)	2 (18.2)	
≥ 2	27 (65.9)	23 (76.7)	4 (36.4)	

*n (%): values are presented in number and percentage, unless otherwise shown. *Median (25-75 percentiles).*

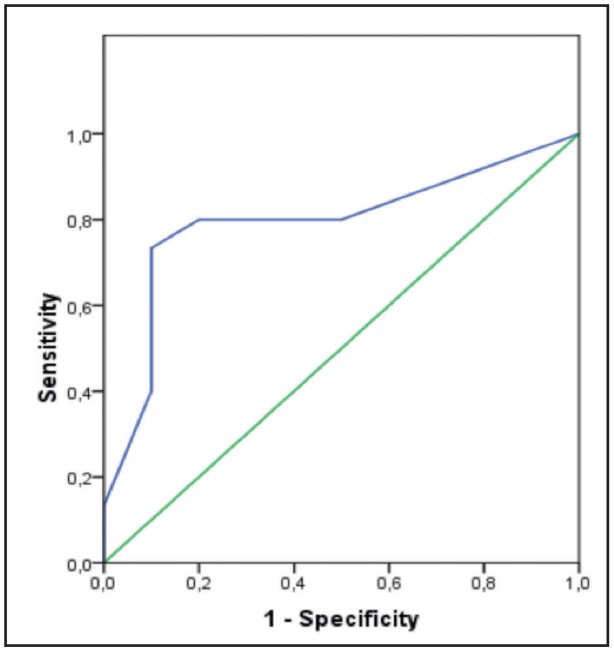

Figure 1.

SEA cut-off points (1 and ≥ 2) determined by the ROC curve in relation to ASG-PPP (B and C). The sensitivity by SEA was 80% (95% CI: 0.48-0.95). Specificity was 80% (95% CI: 0.63-0.91), with an area under the ROC curve (AUC) of 0.79 (95% CI: 0.64-0.95, p = 0.006).

PG-SGA, SGA and Minimal Nutrition Assessment (MNA) are the tools frequently used for nutritional assessment of oncological patients (14).

In our study, there was an overall disagreement among nutritional assessment by PG-SGA, BMI or by serum albumin. These findings further support the fact that either BMI or serum albumin alone did not prove to be consistent methods for this purpose (19), since PG-SGA allowed the identification of malnutrition in 76% of the cases, less than a third of the patients were malnourished by BMI and a little more than one-sixth, by serum albumin.

Likewise, BMI, although significantly reduced in patients with upper GIT tumors and less decreased in those with lower GIT tumors, failed to categorically identify malnutrition, as BMI did not distinguish patients with critical food capacity. On the other hand, by PG-SGA, more than three fourths of malignant neoplasms of the upper GIT cases presented malnutrition and more than half of those with lower GIT cancer had the same diagnosis.

The results for dysphagia by the Atkinson's scale, in a cohort of 110 cases of esophageal cancer, showed 40% of patients presented grade 0 and 1 and 60% presented grades 2 to 4 (24). Similar results were obtained by SEA, as 47% of patients with upper GIT cancer had grade 0 and 1 of dysphagia and 53%, grades 2 to 4. Besides esophagus tumors, other upper GIT tumors, such as those of the liver, pancreas, gallbladder and stomach were included in the SEA and, since dysphagia is uncommon in these tumors (8), SEA results for dysphagia to upper GIT tumors in general proved to be reliable.

Table IV. Association of anthropometric data and inflammatory markers by SEA

Variables	Food capacity - Score of eat-ability (SEA)			p
	Full (0)	Moderate (1)	Critical (≥ 2)	
Weight loss, mean % (SD)				
1 month	0.1 (3.6)	-0.9 (1.1)	3.3 (6.0)	0.154
3 months	2.2 (6.7)†	-0.9 (1.1)†	11.9 (8.4)‡	0.001
6 months	4.7 (7.2)†	-0.9 (1.1)†	14.5 (6.6)‡	< 0.001
BMI (kg/m^2), mean (SD)	25.4 (5.5)	28.5 (0.1)	22.9 (5.2)	0.130
Classification by BMI				
Malnutrition	3 (27.3)	0 (0.0)	9 (34.6)	0.026
Normal	1 (9.1)	0 (0.0)	11 (42.3)*	
Overweight	7 (63.6)*	3 (100)*	6 (23.1)	
PG-SGA				
A	5 (45.5)	3 (100)*	2 (7.7)	< 0.001
B	6 (54.5)*	0 (0.0)	6 (23.1)	
C	0 (0.0)	0 (0.0)	18 (69.2)*	
NLR				
< 5	8 (80.0)	2 (66.7)	12 (54.5)	0.381
≥ 5	2 (20.0)	1 (33.3)	10 (45.5)	
Albumin (g/dl)				
< 3.5	1 (10.0)	0 (0.0)	5 (22.7)	0.481
≥ 3.5	9 (90.0)	3 (100)	17 (77.3)	
CRP (mg/l)				
≤ 10	2 (20.0)	2 (66.7)	4 (23.5)	0.251
> 10	8 (80.0)	1 (33.3)	13 (76.5)	

*n (%): values are presented in number and percentage, unless otherwise shown. BMI: body mass index; PG-SGA: Patient Generated Subjective Global Assessment; NLR: neutrophil/lymphocyte ratio; CRP: C-reactive protein. *Statistically significant association by the test of the residuals adjusted to 5% of significance. †,‡Equal figures do not differ by the Tukey test at 5% significance.*

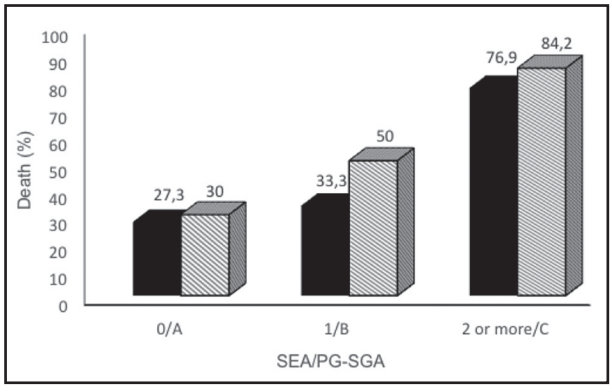

Figure 2.

Incidence of death according to food capacity as determined by the SEA and PG-SGA (both p = 0.01).

Similarly, regarding appetite and food intake, when evaluated independently, no discriminatory power was found between upper and lower tumors. However, it can be observed that 63% *vs* 60% of patients with upper GIT tumors showed alterations, respectively, while these figures were 45% *vs* 36% for lower GIT tumors.

The SEA appetite scale showed appetite loss in 23% of patients with upper GIT cancer, same as it was found in a study that applied the appetite VAS as one of the tools used to compare instruments in the assessment of inpatients anorexia (23). In this study, 23% of the patients were diagnosed with anorexia by the appetite VAS, against only 10% of the cases by the FAACT-ESPEN score (23).

Up to date, there is still no tool that can be considered as a "gold standard" for diagnosing anorexia in cancer patients (7). Moreover, some studies indicated that VAS for appetite in clinical practice better suits the need to track changes over time rather than diagnosing anorexia on a specific day (23). However, in developing countries, the VAS for determining appetite turns into a simpler, more practical, quicker and easier tool to be perceived by the patient when compared to questionnaires with multiple domains, often difficult to understand.

In the SEA, determining the evaluation of intake by a combined VAS on the percentage of estimated solids and liquids taken also allowed greater intake perception by patients as a whole. One of the criteria to indicate enteral nutritional therapy in cancer patients is food intake under 60% of their nutritional needs for more than one to two weeks (1). This would be the case in 47% and 36% of patients with upper and lower GIT tumors, respectively, by using the SEA, resulting in a quick and simple way that provides health professionals with a reliable assessment on patient daily food compliance and clearly avoiding misinterpretation.

When these parameters (dysphagia, appetite and food intake) were evaluated altogether, it became easier to consider that dysphagia is directly involved with intake and secondary and indirectly, with appetite, just as appetite loss is directly implicated with less food intake. SEA allowed better judgment on "*eat-ability"* (food capacity) among upper and lower GIT patients, who are possibly at increased risk of malnutrition.

Malnutrition might be detected in up to 87% of patients with GIT cancer, depending on tumor site and stage (11). In SEA, critical food capacity (SEA ≥ 2) was associated to 92% of malnourishment cases, being also reliably associated with weight loss at three and six months previously, when compared to full and moderate food capacity (SEA 0 or 1), respectively.

Blackburn et al. considered as severe unintentional weight loss greater than 5%, 7.5% and 10% at one, three and six months, respectively (28), as unintentional weight loss > 10% has been considered to be an indicator of nutritional risk (12). In our study, SEA ≥ 2 was consistent with weight loss greater than 10% at three and six months, showing the role of SEA as a predictor of weight loss and high nutritional risk.

Some discrepancy between full and moderate "*eat-ability"* in moderately undernourished and well-nourished patients, respectively, was due to a type II sampling error, since there were no cases in three subgroups of those categories. Although all cases classified as critical "*eat-ability"* were severely malnourished, a greater sample is still needed to validate this combined SEA. Despite this, there was a greatly "*eat-ability"* impairment among patients who died, who were greatly malnourished. Nevertheless, the role of "*eat-ability"* and malnutrition on death risk requires further studies on a large sample, since most patients were in advanced stages of the disease (stages III and IV).

Another deterrent factor in the study is that most of the patients died after hospital discharge, making it difficult to establish if death was directly related to the tumor or to the comorbidities.

Perspectives point out to increase cases evaluated by SEA and to compare it with inflammatory parameters, most probably with c-reactive protein (CRP), since SEA and CRP were similarly increased and CRP was twice NLR positive, and to better determine the role of SEA as a nutritional risk ancillary.

In conclusion, the combined evaluation of food intake, dysphagia and appetite (SEA) was reliable in clearly identifying patients with impaired "*eat-ability"* in more than half and in more than three fourths of those with lower and upper GIT tumors, respectively, that significantly affect nutritional status and risk of death of patients with GIT tumors.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Epidemiología y dietética

Food neophobia, Mediterranean diet adherence and acceptance of healthy foods prepared in gastronomic workshops by Spanish students

Neofobia alimentaria, adhesión de la dieta mediterránea y aceptación de alimentos saludables preparados en talleres gastronómicos por estudiantes españoles

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Abstract

Introduction: food neophobia can affect dietary variety and hedonic acceptance due to rejection of healthy foods.

Objective: to evaluate the impact of dietary neophobia on adherence to the Mediterranean diet and on the hedonic acceptance of healthy foods made in gastronomic workshops by schoolchildren.

Methodology: descriptive cross-sectional study of Primary (8-11) and Secondary (12-18) schoolchildren from Murcia, Spain, participating in gastronomic workshops, where two recipes were prepared and tasted (vegetables + blue fish and fruits). Food neophobia (FN) and adherence to the Mediterranean diet (KIDMED) were identified and each participant assessed the acceptance of each recipe using a hedonic scale (seven points).

Results: a total of 1,491 students (49.5% girls) participated in the study; 13.5% were neophobic and 61.1% presented optimal diet quality. A linear inverse relationship between the degree of neophobia and the quality of the diet (ρ [rho] = -0.31, p = 0.001) was found. High adherence to the Mediterranean diet was associated with lower neophobia and better hedonic scores, compared to intermediate or low adhesions ($p < 0.0001$). Neophobic schoolchildren presented significantly worse results in vegetable consumption, especially at the Secondary level, and in the acceptance of healthy preparations ($p < 0.05$). A good acceptance of the prepared preparations was associated with the usual adequate consumption of fruits, vegetables, fish and legumes.

Conclusion: food neophobia affects the adherence to the Mediterranean diet and the acceptance of healthy foods elaborated in gastronomic workshops by Spanish schoolchildren.

Key words:

Food neophobia. Hedonic acceptance. Mediterranean diet. Gastronomic workshops.

Resumen

Introducción: la neofobia alimentaria puede afectar la variedad dietética y la aceptación hedónica debido al rechazo de alimentos saludables.

Objetivo: evaluar el impacto de la neofobia alimentaria en la adherencia a la dieta mediterránea y en la aceptación hedónica de alimentos saludables realizados en talleres gastronómicos por escolares.

Metodología: estudio descriptivo transversal de escolares de Primaria (8-11) y Secundaria (12-18) de Murcia, España, que participaron en talleres gastronómicos donde se prepararon y probaron dos recetas (verduras + pescado azul y frutas). Se identificaron la neofobia alimentaria (FN) y la adhesión a la dieta mediterránea (KIDMED) y cada participante evaluó la aceptación de cada receta utilizando una escala hedónica (siete puntos).

Resultados: participaron 1.491 alumnos (49,5% niñas); el 13,5% eran neofóbicos y el 61,1% presentaban una calidad óptima de la dieta. Se encontró una relación lineal inversa entre el grado de neofobia y la calidad de la dieta (ρ [rho] = -0,31, p = 0,001). La alta adherencia a la dieta mediterránea se asoció con menor neofobia y mejores puntuaciones hedónicas en comparación con adherencias intermedias o bajas ($p < 0,0001$). Los escolares neofóbicos presentaron resultados significativamente peores en el consumo de vegetales, especialmente en el nivel secundario y en la aceptación de preparaciones saludables ($p < 0,05$). Una buena aceptación de las recetas elaboradas se asoció con el habitual consumo de frutas, verduras, pescado y legumbres.

Conclusión: la neofobia alimentaria afecta la adherencia a la dieta mediterránea y la aceptación de alimentos saludables elaborados en talleres gastronómicos por escolares españoles.

Palabras clave:

Neofobia alimentaria. Aceptación hedónica. Dieta mediterránea. Talleres gastronómicos.

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INTRODUCTION

Exposure to high food diversity in the early years modulates food preferences and improves dietary variety. Children identified with dietary neophobia have a poorly varied diet because they present an important rejection to many foods (1,2). This situation is more common at younger ages and is maintained over the years (3). Some variables associated with the consumption of vegetables (most rejected foods) in young children are: early feeding practices, parental education, and family income (4), low vegetable consumption by parents (5) and home availability (6). Likewise, breastfeeding and the early introduction of fruits and vegetables are related to their consumption (7).

Food neophobia negatively correlates with fruit acceptance and, to a greater extent, with vegetables (8). Vegetables are the least accepted food group by children, and this is probably the reason for their low consumption. It has been identified that the number and type of preparations that the child consumes depend on the type of vegetable, and the best accepted dishes are those that combine them with other foods. Likewise, consumption is greater as the variety of methods of culinary preparation increases (9). Equally, the acceptance of fish by children depends to a great extent on the method of culinary preparation (10). Recently, it has been reported that food manipulation by children through tactile contact may be related to the acceptance of a greater variety of fruits and vegetables, although not with an increase in their consumption (11). In addition, it has been proposed that the participation of children in the kitchen can reduce food neophobia and promote the consumption of foods such as vegetables (12).

Due to the above, it is important to know the impact of food neophobia on the hedonic acceptance of healthy foods, the variety of diet and eating habits in school children, as well as the lack of information about its effects on different aspects associated with the consumption of food, such as participation in the elaboration itself. The objective of the present work was to evaluate the impact of dietary neophobia on adherence to the Mediterranean diet and acceptance of healthy preparations made by students in gastronomic workshops.

METHODS

PARTICIPANTS

A cross-sectional descriptive study was carried out in schoolchildren from Murcia (Spain) aged 8-18 years. The study was carried out in the framework of sensorial gastronomy workshops, where two recipes were cooked and tasted; the main ingredients of these recipes were healthy components of the Mediterranean diet (recipe 1 = with vegetables and blue fish; recipe 2 = with fruits). The City Council of the city of Murcia carries out a program to promote the Mediterranean diet for schoolchildren that takes place in the "Raimundo González" gastronomic classroom located in a local market.

The study comprised eleven schools that voluntarily requested to participate in the project between 2013 and 2015. The total sample was stratified by gender and school level: 8-11 years (Primary level) and 12-18 years (Secondary level). All schoolchildren surveyed participated voluntarily with a written authorization from parents or guardians and with the consent of each school's management.

INSTRUMENTS AND DATA COLLECTION

The recipes were designed by the manager of the community nutrition service and adapted by a professional chef. The questionnaires were sent to the school prior to the workshop in the gastronomic classroom and were self-answered by each participant.

Each workshop consisted in a visit to the gastronomic classroom located in a local market, where the students chose the ingredients. It should be mentioned that the cost of food was covered by tenants of the local market, due to their commitment to the city council. Recipe 1 was a "healthy" pizza with various vegetables and fresh blue fish (anchovies). Recipe 2 consisted of seasonal fruits presented as a dessert and in a colorful way for students. Fruit and vegetables were chosen by children according to availability and seasonality. During the workshop, while the students were preparing and cooking the food, a nutritionist described how these foods are part of the Mediterranean pyramid and how to introduce them into your usual diet. All children participated voluntarily in the tasks related to the purchase, cutting, mixing and cooking of ingredients. Finally, after the preparation, all the children performed the tasting and hedonic evaluation of the prepared foods.

FOOD NEOPHOBIA

Participants responded to a survey assessing the presence of food neophobia (13), which is recognized and consolidated in the scientific literature as a highly reliable instrument for assessing individuals' attitudes towards novel foods (14). The survey consisted of ten questions, rated with a Likert scale of seven points (range 0-70). The presence of neophobia was defined as > 1 standard deviation of the mean, as reported in the literature (13). Before carrying out the statistical analysis, some questions of the scale were inverted in order to be able to obtain valuations in the same sense. According to another reference population, this questionnaire has shown sufficient internal validity for its application in Spanish children (15).

MEDITERRANEAN DIET

The participants answered a questionnaire on adherence to the Mediterranean diet (KIDMED) consisting of 16 items (range 0-12) and validated for the Spanish population in the ENKID

study (16). In this survey, 12 aspects of the Mediterranean diet were positively rated, as the consumption of fruit and vegetables, fish, olive oil, cereal and dairy consumption at breakfast, etc., with four negative points (remaining): the consumption of fast food, sweets and candies, pastries and the omission of breakfast. Three points or less was considered as a low adhesion; 4-7 points, medium adhesion; and ≥ 8 points, good adhesion. For comparative purposes, diet quality was defined as good adherence to those with scores ≥ 8 and improved adherence with seven points or less (16).

HEDONIC EVALUATION

The acceptance of the preparations elaborated with healthy foods typical of the Mediterranean diet was carried out with the support of a hedonic scale of seven points that consisted of images of different facial expressions that represented the following: 1 = super bad, 2 = very bad, 3 = bad, 4 = not good, not bad, 5 = good, 6 = very good, and 7 = super good (15), which was previously used by our working group in school cafeteria users (17). For comparative purposes, scores of 5 to 7 were scored as good acceptance and bad ratings of 1 to 4.

STATISTICAL ANALYSIS

The normal distribution of quantitative variables was verified by the Kolmogorov-Smirnov test and internal consistency analysis of the neophobia scale (Cronbach's alpha) was performed. The associations between food neophobia, adherence to the Mediterranean diet and hedonic food assessment were determined using the non-parametric Pearson χ^2 test. Since the data from the hedonic appreciation were not normal, Mann-Whitney U-analysis was used to establish differences between the groups. A stepwise multivariate logistic regression analysis was also performed to establish the independent predictors of acceptance of each preparation, previously selecting the variables with a value of $p \leq 0.2$ in the univariate analysis. All analyses were performed with the statistical package SPSS version 23.0, considering the probability of 95% confidence.

RESULTS

There were 1,491 students: 478 (32%) in 2013, 592 (40%) in 2014 and 421 (28%) in 2015. The participation of public schools was 84% and of private centers, 16%. The participants were divided into two groups: 1,057 primary schoolchildren between eight and eleven years old (71.6%) and 424 secondary schoolchildren between 12 and 18 years old (28.4%). Of the total number of participants, 49.5% were girls and 50.5% were boys; 4.7% were immigrants and, of all of them, only 22% used the school cafeteria on a regular basis.

FOOD NEOPHOBIA

The mean score of the food neophobia scale was 33.5 ± 11.8 (33.1 ± 11.8 for primary and 32.93 ± 11.8 for secondary), with no significant difference between the groups. No difference was found as well between genders (34.0 ± 12.3 in females and 32.1 ± 11.3 in males). The results indicated that 13.5% of the participants presented food neophobia. The scale had an internal consistency (Cronbach's alpha) of 0.76, indicating that neophobia was reliably quantified (15). An analysis was made of age and the presence of neophobia, noting that at the primary level, the presence of neophobia did not seem to influence dietary habits, although there was a trend towards lower consumption of fruits, vegetables, fish and greater omission of breakfast. However, the secondary level, with food neophobia, did present statistical differences with a lower consumption of vegetables and breakfast cereals or derivatives, as well as greater consumption of candy and sweets ($p < 0.05$). There was also a trend towards lower fish consumption, although this difference was not significant (Table I). In addition, an inverse linear relationship was found between the degree of neophobia and the quality of the diet (ρ [rho] = -0.31; $p = 0.001$).

MEDITERRANEAN DIET

The mean score on the KIDMED scale was significantly lower in Secondary school students than in Primary school (6.9 ± 2.4 *vs* 8.4 ± 2.3; $p < 0.01$). It was also identified that the good adherence to the Mediterranean diet was lower in the Secondary group than in the Primary group (44.2% *vs* 68%, respectively, $p < 0.01$). The poor adherence category was 7.3% in the Secondary group and 4% in the Primary group, with no statistical differences.

An analysis by age and gender was carried out (Table II), showing that in the Primary level, boys consumed more dairy (milk, yogurt) and industrial bakery than girls ($p < 0.05$). On the other hand, in Secondary school, boys were observed to consume less vegetables once a day ($p < 0.05$) and for the second occasion in the day ($p < 0.01$). On the other hand, girls consumed fewer pastas or rice and nuts ($p < 0.5$), and consumed less cereals and derivatives ($p < 0.01$) than boys. In addition, girls skipped more breakfast and consumed more candy and sweets than boys ($p < 0.05$). Although no significant difference was observed, a lower consumption of fish at the Secondary level was found.

SENSORY EVALUATION

In all ages, fruit preparations (recipe 2) were better valued than those containing vegetables and fish (recipe 1) (6.1 ± *vs* 5.4 ±, $p < 0.01$) (Table III). In the Primary group, the students evaluated positively both preparations, with no statistically significant differences between them. The presence of neophobic in Primary school did not affect acceptance since both recipes had high

Table I. Differences in adherence to the Mediterranean diet by educational level and presence of food neophobia

KIDMED - Mediterranean Diet Quality Index	Primary level (8-11 y) n = 1,057			Secondary level (12-18 y) n = 424		
	Without neophobia (%)	With neophobia (%)	Total (%)	Without neophobia (%)	With neophobia (%)	Total (%)
Takes a fruit or fruit juice every day	85.6	78.8	84.7	82.6	76	81.8
Has a second fruit every day	65	60.6	64.4	34.7	24	33.3
Has fresh or cooked vegetables regularly once a day	77.9	66.7	76.3	*72*	*48*	*68.9**
Has fresh or cooked vegetables more than once a day	44.2	46.9	44.5	*36.5*	*12*	*33.3**
Consumes fish regularly (at least 2-3 times per week)	77.1	71.9	76.4	60.7	48	59.1
Goes more than once a week to a fast-food (hamburger) restaurant	21.5	18.8	21.1	22.8	24	22.9
Likes pulses and eats them more than once a week	77.4	83.3	78.2	71.9	60	70.3
Consumes pasta or rice almost every day (5 or more times per week)	76.1	78.8	76.5	69.6	68	69.4
Has cereals or grains (bread, etc.) for breakfast	87.1	84.8	86.8	*70.1*	*48*	*67.2**
Consumes nuts regularly (at least 2-3 times per week)	67.8	63.6	67.2	51.8	56	52.4
Uses olive oil at home	95	100	95.7	98.2	95.8	97.9
Skips breakfast	15.6	24.2	16.8	20.4	33.3	22
Has a dairy product for breakfast (yogurt, milk, etc.)	93	87.5	92.2	83.9	80	83.4
Has commercially baked goods or pastries for breakfast	16.2	9.1	15.2	14.5	20	15.2
Takes two yogurts and/or some cheese (40 g) daily	66.8	51.6	64.8	48.8	48	48.7
Takes sweets and candy several times every day	22.3	9.1	20.4	*20.6*	*52*	*24.7†*

*χ^2, *p < 0.05; †p < 0.01.*

values. However, although this difference was not statistically significant, the preparation with vegetables and fish had an average hedonic acceptance of 5.2 ± 1.9 in neophobic compared to 5.5 ± 1.7 in non-neophobic ($p > 0.05$). In the case of the Secondary group, the neophobics evaluated the recipe with vegetables and fish significantly (3.80 ± 1.6 *vs* 5.1 ± 1.2; $p < 0.01$), although they positively evaluated the recipe with fruits.

Additionally, the relationship between the adherence to the Mediterranean diet and the hedonic valuations given to the elaborations prepared in the gastronomic classroom was explored. It was found that those with a good adherence gave better hedonic scores, in contrast to intermediate or lower adhesions in both age groups, especially of the preparation with vegetables and fish (Table IV).

According to multivariate stepwise logistic regression analysis (Table V), it was found that in the Primary group, independent predictors of acceptance of the recipe with vegetables and fish were consumption of fresh or cooked vegetables more than once a day (OR = 1.5, 95% CI 1.1-2.1), fish consumption at least two or three times per week (OR = 1.5, 95% CI 1.1-2.1) and vegetable consumption once a week (OR = 1.7, CI 95% 1.2-2.5). In the fruit recipe, they consumed a second fruit or fruit juice every day (OR = 2.0, 95% CI 1.2-3.4), fresh vegetables or cooked once a day (OR = 2.1, 95% CI 1.2-3.6), fish at least two or three times per

Table II. Differences in adherence to the Mediterranean diet by educational level and sex

KIDMED - Mediterranean Diet Quality Index	Primary level (8-11 y) n = 1,057			Secondary level (12-18 y) n = 424		
	Girls (%)	Boys (%)	Total (%)	Girls (%)	Boys (%)	Total (%)
Takes a fruit or fruit juice every day	87.7	89.2	88.5	85.2	76.6	81
Has a second fruit every day	65.7	67.9	66.8	38.5	31.9	35.3
Has fresh or cooked vegetables regularly once a day	75.4	70.6	72.9	*76*	*62.8*	*69.5**
Has fresh or cooked vegetables more than once a day	51.7	51	51.3	*38*	*23.4*	*30.8†*
Consumes fish regularly (at least 2-3 times per week)	74.1	74.3	74.2	62	62.8	62.4
Goes more than once a week to a fast-food (hamburger) restaurant	19.6	20.9	20.3	27.5	20.7	24.1
Likes pulses and eats them more than once a week	78.7	73.6	76.1	77.2	68.8	73
Consumes pasta or rice almost every day (5 or more times per week)	73.9	77.5	75.7	*63.3*	*75.9*	*69.5**
Has cereals or grains (bread, etc.) for breakfast	86.9	88.9	87.9	*57.7*	*77.2*	*67.3†*
Consumes nuts regularly (at least 2-3 times per week)	66.9	69.4	68.2	*45.6*	*60.4*	*52.9**
Uses olive oil at home	*95.9*	*92.6*	*94.3**	98	98.6	98.3
Skips breakfast	14.9	11.6	13.2	*27.9*	*16*	*22.0**
Has a dairy product for breakfast (yogurt, milk, etc.)	*88.4*	*92.8*	*90.6**	82.7	89.7	86.1
Has commercially baked goods or pastries for breakfast	*11.9*	*18.5*	*15.2**	10.5	17.2	13.9
Takes two yogurts and/or some cheese (40 g) daily	69.6	67.3	68.4	45.3	53.5	49.3
Takes sweets and candy several times every day	19.1	22.1	20.6	*31.1*	*19.6*	*25.4**

*χ^2, *p < 0.05; †p < 0.01.*

Table III. Impact of food neophobia (FN) on the hedonic assessment of prepared foods by educational level

	Primary level n = 1,057			Secondary level n = 424		
	Without FN (Mean ± DE)	With FN (Mean ± DE)	p	Without FN (Mean ± DE)	With FN (Mean ± DE)	p
Recipe 1	5.6 ± 1.7	5.3 ± 1.9	0.377	5.2 ±1.3	3.8 ± 1.7	*0.000*
Recipe 2	6.4 ± 1	6.3 ± 1.3	0.555	5.8 ± 1.2	5.2 ± 1.9	*0.096*

Mann-Whitney U-analysis was used to establish differences between the groups (with or without FN).

Table IV. Impact of adherence to the Mediterranean diet (MD) on the hedonic assessment of prepared foods by educational level

	Primary level n = 1,057			Secondary level n = 424		
	Low or medium adherence (Mean ± DE)	High adherence (Mean ± DE)	p	Low or medium adherence (Mean ± DE)	High adherence (Mean ± DE)	p
Recipe 1	5.4 ± 1.9	5.7 ± 1.6	0.002	4.9 ± 1.5	5.3 ± 1.3	0.035
Recipe 2	6.2 ± 1.2	6.4 ± 1.0	0.006	5.5 ± 1.4	5.9 ± 1.3	0.026

Mann-Whitney U-analysis was used to establish differences between the groups (low/medium and high adherence to Mediterranean diet).

Table V. Independent predictors associated with the hedonic valuation of foods prepared by educational level

Predictors	Recipe 1 OR (CI 95%)	Recipe 2 OR (CI 95%)
Primary level		
Has a second fruit every day		2.0 (1.2-3.4)
Has fresh or cooked vegetables regularly once a day		2.1 (1.2-3.6)
Has fresh or cooked vegetables more than once a day	1.5 (1.1-2.1)	
Consumes fish regularly (at least 2-3 times per week)	1.5 (1.1-2.1)	1.8 (1.0-3.0)
Likes pulses and eats them more than once a week	1.7 (1.2-2.5)	2.0 (1.2-3.4)
Secondary level		
Food neophobia	0.2 (0.1-0.5)	
Takes a fruit or fruit juice every day		7.0 (2.2-22.1)

Multivariate logistic regression analysis by steps.

week (OR = 1.8, 95% CI 1.0-3.0) and legumes once a week (OR = 2.0, 95% CI 1.6-3.4). On the other hand, in the Secondary group, the only independent predictor for the recipe with vegetables and fish was to be classified as neophobic (OR = 0.2, 95% CI 0.1-0.5) and for the recipe with fruits, consumption of a fruit or fruit juice every day (OR = 7.0, 95% CI 2.2-22.1).

DISCUSSION

The present study shows that dietary neophobia affects dietary variety by adversely affecting adherence to the Mediterranean diet, and both conditions impact on the hedonic perception of healthy foods.

In our study, the prevalence of food neophobia in children and young people aged 8-11 years reached 13.5% of the participants, with an average score of 33.5 ± 11.8, in line with research in Spanish children from the same geographical area showing measurements of 37.9 ± 13.1 and 16.1% prevalence (15), and in German teenagers with a median of 31 ± 21 (18). However, in a study in northern Spain (12) smaller averages are reported, of approximately 21 points in nine year-old children, probably because participation in our program does not present a participation bias, since the intervention is performed in complete classrooms, regardless of the parents' concern or motivation for a healthy diet of their children.

No differences were found in the degree of neophobia according to gender and age, although large studies in Finland and the United States between 2001 and 2010 describe greater neophobia in the upper strata of age and hold controversy over gender effects (19). Our study does not show a decrease in neophobia with age, probably due to the fact that the youngest participants were eight years old and would have exceeded the age at which the peak of neophobia occurs, maintaining stability between 8-18 years, consistent with that described in Spanish children (20). The discrepancies described in the literature on the relationship between gender and food neophobia suggest that more research is needed.

Currently, one of the biggest problems in child nutrition is the low consumption of food considered as an important part of the Mediterranean diet such as fruits, vegetables and fish. It is well known that Spanish children and young adults have a very variable adherence to the pattern of Mediterranean diet, depending on the age and area of the country (1). The KIDMED test is widely used to assess adherence to the Mediterranean diet pattern in children and young adults, and is effective in evaluating the quality and variety of the diet at these ages. In a recent systematic review, there is a clear tendency to abandon this pattern, with only a mean adequate adherence of 10% (1). The average prevalence of adequate adherence to this model in our participants reaches 68% and 44.2% in younger students and 12 years or more respectively, placing us in the upper stratum of prevalence of the reviewed studies. Specifically, a study in adolescents in a geographical area near Murcia found a 30.9% adequate adherence to the Mediterranean diet (21). In the present work, it is described that the adherence to the Mediterranean diet has an inverse relation with age, since the students of the Secondary group have lower scores than those of the Primary level, as reported in a group of ten to 16 (22) and in similar populations (15,21). The diet of the older students presents worse profile than that of the younger ones in 14 of the 16 items that compose the test. Boys consume less vegetables, skip breakfast, and consume more pasta and rice and nuts than girls.

According to our results, the presence of neophobia is negatively correlated with adherence to the Mediterranean diet, so that neophobia decreases the quality of the diet, in line with the results of another study in Spanish children and youngsters (20). In the Secondary group, its effect on the consumption of fruits, vegetables, fish, sweets and candies was identified, as in our study. In addition, our results also showed an effect of cereal consumption at breakfast, which indicates that the diet of older students may be inadequate from the beginning of the day, in congruence with

findings in the Spanish population, where only 18% of young people make an adequate breakfast (22). At the Primary level, our results show a tendency to decrease the consumption of fruits, vegetables, fish and greater omission of breakfast, but without significant differences, unlike the study by Maiz E et al. (20).

The hedonic evaluation of the foods prepared by the students in the gastronomic workshops indicated an effect of the age, since those of the Primary level group positively evaluated both preparations; however, those of the Secondary level group negatively evaluated the preparation, which included vegetables and blue fish, although the valuation of the fruits was positive. Negative assessment of vegetables may be associated with poor participation of adolescents in the preparation of family meals and low self-efficacy for the preparation of these healthy foods, a relationship that has been previously reported (23). In addition, regression analysis indicated that food neophobia was a negative predictor of the hedonic assessment of the recipe with vegetables and fish in the older group.

Little has been explored the influence of the presence of neophobia in the acceptance of foods prepared by the students themselves in an environment outside the home, but according to a recent experimental research, when children participate in the elaboration of healthy foods with fruits and vegetables, they show a higher preference for these processed foods themselves, increase their willingness to try new foods and choose foods that contain vegetables (12). It has also been pointed out that children's participation in household food preparation may favor increased vegetable intake (24) and a better quality of diet for young adults identified as a valuable educational tool in these age groups (25). Likewise, it has been recommended that simple food preparation activities can lead to improved eating habits (26).

Another important finding was that those who had a better adherence to the Mediterranean diet gave higher hedonic assessments, especially to the preparation with vegetables and blue fish in both age groups, so it is clear that familiarity (intake in his habitual diet) with these foods, increased their acceptance (7).

Most recent studies analyze hedonic acceptance by subjecting different recipes to visual or tasting tests primarily in school canteens. There are few studies that have analyzed complex interactions between neophobia, diet quality and hedonic acceptance of key foods in the Mediterranean diet in a participatory context of gastronomic and sensorial workshops developed in the framework of seasonal sales and closeness.

In spite of this, one of the major strengths of the study is the participation mediated by the educational centers, which causes all the students of the courses selected by the center carry out the gastronomic workshop and all the questionnaires of the program, thus saving possible participation biases.

Given the efficacy of the dietary pattern of the Mediterranean diet in its well-known health benefits, it is necessary to promote its consumption not only in non-Mediterranean countries, but also in Mediterranean countries, where adherence has been declining in recent decades. Special attention to children and young people with a clear tendency to rapid abandonment should be paid.

The results of this study demonstrate implications for public health policies that should foster familiarity with a wide variety of foods from the earliest ages in both, families and school canteens. In addition, the introduction of practical workshops on gastronomy and sensory education as part of school programs can contribute to the creation of positive experiences with new flavors to encourage children to try new foods and therefore, increase the variety in their diets. In addition to the implications for health, the influence of these factors on the current trend of control and reduction of food waste in the domestic and community domains should be taken into account.

Among the limitations of the study are the lack of collection of demographic variables related to increased exposure to a variety of foods, such as the level of income and family income and the urban environment, and showing positive effects on neophobia. In addition, as a cross-sectional study, causal relationships cannot be established.

The results of this study indicated that food neophobia affects the adherence to the Mediterranean diet and the acceptance of healthy foods elaborated in gastronomic workshops by Spanish schoolchildren.

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Trabajo Original

Epidemiología y dietética

Salt content in bread in Spain, 2014

Cantidad de sal en el pan en España, 2014

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Abstract

Introduction: excess salt intake is associated to the risk of cardiovascular diseases. Bread is one of the foods that contributes the most salt to the diet in Spain. It is important to monitor the salt content of bread.

Objective: to quantify the amount of salt in bread in Spain in 2014, and to compare it to the amount of salt in 2008.

Methods: this cross-sectional study was conducted in Spain in 2014, and 1,137 loaves of bread (three types: *barra*, a Spanish style, similar in shape to a baguette; baguettes and wholemeal) were purchased at bakeries with and without on-site workrooms and at supermarkets in all of Spain's autonomous communities. Salt content (g/100 g bread) was estimated by determining total sodium. In one subsample, mean salt content was estimated by determining chlorides; it was compared to previous data of 2008 salt content (chloride determination).

Results: the mean salt content was 2.08 g/100 g (SD: 0.32) with a minimum value of 0.30 and a maximum of 3.33. The mean salt content was similar in *barra* and baguette-type breads (2.09 g/100 g) and somewhat lower in wholemeal. The mean salt was 2.07 g/100 g in breads made with fresh dough and 2.12 g/100 g in breads made with frozen dough. The mean salt content (chlorides) was 1.64 g/100 g (SD: 0.42) in 2014 and 1.63 g/100 g (SD: 0.37) in 2008. This was not a significant difference ($p = 0.428$).

Conclusions: the amount of salt in common bread in Spain remains stable from 2008.

Key words:

Bread. Sodium chloride. Food quality. Cardiovascular diseases.

Resumen

Introducción: el consumo excesivo de sal está relacionado con un mayor riesgo de enfermedades cardiovasculares. El pan es uno de los mayores contribuyentes a la ingesta de sal en España y es importante evaluar su contenido en sal.

Objetivo: cuantificar la cantidad de sal en el pan en España en 2014 y compararla con la cantidad de sal que contenía en 2008.

Métodos: este es un estudio transversal realizado en 2014. Se adquirieron 1.137 piezas de pan (barra o similar, baguette y pan integral) en panaderías con y sin obrador y en supermercados de todas las comunidades autónomas de España. El contenido de sal (g/100g de pan) se analizó mediante la determinación de sodio total. En una submuestra se estimó el contenido de sal mediante determinación de cloruros y se comparó con el contenido de sal con datos previos de 2008 (cloruros).

Resultados: el contenido medio de sal fue 2,08 g/100 g (DE: 0,32), con un mínimo de 0,30 y un máximo de 3,33. El contenido medio de sal fue similar en barras y baguettes (2,09) y más bajo en pan integral. La media de sal fue de 2,07 g/100 g en pan elaborado con masa fresca y 2,12 g/100 g en pan de masa congelada. El contenido medio de sal medido mediante cloruros fue 1,64 g/100 g (DE: 0,42). La media de sal en resultados previos de 2008 era 1,63 g/100 g (DE: 0,37). La diferencia no fue significativa ($p = 0,428$).

Conclusiones: la cantidad de sal en España permanece estable en los diferentes tipos de pan desde 2008.

Palabras clave:

Pan. Sal. Calidad de los alimentos. Enfermedades cardiovasculares.

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INTRODUCTION

Of the 56 million deaths worldwide in 2012, 38 million were caused by noncommunicable diseases (NCDs), particularly cardiovascular disease (17.5 million, 46.2% of all NCD deaths) (1). High blood pressure is the largest risk factor for NCDs; between 13-16% of all deaths are attributed to this (2,3). According to the World Health Organization (WHO), high blood pressure is responsible for at least 45% of deaths due to heart disease and 51% of deaths due to stroke (4). The worldwide prevalence of high blood pressure (arterial systolic and/or diastolic blood pressure ≥ 140/90 mmHg) in adults (aged 18 or over) is estimated at 22% in 2014 (1). The prevalence of high blood pressure in adults in Spain was estimated at 33% in 2010, although this figure reaches almost 70% in people aged over 65 (5).

One element of the diet that is associated with the risk of high blood pressure and cardiovascular disease is excess salt intake. The quantity of salt ingested in the diet is a highly significant determinant of blood pressure levels and cardiovascular risk (6-11). Excess salt intake is estimated to have been responsible for 1.7 million deaths due to cardiovascular disease (12). Excess salt intake has also been linked to other NCDs, such as stomach cancer (13); research has even been done into a possible link as a determinant of obesity (14). The WHO recommends a maximum daily salt intake of 5 g (15). The worldwide average daily salt intake in adults is estimated at 9.88 g per person (range: 5.45-13.78), with 99.2% of the world's population having an average daily salt intake that exceeds the WHO recommendations (12). Average daily salt intake in Spain is estimated at 9.8 g (SD: 4.6 g) (16). In other words, salt intake in Spain is very close to the worldwide average, almost twice the level recommended by the WHO.

Over 75% of dietary salt is found in processed foods (17). It is therefore important to address reformulating the salt content of foods in order to enable salt intake to be reduced. One food of particular importance is bread, as shown by the European Commission High Level Group on Nutrition and Physical Activity (18). Bread represents one of the foods that contributes the most salt to the diet, due both to its salt content and to its high consumption frequency. Bread is also consumed very frequently in Spain (19) and, in addition to this, it is an important food due to its inclusion in the Mediterranean diet (20). For this reason, it is considered important to know, and where possible to reduce, the salt content of bread (19). Within this type of bread, the varieties most frequently consumed in Spain are the *barra* and the baguette, followed by wholemeal bread (21). Various studies and initiatives have demonstrated that it is possible to gradually reduce the salt content of bread without the consumer perceiving this (22-24). A collaboration agreement was signed in 2004 between the Spanish Agency for Food Safety and Nutrition (AESAN, now AECOSAN), the Spanish Confederation of Bakers (CEOPAN) and the Spanish Association of Manufacturers of Frozen Dough (ASEMAC), whereby said institutions made a commitment and, in four years, reduced salt content of common bread by 25%, reaching an average amount of 1.63 g/100 g product (25,26). Since 2008, the development of this salt content has not been evaluated. That evaluation in 2008 was done by determining chlorides. Currently, the method of reference is the determination of total sodium, so it was necessary to estimate the salt content in a subsample of pieces of bread by determining chlorides, in order to compare it to the salt content in 2008.

This study aimed to establish the mean salt content of common bread in Spain in 2014 and whether there was any change in salt content in bread in Spain since the reduction achieved in 2008.

METHODS

SAMPLING

It was necessary to collect a sample of loaves of bread representing the common bread available in Spain, which is administratively organized into autonomous communities. A calculation was carried out to determine the sample size necessary to obtain an estimate of the mean salt content in bread (measured in grams salt per 100 grams product), with an error of ± 0.1 g and α of 0.025. The calculation also accounted for a standard deviation of 0.36 for this mean value in a previous study evaluating salt content in bread. The result was a necessary sample size of 50. A design effect of 1.2 was applied, bringing the total samples needed in each Autonomous Community to 60. Therefore, the minimum sample size required was 60 x 19, or 1,140 samples.

In autonomous communities with multiple provinces, one or two provinces were selected by simple random sampling. The provinces of single-province communities and the autonomous cities of Ceuta and Melilla were also selected. In each province selected, sampling was carried out in the capital and at least two other municipalities. In each municipality, where possible, samples were acquired at three types of establishment: bakeries with on-site ovens, bakeries without on-site ovens, and food shops or small and medium grocery stores.

The bread purchased was the bread that is most consumed in Spain, comprising two main varieties: *barra* or similar and baguette or similar. Loaves of wholemeal bread, the third most consumed variety, were also purchased. The loaves were bought in bakeries with and without on-site workrooms and in supermarkets (27).

Having obtained the samples, these were kept in paper bags labelled with all identifying information on bread type, municipality and place of purchase. Within five days of purchase, the samples were transported to the laboratory, where they were frozen until the time of analysis. All samples were obtained in October and November 2014.

ANALYTICAL METHODS

The NaCl analysis of dried extracts was calculated based on sodium analysis (flame atomic absorption spectrophotometry [AAS]), as per the legislation in force, Regulation (EU) no. 1169/2011 of the European Parliament and of the Council, of

25 October 2011, on the provision of food information to consumers. For the analysis, first humidity was measured and then the calculated content of sodium does not take into account the humidity variation.

As the salt content in the previous 2008 study (800 bread loaves from all Spanish regions) was measured with chloride determination, to compare 2008 data with the current study a random subsample of 20 loaves (*barra* type) was used for chloride-based NaCl analysis. This subsample was analysed according to method AOAC 971.27, consisting in potentiometric titration with silver nitrate (AgNO3) specific for vegetable matter.

STATISTICAL ANALYSIS

A descriptive study was carried out for the type of bread analysed, the type of dough used and the type of establishment where the samples were obtained. Salt content (g/100 g product) was quantified and described according to the type of bread analysed, the type of dough used and the type of establishment. Student's t-test for independent samples and ANOVA were applied to assess whether there were significant differences in mean salt content according to type of bread, type of dough and type of establishment.

Mean salt content (g/100 g product) based on the 2014 chloride determination was compared to the value found in 2008. The Mann-Whitney U test was carried out to evaluate the statistical significance of the difference.

RESULTS

The analysis was carried out on 1,137 loaves of bread from all the autonomous cities and communities of Spain. Figure 1 shows the distribution of the loaves of bread by Autonomous City or Community.

Of the 1,137 samples, 527 (46.3%) were *barra*-type, 498 (43.8%) were baguette-type, and 112 (9.9%) were wholemeal-type; 82.7% of the loaves were made from fresh dough and 17.3%, from frozen dough. In addition, 43.7% were purchased in bakeries with on-site workrooms, 49.6% in bakeries without on-site workrooms, and 6.7% in supermarkets (Table I).

The mean salt content for the sample as a whole was 2.08 g/100 g. According to bread type, the mean salt content was the same in *barra*- and baguette-type bread (2.09 g/100 g product) while it was lower in wholemeal bread (1.99 g/100 g) (Table II). This was a statistically significant difference ($p = 0.005$). The mean salt content in bread made from fresh dough was 2.07 g/100 g, while in bread made from frozen dough it was 2.12 g/100 g. This was a statistically significant difference. Differences in salt content according to type of establishment were not statistically significant. In bakeries with on-site workrooms, mean salt content was 2.07 g/100 g; in bakeries without on-site workrooms it was 2.10 g/100 g; and in supermarkets it was 2.06 g/100 g.

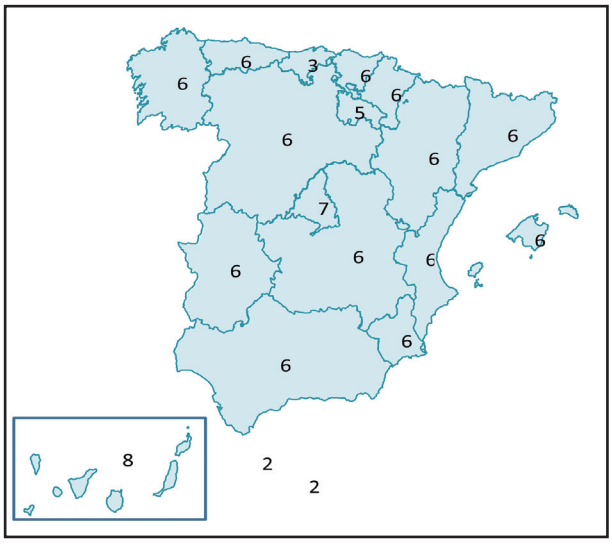

Figure 1.

Number of loaves of bread purchased in each Spanish Autonomous City and Community.

The mean salt content found through chloride determination in the subsample of 20 loaves from 2014 was 1.64 g/100 g product (SD: 0.42). The 2008 mean salt content was 1.63 g/100 g (SD: 0.37). The difference between these amounts was not statistically significant ($p = 0.428$). In addition, the mean salt content found through sodium determination in the same subsample of 20 loaves from 2014 was 2.09 g/100 g (SD: 0.22), similar to the salt content found in the whole sample.

DISCUSSION

Given that bread is a highly consumed food (not only in Spain) and that it contains a significant amount of salt, the impact of reformulation on salt is very relevant. The initiative run in Spain between 2004 and 2008 surpassed its proposed objectives (25). With this reduction yielding successful results, it was important to carry out a second evaluation due to the possibility that a "relaxation" may have occurred following the completion of AECOSAN's collaboration agreement with bread manufacturers, causing a rise in salt content.

The study's results include several important findings. Firstly, salt content is quite uniform across the different breads on sale in Spain. Only very slight differences were detected between different types of bread, especially the most popular varieties, *barra*-type and baguette-type breads. There was, however, a somewhat smaller amount of salt in wholemeal bread, probably due to the special characteristics of this type of bread, making it an even healthier option. A significant difference in salt content was also found between breads made from fresh and from frozen dough; nonetheless, the magnitude of this difference (0.04 g/100 g product) is so low that it has no practical repercussions, and

Table I. Description of the bread samples obtained

	Type of dough				Type of establishment					
	Fresh		Frozen		With on-site workroom		Without on-site workroom		Supermarket	
	n	%	n	%	n	%	n	%	n	%
Type of bread										
Barra	462	87.7	65	12.3	230	43.6	261	49.5	36	6.8
Baguette	379	76.1	119	23.9	211	42.4	252	50.6	35	7.0
Wholemeal	99	88.4	13	11.6	55	49.1	52	46.4	5	4.5
Total	940		197		496		565		76	

Table II. Salt content of bread in Spain, 2014 (g/100 g product)

	Median	Minimum	Maximum	Mean	SD	p
Total	2.10	0.30	3.33	2.08	0.32	
Type of bread						
Barra	2.13	0.55	3.20	2.09	0.30	
Baguette	2.10	0.88	3.33	2.09	0.30	
Wholemeal	2.00	0.30	3.20	1.99	0.47	0.005
Type of dough						
Fresh	2.10	0.30	3.20	2.07	0.33	
Frozen	2.10	0.88	3.33	2.12	0.26	0.041
Type of establishment						
With on-site workroom	2.10	0.73	3.05	2.07	0.31	
Without on-site workroom	2.13	0.30	3.33	2.10	0.31	
Supermarket	2.06	0.88	2.98	2.06	0.32	0.317

SD: standard deviation. p: p-value of statistical significance.

the medians in both types of bread are equal. Similarly, and as expected, salt content is similar between breads purchased from different establishments.

Despite the limitations of the analysis of this small sample for comparison with the 2008 data, it seems that since the achievement of salt content reduction of over 20% in 2008, there has been no rise to date, with salt content remaining at the amount achieved following that reduction. The fact that the two studies followed different methodologies owes to a change in the laboratory method of choice since the original study; however, this does not influence the comparison.

Reducing salt content is one of the main aims in improving the quality of nutritional composition of foods. Numerous initiatives by governments, public authorities and other institutions aim to make the foods available increasingly healthy, and the continuous reduction of salt content is an important part of this (24,28-32). Salt reformulation actions have also been carried out in Spain; these have yielded results in several food groups, including industrially produced bread (33).

One of the main issues with reducing salt content in foods is the risk that they may be less accepted by consumers due to changes in flavour. For this reason, manufacturers may express concern and resistance regarding reformulation. However, it has been demonstrated that by making changes gradually in terms of quantity and time, this problem can be bypassed effectively (22,34,35). This study's findings reinforce the fact that a gradual, significant reduction can be made with no adverse effects on the organoleptic properties of the product, and therefore, without increasing the likelihood of consumers potentially rejecting the food.

One limitation of this study is that the data of 2008 are not so complete as those of 2014, and we have not available data of the different types of bread. In addition, the method used in 2008 was chloride determination, which provides quite different estimations of salt content. However, for trend assessment purposes, the use of chlorides is valid. In addition, the small sample size in the subsample in 2014 that was analysed with chloride determination could be a limitation, but as the results of salt content in 2014 were really homogeneous, the sample size would be enough.

The different results found depending on the method used (chlorides or total sodium) must warn us about the consequences in several aspects. For example, the salt content in the nutritional

labelling could be quite different depending on the method, and the food composition tables and even the nutritional recommendations of salt intake could be affected as well.

The main conclusion from the study is that the quantity of salt in common bread (not including industrially produced breads) in Spain remains stable following a significant reduction.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Epidemiología y dietética

Evolución de la función renal en pacientes con enfermedad renal crónica con dieta restringida en proteínas suplementada con una mezcla de aminoácidos y cetoanálogos

Progression of renal function in patients with chronic kidney disease on a low-protein diet supplemented with aminoacids and ketoanalogues

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Resumen

Introducción: la enfermedad renal crónica (ERC) es un problema de salud pública. Se ha evaluado el uso de dietas con bajo contenido proteico suplementadas con cetoácidos y aminoácidos esenciales en diferentes estadios de la ERC.

Objetivo: observar la evolución de la función renal durante un año en pacientes adultos con ERC estadios 3b y 4 con dieta controlada en proteínas y suplementada con aminoácidos y cetoanálogos.

Métodos: estudio retrospectivo, descriptivo de una intervención. Intervención nutricional: aporte proteico-calórico: 0,4-0,6 g/kg/día y 30-35 kcal/kg/día más un comprimido de alfacetoanálogos (Ketosteril®)/5 kg de peso. Se evaluaron el estado nutricional, el filtrado glomerular (FG), la creatinemia, la uremia y la albuminemia a los 0, 3, 6, 9 y 12 meses. Se utilizó el programa SPSS versión 18 para el análisis estadístico.

Resultados: fueron estudiados 33 pacientes, un 67% de ellos masculinos, con un promedio de edad de 59,7 años (r: 24-87). Aporte proteico-calórico: 0,55 ± 0,20 g/kg/día y 34 ± 4,51 kcal/kg/día. Consumo de Ketosteril®: 11,87 comprimidos diarios (r: 9-14). FG inicial: 24,97 ± 6,64 ml/min/1,73 m^2, con un aumento significativo entre los tres y los 12 meses (25,51 ± 8,57 y 29,26 ± 10,33 ml/min/1,73 m^2; p = 0,006). Nitrógeno ureico: disminuyó significativamente a los seis meses respecto del valor inicial (p < 0,005). Índice de masa corporal: sin cambios significativos al inicio (26,63 ± 4,08 kg/m^2) y al final (26,78 ± 3,98 kg/m^2). Albuminemia: 3,53 ± 0,64 g/l y 4,00 ± 0,53 g/l al inicio y al final (p = 0,079).

Conclusión: los pacientes con ERC estadios 3b y 4 tratados con una dieta baja en proteínas y cetoanálogos mantuvieron el estado nutricional y el equilibrio mineral, mejoraron significativamente el FG y disminuyeron la uremia.

Palabras clave:

Dieta restringida en proteínas. Cetoanálogos. Insuficiencia renal crónica.

Abstract

Introduction: chronic kidney disease (CKD) is a public health problem. Low-protein diets supplemented with ketoacids and essential aminoacids have proved effective at different CKD stages.

Aim: to assess the progression of renal failure in adult patients with CKD stages 3b and 4 receiving a protein-controlled diet supplemented with aminoacids and ketoanalogues.

Methods: retrospective, descriptive intervention study. The nutritional intervention consisted of a protein/calorie intake of 0.4-0.6 g/kg/day and 30-35 kcal/kg/day plus a tablet of ketoanalogues (Ketosteril®)/5 kg weight. We assessed nutritional condition, glomerular filtration (GF) and creatinine, urea and albumin levels at 0, 3, 6, 9 and 12 months. SPSS version 18 was used for data statistical analysis.

Results: thirty-three patients were studied (67% male; mean age 59.7 years, r: 24-87). Protein/calorie intake was 0.55 ± 0.20 g/kg/day and 34 ± 4.51 kcal/kg/day. Ketosteril® intake was 11.87 tablets/day (r: 9-14). Initial GF was 24.97 ± 6.64 ml/min/1.73 m^2, showing a significant increase between three and 12 months (25.51 ± 8.57 and 29.26 ± 10.33 ml/min/1.73 m^2; p = 0.006). Urea nitrogen decreased significantly at six months compared with the initial level (p < 0.005). Body mass index did not change significantly (initial, 26. 63 ± 4.08 kg/m^2; after a year, 26.78 ± 3.98 kg/m^2). Initial and final albumin levels were 3.53 ± 0.64 g/l and 4.00 ± 0.53 g/l, respectively (p = 0.79).

Conclusion: a low-protein diet supplemented with ketoanalogues administered to patients with CKD stages 3b and 4 preserved nutritional condition and mineral balance, improved GF significantly and decreased urea levels.

Key words:

Low-protein diet. Ketoanalogues. Chronic kidney disease.

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INTRODUCCIÓN

La enfermedad renal crónica (ERC) es un problema de salud pública en aumento a nivel mundial (1), cuya prevalencia supera el 10% de la población. En los países con menores ingresos la ERC presenta un mayor incremento, mientras que en las poblaciones en riesgo de desarrollarla (con hipertensión arterial, síndrome metabólico y diabetes) supera el 50% (2,3).

Existe una fuerte asociación entre ERC y malnutrición calórico-proteica (MCP) y una correlación directa entre esta última y la morbimortalidad del paciente (4). Aunque la MCP es una condición poco apreciada en los inicios de la ERC, su prevalencia ronda el 20-25% y se incrementa a medida que la insuficiencia renal progresa, constituyéndose en un fuerte predictor de resultados adversos. La MCP se asocia con la activación de citoquinas pro-inflamatorias combinada con estados hipercatabólicos y descenso del apetito, entre otras causas (5). Esta alteración del apetito conduce a una ingesta calórico-proteica inadecuada que puede agravarse por restricciones en la dieta prescrita, más aún si el seguimiento y la supervisión del estado nutricional del paciente por parte del equipo de salud es inadecuado.

Muchos pacientes con ERC reducen espontáneamente el consumo de nutrientes a medida que disminuye la función renal (6). La falta de un aporte adecuado de energía puede deberse a múltiples causas tales como anorexia, náuseas, anemia, dietas restrictivas, comorbilidades asociadas, edad y factores psicosociales (6).

La manipulación de la ingesta proteica es el punto principal del tratamiento nutricional de pacientes con ERC y su objetivo es reducir la carga de toxinas urémicas para disminuir la toxicidad de la uremia y retrasar la indicación de ingreso a diálisis. Existe consenso respecto al beneficio de la restricción proteica progresiva que permita retrasar la progresión del fallo renal y la necesidad de diálisis, siempre que se provea un aporte adecuado de energía (7-9).

Durante décadas se utilizaron las dietas restringidas en proteínas para disminuir la acumulación de productos de desecho y la presencia de complicaciones como acidosis metabólica, alteración del metabolismo óseo-mineral, insulinorresistencia, proteinuria y deterioro de la función renal, así como para aliviar también los síntomas urémicos (10,11).

La dieta controlada en proteínas considera un aporte de 0,6-0,8 g/kg/día y un 50% de las proteínas deben ser de alto valor biológico (3). Dicha restricción en el aporte proteico debe ir acompañada de un adecuado aporte calórico para lograr un balance neutro de nitrógeno. Se recomiendan 35 kcal/kg/peso en menores de 60 años y 30 kcal/kg/peso en mayores de 60 años (12). Para lograr estos objetivos nutricionales, el paciente debe estar incorporado a un programa de educación dietética y realizar controles frecuentes por parte de un equipo especializado (13).

El síndrome urémico deriva de la retención de moléculas y toxinas resultantes del catabolismo de las proteínas exógenas. Una forma de proteger la función renal residual y ralentizar la progresión de la enfermedad renal es reducir la hiperfiltración e hipertrofia glomerular, reduciendo la ingesta proteica. La dieta muy baja en proteínas proporciona 0,3-0,6 g/kg/día, dependiendo del estadio de la enfermedad renal (3b a 5). La suplementación de dicha dieta con una mezcla de aminoácidos esenciales y cetoanálogos tiene como ventaja la reducción más marcada de los compuestos urémicos y, consecuentemente, de los síntomas urémicos. Además de mejorar la sensibilidad a la insulina, esta dieta permite controlar la presión arterial, reducir la proteinuria, corregir la acidosis metabólica y los trastornos óseos y minerales, enlentecer la progresión del daño renal, retrasar el inicio de la diálisis y preservar el estado nutricional (14,15).

A pesar de la importancia de la restricción proteica, este no es el único aspecto en el plan de cuidado del paciente con ERC. Otras características del tratamiento nutricional incluyen un aporte calórico adecuado, modificaciones del sodio y del fósforo, así como el origen animal o vegetal de la fuente proteica o lipídica. Los suplementos juegan un importante rol para obtener efectos nutricionales beneficiosos y seguros. En este sentido, los aminoácidos esenciales y los cetoácidos son los suplementos más utilizados en pacientes con ERC y regímenes de baja ingesta proteica para prevenir la malnutrición (16).

La suplementación de la dieta controlada en proteínas con aminoácidos esenciales y cetoanálogos permite que el paciente se beneficie con una mayor variedad y palatabilidad en la selección de alimentos, ya que no debería considerar que el 50% de las proteínas ingeridas sean de alto valor biológico. El logro de los objetivos de dicho tratamiento demanda un seguimiento individual o periódico por parte del equipo de salud, con nutricionistas capacitados en el área renal (17). Sin embargo, algunos autores plantean la necesidad de realizar más estudios para fortalecer las evidencias clínicas del impacto de los cetoanálogos y de las dietas restringidas en proteínas en el paciente con ERC (18).

El objetivo del presente estudio fue observar la evolución clínica de un grupo de pacientes con ERC en los estadios 3b y 4 seguidos durante un año y tratados con una dieta controlada en proteínas y suplementada con aminoácidos esenciales y cetoanálogos de aminoácidos esenciales.

MATERIAL Y MÉTODOS

DISEÑO DEL ESTUDIO

El estudio fue de tipo retrospectivo, descriptivo de una intervención de pacientes seguidos durante un año de tratamiento por ERC estadios 3b y 4. Se realizó en servicios de Nefrología de nueve ciudades de Argentina por profesionales que integran el grupo RIANA (Red Interdisciplinaria de Atención Nutricional Ambulatoria) de enero de 2015 a mayo de 2017. Se incluyeron pacientes adultos mayores de 21 años de edad con ERC que al momento del ingreso presentaron los estadios 3b o 4. Se constató que hubieran completado un año de seguimiento por parte de un equipo que garantizara la atención del paciente (un médico nefrólogo responsable del paciente y un nutricionista con asistencia semanal) (19). Se consideraron criterios de exclusión los pacientes con ERC en estadio 5, en tratamiento sustitutivo (hemodiálisis o diálisis peritoneal), oncológicos, inmunodeprimidos, embarazadas, mujeres en periodo de lactancia y aquellos que

no cumplieron con las indicaciones médicas y nutricionales, tales como controles y adherencia a la dieta propuesta.

El seguimiento nutricional consistió en adecuar un plan nutricional cuyo aporte de calorías se ajustara a los requerimientos del paciente, resultando en un aporte proteico de 0,4-0,6 g/kg/día más la incorporación de un comprimido de alfacetoanálogos de aminoácidos esenciales (Ketosteril® Fresenius-Kabi, Alemania) cada 5 kg de peso ideal. Junto con el plan de alimentación controlado en proteínas, el paciente recibió material educativo con menús hipoproteicos ejemplificados y cuantificados para combinar con alfacetoanálogos en el tratamiento de la ERC. Se realizaron seguimiento nutricional y control antropométrico semanal y control médico mensual.

Teniendo en cuenta los registros, las variables se estudiaron y analizaron a los 0, 3, 6, 9 y 12 meses.

Función renal

Se consideraron los siguientes indicadores: filtrado glomerular (FG), creatinemia (valores de referencia de creatinina: 0,7-1,3 y 0,6-1,1 mg/dl para hombres y para mujeres, respectivamente) y uremia (valores de referencia: 4,7-23,4 mg/dl). La estimación del FG (eFG) se realizó mediante la ecuación MDRD-4 (20).

Estado nutricional

Para la evaluación de esta variable se utilizaron los siguientes indicadores: índice de masa corporal (IMC) (peso [kg]/talla^2 [m]; valor normal: 18-25 kg/m^2), albúmina (valor de referencia: 3,4-5, 4 g/dl) y anemia (indicador: Hb < 11 g/dl).

Equilibrio mineral fosfocálcico

Para su evaluación, se utilizaron los siguientes indicadores: calcemia (valor de referencia: 8,5-10,5 mg/dl para hombres y mujeres) y fosforemia (valor de referencia: 2,5-5,6 mg/dl).

Equilibrio hidroelectrolítico

Se evaluaron sodio (136-146 mmol/l) y potasio (3,5-5, 1 mmol/l). Las determinaciones se realizaron con los siguientes métodos: Jaffé automatizado (creatinina), cinético UV automatizado (uremia y fósforo sérico), electroforesis (hemoglobina y albúmina), método colorimétrico automatizado (calcio sérico) y electrodo ion selectivo (potasio).

ANÁLISIS ESTADÍSTICO

El análisis de los datos obtenidos se realizó con el *software* SPSS versión 18. Se evaluó la normalidad de los datos y se expresaron como media y desviación estándar o mediana y rango intercuartílico, según correspondiera. Se compararon las medias al año y al inicio del estudio mediante la prueba t de Student pareada o la prueba de Wilcoxon de rangos signados, según correspondiera.

En cada uno de los cinco puntos de evaluación clínica, se compararon las medias de FG, IMC y de las concentraciones séricas de urea, potasio, calcio, fósforo y albúmina. Para las variables cuya distribución fue compatible con la normal se usó la prueba de ANOVA de medidas repetidas, mientras que para aquellas con distribución distinta de la normal se usó la prueba de Friedman. Cuando se encontró significancia estadística, la comparación de a pares *post hoc* se realizó a través de la prueba t de Student pareada o la prueba de Wilcoxon de rangos signados, según correspondiera, en ambos casos usando la corrección de Bonferroni.

RESULTADOS

Se estudiaron 33 pacientes con ERC. El 67% correspondió al sexo masculino y la edad promedio fue de 59,7 años (r: 24-87). Se realizó diagnóstico de glomerulopatía (n = 8), diabetes (n = 7), hipertensión (n = 5), vejiga neurogénica (n = 3), poliquistosis (n = 3), riñón senil (n = 6) y etiología desconocida (n = 1). Todos los pacientes sostuvieron una dieta con un aporte promedio de proteínas de 0,55 ± 0,20 g/kg/día y un aporte calórico de 34 ± 4,51 kcal/kg/día. En promedio, los pacientes consumieron 11,87 comprimidos de Ketosteril® por día (r: 9-14).

Los resultados correspondientes a FG y nitrógeno ureico (UN) se presentan en la tabla I. El FG al inicio del tratamiento fue 24,57 ± 6,64 ml/min/1,73 m^2, con un aumento significativo luego de un año (29,26 ± 10,33 ml/min/1,73 m^2; p = 0,006) (n = 33). La figura 1 muestra la evolución del FG a lo largo del año en las cinco

Tabla I. Filtrado glomerular y nitrógeno ureico en los cinco cortes estudiados

	Tiempo (meses)					
	0	**3**	**6**	**9**	**12**	**p***
FG	25,0 (22,6-27,4)	25,5 (24,4-26,6)	26,7 (25,7-27,8)	27,3 (26,2-28,5)	29,3† (27,8-30,7)	0,019
NU	108,4 (98,8-118,1)	86,7 (81,9-91,5)	80,9‡ (77,0-84,8)	81,7‡ (77,7-85,7)	82,6‡ (79,2-86,0)	0,002

*FG: filtrado glomerular (ml/min/1,73 m^2); NU: nitrógeno ureico (mg/dl). Los resultados se expresan como medias e intervalos de confianza del 95%. *Valor de p correspondiente a ANOVA de medidas repetidas. †Valor de p < 0,05 con respecto a tres meses. ‡Valor de p < 0,05 con respecto a cero meses.*

evaluaciones trimestrales. El aumento fue significativo entre los tres y los 12 meses (25,51 ± 8,57 y 29,26 ± 10,33; p = 0,006).

El nivel de la uremia disminuyó significativamente entre el valor del inicio (x = 95,97 ± 31,69 g/l) y el control final al año (77,03 ± 19,04 g/l) (p = 0,001). La figura 2 ilustra la evolución de la urea a lo largo del año en los cinco cortes estudiados. La diferencia fue significativa entre el inicio y los seis, nueve y 12 meses (p = 0,02, 0,038 y 0,012, respectivamente).

El IMC se mantuvo sin cambios significativos a lo largo del estudio (inicio: 26, 63 ± 4,08 kg/m^2; luego de un año: 26,78 ± 3,98 kg/m^2).

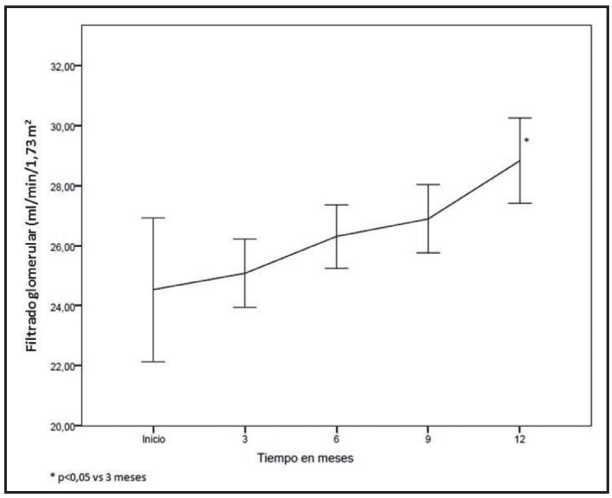

Figura 1.

Filtrado glomerular en los cinco cortes estudiados. Los resultados se expresan como medias e intervalos de confianza del 95%.

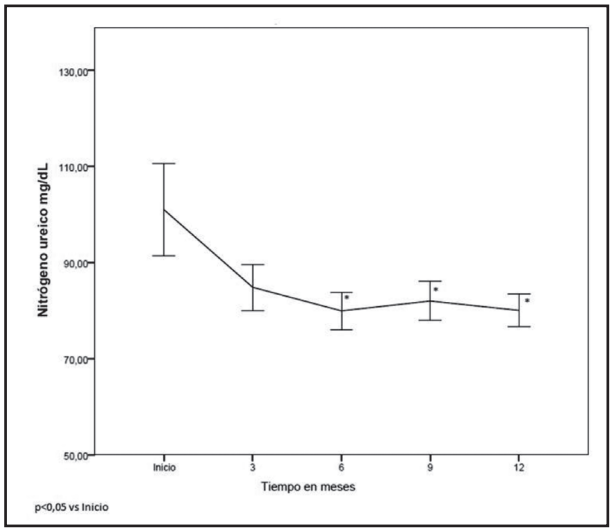

Figura 2.

Nitrógeno ureico en los cinco cortes estudiados. Los resultados se expresan como medias e intervalos de confianza del 95%.

El nivel de albuminemia fue 3,53 ± 0,64 g/l al inicio y 4,00 ± 0,53 g/l al final del estudio; sin embargo, la diferencia no fue significativa (p = 0,079).

No se observaron cambios significativos durante la revisión de resultados de Hb al inicio y al final (x: 11,28 ± 1,68 *versus* 11,81 ± 1,43 g/l). Tampoco se registraron cambios significativos en la calcemia inicial y final (x: 9,35 ± 0,60 y 9,12 ± 0,54 mg/dl) ni en la fosforemia (x: 4,3 ± 1,15 y 4,12 ± 0,60 mg/dl). Por su parte, el valor de la potasemia inicial fue 4,53 ± 0,46 mEq/l y 4,38 ± 0,45 mEq/l a los 12 meses (NS).

DISCUSIÓN

Numerosas revisiones y metaanálisis de los últimos años analizaron resultados que permitieron precisar la eficacia del uso de dietas con bajo contenido proteico suplementadas con cetoácidos y aminoácidos esenciales en diferentes grados de la ERC (5,11,12).

Nuestros resultados muestran un aumento significativo del FG, una disminución significativa de la uremia y mantenimiento de los valores de índice de masa corporal, albuminemia, sodio, fósforo y potasio.

Otros estudios mostraron que el uso de aminoácidos esenciales y cetoanálogos disminuyó la velocidad de progresión de la ERC en un importante número de pacientes. A diferencia del nuestro, incorporaron pacientes grados 3 a 5 (21). En un trabajo prospectivo, aleatorizado, doble ciego con placebo realizado en Nueva Delhi, India, en 34 pacientes en periodo de prediálisis se evaluó si una intervención con cetoanálogos y aminoácidos esenciales combinada con una dieta muy baja en proteínas *versus* una dieta con 0,6 g/kg/día más placebo retardaba la progresión de la ERC y mantenía el estado nutricional (14). Se demostró que en los pacientes que recibieron 0,3 g/kg/día de proteínas más una tableta de Ketosteril® durante nueve meses el FG se mantuvo sin cambios significativos (28,1 ± 8,8 antes y 27,6 ± 10,1 ml/min/1,73 m^2 al finalizar el estudio), mientras que en el grupo control disminuyó de 28,6 ± 17,6 a 22,5 ± 15,9 ml/min/1,73 m^2 (p = 0,015) (14). Cabe destacar que para sostener nutricionalmente una dieta muy baja en proteínas es necesario suplementarla con cetoanálogos y aminoácidos esenciales (22).

Una reciente revisión (15) incluye resultados de Subhramanyam y cols., quienes evaluaron un grupo de pacientes con ERC grados 3 a 5 con dieta baja en proteínas (0,6 g/kg/día) suplementada con una tableta de Ketosteril®/10 kg de peso y otro grupo con 0,3 g/kg/día de proteínas y una tableta de Ketosteril®/5 kg de peso. En el primer grupo, el *clearance* de creatinina aumentó significativamente mientras que la uremia disminuyó, como en nuestro caso. Estos autores no utilizaron el FG como parámetro de evaluación como se hizo en nuestro trabajo.

En otro estudio, pacientes con ERC grados 4 y 5 que recibieron Ketosteril® y dieta baja en proteínas mostraron un enlentecimiento del 57% en la tasa de progresión de la ERC (23).

También se han estudiado otros aspectos de la intervención con cetoanálogos en pacientes en prediálisis. Como en nuestro caso,

los autores hacen referencia en sus resultados al mantenimiento del estado nutricional en pacientes con dietas bajas o muy bajas en proteínas suplementadas con cetoanálogos, atribuyéndoles un efecto anabólico o anticatabólico, especialmente a leucina e isoleucina (18-26).

También se ha abordado el mantenimiento del equilibrio de minerales y proteínas séricas con este tratamiento dietético nutricional, mostrando, como en nuestro caso, que se pueden sostener los niveles de calcio, fósforo y albuminemia (15,26).

La selección estricta del paciente, el monitoreo nutricional y la consejería dietética con clínicos nefrólogos y nutricionistas que trabajen en contacto permanente junto con los pacientes para sostener la propuesta dietética se torna fundamental a largo plazo para obtener buenos resultados (15,17).

La debilidad de nuestro estudio es que se trata de un estudio retrospectivo descriptivo. La falta de un grupo control no permite diferenciar la fuerza de la intervención a través de una dieta baja en proteínas o la de los cetoanálogos. Sin embargo, la revisión bibliográfica permite inferir la importancia de los dos factores en la obtención de los resultados que mostramos.

En la mayoría de los estudios se mostró una disminución de la velocidad de la caída o mantenimiento del FG. En nuestro estudio hallamos una mejoría significativa que debería corroborarse con la incorporación de un mayor número de pacientes.

CONCLUSIÓN

En los pacientes con ERC grados 3b y 4 tratados con una dieta baja en proteínas y cetoanálogos se pudo mantener el estado nutricional y el equilibrio mineral, mejorar significativamente el FG y disminuir la uremia.

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Otros

Percepción y distorsión de la imagen corporal en bailarinas españolas en función del curso académico y de la edad

Perception and distortion of body image in Spanish women dancers based on academic year and age

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Resumen

Introducción: las bailarinas presentan un elevado riesgo de sufrir trastornos de la imagen corporal desde la etapa de formación.

Objetivo: analizar la percepción y distorsión de la imagen corporal en bailarinas en formación en función del curso académico y la edad.

Metodología: se evaluó a 298 bailarinas, con edades comprendidas entre 11 y 24 años, que cursaban entre 1º y 6º de Enseñanzas Profesionales. Se les solicitó que completaran el "test de siluetas para adolescentes" para poder valorar su percepción de la figura femenina y masculina, así como su imagen percibida e ideal, y sus índices de distorsión, insatisfacción y real-ideal.

Resultados: las participantes fueron más severas al valorar las figuras masculinas que las femeninas. Las bailarinas de los cursos inferiores, especialmente las de 1º, así como las de menor edad fueron quienes presentaron un mayor índice de distorsión y real-ideal, entendiendo que eran menos delgadas, pero considerando ideal estar más gruesas de como en realidad eran ($p < 0,001$). Respecto al índice de insatisfacción, se detectó un deseo de querer estar más delgadas, sin diferencias en función del curso o la edad ($p > 0,05$). Diez bailarinas presentaron un riesgo elevado de poder desarrollar desórdenes alimenticios.

Conclusiones: las bailarinas de los cursos iniciales y con menor edad se ven más gruesas de como están, quieren ser más delgadas de como se ven, pero están más delgadas de lo que les gustaría ser. Esto podría favorecer la aparición de trastornos de insatisfacción corporal.

Palabras clave:

Adolescencia. Desórdenes de la conducta alimentaria. Ejercicio.

Abstract

Introduction: young dancers are at a higher risk of developing body image distortion.

Objective: to analyze body image perception and distortion in dancer students based on academic year and age.

Methods: two hundred and ninety-eight women dancers between 11 and 24 years, who were studying between the 1st and 6th year of Professional Program, were evaluated. Dancers completed the "silhouette scale for adolescents" in order to determine their perception of the female and male figures, their perceived and ideal images, and the distortion, dissatisfaction and real-ideal indexes.

Results: participants were more severe with male figures than with female ones. Dancers of the lower courses, especially from the 1st year, and youngest showed the highest values in distortion and real-ideal indexes. They thought that they look like thicker than they are, but their ideal figure was thicker than they really were ($p < 0.001$). In relation to the dissatisfaction index, all dancers desired to be thinner, without differences based on academic year or age ($p > 0.05$). Ten dancers showed a high risk to develop an eating disorder.

Conclusions: dancers of the initial courses and youngest have a tendency to see themselves fatter than they are. They want to look thinner, but they are thinner than they would like to be. This could act as a trigger for developing body dissatisfaction.

Key words:

Teenage. Eating disorders. Exercise.

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INTRODUCCIÓN

Grogan (1) define la imagen corporal como "las percepciones, sentimientos y pensamientos de una persona acerca de su cuerpo". El concepto de belleza que maneja la sociedad termina incidiendo de manera directa en la manera en que las personas perciben su imagen corporal (2). La imagen corporal refleja la relación que los individuos tienen consigo mismos y la misma se va modificando conjuntamente con los cambios físicos de las personas (3). El entorno familiar, los medios y el entorno social son canales socioculturales fundamentales en la formación de los estereotipos ideales (4). Si bien el grupo social ejerce una importante influencia en el adolescente, el afán por alcanzar determinado estereotipo físico dependerá del valor que ellos le otorguen al físico (5).

La internalización, que se refiere al grado en que los ideales irreales a nivel físico son tomados como propios, también influye en la valoración personal (6). Es más común que suceda en la mujer y que esta presente una peor estima (7). El mayor predominio de la insatisfacción corporal femenina quizás se deba a que mientras se promueve un físico esbelto y musculoso para el hombre, alcanzar un cuerpo delgado y magro es lo que se espera en la mujer (8). La internalización por tener una delgada silueta termina incidiendo en la satisfacción corporal. No lograr la delgadez que promueve la cultura aumenta el riesgo de desarrollar trastornos de la imagen corporal (9). Heshmat y cols. (10) identificaron que hasta en un 40% de las mujeres adolescentes existía una distorsión entre la imagen real y la autopercibida.

La adolescencia es la etapa de mayor riesgo de sufrir trastornos de la imagen corporal. No está claro qué etapa dentro de este periodo es la más crítica. Mientras que algunas investigaciones apuntan a que el peligro es mayor al inicio de la misma (11,12), otras establecen que prevalece más al final de esta etapa (13,14). No obstante, en todas las etapas el objetivo es querer disminuir el peso corporal (15). También se ha encontrado que las maduradoras tempranas suelen presentar un peso corporal más elevado que sus pares (16), lo que les lleva a mostrar una mayor insatisfacción corporal y a tener una mayor predilección por estar delgadas (17). En un estudio se pudo determinar incluso que, si bien las niñas presentaban un menor índice de masa corporal (IMC) que los niños, su satisfacción corporal era menor (18).

El nivel de autoestima que presentan los individuos también ejerce cierto rol sobre la imagen corporal. En este sentido, se ha encontrado que los adolescentes, sobre todo en el caso de las niñas, se perciben más gruesas de lo que están, lo cual afecta a sus condicionantes psicológicos (19,20).

No existe una relación clara sobre la práctica de ejercicio físico y la imagen corporal en deportistas recreacionales en comparación con sujetos sedentarios (21,22). De hecho, se ha propuesto que aquellos deportistas que practican disciplinas donde el peso corporal cobra una gran importancia tienen una mayor prevalencia de trastornos de la conducta alimenticia (TCA) y trastornos de la imagen corporal (23). Dado que la danza es una disciplina artística-deportiva donde prevalece la composición corporal y el peso tienen una gran importancia, las bailarinas en edad de formación tienen elevados riesgos de sufrir trastornos de la imagen corporal por su edad, sexo y disciplina deportiva (24). Se ha encontrado que la danza es una disciplina con una incidencia importante de casos de bulimia, insatisfacción corporal y deseo de querer alcanzar la delgadez. Esto se debe a la gran importancia que tiene el aspecto físico en la valoración de su disciplina, unido a la predilección por el perfeccionismo (24). Incluso, aunque ellas consideren que su peso corporal es apropiado, existe una tendencia importante a querer realizar algún tipo de dieta para poder cambiar su silueta (25). Llevar una alimentación inapropiada y baja en calorías puede terminar afectando el normal funcionamiento del metabolismo basal (26) y puede dar lugar al desarrollo de la tríada femenina. En un grupo de bailarinas se pudo detectar que un 14% de ellas tenían amenorrea (27), mientras que en otra investigación se halló que un 12% de las bailarinas llegan a desarrollar TCA (28).

Aquellas bailarinas que aún no han iniciado su desarrollo biológico o aquellas que están iniciando este proceso presentan una menor aparición de síntomas bulímicos y preocupaciones por el peso corporal que sus pares (29). Siguiendo esta línea, otra investigación identificó que las participantes de los grupos de danza que se encuentran en cursos superiores suelen buscar con mayor frecuencia cambios en su peso corporal y suelen presentar con mayor frecuencia alteraciones en su alimentación para intentar adaptar su silueta al modelo pro-delgadez (30).

No obstante, son pocos los estudios que han comparado la incidencia del curso académico en las variables relacionadas con la imagen corporal en bailarinas jóvenes. Por todo ello, el objetivo de la presente investigación fue analizar la percepción y distorsión de la imagen corporal de bailarinas en formación en función del curso académico de danza y la edad de las participantes.

MATERIAL Y MÉTODOS

PARTICIPANTES

Se estudió a 298 bailarinas con edades comprendidas entre los 11 y los 24 años (media de edad: 16,24 ± 3,10 años), estudiantes de enseñanzas profesionales del Conservatorio Profesional de Danza de Murcia. La distribución de alumnas por curso fue la siguiente: 1º (n = 34), 2º (n = 43), 3º (n = 60), 4º (n = 71), 5º (n = 53), 6º (n = 37). Los criterios de inclusión fueron: a) ser mujer; b) no tener ningún TCA diagnosticado por profesionales médicos, siguiendo el criterio establecido por el *Manual diagnóstico y estadístico de los trastornos mentales* (DSM V) (31); c) haber comenzado sus estudios desde 1º en el Conservatorio Profesional de Danza; y d) asistir al menos al 80% de las sesiones.

DISEÑO DEL ESTUDIO

El Comité de Bioética institucional aprobó la ejecución de la investigación. También el cuerpo docente y directivo del Conservatorio consintió la realización del presente estudio. Se informó sobre la forma de proceder a los participantes y los tutores legales

en el caso de las menores de edad. Posteriormente, de forma voluntaria accedieron a firmar el consentimiento informado.

Las participantes autocumplimentaron el "test de siluetas para adolescentes" (TSA) de Maganto y Cruz (32). Este cuestionario tiene como objetivo poder conocer el grado de distorsión de la imagen corporal de las adolescentes, cuál es su nivel de insatisfacción corporal y conocer qué parámetro físico establece el individuo como ideal. El TSA está formado por ocho figuras masculinas y femeninas que muestran un aumento progresivo de la silueta corporal, pero no de la estatura. Existe una relación entre cada figura y un determinado IMC, siguiendo un patrón estadístico. Solamente los investigadores conocían esta información.

Se solicitó a las participantes que clasificaran cada una de las siluetas como delgadas, normales o gordas a fin de poder conocer qué parámetro estético utilizan las bailarinas para evaluar tanto su propia silueta como la de las demás personas.

Posteriormente, a fin de poder conocer la valoración de su imagen corporal, se les pidió que marcaran la figura que más se asemejaba a su silueta ($imagen_{percibida}$). Para conocer sus preferencias, se les pidió que indicaran qué figura consideraban como ideal ($imagen_{ideal}$).

Para el establecimiento de la silueta real que le correspondía a cada participante ($imagen_{real}$) se calculó el IMC real de la misma. Para ello se valoraron la talla y el peso corporal, siguiendo los criterios establecidos por la *International Society for the Advancement of Kinanthropometry* (ISAK) (33). Las medidas fueron realizadas por un antropometrista ISAK nivel 4, midiéndose por duplicado y realizando la media de ambos valores si las diferencias entre ellas eran menores del 1%, y haciendo una tercera medida y calculando la mediana en caso de que se superara este porcentaje. Una vez obtenidos el peso y la talla de cada participante, se calculó el IMC con la fórmula IMC (kg/m^2) = peso (kg)/talla (m^2). Para la valoración antropométrica se estableció la temperatura de la sala de valoración en 25 °C y se solicitó a las bailarinas que evitaran la realización de cualquier tipo de ejercicio y las comidas pesadas durante las 24 horas previas a la valoración.

Adicionalmente, se comparó la clasificación de la figura que las bailarinas seleccionaron como propia con la clasificación que ellas habían realizado de esta misma figura.

A partir de estos datos se calculó el índice de distorsión de la imagen corporal. Para ello se restó a la $imagen_{percibida}$ la $imagen_{real}$. Si el índice de distorsión era igual a 0, significaba que no existía distorsión de la imagen corporal en la participante, valores negativos referían que la bailarina se veía más delgada de lo que estaba y valores positivos, lo contrario. Si la bailarina obtenía puntuaciones mayores a 3 se consideró que presentaba un altor riesgo de desarrollar TCA, de acuerdo a los parámetros establecidos en el TSA (32).

Para poder conocer cuánto deseaba la bailarina poder cambiar su figura corporal se calculó el índice de insatisfacción. Para hallarlo, se restó la $imagen_{percibida}$ a la $imagen_{ideal}$. Un índice de insatisfacción igual a 0 significó que la bailarina no deseaba modificar su figura. Cuando el índice mostró valores positivos se consideró que a la participante le gustaría verse más delgada, mientras que un valor negativo revelaba que le gustaría aumentar su peso corporal. Se consideró que aquellas bailarinas con una puntuación mayor de 3 tenían un riesgo elevado de sufrir TCA (32).

Por último, se calculó el índice real/ideal. El mismo se obtuvo a partir de la diferencia entre la $imagen_{real}$ y la $imagen_{ideal}$. Si el índice era igual a 0, significaba que ambas figuras coincidían. Si la relación era positiva, la bailarina consideraba como ideal una figura con un IMC menor que el suyo, mientras que valores negativos reflejaban lo contrario.

ANÁLISIS ESTADÍSTICO

La distribución de los datos fue inicialmente valorada mediante el test de normalidad de Kolmogorov-Smirnov. Puesto que las variables seguían una distribución normal, se realizó un análisis estadístico en base a pruebas paramétricas. Para la obtención de los resultados se realizó una estadística descriptiva con la obtención de los valores medios y desviación típica. Un análisis ANOVA de un factor fue realizado para establecer las diferencias en cada una de las variables analizadas en función del curso académico. El nivel de significación fue establecido *a priori* a $p < 0,05$. En caso de encontrar un efecto significativo, se realizó una comparación por pares usando la corrección de Bonferroni para comparaciones múltiples con un criterio de significación ajustado a $p < 0,017$. Para conocer el coeficiente de correlación entre la edad y las variables de imagen corporal se utilizó el coeficiente de correlación de Pearson. El análisis estadístico se realizó con el programa estadístico Statistical Package for the Social Sciences (SPSS), versión 21.0.

RESULTADOS

En la tabla I se encuentran los valores descriptivos de edad y variables antropométricas en función del curso académico.

Tabla I. Variables descriptivas en función del curso académico

	1º (n = 34)	2º (n = 43)	3º (n = 60)	4º (n = 71)	5º (n = 53)	6º (n = 37)	Valor de significación (F y p)
Edad (años)	13,2 ± 1,3	14,7 ± 2,0	15,4 ± 1,8	16,6 ± 2,3	17,3 ± 1,8	18,0 ± 1,2	F = 36,3; p < 0,001
Peso (kg)	48,9 ± 7,4	51,9 ± 7,9	52,2 ± 7,4	55,2 ± 8,6	54,3 ± 5,9	54,3 ± 6,1	F = 4,2; p < 0,001
Talla (cm)	156,8 ± 7,0	158,6 ± 5,5	160,6 ± 6,9	162,5 ± 6,8	160,5 ± 6,1	161,8 ± 5,4	F = 4,7; p < 0,001
IMC (kg/m^2)	19,9 ± 3,3	20,6 ± 2,5	20,2 ± 2,0	20,8 ± 2,5	21,0 ± 1,7	20,7 ± 1,8	F = 1,6; p = 0,17

Se encontraron diferencias significativas para la edad, el peso y la talla, mostrando en todos los casos las bailarinas de los cursos inferiores valores menores a los de las bailarinas de los cursos superiores. Para la edad se encontraron diferencias significativas al comparar por pares todos los cursos, a excepción de 2º con 3º, 4º con 5º y 5º con 6º ($p < 0,05$). Se hallaron diferencias significativas para el peso corporal en las alumnas de 1º en relación con las de 4º, 5º y 6º ($p < 0,05$). La talla corporal varió significativamente entre las alumnas de 1º y las de 4º y 6º, y entre las de 2º y las de 4º ($p < 0,05$). En cuanto al IMC no se detectaron diferencias significativas en función del curso académico. Además, se encontró una relación lineal positiva estadísticamente significativa al correlacionar la edad de las bailarinas con el curso académico ($r = 0,6$; $p < 0,001$), peso ($r = 0,3$; $p < 0,001$), talla ($r = 0,2$; $p = 0,001$) e IMC ($r = 0,3$; $p < 0,001$).

La valoración de cada una de las figuras en función del curso académico se puede apreciar en la tabla II. En términos generales, se observó que las bailarinas fueron propensas a ser menos severas con las figuras femeninas que con las masculinas. La gran mayoría marcó a las primeras tres figuras como delgadas para ambos sexos. En las figuras tercera y cuarta, fue mayor la tendencia a clasificar como delgada la figura femenina y como normal la silueta masculina. En la quinta figura, prevaleció la valoración de normalidad en la figura femenina y gruesa para la masculina. Para la sexta figura hubo una mayor tendencia a clasificar la figura masculina como gruesa en comparación con la femenina. Casi todas las bailarinas clasificaron como gruesas las figuras séptima y octava, independientemente de si la imagen era masculina o femenina.

En la tabla III se presenta la valoración de la figura corporal que realizan las bailarinas de las siluetas que han marcado como aquella que las representa. Predominó la clasificación de normalidad para todos los cursos.

En la tabla IV se pueden apreciar los valores descriptivos para $imagen_{real}$, $imagen_{percibida}$ e $imagen_{ideal}$ y los índices de distorsión, insatisfacción y real/ideal obtenidos a través del TSA. Se encontraron diferencias significativas para la $imagen_{real}$ en función del curso académico ($F = 2,454$; $p < 0,001$), observándose que las bailarinas de 1º presentaban una $imagen_{real}$ significativamente más delgada que las de 5º ($p < 0,001$). Al correlacionar la edad de las bailarinas con la imagen real se encontró una relación directa estadísticamente significativa ($r = 0,3$; $p < 0,001$). No se encontró una diferencia significativa del ANOVA para la $imagen_{percibida}$ y la $imagen_{ideal}$ en función del curso académico ni una correlación estadísticamente significativa entre la edad y estas variables ($p > 0,05$).

Respecto al índice de distorsión, se halló un efecto significativo del curso académico sobre esta variable ($F = 3,084$; $p < 0,001$). En casi todos los cursos académicos se pudo apreciar que este índice era positivo, a excepción de 5º y 6º, donde la tendencia fue la opuesta. Las bailarinas de 1º mostraron un índice de distorsión

Tabla II. Porcentajes de clasificación para cada una de las figuras en función del curso académico

Curso académico		1		2		3		4		5		6		7		8	
		H	M	H	M	H	M	H	M	H	M	H	M	H	M	H	M
1 (n = 34)	Delgada	100	100	97,1	97,1	67,6	82,4	5,9	14,7	0	0	0	0	0	0	0	0
	Normal	0	0	2,9	2,9	32,4	17,6	91,2	82,4	85,2	91,2	8,8	20,6	0	0	0	0
	Gorda	0	0	0	0	0	0	2,9	2,9	14,7	8,8	91,2	79,4	100	100	100	100
2 (n = 43)	Delgada	100	100	100	100	65,1	88,4	9,3	20,9	0	2,3	0	0	0	0	0	0
	Normal	0	0	0	0	34,9	11,6	88,4	79,1	81,4	88,4	11,6	27,9	0	0	0	0
	Gorda	0	0	0	0	0	0	2,3	0	18,6	9,3	88,4	72,1	100	100	100	100
3 (n = 60)	Delgada	100	100	100	98,3	76,7	88,3	11,7	15	1,7	3,3	1,7	0	1,7	0	1,7	0
	Normal	0	0	0	1,7	23,3	11,7	88,3	85	90	83,3	20	20	1,7	0	0	0
	Gorda	0	0	0	0	0	0	0	0	8,3	13,3	78,3	80	96,7	71,7	98,3	100
4 (n = 71)	Delgada	100	98,6	100	98,6	77,5	81,7	21,1	21,1	2,8	0	1,4	1,4	1,4	1,4	1,4	1,4
	Normal	0	0	0	0	22,5	16,9	74,6	76,1	87,3	85,9	12,7	25,3	2,8	0	1,4	0
	Gorda	0	1,4	0	1,4	0	1,4	4,2	2,8	9,9	14,1	85,9	73,2	95,8	98,6	97,2	98,6
5 (n = 53)	Delgada	100	100	100	100	84,9	90,6	20,9	26,4	13,2	13,2	1,9	0	1,9	0	1,9	0
	Normal	0	0	0	0	15,1	9,4	79,2	71,7	77,4	79,2	7,5	26,4	0	0	0	0
	Gorda	0	0	0	0	0	0	0	1,9	9,4	7,5	90,6	73,6	98,1	100	98,1	100
6 (n = 37)	Delgada	100	100	100	100	83,8	81,8	10,8	27	0	0	0	0	0	0	0	0
	Normal	0	0	0	0	15,2	18,9	89,2	70,3	78,5	83,8	13,5	13,5	2,7	2,7	0	0
	Gorda	0	0	0	0	0	0	0	2,7	21,6	15,2	86,5	86,5	97,3	97,3	100	100

H: hombre; M: mujer.

Tabla III. Clasificación figura percibida en función del curso académico

	1 (n = 34)	2 (n = 43)	3 (n = 60)	4 (n = 71)	5 (n = 53)	6 (n = 37)	Total
Delgada	2 (5,9%)	4 (9,3%)	8 (13,3%)	8 (11,3%)	12 (22,6%)	6 (14,6%)	40 (13,4%)
Normal	30 (88,2%)	33 (76,7%)	41 (68,3%)	50 (70,4%)	36 (67,9%)	28 (73,2%)	218 (73,2%)
Gorda	2 (5,9%)	6 (14,0%)	11 (18,3%)	13 (18,3%)	5 (9,4%)	3 (12,2%)	40 (13,4%)

Tabla IV. Imagen corporal de las bailarinas en función del curso académico

	1 (n = 34)	2 (n = 43)	3 (n = 60)	4 (n = 71)	5 (n = 53)	6 (n = 37)	Valor de significación (F y p)
$Imagen_{real}$	3,76 ± 1,63	4,28 ± 1,70	4,07 ± 1,49	4,44 ± 1,61	4,79 ± 1,25	4,46 ± 1,30	F = 2,454; p = 0,034
$Imagen_{percibida}$	4,53 ± 7,48	4,79 ± 8,33	4,51± 1,02	4,62± 0,82	4,63 ± 0,79	4,39 ± 0,81	F = 1,062; p = 0,381
$Imagen_{ideal}$	4,12 ± 0,59	4,23 ± 0,47	4,09 ± 0,61	4,06 ± 0,70	4,15 ± 0,63	4,18 ± 0,71	F = 0,522; p = 0,759
Índice de distorsión	0,76 ± 1,33	0,51 ± 1,40	0,44 ± 1,24	0,18 ± 1,19	-0,16 ± 1,21	-0,07 ± 0,22	F = 3,084; p = 0,010
Índice de insatisfacción	0,41 ± 0,61	0,56 ± 0,67	0,42 ± 0,74	0,56 ± 0,73	0,48± 0,64	0,22± 0,81	F = 1,433; p = 0,212
Índice real/ideal	-0,35 ± 1,54	0,05 ± 1,7	-0,02 ± 1,4	0,38 ± 1,54	0,64 ± 1,26	0,28± 1,31	F = 2,533; p = 0,028

significativamente mayor que las bailarinas de 5º ($p < 0,001$). En la misma línea, se encontró una relación inversa entre la edad y el índice de distorsión de las bailarinas ($r = -0,3$; $p < 0,001$). Además, de acuerdo a la puntuación de este índice, diez bailarinas presentaron riesgo de desarrollar TCA. Una de ellas se encontraba en 2º (2,94%), dos en 3º (4,7%), cuatro en 4º (5,63%), una en 5º (1,9%) y dos en 6º (5,4%).

En el índice de insatisfacción se detectó que todos los cursos académicos presentaron valores positivos, es decir, consideraban apropiado estar más delgadas de cómo se percibían. No obstante, no se encontró un efecto significativo del curso académico sobre esta variable. Tampoco se halló una correlación significativa entre la edad y este índice ($p > 0,05$). Además, no se encontraron casos de bailarinas con probabilidad de desarrollar un TCA de acuerdo a los valores de referencia.

En el índice real/ideal también se encontró un efecto significativo del curso académico sobre este parámetro ($F = 2,533$; $p < 0,001$). Las bailarinas de 1º mostraron valores negativos en esta variable, lo que significa que veían como ideal un IMC mayor del suyo propio. Por su parte, las participantes de 2º y 3º mostraron un valor de cero, es decir, querían ser exactamente como eran en realidad. Las bailarinas de 4º en adelante tuvieron valores positivos, es decir, veían como ideal figuras con un menor IMC del que en realidad tenían. Para este índice se pudieron detectar diferencias significativas entre las alumnas de 1º y 5º ($p < 0,001$). También se halló una correlación directa entre la edad de las bailarinas y el índice real/ideal ($r = 0,28$; $p < 0,001$).

DISCUSIÓN

El objetivo de esta investigación fue estudiar la distorsión de la imagen corporal en bailarinas en etapa de formación en función del curso académico en el que se encontraban y su edad. Entre los principales hallazgos destacan las diferencias encontradas en el índice de distorsión entre los cursos iniciales comparados con los cursos superiores, así como una correlación inversa entre la edad y el índice de distorsión. Esto supone que las bailarinas de menor edad y curso académico creían tener un mayor IMC del que realmente tenían, mientras que las bailarinas que se encontraban cursando los cursos superiores y/o tenían mayor edad ajustaban mejor su autopercepción al peso corporal que realmente presentaban. Por tanto, se puede apreciar un mayor grado de alteración respecto a la imagen autopercibida en quienes se encuentran iniciando la adolescencia. Esto coincide con lo investigado por Esnaola (34), quien concluyó que, como consecuencia de los cambios que sufren los individuos durante la pubertad, terminan adquiriendo cierto grado de madurez psicológica. Estos resultados también podrían deberse a que las alumnas de mayor edad llevan más tiempo en el mundo de la danza y, por tanto, han podido incorporar mayores conocimientos sobre cuál es su físico real y también el físico esperado como bailarinas (35). Sin embargo, en otra investigación se encontró que las bailarinas con una formación superior tienden a tener un mayor afán por alcanzar un cuerpo esbelto y a presentar TCA (30). Es contradictoria la evidencia vigente sobre en qué momento se alcanza

el mayor descontento físico, habiendo pocos estudios realizados en danza. Algunos autores consideran que es mayor el riesgo al aproximarse a la adultez (14), mientras que otros investigadores concluyeron que la adolescencia es el periodo de mayor riesgo para desarrollar trastornos de la imagen corporal (11,12). Es por esto que se requiere de mayores investigaciones que analicen la relación entre el índice de distorsión, el curso académico y la edad de las bailarinas.

Otro de los hallazgos de la presente investigación fueron los relacionados con el índice real/ideal. Las participantes de los cursos inferiores y con menor edad determinaron como ideal figuras con un IMC mayor o similar del que en realidad presentaban, mientras que las de los cursos superiores y con mayor edad marcaban como ideal estar más delgadas. Debido a que no se encontraron diferencias significativas en la imagen ideal en función del curso académico ni de la edad de las participantes, los resultados detectados en el índice real/ideal responden a un incremento progresivo de la imagen real con el paso de los años. La imagen real se establece con la relación de peso y talla, por lo que las diferencias encontradas en las participantes en función del curso académico y de la edad podrían estar influenciadas por la existencia de la maduración biológica de las bailarinas analizadas al encontrarse las mismas en edad de desarrollo (36). No en vano, en la presente investigación se encontró una relación positiva y significativa entre la edad de las participantes y el IMC, lo que respalda esta teoría.

En relación a la preferencia existente en los cursos superiores y entre las bailarinas de más edad a estar más delgadas de lo que en realidad estaban, los resultados son acordes a lo encontrado en estudios previos realizados en bailarinas y practicantes de deportes estéticos (23,24). Esto podría deberse a que las bailarinas de mayor edad y de los cursos superiores son las que se encuentran practicando danza desde hace más tiempo y las que mayor presión tienen por alcanzar el profesionalismo. En esta línea, estudios previos han señalado que la insatisfacción corporal es elevada cuando la apariencia y el peso corporal son determinantes (23,24). Dicho estrés podría favorecer un desarrollo elevado de perfeccionismo y exigencia, favoreciendo la aparición de TCA (24,30). Sin embargo, debido a la escasa evidencia encontrada sobre esta temática, resultaría de suma utilidad que futuros estudios se centren en estudiar la relación entre dichos parámetros.

No se encontró en las bailarinas un elevado índice de insatisfacción, hallándose en todas las participantes una tendencia similar, sin importar su curso académico ni su edad, a desear estar más delgadas. Estos resultados no resultan sorprendentes, ya que es sumamente común encontrar en la mujer una tendencia hacia la reducción de su peso corporal (15). Estudios previos determinaron que, en cierta medida, esto se debe a que se espera que ellas puedan alcanzar un cuerpo delgado y magro (8). No alcanzar este parámetro establecido puede provocar que las mujeres desarrollen insatisfacción corporal y trastornos de la imagen corporal, independientemente de su edad (2,9). Adicionalmente, la presión que ejerza el entorno de las bailarinas puede terminar agravando este deseo de querer conseguir un cuerpo delgado (4). A su vez, una fuerte identificación como bailarina eleva los riesgos de que se vea alterada la valoración corporal (37). Todo esto alcanzaría a repercutir en quienes practican danza, por lo que podría provocar una mayor persecución por alcanzar el estereotipo ideal establecido para esta disciplina (38). De hecho, investigaciones previas han encontrado una menor preocupación por el peso corporal en aquellas bailarinas que no habían madurado biológicamente (29). En esta misma línea, otro estudio detectó que las bailarinas con mayor formación en danza solían buscar con mayor asiduidad alterar su peso corporal (30). No obstante, los grados de distorsión mostrados por la presente muestra no revelaron una posible aparición de TCA según los criterios establecidos por los autores del test (32).

Otro dato de interés de la presente investigación fue que diez personas de la muestra analizada mostraron un índice de distorsión elevado, pudiendo ser categorizadas con posible riesgo de padecer TCA, de acuerdo al baremo creado por los autores del TSA (32). Este dato concuerda con otro estudio, el cual detectó que en dicha población es frecuente encontrar trastornos de la imagen corporal y TCA (24). Adicionalmente, un metaanálisis concluyó que los TCA en esta población suelen prevalecer en el 12% de las bailarinas (28). Incluso, en un 14% de las bailarinas suelen aparecer alteraciones de su ciclo menstrual (27).

El bajo número de bailarinas con posible riesgo de desarrollar TCA podría estar relacionado con que son mujeres que aún se encuentran en el proceso formativo; por tanto, quizás el nivel de exigencia al cual están siendo sometidas no sea tan estricto como ocurre a nivel profesional, lo cual favorece en cierta medida que no se dispare la prevalencia de participantes con posible riesgo de desarrollar TCA (39). Un grupo de investigadores encontró que la prevalencia de TCA en bailarinas suele reducirse a medida que ellas van creciendo (30). Por otra parte, en otra investigación se halló que uno de los factores que termina condicionando la aparición de TCA es el ambiente y grado de aceptación que exista en el centro académico de danza en torno a la delgadez (35,28). De todos modos, en los centros de formación de bailarinas es sumamente importante instruir adecuadamente al personal docente. Torres-McGehee y cols. (40) encontraron que quienes suelen trabajar en dichos centros presentan un nivel de conocimiento insuficiente para poder identificar de forma anticipada los TCA en el alumnado. Es por esto que sería sumamente importante educar desde los inicios a las bailarinas sobre cuál es el peso corporal adecuado para su rendimiento deportivo. No obstante, se ha de tener en cuenta que solo se consideró la insatisfacción y distorsión de la imagen corporal de las bailarinas para predecir el potencial riesgo de desarrollar TCA, cuando la aparición de este trastorno depende de numerosos factores (25). Por tanto, son recomendables más estudios en bailarinas de diferentes edades que evalúen los diferentes factores de riesgo para sufrir un TCA.

A la hora de analizar la clasificación de las figuras se pudo apreciar que en la mayoría de los casos la respuesta fue apropiada al IMC de la silueta y parecida para ambos sexos, pudiendo deberse las diferencias a los diferentes roles que marca el modelo pro-delgadez para los hombres y las mujeres (2). No obstante, la mayoría de las bailarinas eligieron como propia una figura que previamente habían clasificado como normal, a pesar de que según su IMC eran delgadas. Esta diferencia entre la clasificación

inter e intrasujetos quizás responda a que las bailarinas se ven influenciadas por los patrones estéticos, lo que conlleva a que se exijan a sí mismas más por alcanzar un cuerpo magro y atractivo que al resto (2,4). A su vez, otro de los factores que podrían explicar esto es que tienen un elevado grado de internalización por un físico delgado (6,9). Cuando la internalización por alcanzar un cuerpo fino es elevada, aumenta el riesgo de que desarrollen insatisfacción corporal y TCA (8,23,24).

En cuanto a las limitaciones con las cuales contó la presente investigación, al emplear una investigación de corte transversal no se pudo valorar cómo evolucionaron los parámetros examinados en función del tiempo. Aplicar un estudio de carácter longitudinal podría ser de utilidad para dilucidar cómo se comportan las variables analizadas a medida que transcurre el tiempo. Una segunda limitación se debe a que resulta difícil poder determinar el nivel de veracidad con el cual las bailarinas contestaron al cuestionario, a pesar de que la participación fue voluntaria. Como tercer aspecto, cabe destacar que son numerosos los factores que inciden en la aparición de TCA. En la presente investigación solo se evaluó la percepción y distorsión de la imagen corporal y no se utilizaron otros instrumentos, por lo que los resultados sobre este parámetro deben ser tomados con cautela.

En conclusión, se pudo observar que las bailarinas de los cursos iniciales y menor edad se veían más gruesas de lo que realmente estaban. Asimismo, también fueron estas quienes presentaron un menor peso corporal. En consecuencia, esto podría estimular una preocupación excesiva por su imagen corporal, favoreciendo la aparición de una insatisfacción corporal y alteraciones en su alimentación. De todos modos, el número de personas identificadas con riesgo potencial de poder llegar a desarrollar TCA fue bajo. Por todo esto, resulta conveniente comenzar a educar desde edades tempranas a las bailarinas sobre cuál es la imagen corporal apropiada para maximizar su rendimiento sin tener que sacrificar su salud, y que a su vez sea compatible con lo establecido dentro de la exigencia profesional. El trabajo realizado contribuye a vislumbrar la valoración de la imagen corporal en las bailarinas y ayuda a poder identificar de forma temprana a aquellas bailarinas con riesgo de desarrollar TCA.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Otros

Cachexia in hospitalized patients with heart failure

Caquexia en pacientes con insuficiencia cardiaca hospitalizados

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Abstract

Aims: to evaluate cachexia prevalence in hospitalized heart failure (HF) patients by comparing two methods for diagnosing cachexia and alterations in each component involved in its diagnosis.

Method: a cross-sectional study, involving patients diagnosed with HF and admitted between April and August 2015 to a public hospital in the Brazilian Northeast. Cardiac cachexia was defined using the Cachexia Consensus criteria (Washington, DC), which defines cachexia as ≥ 5% unintentional weight loss in the previous 12 months or a body mass index (BMI) ≤ 20.0 kg/m², in combination with at least two of the following criteria: fatigue, anorexia, low hand grip strength, low muscle strength, and biological alterations (hemoglobin < 12 g/dl, albumin < 3.2 g/dl, and PCR ≥ 5 mg/dl), and for comparative purposes a diagnostic criterion which considers weight loss ≥ 6% in at least six months as a cachexia diagnosis.

Results: one hundred and fifty-six individuals were evaluated, with an average age of 59.1 (± 15.3). Cachexia prevalence was 37.2% and associated with a low BMI ($p < 0.001$), low muscle mass ($p < 0.001$), reduced ejection fraction ($p = 0.005$), hypoalbuminemia ($p = 0.040$), and anemia ($p = 0.002$). Among the diagnostic components, the greatest alterations were observed in relation to fatigue (88.2%), anorexia (72.1%) and weight loss (61.7%).

Conclusions: the high prevalence of diagnosed cachexia indicates that this condition is common and is associated with poor nutritional state and clinical condition.

Key words:

Cachexia. Heart failure. Nutritional status.

Resumen

Objetivos: evaluar la prevalencia de caquexia en pacientes con insuficiencia cardiaca (IC) hospitalizados comparando dos métodos de diagnóstico de la caquexia, así como analizar los factores asociados a la caquexia y las alteraciones de cada componente involucrado en su diagnóstico.

Métodos: estudio transversal en pacientes con diagnóstico de IC hospitalizados durante el periodo de abril a agosto de 2015 en un hospital público en el noreste brasileño. La caquexia cardiaca se definió utilizando los criterios de consenso sobre la caquexia (Washington, DC), que definen la caquexia como una pérdida no intencionada de peso ≥ 5% en los últimos 12 meses o un índice de masa corporal (IMC) ≤ 20,0 kg/m², asociados a, al menos, dos de los siguientes criterios: fatiga, anorexia, baja fuerza de asimiento manual, baja masa muscular y cambios bioquímicos (hemoglobina < 12 g/dl, albúmina < 3,2 g/dl y PCR ≥ 5 mg/dl). Para fines comparativos se utilizó otro criterio que considera como diagnóstico de caquexia la presencia de pérdida de peso ≥ 6% en al menos seis meses.

Resultados: fueron evaluados 156 individuos, con una media de edad de 59,1 (± 15,3) años. La prevalencia de caquexia fue del 37,2% y se mostró asociada a IMC bajo ($p < 0,001$), baja masa muscular ($p < 0,001$), fracción de eyección reducida ($p = 0,005$), hipoalbuminemia ($p = 0,040$) y anemia ($p = 0,002$). Entre los componentes diagnósticos, las mayores alteraciones fueron observadas en relación a la fatiga (88,2%), la anorexia (72,1%) y la pérdida de peso (61,7%).

Conclusiones: la elevada prevalencia de caquexia diagnosticada indica que esta condición es común y está asociada con un estado nutricional y una condición clínica peores.

Palabras clave:

Caquexia. Insuficiencia cardiaca. Estado nutricional.

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INTRODUCTION

Heart failure (HF) is a progressive syndrome with high morbidity and mortality, characterized by cardiac dysfunction, which causes inadequate blood supply to meet metabolic and tissue needs, and presenting survival rates and losses in years of life which are equally as poor as those associated with cancer (1,2). Cardiac cachexia is a grave condition that affects patients with HF, involving a metabolic and neuroendocrine syndrome marked by an exacerbated inflammatory state (3).

Various definitions are proposed for cardiac cachexia, resulting in a prevalence which varies from 10 to 60%, according to the diagnostic criterion used and population evaluated (4-6). Patients diagnosed with cardiac cachexia present a mortality rate of 50% in 18 months, with these high mortality rates associated with cachexia independent of other variables, such as functional classification (FC), sodium levels, VO_2 (volume of oxygen) peak, and age (3).

In light of the negative impact of cachexia on patient prognosis and the lack of a universal definition for diagnosing it, in 2006 a consensus was elaborated by the Cachexia Society (Washington, DC) for diagnosing cachexia, based on the main characteristics of this condition, including criteria which address biochemical and nutritional alterations that reflect the complex physiology of this syndrome (7). The Cachexia Consensus allows clearer diagnosis to be carried out, indentifying alterations in the components of this syndrome, and differentiating cachexia from other conditions, such as sarcopenia, malnutrition without inflammation, and anorexia. This consensus has not been applied sufficiently yet, and until now only one study has been identified which adopted the proposed methodology (8). Thus, it is possible that the magnitude of cachexia has not yet been sufficiently described, and more studies are needed to estimate its prevalence and describe the nutritional and biochemical alterations in patients with cachexia, since most definitions use only weight loss to diagnose it.

With the previous criterion, which uses only weight loss to diagnose cachexia, it was not possible to carry out a clear diagnosis and distinguish cachectic patients from other less serious conditions. Therefore, it is possible that cachexia is not adequately diagnosed, resulting in a lack of treatment and bad prognosis for these patients. In this context, the aim of this study was to evaluate cachexia prevalence in hospitalized HF patients according to the Cachexia Consensus criteria, comparing it with another diagnostic method for cachexia, in order to evaluate the factors associated with it and analyze alterations in the components involved in diagnosing it.

METHODS

A cross-sectional study was carried out at a public hospital of reference in Cardiology, located in the Brazilian Northeast, and involving adult and elderly patients of both sexes diagnosed with HF and admitted between April and August 2015. Patients aged < 18 were excluded, along with those in the post-operative phase immediately after cardiac surgery; those with ascites, anasarca, upper or lower limb amputations; pregnant women; patients with a reported diagnosis of hepatic disease, hypo or hyperthyroidism or neoplasm; those living with acquired immunodeficiency virus (HIV); and those with renal disease in dialysis treatment.

The sample calculation was carried out considering 350 admissions occurring last year between April and August, with a 16.4% prevalence (5), 5% precision, and 95% confidence interval (CI), resulting in a minimum number of 131 patients to be studied. To correct for potential losses, this number was increased by 20%, bringing the total to 158 patients.

To diagnose cachexia, the criteria proposed by the Cachexia Society Consensus (7) were used, and for comparative purposes the diagnostic criterion proposed by Anker et al. (2003) was also used, which considers ≥ 6% weight loss in at least six months as a cachexia diagnosis (9). The Cachexia Consensus establishes a set of diagnostic criteria for cachexia, the main component of which is ≥ 5% non-edematous weight loss in the previous 12 months, or a body mass index (BMI) of < 20 kg/m^2 when this weight loss cannot be documented, which should be combined with at least three characteristic markers of cachexia: loss in muscle strength, fatigue, anorexia, low muscle mass index, and/or biochemical alterations, such as inflammation, anemia, or hypoalbuminemia. Weight loss history was obtained in interviews with the patients, and the weight loss percentage was obtained by subtracting usual weight reported by the patients from the weight obtained at the time of anthropometric evaluations for the study.

The anthropometric measurements and application of questionnaires regarding fatigue, anorexia, and demographic data was carried out by two nutritionists trained for the study and using those patients admitted to the hospital over the research period and who met the study criteria.

Reduced muscle strength was evaluated using handgrip strength (HGS), which was measured with the help of a Jamar brand digital dynamometer, adopting kilograms (kg) as the measuring unit. The technique adopted follows the American Society of Hand Therapists' instructions (10). To classify HGS as low, the lower third for age and sex was considered (7). The fatigue evaluation was carried out using the Dutch Fatigue Scale (DUFS) (11), considering that a total score of ≥ 14.5 indicates the presence of fatigue. The anorexia evaluation was carried out using the simplified nutritional questionnaire on appetite (SNQA), and indices of ≤ 14 indicate risk of weight loss and the presence of anorexia (12).

Muscle mass was evaluated using the mid arm muscle circumference (MAMC). MAMC was obtained based on the mid arm circumference (MAC) and triceps skinfold (TSF) values taken from the non-dominant arm. The MAMC results were compared with the Frisancho (1981) standard for age groups up to 59 years old (13), and the Third National Health and Nutrition Examination Survey-NHANES III (1988-1994) standard was considered for the ≥ 60 age group (14). Muscle mass was considered to be low when MAMC was below the percentile 10 for age and sex.

Among the biochemical alterations for cachexia, the following were considered: anemia (hemoglobin < 12 g/dl), hypoalbuminemia, when albumin < 3.2 g/dl, and an inflammatory state, evaluated using the C-reactive protein (CRP ≥ 5.0 mg/l) (7).

The data regarding patient clinical variables were collected from the patient records: HF based illness, HF functional class (defined according to the New York Heart Association criteria), existing comorbidities (systemic arterial hypertension, diabetes mellitus, chronic rheumatic disease, and chronic renal disease), and the ejection fraction percentage of the left ventricle (%EFLV) (obtained from a cardiogram carried out during admittance). A %EFLV of < 50% was considered as being reduced. Nutritional state was evaluated using BMI, with adults classified according to the World Health Organization proposal (1997) (15) and the elderly classified using the cut-off point proposed by Lipschitz (1994) (16). Corrected mid arm muscle area (cMAMA) and mid arm fat area (MAFA) were evaluated, in accordance with the Frisancho equation (1990) (17).

The study was approved by the Committee on Ethics in Research involving human beings of the HUOC/PROCAPE hospital complex, in accordance with Resolution No. 466/2012 of the National Health Council/Health Ministry, under protocol number 980.472/2015. All of the patients and those responsible who agreed to participate in the study signed an informed consent form (ICF).

The data were tabulated and analyzed with the help of the SPSS statistical package, version 13.0 (SPSS Inc., Chicago, IL, USA). A descriptive analysis of the variables was carried out by calculating the frequency distributions and central tendency measures. The continuous variables were tested according to distribution normality using the Kolmogorov-Smirnov test. When they presented normal distribution, they were described in means and standard deviations and the respective parametric test was applied (Student's t test for comparing two means). When they presented abnormal distribution, they were described in medians and interquartile intervals, applying the non-parametric test (Mann-Whitney U test for comparing two medians). The factors associated with cardiac cachexia were analyzed using the Pearson's Chi-squared test or Fischer's exact test. To evaluate agreement between two diagnostic criteria for cachexia, the kappa index was used. The level of significance adopted for all of the tests was less than 0.05.

RESULTS

Of the 322 patients admitted during the period the study was carried out, 150 patients did not meet the eligibility criteria: edema (38), ascites (6), limb amputation (5), bed ridden patients for whom it was not possible to carry out the proposed evaluations (12), renal disease in dialysis treatment (18), HIV (4), cancer (3), post-surgery (17), endocarditis and other types of infection (29), mental disability (13), hypothyroidism (2), and hepatic disease (3). After eliminating losses from early hospital release (13), or inconsistent data (3), 156 individuals were included in the study, with an average age of 59.1 (± 15.3) and homogeneous distribution between sexes (Table I).

Among the patients with a HF diagnosis, the most prevalent functional class was functional class III (FCIII) (41.6%). A high percentage of patients with ejection fractions lower than 50% (51%) was verified. The most prevalent comorbidity in the sample was arterial hypertension (79.4%) (Table I).

Table I. General characteristics of hospitalized patients with heart failure, Northeastern Brazil (n = 156)

Variables	n	%
Age range		
Adult	77	49.4
Elderly (≥ 60 years)	79	50.6
Gender		
Male	76	48.7
Female	80	51.3
NYHA		
I	22	16.1
II	43	31.4
III	57	41.6
IV	15	10.9
LVEF		
< 50%	71	51.1
≥ 50%	68	48.9
Comorbidities		
Diabetes mellitus	30	19.5
Arterial hypertension	123	79.4
Chronic renal failure*	17	11.0
Nutritional status		
Low weight	27	17.5
Normal weight	76	49.4
Overweight	51	33.1

*NYHA: New York Heart Association functional class; LVEF: left ventricular ejection fraction. *Chronic renal failure no dialysis.*

Using the Cachexia Society Consensus criterion (7), 37.2% cachexia prevalence was verified, whereas the prevalence according to the Anker et al. criterion (8) was 49.3% (kappa = 0.401). In accordance with the Consensus criteria, the alterations in each parameter were analyzed, with fatigue and anorexia being the most prevalent aspects (88.2% and 72.1%, respectively). A ≥ 5% weight loss in the previous 12 months was observed in 61.7% of the sample, with low muscle mass found in 46.7% of the patients. PCR, an inflammation marker also used as a diagnostic criterion, was altered in 50.7% of the patients (Table II).

When the factors associated with cachexia were analyzed (Table III), there were no significant differences in prevalence in relation to age, sex, functional class, and comorbidities. Cachexia was most prevalent among the individuals with low BMI ($p < 0.001$), individuals with low muscle mass ($p < 0.001$), among the patients with an EFLV under 50% ($p = 0.005$), with low HGS ($p < 0.001$), with hypoalbuminemia ($p = 0.040$), and with anemia ($p = 0.002$).

Table II. Prevalence of cardiac cachexia changes the proposed diagnostic criteria for Consensus in hospitalized patients with heart failure, Northeastern Brazil (n = 156)

Variables	n	%
Cardiac cachexia	58	37.2
Weight loss ≥ 5% at 12 months	82	61.7
Body mass index < 20 kg/m²	23	14.7
Low muscle strength*	37	24.0
Fatigue†	135	88.2
Anorexia‡	111	72.1
Reduced muscle tissue§	70	46.7
Hypoalbuminemia (< 3.2 g/dl)	14	10.7
CRP high (> 5.0 mg/l)	76	50.7
Anemia (hemoglobina < 12 g/dl)	54	34.6

*CRP: C-reactive protein. *Low muscle strength: lower tertile for sex and age. †Score ≥ 14, assessed according to the Dutch Fatigue Scale (DUFS). ‡Score ≤ 14, assessed by Simplified Nutritional Appetite Questionnaire (SNAQ). §Assessed by arm muscle circumference. < percentile 10 for sex and age.*

Lower averages were verified among the cachectic patients for weight ($p < 0.001$), BMI ($p < 0.001$), mid arm muscle circumference ($p = 0.001$), mid arm muscle circumference corrected ($p < 0.001$), arm fat area ($p = 0.001$), triceps skinfold ($p = 0.001$), and handgrip strength ($p = 0.001$) (Table IV).

DISCUSSION

The clinical symptoms commonly observed in HF, such as fatigue, dyspnea, and anorexia, associated with hypermetabolism and greater loss in nutrients, represent important factors which culminate in accentuated weight loss among these patients, and are responsible for a deteriorating nutritional state until serous conditions appear such as cachexia, which is an important predictor of poor clinical prognosis.

Cachexia is a syndrome that can affect HF patients and must be evaluated systematically during clinical monitoring of these individuals. There are various definitions and methods for diagnosing cachexia, resulting in differences in prevalences found. In our study, we used the most recent definition proposed by the Cachexia Society Consensus (7), and a high prevalence of 37.2% was found. Considering its repercussions in terms of a worse clinical evolution, reduced survival rate, and impact on hospital admittance numbers and costs, this high prevalence indicates a need for more attention to be paid by the whole multi-professional healthcare team. Previous studies that used only weight loss in the previous six months as the diagnostic criterion, and adopted different percentages (≥ 5%, ≥ 7.5%, > 6.0%), found cardiac cachexia prevalences which varied between 10.5%, 40.4%, and 19.0%, respectively (4,18,19). Letilovic and Vrhovac (2013), using the same consensus criteria adopted in this investigation in a sample of hospitalized HF and cancer patients, found a 21.8% prevalence of cachexia (8).

For comparative purposes, a previous definition was also used which involved only weight loss (≥ 6% in at least six months), identifying a higher cachexia prevalence (49.3%) than when the criteria proposed by the consensus was used (37.2%), and moderate agreement between the methods (kappa = 0.401). These differences in the prevalence found could possibly be attributed to the fact that the patients with weight loss only presented other conditions which are easily confused with cachexia, such as malnutrition without inflammation, malnutrition related with social and psychological conditions, and sarcopenia.

The findings in this study show ≥ 5% weight loss in 61.7% of the sample, which is higher than in the data presented by Letilovic and Vrhovac (2013), who evaluated hospitalized patients (8) diagnosed with cancer and HF (30.6%) and also higher than in the study with stable HF patients seen as outpatients, which showed ≥ 5% prevalence of weight loss in 42% of the sample (9). It is possible that the high prevalence of weight loss found in this study is influenced by the sample having been composed of patients admitted to hospital in a developing country with low social conditions and healthcare.

Weight loss in HF is considered to be the most sensitive indicator of clinical changes in cachectic patients, especially in patients with cardiac cachexia for whom weight loss mainly affects muscle, including cardiac muscle (20). Various factors can contribute to weight loss in HF patients, such as anorexia, poor nutrient absorption, dyspnea, and increased inflammatory cytokines (21). Although weight loss is the most important component of cachexia diagnosis, we believe isolated weight loss does not reflect the complex physiology of this syndrome. Moreover, weight loss evaluations with HF should be carried out with caution, given that these patients evolve with edema, and weight variations resulting from hydric retention are common, and thus nutritional evaluations should be carried out after edema resolution. Another aspect to be highlighted is that isolated weight loss does not differentiate cachexia from other conditions which also involve weight loss, such as anorexia, sarcopenia, and malnutrition without inflammation (22). Thus, we believe that the current consensus better represents cardiac cachexia due to it providing a systemic evaluation of this condition.

Studies show that despite cachectic patients presenting generalized loss of adipose and osseous tissue, muscle mass is compromised most, notably affecting the skeletal muscle (23). In our study, muscle loss was observed in 46.7% of the sample and 55.7% of the cachectic patients, which is a higher result than that reported by Fulster et al. (24) in a study with HF patients (19.5%) using DEXA (dual energy X-ray absorptiometry) to evaluate muscle mass, which is considered as the gold standard, instead of CBM, which is adopted in our investigation.

Involuntary weight loss plays a relevant part in compromising lean mass, given that it has been demonstrated that in some situations of unintentional loss in body weight, such as hypercatabolic clinical conditions, there is a disproportionate reduction in body

Table III. Comparative analysis of variables associated with cardiac cachexia in hospitalized patients with heart failure, Northeastern Brazil (n = 156)

Variables	With cachexia		Without cachexia		p-value*
	n	%	n	%	
Age range					
Adults (< 60 years)	24	31.2	53	68.8	0.125
Elderly (≥ 60 years)	34	43.0	45	57.0	
Gender					
Male	28	36.8	48	63.2	0.932
Female	30	37.5	50	62.5	
Etiology of HF					
Cardiomyopathy	36	62.1	22	37.9	0.565
Valvulopathy	55	63.2	32	36.8	
Cardiomyopathy and valvulopathy associated	3	42.9	4	57.1	
NYHA class†					
I or II	22	34.4	42	65.6	0.205
III or IV	32	45.1	39	54.9	
LVEF (%)					
< 50%	34	47.9	37	52.1	0.005
≥ 50%	17	25.0	51	75.0	
Arterial hypertension					
Yes	42	34.1	81	65.9	0.099
No	16	50.0	16	50.0	
Diabetes mellitus					
Yes	10	33.3	20	66.7	0.642
No	47	37.9	77	62.1	
Nutritional status‡					
Low weight	19	70.4	8	29.6	< 0.001
Normal weight	27	35.5	49	64.5	
Overweight	11	21.6	40	78.4	
Muscle tissue					
Normal	16	20.0	64	80.0	< 0.001
Low	39	55.7	31	44.3	
*Muscle strength**					
Normal	34	29.05	83	70.94	< 0.001
Low	23	62.16	14	37.83	
C-reactive protein					
High (> 5 mg/l)	33	43.4	43	56.6	0.082
Normal (≤ 5 mg/l)	22	29.7	52	70.3	
Albumin					
Low (< 3.2 g/dl)	9	64.3	5	35.7	0.040
Normal (≥ 3.2 g/dl)	42	35.9	75	64.1	
Anemia					
With anemia (hemoglobin < 12 g/l)	29	53.7	25	46. 29	0.002
Without anemia (hemoglobin ≥ 12 g/l)	29	28.43	73	71.56	

*LVEF(%): left ventricular ejection fraction. *The Chi-squared test or Fisher's exact. †NYHA: New York Heart Association functional class. ‡Nutritional status according to body mass index (OMS, 1997). Muscle tissue assessed by arm muscle circumference. Muscle strength assessed by handgrip strength (kg), considering the lowest tertile for sex and age.*

Table IV. Comparability of anthropometric, biochemical markers and muscle strength according to the presence of cachexia in hospitalized patients with heart failure, Northeastern Brazil

Variables	With cachexia (n = 58)	Without cachexia (n = 98)	p-value*
Weight (kg)	56.77 (± 11.8)	68.05 (± 16.4)	< 0.001
Body mass index (kg/m^2)	24.79 (± 5.43)	26.20 (± 5.4)	< 0.001
Mid arm muscle circumference	22.31 (± 3.2)	22.94 (± 2.9)	0.001
Mid arm muscle circumference corrected (cm^2)	32.43 (± 10.7)	34.54 (± 10.0)	0.001
Arm fat area (cm^2)	16.4 (± 9.2)	21.41 (± 7.7)	0.001
Triceps skinfold (mm)	17.98 (± 9.7)	23.71 (± 10.8)	0.001
Handgrip strength (kg)	19.9 (± 7.4)	26.6 (± 10.5)	0.001

**Student's t test.*

stocks, originating an excessive loss of muscle tissue, which can be up to 72%, and a reduction of only 28% in adipose tissue, unlike with intentional weight loss, in which a reduction of 80% in fat mass and only 20% in lean mass are observed (25). The potential mechanisms involved in the preferential loss of muscle tissue result from excessive production of inflammatory cytokines, characterizing the exacerbated inflammatory state of cachexia, as well as increased catabolic hormone production, creating a disequilibrium between anabolic and catabolic processes. Cytokines have a direct negative effect on muscle mass, resulting in ingestion suppression, and the increase in catabolic hormones activates the ubiquitin proteasome pathway, which is the predominant pathway for protein degradation (23).

Although in our study PCR was not significantly associated with cachexia, it is known that this protein is not a sensitive and specific marker of inflammatory states, and for this reason the use of PCR was a limitation of our study. We suggest that another specific marker for evaluating cachexia inflammatory states, such as TNFα, would be more appropriate for evaluating this condition in future studies.

Fatigue is one of the most frequent symptoms of HF, especially in patients with functional class III and IV, involving symptoms of tiredness, exhaustion, and lack of energy, and associated with limitations in maintaining a lifestyle compatible with a desired sense of autonomy and independence, and is a limiting factor for physical activity among patients (26). Fatigue is one of the two most common symptoms (together with dyspnea) reported by HF patients (26,27), thus our results, which indicate a high percentage of this symptom (88.2%), were expected. The physiopathological causes of fatigue in HF are multifactorial (27) and include low cardiac debit, poor tissue perfusion, metabolic muscular abnormalities, abnormalities in the autonomous nervous system, physical deconditioning, and endothelial dysfunction.

Anorexia, present in 72.1% of the sample, may be related to HF via a connection with its main symptoms (fatigue and dyspnea). Anorexia can be a symptom of cachexia, however, it is a symptom that should be analyzed carefully, given that it also occurs in other conditions that are not associated with cachexia, such as the use of certain medications, depression, advanced ageing, and gastrointestinal problems. Moreover, anorexia can be due to a collateral effect of digitalis, angiotensin conversion enzyme inhibitors, intestinal edema, and sodium restricted diets (28,22).

Handgrip strength (HGS) is a fragility marker, is correlated with global muscle strength, and is considered as an independent predictor of a poor prognosis for HF patients. We identified low HGS in cachectic patients, with an average of 19.9 (± 7.4) kg, which is lower than in the data presented in a study of Japanese men (29) with HF (33.3 ± 8.6 kg), and lower than in the results from another investigation (30) involving patients with advanced HF (381 ± 7.9 kg). One previous study suggested a HGS value lower than 32.2 kg in HF patients as a predictor of mortality. As patients with cardiac cachexia present global myopathy, this would be expressed in an evident decrease in HGS, contributing to lower functional capacity, greater severity HF, and fatigue. The underlying mechanisms in HGS reduction include alterations in the ultra-structure and biochemistry of the skeletal muscle (30).

Anemia is a common condition in HF patients, causing a reduction in oxygen supply to the periphery, contributing to intolerance to exercise, and associated with greater clinical severity, rapid HF deterioration, and increased mortality. In our study, we found that anemia was significantly greater in cachectics (53.7%), and this result agrees with previous studies that demonstrate a high prevalence of anemia in HF patients, which is greater the worse the gravity of NYHA functional class, varying from 7.0% to 9.1% for FCI, and 65.9-79.1% for FCIV (31,32). In cachectic patients, some studies which evaluated anemia identified a prevalence which varied from 24% to 70% (18,33), independently of functional class. In cardiac cachexia, an increase in TNF occurs as a result of the inflammatory state of this condition, with this cytokine involved in bone marrow depression, induced erythropoietin insensitivity, and interference in iron release and use, and it is also known that inflammation reduces these patients' appetite, resulting in low iron ingestion (32).

Hypoalbuminemia is a common finding in cardiac cachexia patients, with prevalences varying from 18% to 89% (34). In our study, the cachectic patients presented significantly lower levels of

albumin (64.3%), and the possible cause factors for this condition include malnutrition and systemic inflammation, which causes an increase in PCR levels. Other factors that explain hypoalbuminemia in these patients and that were not evaluated would be: intestinal losses caused by splenic congestion, renal insufficiency, and protein catabolism (34). The importance of evaluating albumin levels in these patients is due to its importance as an independent predictor of poor prognosis: it causes pulmonary congestion, results in greater oxidative stress and inflammation, favors edema of the myocardium, and subsequently aggravates myocardial dysfunction, contributing to fluid retention.

In our study, reduced %EFLV was significantly associated with cardiac cachexia. On the other hand, NYHA functional class did not present any relationship. Some studies demonstrate that reduced %EFLV and higher functional class (III-IV) are related with HF gravity and the occurrence of cardiac cachexia, and both have been used in evaluating HF prognosis, as independent mortality markers (18). Reduced %EFLV results in low cardiac debit, resulting in impaired peripheral blood flow. Hypoflux in cardiac cachexia has been shown to be an independent predictor of lower exercise capacity, loss of muscle strength, and an earlier onset of fatigue. In particular, hypoflux in the muscular skeleton causes ischemia of the tissue and hypoxia, causing significant alterations in the skeletal muscle via endothelial dysfunction, damaged vascular perfusion, the development of resistance to insulin, cellular death, and loss of muscle mass, causing weakening of the skeletal muscle. Moreover, hypoxia resulting from hypoflux is a determining factor for the pathogenesis of the metabolic alterations present in cardiac cachexia. In hypoxia, oxygen reduction causes a deviation of the metabolism to anaerobic pathways, resulting in increased mobilization of fatty acids, anaerobic glycolysis, and neoglucogenesis, causing increased catabolism (proteolisis) and reduced anabolism. In addition to these factors, hypoxia is considered to be the main stimulus for increased TNF production in HF patients. Therefore, hypoxia leads to a hypercatabolic and inflammatory state, which characterize cachexia syndrome (35).

Although cachexia was obviously greater among the malnourished, it is important to highlight that 35.5% of normal weight individuals and 21.6% of overweight individuals presented cachexia, showing that this condition is not restricted to low BMI cases. Not evaluating the cachexia criteria merely because patients have an apparently preserved nutritional state will hamper tracking individuals with this syndrome. Most of the time cachexia is only diagnosed and receives due importance when the patient reaches a devastating state of nutritional impairment. However, if patients are not systematically evaluated, their final evolution will be the characteristic underweight profile associated with cachexia.

In this study we identified the nutritional alterations in cachectic patients, and the factors which are associated with the occurrence of cachexia. Our study presented some limitations. First, the cross-sectional study design means it is not possible to establish cause and effect relationships. Moreover, we presented an investigation from only one center and did not evaluate inflammation with a specific inflammatory marker. Thus, any generalization of the data presented for other HF patient groups should be made with due caution.

Although a previous study (8) considered that the application of secondary Cachexia Consensus criteria means we lose high risk patients due to reducing cachexia prevalence, in this study we verified that using the consensus criteria allowed for a distinction to be made between patients that present complex alterations which are characteristic of cachexia and those that only present weight loss. Applying the secondary criteria means we do not lose at-risk patients and allows for attention to be concentrated on cachectic patients in an institution with adequate treatment measures. Thus, we believe that patients who have only lost weight cannot be attributed the same gravity which cachexia represents, although they do obviously require attention and nutritional interventions.

CONCLUSIONS

A high prevalence of cardiac cachexia was observed and the affected patients presented increased loss of muscle mass, adipose tissue, low handgrip strength, a substantial presence of fatigue and anorexia, and biochemical alterations (anemia, raised PCR, and hypoalbuminemia), confirming the clinical deterioration in these patients. These results reinforce the need for cachexia to be routinely investigated so that preventative measures can be adopted and specific therapeutic interventions are implemented in the treatment of this syndrome.

Applying a new definition to cachexia allowed us a global overview of the modifications that occur in cachectic patients, and made it possible to identify the main altering factors in cachexia and those which were associated with this condition.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Otros

Malnutrition is a key prognostic factor related to high mortality-rate in patients with severe alcoholic hepatitis

La desnutrición es un factor pronóstico clave relacionado con elevada mortalidad en pacientes con hepatitis alcohólica severa

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Abstract

Background and aim: comparatively with European or North-American populations, severe alcoholic hepatitis has a high mortality rate in Mexican population, becoming as high as 50 to 81% in those classified as ABIC B or C; this is true even when they receive specific therapy with steroids or pentoxifylline. The aim of this study was to know which clinical factors are related to early mortality (first 30 days) in Mexican patients with severe alcoholic hepatitis.

Subjects and methods: this was a retrospective cohort study that included patients with severe alcoholic hepatitis, defined by a Maddrey's discriminant function ≥ 32, treated at a tertiary care center in a period of five years (2010 to 2015).

Results: seventy-six patients were included, 72 (94.7%) were males, mean age was 43 ± 9.1 year-old, and 58 (76.3%) had also cirrhosis. According to the subjective global assessment (SGA), 38 (50%) had severe malnutrition, 22 (28.9%) were at risk of malnutrition, and 16 (21.1%) were well-nourished. At 30 days, 46 patients (60.5%) died. In the multivariate analysis, only the presence of severe malnutrition was associated with 30-day mortality: OR = 6.4; 95% CI: 1.9-22.1; p = 0.003.

Conclusions: the nutritional status seems to be a cardinal prognostic factor associated with early mortality (first 30 days). Malnutrition can explain the high mortality rate observed in Mexican patients with severe alcoholic hepatitis.

Key words:

Alcoholic hepatitis. Malnutrition. Mortality. Subjective global assessment. Risk factors.

Resumen

Antecedentes: en comparación con otras poblaciones europeas o norteamericanas, la hepatitis alcohólica severa tiene una mortalidad muy elevada en población mexicana atendida en hospitales federales (generalmente, pacientes de medio socioeconómico bajo) y llega a alcanzar entre el 50% y el 81% en aquellos catalogados como ABIC B o C; esto es cierto a pesar del tratamiento específico con esteroide o pentoxifilina.

Objetivo: conocer qué factores clínicos están asociados a una mortalidad temprana (30 días) en pacientes mexicanos con hepatitis alcohólica severa.

Material y métodos: se realizó un estudio de cohorte histórica que incluyó a pacientes con hepatitis alcohólica severa, definida por una función discriminante de Maddrey mayor a 32, atendidos en el Hospital General de México durante un periodo de cinco años (2010-2015).

Resultados: se incluyeron 76 pacientes, de los cuales 72 (94,7%) fueron hombres, la media de edad fue de 43 ± 9,1 años; 58 (76,3%) de ellos tenían alteraciones sugestivas de cirrosis en el ultrasonido. De acuerdo con la valoración global subjetiva (VGS), 38 (50%) presentaban desnutrición grave, 22 (28,9%) se encontraban en riesgo de desnutrición y 16 (21,1%) estaban bien nutridos. La mortalidad global a 30 días en esta cohorte fue de 46 pacientes (60,5%). En un modelo multivariado, solo la desnutrición severa se asoció con mortalidad a 30 días: OR = 6,4; IC 95%: 1,9-22,1; p = 0,003.

Conclusión: el estado nutricional es el determinante más importante asociado a mortalidad temprana (30 días). La desnutrición severa explica claramente la elevada mortalidad que se observa en pacientes con hepatitis alcohólica severa, en población mexicana.

Palabras clave:

Hepatitis alcohólica. Desnutrición. Mortalidad. Valoración global subjetiva. Factores de riesgo.

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INTRODUCTION

Comparatively with European or North-American populations, severe alcoholic hepatitis (SAH) has a very high mortality rate in Mexican population, being as high as 50 to 81% in those classified as Age-Bilirubin-INR-Creatinine score (ABIC) B or C; this is true in spite of specific treatment with steroids or pentoxifylline (1).

Recently, STOPAH trial demonstrated that neither steroid nor pentoxifylline treatment has a significant impact on the long-term mortality-rate of patients with SAH. But steroids can be helpful to improve 30-day survival in these patients (2).

Risk factors associated with early mortality in patients with SAH are: age, raise on serum creatinine, hyperbilirubinemia, leukocytosis, and alcohol intake > 120 g/day (1). One of the most important factors related to 30-day mortality is the development of acute renal failure (ARF); moreover, the amount of alcohol intake (median 219 g/day) is related to the development of ARF. The development of two or three simultaneous complications, such as ARF, hepatic encephalopathy, or variceal bleeding, increase the mortality risk in patients with SAH (3).

The liver failure is a condition that accelerates starvation; therefore, malnutrition is a common complication of liver disease. The prevalence of clinically significant malnutrition varies from 65% to 100% among patients with chronic liver disease (4). Malnutrition as a risk factor associated with mortality in patients with SAH has been evaluated in a few studies (5-7), but never was evaluated specifically in Mexican patients, a population with a high early mortality-rate (1,3).

The aim of this study was to explore which clinical factors are related to early mortality (at 30 days) in a population with a high mortality rate despite specific therapy for SAH, and to identify if malnutrition has influence in survival of patients with SAH.

SUBJECTS AND METHODS

TYPE OF STUDY AND SELECTION CRITERIA

A retrospective cohort study, which included patients with SAH, defined by a Maddrey's discriminant function ≥ 32, attended at tertiary care center, from January 2010 to July 2015. Patients with the following comorbidities were excluded: diabetes, viral hepatitis, patients who requested voluntarily their discharge from hospital, who were not treated with prednisone or pentoxifylline, co-infected with human immunodeficiency virus, or with diagnosis of hepatocarcinoma.

PROCEDURE

Demographic, clinical and biochemical data were collected. The following data were registered: amount of alcohol intake, development of ARF, hepatic encephalopathy, variceal bleeding, bacterial infections, suggestive changes of cirrhosis reported in the ultrasonography. The nutritional status determined through the global subjective assessment (GSA) (8) at patient admission classified patients in one of three different categories: well-nourished, at risk of malnutrition, or severe malnourished. Treatment with prednisone or pentoxifylline was also verified. Also, the outcome (death or survival) since the admission to hospital until a 30-day follow-up was registered.

STATISTICAL ANALYSIS

Quantitative variables were resumed with mean and standard deviation when their distribution was normal, or with median and range in case of non-parametric distribution. For qualitative variables proportions and percentages were employed. The characteristics between groups were compared using Student's t test for independent samples or Mann-Whitney U test in case of continuous variables, and through Chi-squared test of Fisher's exact test for categorical variables. For the survival analysis, Kaplan-Meier curves and the log rank test were used. The association between risk factors and 30-day mortality was determined through hazard ratios (HR) and their respective 95% confidence intervals were calculated using Cox regression models. All those significant variables with a p value ≤ 0.05 identified in the univariate analysis were included in the multivariate analysis. The SPSS version 19.0 (Chicago, Illinois, USA) was used.

RESULTS

Seventy six patients were included, 72 (94.7%) were male, mean age was 43 ± 9.1 year-old, and 58 (76.3%) had changes compatible with cirrhosis in the ultrasonography. According to the GSA, 38 (50%) had severe malnutrition, 22 (28.9%) were at risk of malnutrition, and 16 (21.1%) were well-nourished. The overall 30-day mortality in this cohort was 46 patients (60.5%). The characteristics of patients at admission to hospital according to their outcome at 30 days of follow-up are summarized and compared in table I.

In the univariate analysis, the following variables were associated with 30-day mortality: concomitant cirrhosis (OR = 2.3; 95% CI: 1.5-3.4; p < 0.0001), development of hepatic encephalopathy (OR = 5.6; 95% CI: 2.5-12.5; p < 0.0001), development of ARF (OR = 6.2; 95% CI: 2.5-15.6; p < 0.0001), variceal bleeding (OR = 4.4; 95% CI: 1.7-11.3; p < 0.0001), bacterial infection (OR = 2.7; 95% CI:1.3-5.8; p = 0.004), at risk of malnutrition according to the GSA (OR = 2.0; 95% CI: 1.2-3.3; p = 0.01), and severe malnutrition according to the GSA (OR = 5.8; 95% CI: 2.0-16.4; p < 0.0001). Neither therapy with prednisone nor therapy with pentoxifylline improved survival in patients with SAH. Neither was difference between the treatment groups (Table II).

When all significant variables in the univariate analysis were adjusted in a multivariate analysis, only severe malnutrition was associated with 30-day mortality (OR = 6.4; 95% CI: 1.9-22.1; p = 0.003) (Table III and Fig. 1).

Table I. Characteristics of patients at admission to hospital and comparison according to outcome at 30-day follow-up

Characteristic	Dead n = 46	Alive n = 30	p
Age in years	44.2 ± 8.7	41.0 ± 9.5	0.13
Male sex, n (%)	44 (95.7)	28 (93.3)	0.65
Maddrey's discriminant function	101.5 ± 73.5	73.0 ± 28.3	0.02
MELD	34.6 ± 7.7	27.4 ± 4.3	< 0.0001
MELD-Na	35.1 ± 5.6	30.0 ± 3.7	< 0.0001
Glasgow	10.3 ± 1.1	9.5 ± 1.1	0.001
ABIC	9.1 ± 1.8	7.9 ± 1.3	0.003
Alcohol (g/day)	361.0 ± 210.3	333.7 ± 134.8	0.49
Urea (mg/dl)	87.2 ± 67.8	38.2 ± 32.9	< 0.0001
Creatinine (mg/dl)	2.3 ± 1.1	1.4 ± 0.8	< 0.0001
Sodium (mEq/l)	129.6 ± 5.8	132.7 ± 4.7	0.01
Albumin (mg/dl)	1.7 ± 0.4	1.9 ± 0.3	0.009
Bilirubin (mg/dl)	24.6 ± 9.9	23.9 ± 11.3	0.70
AP (UI/l)	200 ± 96	227 ± 88	0.22
GGT (UI/l)	323 ± 252	322 ± 323	0.99
AST (UI/l)	224 ± 174	183 ± 85	0.24
ALT (UI/l)	77 ± 96	50 ± 28	0.14
Leukocytes (cel x 10^3)	21.9 ± 9.9	16.5 ± 7.5	0.26
Neutrophiles (cel x 10^3)	18.1 ± 9.4	16.5 ± 8.3	0.42
Hemoglobin (g/dl)	11.0 ± 2.9	11.7 ± 2.8	0.27
Platelets (cel x 10^9)	171.1 ± 121.4	182.7 ± 107.3	0.67
Protrombin time (sec)	28.8 ± 16.1	22.6 ± 6.3	0.02
INR	2.5 ± 1.6	1.9 ± 0.5	0.02

ABIC: age-bilirubin-INR-creatinine; ALT: alanine aminotransferase; AP: alkaline phosphatase; AST: aspartate aminotransferase; GGT: gamma glutamiltransferase; INR: international normalized ratio; MELD: Model for End-stage Liver Disease; MELD-Na: Model for End-stage Liver Disease-Sodium. t de Student, Chi-squared: statistical significance p < 0.05.

DISCUSSION

In Mexico, mortality related to chronic liver disease is among the main causes of general mortality, occupying the fourth place (9), making it one of the countries with the highest rates of liver-related mortality (10). The Ministry of Health estimated an average of 25,000 deaths from cirrhosis between 2000 and 2010 (11). In Mexico, alcohol is the leading cause of cirrhosis, followed by hepatitis C and non-alcoholic steatohepatitis. In addition, when patients seek medical attention, they are often at advanced stage of the disease (Child-Pugh C) with obvious manifestations of decompensation, and they often continue to intake alcohol despite the diagnosis of liver disease. All these factors contributed to high mortality at productive age (12,13).

SAH is characterized by the rapid onset of jaundice and coagulopathy in patients with active and chronic alcohol intake (14). The reported mortality, as well as the response to therapy with steroids or pentoxifylline, is extremely variable among different populations. Some authors report mortality greater than 50% at two months without specific treatment (steroids) (15-17). In France, treatment with prednisolone has been shown to be effective reducing mortality to 35% at six months of follow-up (18-20). Nevertheless, up to 40% of patients do not respond to steroid therapy, and particularly in these non-responder patients, mortality has been reported greater than 75% (16,21). On the other hand, several studies in Mexican population have found high mortality-rate and failure to steroid and pentoxyfilline treatments. A cohort study in Mexican population found that near to 90% of patients with SAH were non-responders to steroid therapy according to the Lille model (Lille score value > 0.45 after seven days of treatment with prednisone) (22). A retrospective study by Garrido-García et al. found a mortality-rate as high as 59.9% at 28 days of follow-up, despite treatment with prednisone (23). In English population, the STOPAH trial, which included the greatest number of patients with SAH in a clinical trial, did not show usefulness of steroids or pentoxifylline; however, mortality-rate at 28 days in all groups

Table II. Univariate analysis comparing the clinical characteristics of surviving *versus* non-surviving patients during the 30-day follow-up

Characteristic	Dead n = 46	Alive n = 30	p	OR (95% CI)
Cirrhosis in the USG, n (%)	45 (97.8)	1 (3.3)	< 0.0001	2.3 (1.5-3.4)
Development of HE, n (%)	43 (93.5)	5 (16.7)	< 0.0001	5.6 (2.5-12.5)
Development of ARF, n (%)	38 (82.6)	4 (13.3)	< 0.0001	6.2 (2.5-15.6)
Development of VB, n (%)	27 (58.7)	4 (13.3)	< 0.0001	4.4 (1.7-11.3)
Development of infection, n (%)	25 (54.3)	6 (20.0)	0.004	2.7 (1.3-5.8)
GSA: nutritional status				
Well-nourished, n (%)*	3 (6.5)	16 (53.3)		
At risk of malnutrition, n (%)†	13 (28.2)	11 (36.7)	0.01§	2.0 (1.2-3.3)§
Severe malnutrition, n (%)‡	30 (65.2)	3 (10.0)	< 0.0001ǀ	5.8 (2.0-16.4)ǀ
Treatment				
Prednisone, n (%)	20 (51.3)	19 (48.7)	0.15	0.7 (0.4-1.1)
Pentoxifylline, n (%)	26 (70.3)	11 (29.7)		1.5 (0.9-2.6)

*ARF: acute renal failure; GSA: global subjective assessment; HE: hepatic encephalopathy; OR: odds ratio; USG: ultrasonography; VB: variceal bleeding. §Comparison using Chi-squared between * and †. ǀComparison using Chi-squared between * and ‡. Statistical significance p ≤ 0.05.*

Table III. Multivariate analysis to identify risk factors associated with early mortality in patients with severe alcoholic hepatitis

Characteristic	Dead n = 46	Alive n = 30	p	OR (IC 95%)
Cirrhosis in the USG, n (%)	45 (97.8)	1 (3.3)	0.31	3.4 (0.3-34.5)
Development of HE, n (%)	43 (93.5)	5 (16.7)	0.12	3.9 (0.7-21.0)
Development of ARF, n (%)	38 (82.6)	4 (13.3)	0.15	2.0 (0.8-5.1)
Development of VB, n (%)	27 (58.7)	4 (13.3)	0.70	1.1 (0.6-2.2)
Development of infection, n (%)	25 (54.3)	6 (20.0)	0.78	1.1 (0.6-2.1)
GSA: nutritional status				
Well-nourished, n (%)*	3 (6.5)	16 (53.3)		
At risk of malnutrition, n (%)†	13 (28.2)	11 (36.7)	0.06§	3.5 (1.0-13.0)§
Severe malnutrition, n (%)‡	30 (65.2)	3 (10.0)	0.003ǀ	6.4 (1.9-22.1)ǀ

*ARF: acute renal failure; GSA: global subjective assessment; HE: hepatic encephalopathy; OR: odds ratio; USG: ultrasonography; VB: variceal bleeding. Cox regression model. §Comparison between * and †. ǀComparison between * and ‡. Statistical significance p ≤ 0.05.*

was extremely low: 17% in the p lacebo group, 14% in the prednisolone group, 19% in the pentoxifylline group, and 13% in the prednisolone plus pentoxifylline group (2).

Several studies have tried to explain which factors are related to a higher mortality in patients with SAH. The development of ARF is one of the most important mortality predictive factors (24). Interleukin-2 has been identified as a factor related to steroid treatment resistance (25). The amount of alcohol intake > 120 g/day has been also related to higher mortality-rate (1). Other factors associated with higher mortality-rate are age, raised serum creatinine, hyperbilirubinemia, leukocytosis, and also the synergistic effect of the development of two or three simultaneous complications as ARF, hepatic encephalopathy, or variceal bleeding (1,3). In the univariate analysis, our study confirmed ARF, variceal bleeding, hepatic encephalopathy, and infection are clinical factors related to a higher mortality-rate in patients with SAH.

Malnutrition is a prevalent comorbid condition in Mexican alcoholic patients. The prevalence of malnutrition and its degree correlates with the severity of chronic liver disease and its complications (26). But, until now no study has previously evaluated the impact of malnutrition on mortality of Mexican patients with SAH. Our study shows that severe malnutrition is a determinant factor which explains the high mortality-rate in Mexican patients with SAH. As the Kaplan-Meir curves and the multivariate analysis show, malnutrition resulted to be the most important risk factor related to high early mortality in these patients.

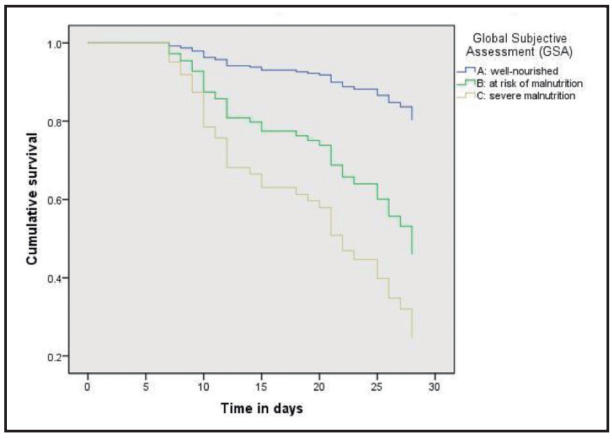

Figure 1.

Kaplan-Meier curves showing 30-day survival according to nutritional status in a cohort of patients with severe alcoholic hepatitis. Cox regression, p = 0.008. Adjusted model for the following co-variables: development of hepatic encephalopathy, variceal bleeding, acute renal failure, infection, concomitant cirrhosis on the ultrasonography.

The prevalence of malnutrition in patients with cirrhosis is widely variable; it has been reported from 25% to 80%, depending on the clinical severity of the disease and the specific evaluation method used (27-29).

The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend clinical methods, as the GSA, to evaluate the nutritional status in patients with liver diseases (30,31). The GSA is a routinely used tool in our hospital to evaluate nutritional status in patients with liver diseases. In our study, a high frequency of severe malnutrition was found, which is in agreement with previous findings reported by other authors (27-29).

The liver participates in the caloric homeostasis regulation (32). Patients with liver disease are susceptible to malnutrition due to several factors such as poor ingestion, fat malabsorption, intestinal loss of proteins, decreased protein synthesis, hypermetabolic state, symptoms as nausea, vomiting, early satiety, insulin resistance, gastroparesis, ascites, bacterial overgrowth (33). There is also over-regulation of inflammatory mediators that interfere with appetite, such as the tumor necrosis factor-alpha (34), which is significantly elevated in patients with SAH (14).

Sarcopenia is a common complication in patients with chronic liver disease and it worsens as chronic liver disease worsens (35,36); likewise, malnutrition is a predictor of morbidity and mortality in patients with chronic liver disease (34). Similarly to our finding about the association between malnutrition and higher mortality at 30 days, other authors have found in different populations a relationship between malnutrition and higher mortality-rate at 30-day, 6-month and 12-month follow-up in patients with SAH (5-7).

The American Association for the Study of Liver Disease and the European Association for the Study of the Liver recommend enteral nutrition with the objective of preserving the integrity of the intestinal barrier and avoiding the pathological increase in intestinal permeability, as well as to prevent the risk infection due to bacterial translocation infection, promote the anabolism to preserve muscle mass and prevent sarcopenia, and restore deposits of glutathione, a potent cellular antioxidant which is severely depleted in SAH (37).

CONCLUSIONS

This study confirms that nutritional status is an important factor associated with early mortality (first 30 days) in patients with SAH. Severe malnutrition clearly explains the high mortality observed in Mexican patients with SAH. The evaluation of nutritional status is essential as part of the initial assessment of patients with SAH since it behaves as a prognostic factor. Strategies to prevent nutritional deterioration are crucial in order to improve the survival of these patients.

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Nutrición Hospitalaria

Trabajo Original

Otros

Maximal expiratory pressure predicts mortality in patients hospitalized in medical and surgical wards

La presión espiratoria máxima es un predictor de mortalidad en pacientes hospitalizados en servicios de medicina o cirugía

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Abstract

Background: the prognostic value of maximal inspiratory and expiratory pressures on functional capacity and mortality of hospitalized patients are not well established.

Aim: to evaluate the prognostic value of respiratory pressures in hospitalized patients.

Methods: patients admitted to a general hospital in Santiago-Chile were prospectively studied. Within 48 hours of admission, handgrip strength and inspiratory and expiratory pressures were measured. Subjective global assessment of nutritional status (SGA) was determined and Apache II score was calculated. Functional status was assessed using the Karnofski index. Patients were followed for a period of 30 days. Mortality and decline in functional capacity, defined as a reduction in at least two stages of the Karnofski index were determined. Normal values for handgrip strength and respiratory pressures were obtained in 366 healthy subjects aged 20 to 89 years, thus the results obtained in patients were expressed as age and sex matched z-scores.

Results: one hundred and eight patients were recruited and 18 had to be excluded. Thus, 90 patients aged 58 ± 16 years (46 females) were studied. During the observation period, six patients died and nine experienced a decline in functional status. Patients who died had significantly lower maximal inspiratory and expiratory pressures, hand grip strength and worse SGA. Logistic regression analysis only accepted maximal expiratory pressure expressed as z-score as a predictor of mortality. In addition, it was the only significant predictor of death or functional decline.

Conclusions: maximal expiratory pressure on admission was a predictor of death or functional decline at 30 days.

Key words:

Maximal inspiratory pressure. Maximal expiratory pressure. Prognosis. Handgrip strength.

Resumen

Antecedentes: el valor pronóstico de las presiones inspiratoria y espiratoria máximas para determinar pérdida de capacidad funcional y mortalidad en pacientes hospitalizados, no está bien establecido.

Objetivo: determinar el valor pronóstico de presiones respiratorias en pacientes hospitalizados.

Métodos: se estudiaron pacientes ingresados a un hospital general en Santiago, Chile. Dentro de las primeras 48 horas de internación se midió fuerza de agarre de la mano, presión inspiratoria y espiratoria máximas. Se efectuó una evaluación global subjetiva del estado nutritivo (EGS) y se calculó el puntaje Apache II. El estado funcional se evaluó con el índice de Karnofski. Los pacientes fueron seguidos durante 30 días. Se determinó mortalidad y declinación de la capacidad funcional, definida como una pérdida de 2 o más etapas del índice de Karnofski. Se determinaron valores normales de presiones respiratorias y fuerza de agarre de la mano en 366 personas sanas con edades entre 20 y 89 años. Los resultados obtenidos en los pacientes se expresaron como puntaje z de estos valores, de acuerdo a sexo y edad.

Resultados: se reclutaron 108 pacientes y 18 fueron excluidos. Por lo tanto se estudiaron 90 pacientes con una edad de 58 ± 16 años (46 mujeres). Durante el periodo de observación, seis pacientes murieron y nueve tuvieron un deterioro de su capacidad funcional. Los pacientes que murieron tuvieron presiones inspiratorias y espiratorias, y fuerza de agarre de la mano más baja y una EGS menor. La regresión logística solo aceptó a la presión espiratoria máxima expresada como puntaje z, como predictor de mortalidad. También fue el único predictor de mortalidad o declinación funcional.

Conclusiones: la presión espiratoria máxima al ingreso, fue un predictor de mortalidad o declinación funcional a 30 días en pacientes hospitalizados.

Palabras clave:

Presión inspiratoria máxima. Presión espiratoria máxima. Pronóstico.

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INTRODUCTION

Sarcopenia or the loss of muscle mass and function is an inevitable consequence of aging, malnutrition, chronic or terminal diseases. Patients hospitalized in intensive care units experience a dramatic loss of muscle mass, associated with an increased muscle catabolism. The net loss of muscle mass predicts the appearance of multiple organ failure (1). Among cancer patients, the loss of muscle mass and function is probably the consequence of the increased secretion of cytokines and other tumor-derived factors (2). It is also an important prognostic factor (3,4). An inadequate nutritional intake, especially of dietary protein, also contributes to the loss of muscle mass (5) and is a usual problem among patients with acute diseases or decompensated chronic conditions. Therefore, sarcopenia can also become a relevant problem in the acute care setting.

Among older people, sarcopenia assessed as a low muscle mass or function has a long term prognostic value for mortality (6) and functional impairment (7). However, there is less information concerning its prognostic value in the hospital setting. Since pneumonia acquired during hospitalization and dependence on ventilator assistance are relevant for the outcome of hospitalized patients (8), assessment of respiratory muscle function may be an important tool to determine the short term prognosis of sarcopenia. Measurement of maximal inspiratory and expiratory pressures requires an inexpensive equipment and it is not bothersome for the patient (9). In cardiac surgery, it is associated with time on mechanical ventilation (10). Therefore, it is worth exploring if these parameters could have a prognostic value in patients hospitalized in general medical and surgical wards.

Thus, the aim of this study was to explore the prognostic value of maximal inspiratory, expiratory and handgrip strength on the functional capacity and mortality of patients admitted to medical and surgical wards of a general hospital.

PATIENTS AND METHODS

Non-critical patients of both genders and over 18 years of age hospitalized in the medical and surgical wards of El Pino Hospital in Santiago de Chile were studied. Exclusion criteria were a projected hospitalization of less than five days, being pregnant, being admitted for scheduled elective surgery with an expected hospital stay of less than five days, physical conditions that prevented the measurement of grip strength and maximal respiratory pressures such as myopathies or neurological conditions, and patients with respiratory illness as cause of hospitalization. Both the Ethics Committee of the South Metropolitan Health Service and the Institute of Nutrition and Food Technology of the University of Chile approved the study. All patients gave written informed consent. All assessments were performed within the first 48 hours of hospital admission.

All demographic data, diagnoses, and treatments were obtained from the medical record of each patient. A single researcher performed all histories, physical examination, respiratory pressure and handgrip strength measurements (EC). Body weight and height were measured. Maximal respiratory pressures were measured using a DPM Collins manometer connected to a small chamber (20 mm length and 30 mm inner diameter) with a mouthpiece. A small leak in the chamber prevented the patients from using buccal muscles to generate the pressure. For maximal inspiratory pressure the patients were instructed to expire and to stop breathing at residual lung volume and try to sustain a maximal negative pressure for approximately one to two seconds. For maximal expiratory pressure, the patients were instructed to inspire and stop breathing at total lung capacity and to sustain a maximal positive pressure for one or two seconds (11). The patients were instructed how to perform the test and three measurements were done, recording the highest readings.

Maximal isometric handgrip strength was measured with a 1 kg precision 78010 Lafayette dynamometer. Measurements were performed with the patient in the sitting position, adducted shoulder, neutral forearm rotation, and with the elbow bent at 90 degrees. Three measurements were obtained in each hand and the highest reading was recorded. No dominance was considered.

Global subjective assessment of nutritional status was carried out using the protocol proposed by Detsky et al. (12), using a Spanish translation previously used by us (13). Patients were classified as A = well nourished, B = moderately malnourished or at risk for malnutrition and C = severely malnourished.

Apache II score was calculated using laboratory and clinical data of patients, also within 72 hours of admission, using the French Society for Anesthesia and Resuscitation calculator (14).

Functional status was determined on admission, and at 15 and 30 days after hospital admission using the Karnofsky performance scale (15). The procedure was performed at the patient bed if still hospitalized, or on an ambulatory basis if the patient was already discharged from hospital. After 30 days of hospitalization, a decrease in two categories in the scale, compared to the initial score, was considered as a decline in functional status. Survival during the same period was also recorded.

DATA ANALYSIS AND STATISTICAL CALCULATIONS

To obtain normal values for handgrip strength and maximal inspiratory and expiratory pressures, measurements were performed in 366 healthy subjects aged 20 to 89 years (255 females) of a similar socioeconomic status of the studied patients. The mean value for each parameter and its standard deviation were calculated for each gender in ten year intervals from 20 years of age to over 80. Measurements obtained in patients were expressed as absolute values and z-scores of age and gender normal values.

Normality of variable distribution was determined using the Shapiro-Wilk test. Variables with a normal distribution are expressed as mean ± standard deviation, otherwise as median (interquartile range). The Student's t test or the Kruskal-Wallis test were used to compare variables with normal or non-normal

distributions. Proportions were compared with Chi-squared tests, with Yates correction when necessary. Logistic regression models were used to determine which parameters predicted mortality or functional decline in the studied patients. In these models, categorical variables such as gender or subjective global assessment were expanded into indicator variable sets, also called dummies. Models were designed with those variables that were significantly different in univariate analysis. Maximal inspiratory and expiratory pressures and handgrip strength were included as absolute values or z-scores in different models. All statistical calculations were done on Stata 12 for Windows (Statacorp. Texas 77845, United States).

RESULTS

During a three months period, 108 patients who met the inclusion criteria were recruited. Of these, ten were excluded due to a hospital stay of less than five days and eight due to a failure in obtaining all the clinical data necessary for the study. Therefore, 90 patients aged 58 ± 16 years (46 women) were studied. Of these, 35 had cardiovascular diseases; 25, gastrointestinal conditions; 14, infections; nine, kidney diseases; two, diabetes; and two, cancer. Baseline clinical features, respiratory and handgrip strength values of studied patients are shown in table I. No differences in these features were observed according to the underlying diagnoses of patients.

During the 30 days observation period, six patients died and nine had a decline in Karnofsky performance scale. Baseline features of patients who survived or died during the observation period are shown in table II. Deceased patients had a worst baseline subjective global assessment, lower maximal expiratory pressure and handgrip strength. The differences were significant when the later parameters were expressed as absolute values or z-scores. Baseline features of patients who did no experience a functional decline, those whose functional status declined or died

Table I. Baseline features of studied patients (mean ± standard deviation)

	Women (n = 46)	Men (n = 44)	p*
Age (years)	56.6 ± 19.1	59.1 ± 12.4	NS
Body mass index (kg/m^2)	28.1 ± 7.3	28.9 ± 3.0	NS
Apache II score	7.2 ± 4.1	7.0 ± 4.9	NS
Maximal inspiratory pressure (mmHg)	35.6 ± 17.7	54.9 ± 24.3	< 0.01
Maximal inspiratory pressure (z-score)	-2.4 ± 2.0	-1.4 ± 0.9	< 0.01
Maximal expiratory pressure (mmHg)	21.4 ± 15.2	35.4 ± 20.2	< 0.01
Maximal expiratory pressure (z-score)	-4.4 ± 4.9	-2.0 ± 1.2	< 0.01
Maximal hand grip strength (kg)	17.3 ± 6.0	31.0 ± 8.7	< 0.01
Maximal hand grip strength (z-score)	-1.7 ± 1.4	-1.0 ± 1.7	NS

**Probability for differences between men and women.*

Table II. Baseline features of patients who survived or died during the observation period expressed as mean ± standard deviation or median (interquartile range)

	Surviving patients (n = 84)	Patients who died (n = 6)	p*
Sex (women/men)	42/42‡	4/2‡	NS
Age (years)	57.1 ± 16.3	68.5 ± 9.0	NS
Body mass index (kg/m^2)	28.3 ± 5.8	31.2 ± 1.2	NS
Subjective global assessment (A/B/C)†	30/46/8‡	0/3/3‡	0.01
Karnofski index	65 (50-80)	55 (40-70)	NS
Apache II score	6.9 ± 4.5	10.0 ± 3.5	NS
Maximal inspiratory pressure (mmHg)	45.9 ± 23.5	32.5 ± 14.4	NS
Maximal inspiratory pressure (z-score)	-2.0 ± 1.7	-1.5 ± 0.6	NS
Maximal expiratory pressure (mmHg)	29.4 ± 19.1	12.2 ± 8.3	0.03
Maximal expiratory pressure (z-score)	-3.0 ± 3.2	-7.3 ± 7.4	0.01
Maximal hand grip strength (kg)	24.8 ± 9.8	13.3 ± 7.9	0.01
Maximal hand grip strength (z-score)	-1.3 ± 1.5	-2.6 ± 2.2	0.01

**Probability for differences between groups. †A: well nourished; B: moderately malnourished; C: severely malnourished. ‡Number of patients per category.*

or those whose functional status declined but survived are shown in table III. Patients who experienced a functional decline or died were older and had a lower maximal expiratory pressure, either expressed as absolute value or as z-score and a lower absolute value of handgrip strength. Among those who experienced a functional decline but survived, no significant differences in any parameter, were observed.

Logistic regression models for mortality and functional decline are shown in table IV. The only significant predictor of 30 days mortality or functional decline and mortality was maximal expi-

Table III. Baseline features of patients according to their functional decline during the observation period expressed as mean ± standard deviation or median (interquartile range)

	No functional decline (n = 75)	Functional decline (n = 15)	p*	Functional decline alive (n = 9)	p*
Sex (female/male)	37/38‡	9/6	NS	5/5	NS
Age (years)	56.1 ± 16.5	66.5 ± 10.6	0.0	65.2 ± 11.8	NS
Body mass index (kg/m^2)	28.6 ± 5.9	28.2 ± 4.9	NS	26.2 ± 5.7	NS
Subjective global assessment (A/B/C)†	28/40/7	2/9/4	NS	2/6/1	NS
Karnofski index	60 (50-80)	70 (50-80)	NS	80 (60-90)	NS
Apache II score	6.7 ± 4.6	9.1 ± 3.7	NS	8.6 ± 3.9	NS
Maximal inspiratory pressure (mmHg)	46.3 ± 23.9	38.7 ± 18.5	NS	42.9 ± 20.5	NS
Maximal inspiratory pressure (z-score)	-2.0 ± 1.7	-1.4 ± 1.0	NS	-1.3 ± 1.2	NS
Maximal expiratory pressure (mmHg)	30.2 ± 19.5	18.7 ± 13.2	0.03	23.1 ± 14.5	NS
Maximal expiratory pressure (z-score)	-2.9 ± 3.1	-5.1 ± 5.8	0.04	-3.6 ± 4.2	NS
Maximal hand grip strength (kg)	25.1 ± 10.0	18.5 ± 8.8	0.02	21.9 ± 8.0	NS
Maximal hand grip strength (z-score)	-1.3 ± 1.6	-1.8 ± 1.7	NS	-1.2 ± 1.0	NS

**Probability for differences with patients without functional decline. †A: well nourished; B: moderately malnourished; C: severely malnourished. ‡Number of patients per category.*

Table IV. Logistic regression models for mortality or functional decline including only those variables that were significant on univariate analysis

	30 days mortality	p*	Decline in functional status at 30 days	p	Decline in functional status excluding deaths	p*
Models using absolute values of strength measures						
Age (years)			1.03 (0.98-1.08)‡	NS		
Subjective global assessment B†	0 (0-0)	NS				
Subjective global assessment C†	0 (0-0)	NS				
Maximal inspiratory pressure	1.08 (0.98-1.19)	NS	1.04 (0.99-1.09)	NS	1.03 (0.97-1.08)	NS
Maximal expiratory pressure	0.9 (0.8-1.02)	NS	0.95 (0.9-1.01)	NS	0.96 (0.9-1.02)	NS
Maximal hand grip strength	0.84 (0.68-1.03)	NS	0.93 (0.86-1.02)	NS	0.96 (0.87-1.05)	NS
Models using z-scores of strength measures						
Age (years)			1.05 (0.99-1.11)	NS		
Subjective global assessment B†	0 (0-0)	NS				
Subjective global assessment C†	0 (0-0)	NS				
Maximal inspiratory pressure	2.18 (0.65-7.28)	NS	1.29 (0.69-2.4)	NS	1.47 (0.83-2.61)	NS
Maximal expiratory pressure	0.83 (0.69-0.99)	0.04	0.88 (0.78-0.99)	0.04	0.95 (0.8-1.13)	NS
Maximal hand grip strength	0.53 (0.26-1.1)	NS	0.71 (0.47-1.08)	NS	0.96 (0.89-1.04)	NS

**Probability. †Subjective global assessment of nutritional status; A: well nourished, B: moderately malnourished and C: severely malnourished. ‡Odds ratio (95% confidence intervals).*

ratory pressure, expressed as a z-score. Again, in the models in which functional decline excluding deceased patients was used as the dependent variable, none of the tested parameters had a significant predictive capacity.

DISCUSSION

The main result of this observational study is that maximal expiratory pressure upon admission was an independent and significant predictor of mortality and functional decline in this group of hospitalized patients.

The prediction of mortality, incidence of complications and functional impairment is of utmost importance among hospitalized patients. The Acute Physiology and Chronic Health Evaluation II (APACHE II) (16) score was developed to predict mortality among intensive care patients, and it is still a reliable instrument (17). This score is calculated from disease related items and organ function. Nutritional status assessment should predict the incidence of complications. Among the nutritional scores with high predictive value, we chose the subjective global assessment, which is easy to apply and has a low interrater variability (18). Functional impairment prior or during hospital stay is especially relevant in older people, since it predicts outcomes in terms of independence and is also associated with a higher rate of readmission (19) and mortality (20). The importance of maintaining mobility and functionality during hospital stay is underscored by trials showing that mobility enhancing programs improve outcomes in terms of independence after discharge (21).

Since mobility and functionality are important prognostic factors during hospital stay, assessment of muscle performance should be a valuable tool to assess clinical outcome. The long term prognostic value of hand grip strength and other functional measures is undisputable (22). In the hospital setting we showed that this measurement predicts functional impairment during hospital stay (23,24). Maximal inspiratory and expiratory pressures measure thoracic muscle strength, without interferences from airflow limitations (25). These muscles are important to maintain an adequate respiratory capacity, thus influencing oxygen and artificial ventilation requirements, but should also serve as global indicators of muscle mass and function. The finding of this study showing that maximal expiratory pressure predicts mortality and functional impairment in hospitalized patients is novel. The logistic regression models show that this measurement outweighs handgrip strength and subjective global assessment as prognostic indicators. However, a study with a larger number of patients should be performed to determine the additive significance in prognosis that a combination of these assessments could have.

As shown in the results, maximal expiratory pressure is a significant predictive tool only when it is expressed as a z-score of normative values in healthy age and gender matched individuals. Since muscle strength measurements are so dependent on age and gender, informing them as absolute values can be misleading (26). Moreover, normal values cannot be extrapolated from one region to another. Those obtained in North American populations are different to those of Latin American subjects (27). Therefore, obtaining local standards in subjects of the same country and socioeconomic status becomes relevant. For the present study, handgrip and respiratory muscle strength were measured in a significant number of healthy people; therefore, our z-score calculation can be considered as reliable.

The main weakness of this study is the low number of patients studied and that they all were admitted to the same hospital. The ideal would be to perform the study in several hospitals to observe if results were maintained. This is a pending task that should be carried out in the future. However, we detected that maximal expiratory pressure has a significant predictive value for death and functional impairment, even with the low number of observations, which increase the validity of the observation. The strengths of the study are that all the observations and measurements were carried out by the same researcher (EC), that in very few patients we were not able to obtain all the required clinical data and having a significant number of measurements in healthy people to be able to calculate accurate z scores.

In conclusion, maximal expiratory pressure deserves future studies to determine its real value as a prognostic parameter, along with hand grip strength, in hospitalized patients.

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Trabajo Original

Otros

Estudio comparativo de las variables determinantes de la condición física y salud entre jóvenes deportistas y sedentarios del género masculino

Comparative study of the variables of physical fitness and health among young athletes and sedentary males

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Resumen

Introducción: hoy en día, la práctica de actividad física durante la adolescencia aporta importantes beneficios físicos-saludables que ayudan a desarrollar un bienestar futuro en años posteriores de la vida.

Objetivos: el objetivo del presente estudio comparativo fue evaluar la condición física, composición corporal y capacidad cardiorrespiratoria entre jóvenes deportistas y sedentarios de la Comunidad Autónoma de Extremadura (España).

Métodos: doscientos veinticinco sujetos varones, con edades comprendidas entre 12 y 18 años, fueron divididos en dos grupos: 175 deportistas, divididos a su vez en grupo aeróbico (AEG), grupo anaeróbico (ANAEG) y grupo de deportes mixtos (MG); y 50 sedentarios (SG) o grupo control. Se les evaluó la capacidad respiratoria (volumen espiratorio forzado [FEV], flujo espiratorio máximo [PEF], capacidad vital [CV], ventilación máxima voluntaria [MVV]) y la composición corporal. También se les realizó el test del escalón de "Forest Service" para hallar el VO_2max. Se registraron asimismo la frecuencia cardiaca (FC) previa al escalón, la FC máxima durante el test y la FC en la recuperación posterior. Así como la presión arterial previa y posterior al test.

Resultados: se hallaron diferencias significativas en la composición corporal, la presión arterial, la FC y la capacidad respiratoria en relación a los deportistas con respecto al grupo control ($p < 0,05$).

Conclusiones: la actividad física aporta beneficios en aspectos como la composición corporal y la función cardiorrespiratoria.

Palabras clave:

Sedentarismo.
Condición física.
Ejercicio físico. Salud.
Adolescencia.

Abstract

Introduction: today, the practice of physical activity during adolescence brings important physical-health benefits that help develop a future well-being in later life.

Objectives: the objective of this comparative study was to evaluate the physical condition, body composition and cardiorespiratory capacity among young athletes and sedentary people of the Autonomous Community of Extremadura (Spain).

Methods: two hundred and twenty-five male subjects, aged between 12 and 18 years, were divided into two groups: 175 athletes, divided into aerobic group (AEG), anaerobic group (ANAEG) and mixed sports group (MG); and 50 sedentary (SG) or control group. Their respiratory capacity (forced expiratory volume [FEV], peak expiratory flow [PEF], vital capacity [VC], maximum voluntary ventilation [MVV]) and body composition were assessed. They also performed the "Forest Service" step test by finding the VO_2max. Also, the heart rate (HR) was recorded before the step, the maximum heart rate during the test and the HR in the subsequent recovery, as well as pre and post-test blood pressure.

Results: there were significant differences in body composition, blood pressure, heart rate and respiratory capacity in relation to athletes compared to the control group ($p < 0.05$).

Conclusions: physical activity provides benefits in aspects such as body composition, and cardio-respiratory function.

Key words:

Physical inactivity.
Physical exercise.
Health. Adolescence.

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INTRODUCCIÓN

La actividad física es recomendable en todas las edades, pero es en la juventud donde juega un papel fundamental a la hora de adquirir hábitos saludables. La población puberal y adolescente se encuentra en un periodo crítico donde comienzan a adoptarse actitudes y hábitos perjudiciales para la salud, tales como puede ser el consumo de tabaco, alcohol y otras drogas, así como el abandono de prácticas deportivas realizadas en edades infantiles.

En este sentido, ha sido reportado que los adolescentes desarrollan una variedad de comportamientos sedentarios, así como una menor prevalencia del tiempo libre activo en sus estilos de vida. Parece prudente, por lo tanto, alentar a los jóvenes a adoptar estilos de vida saludables en general, con una favorable combinación de ambas actividades activas y sedentarias (1).

Es en la etapa de la adolescencia donde, por norma general, se desarrollan estilos de vida más activos. Sin embargo, hay un porcentaje elevado de adolescentes que no alcanzan el nivel de actividad física recomendado. Este hecho puede ser debido al incremento del uso de los videojuegos y de los ordenadores, que repercute en la salud. El sedentarismo se ve directamente relacionado con enfermedades de sobrepeso, factores de riesgos coronarios, mentales, diabetes tipo II y síndrome metabólico (2-4). En 2010, Piñeros y cols. reportaron bajos niveles de actividad física en cinco ciudades de Colombia (5).

En España, la población de adolescentes con sobrepeso sufre el mismo incremento que en países europeos (6). Según los datos de la European Heart Network, la proporción de adolescentes inactivos en España en 2001 era del 33%. Además, en el estudio HELENA se observó que, en chicas adolescentes, un mayor nivel de sedentarismo era asociado con una disminución de la capacidad cardiorrespiratoria (7).

En una reciente revisión científica se observó cómo las combinaciones de actividad física, comportamiento sedentario y sueño se asocian con indicadores de salud en niños y jóvenes. Así, la actividad física y el nivel alto de sueño se asociaron con beneficios cardiometabólicos y en la adiposidad. Por otro lado, actividad física y bajo nivel de sueño se relacionaron con beneficios cardiometabólicos, de adiposidad y fitness general en comparación con un bajo nivel de actividad física (8).

La bibliografía científica sugiere que mayores niveles de actividad física se asocian a mejores niveles en marcadores de salud en adolescentes. Por ello, el objetivo del presente estudio fue evaluar la composición corporal, la condición física y la capacidad cardiorrespiratoria en jóvenes activos en comparación con adolescentes sedentarios.

MÉTODOS

MUESTRA

En este estudio participaron un total de 225 sujetos varones, con edades comprendidas entre 12 y 18 años, todos ellos ciudadanos de la Comunidad Autónoma de Extremadura, región ubicada en España, al suroeste del país. Los participantes se dividieron en dos grupos: grupo deportistas (DG), con 175 deportistas procedentes de las federaciones extremeñas de diferentes modalidades deportivas; y grupo sedentario (SG), compuesto por 50 adolescentes sedentarios provenientes de centros educativos públicos y concertados de la región extremeña.

El DG se subdividió a su vez en tres grupos: grupo aeróbico (AEG), grupo anaeróbico (ANAEG) y grupo mixto (MG), según las características fisiológicas de los deportes que practicaban los sujetos. Así pues, el grupo aeróbico (AEG) contenía sujetos que practicaban deportes de resistencia como triatlón, orientación, natación y atletismo de fondo. El grupo anaeróbico (ANAEG) estuvo constituido por deportistas con modalidades principalmente anaeróbicas (salvamento y socorrismo, kárate, tenis y pruebas cortas de atletismo y natación). Por último, el grupo mixto (MG) se caracterizó por participantes en deportes interválicos (balonmano). El SG no realizaba más actividad física que las horas de Educación Física en horario lectivo. Fueron excluidos de este estudio los adolescentes que no tenían el consentimiento de sus padres y aquellos que padecían enfermedades cardiorrespiratorias o cardiometabólicas.

La evaluación de los deportistas tuvo lugar durante las concentraciones de la Selección extremeña de los respectivos deportes. Las mediciones de los sujetos sedentarios tuvieron lugar en sus respectivos centros de estudios. En la tabla I figuran las características generales de la muestra y segmentadas por grupo.

VALORACIÓN ANTROPOMÉTRICA Y DE COMPOSICIÓN CORPORAL

Las mediciones se realizaron en las mismas condiciones, en el mismo orden, con el mismo protocolo y por los mismos medidores (encargados cada uno de una parte de las mediciones en todos

Tabla I. Características generales del total de la muestra

	Muestra total (n = 225)	SG (n = 50)	ANAEG (n = 73)	AEG (n = 40)	MG (n = 62)
Edad (años)	14,53 ± 1,70	14,28 ± 2,01	14,14 ± 1,58	15,47 ± 1,67	14,47 ± 1,51
Peso (kg)	61,06 ± 12,97	56,89 ± 13,73	57,75 ± 13,12	60,48 ± 9,81	67,03 ± 12,38
Altura (cm)	1,69 ± 0,11	1,65 ± 0,1	1,66 ± 0,12	1,70 ± 0,08	1,73 ± 0,09

SG: grupo sedentario; ANAEG: grupo anaeróbico; AEG: grupo aeróbico; MG: grupo de deportes mixtos.

los sujetos) y siguiendo todas las directrices del Grupo Español de Cineantropometría (9).

Para la valoración antropométrica se utilizó una báscula de la marca Seca® con una precisión de ± 100 g para evaluar el peso (kg), con tallímetro de pared con una precisión de ± 1 mm para la altura (m), un compás de pliegues cutáneos o plicómetro de marca Holtain con una precisión de ± 0,2 mm para los pliegues cutáneos, un compás de diámetros óseos o paquímetro de la misma marca con precisión de ± 1 mm y una cinta métrica Holtain con precisión de ± 1 mm para valorar los perímetros corporales.

Los pliegues cutáneos evaluados (medidos en mm) fueron el abdominal, suprailiaco, tricipital, subescapular, del muslo y de la pierna. Los perímetros musculares (medidos en cm) de brazo relajado y pierna relajada se evaluaron con la musculatura relajada. Las ecuaciones empleadas para hallar la masa muscular (ecuación de Porta y cols.), grasa (ecuación de Yuhazs) y ósea (ecuación de Van Dobleny Rocha) fueron las que establecen Porta y cols., del Grupo de Cineantropometría (10).

VALORACIÓN DE LA CONDICIÓN FÍSICA

Previo a la medición de la condición física se realizó un calentamiento de cinco minutos de duración basado en la movilidad articular y trabajo de flexibilidad. Para la estimación del VO_2max se realizó la prueba del escalón de Forest Service. El VO_2max, expresado en ml/kg/min, fue calculado según las tablas estimativas de Sharkey, teniendo como referencia el peso del sujeto y los valores de FC obtenidos tras la "prueba del escalón" (11).

VALORACIÓN CARDIORRESPIRATORIA

Para medir tanto la FC por minuto (ppm) como la presión arterial de los sujetos tanto en reposo como tres minutos tras la realización de la prueba del escalón del Forest Service, se utilizó un tensiómetro de la marca OMRON 705 IT Intellisense™.

Los valores espirométricos fueron medidos con un espirómetro portátil de marca Medgraph Ltd. Spirobank G®. Fueron registrados el pico de flujo espiratorio (PEF), el volumen espiratorio forzado en el primer segundo (VEMS), la capacidad vital forzada o máximo volumen de aire espirado (CV) y la máxima ventilación voluntaria (MVV).

ANÁLISIS ESTADÍSTICO

Para la valoración estadística se utilizó el programa estadístico IBM SPSS, en la versión 21.0 para Windows (SPSS Inc., Chicago, IL, Estados Unidos), representándose los datos según su media ± desviación estándar.

Previamente al tratamiento de los datos, se procedió a establecer las pruebas de normalidad a través de la prueba estadística Kolmogorov-Smirnov y de homocesticidad de la muestra mediante la prueba de homogeneidad de las varianzas.

Para establecer la diferencia de los datos de los sujetos sedentarios con respecto a los deportistas aeróbicos, anaeróbicos y mixtos por separado, se aplicó el tratamiento ANOVA de un factor con comparaciones múltiples post hoc de Bonferroni y Tukey, con un nivel de significación de $p < 0,05$; los valores inferiores a 0,01 se consideraron diferencias muy significativas.

RESULTADOS

Las tablas muestran una comparativa de variables entre los resultados obtenidos por el SG, con respecto a los grupos AEG, ANAEG Y MG.

A continuación, se presentan los resultados de altura, peso e índice de masa corporal (IMC) en la tabla II.

Se apreciaron diferencias significativas en el peso y la altura entre el SG y el MG ($p < 0,01$), con valores mayores en el segundo grupo. Sin embrago, no hubo diferencias en estos parámetros entre el SG y los grupos AEG Y ANAEG. En el IMC no se observaron

Tabla II. Medidas antropométricas

Variables	Sedentarios (n = 50)	Deportistas (n = 175)		Sig.
Peso (kg)	56,89 ± 13,74	AEG (n = 40)	60,48 ± 9,81	NS
		ANAEG (n = 73)	57,75 ± 13,12	NS
		MG (n = 62)	67,04 ± 12,38	†
Altura (m)	1,65 ± 0,11	AEG (n = 40)	1,70 ± 0,08	NS
		ANAEG (n = 73)	1,67 ± 0,12	NS
		MG (n = 62)	1,74 ± 0,12	†
IMC (kg/m²)	20,62 ± 3,92	AEG (n = 40)	20,81 ± 2,40	NS
		ANAEG (n = 73)	20,50 ± 2,70	NS
		MG (n = 62)	22,09 ± 2,95	NS

*ANAEG: grupo anaeróbico; AEG: grupo aeróbico; MG: grupo de deportes mixtos; NS: no significación; IMC: índice de masa corporal. *p < 0,05; †p < 0,01.*

diferencias y todos los grupos evaluados se encontraron dentro de los parámetros de normopeso.

En la tabla III se recopilan los valores netos y porcentajes de peso corporal de los diferentes grupos. Se observan diferencias significativas en la masa grasa, teniendo mayor porcentaje el SG que el AEG y el ANAEG en el porcentaje ($p < 0,01$) como en el peso neto ($p < 0,05$). En relación a la masa muscular se observan diferencias significativas también de los grupos ANAEG, AEG y MG con respecto al SG tanto en el porcentaje ($p < 0,01$) como en el peso neto ($p < 0,05$). Solamente se observan diferencias significativas en la masa ósea en el porcentaje, siendo mayor el peso neto de masa ósea del MG que del SG ($p < 0,05$). En la masa magra también se observan diferencias, con menor porcentaje del SG que del ANEG y del AEG; esta última comparación es muy significativa en el peso neto ($p < 0,01$).

En la tabla IV se muestran los resultados de la presión arterial inicial, en reposo y en recuperación, así como la diferencia recuperación-basal en comparación con el SG tras la prueba del escalón.

Se observan diferencias significativas en la presión arterial diastólica en reposo ($p < 0,01$) y en la presión arterial sistólica ($p < 0,01$) y diastólica ($p < 0,01$) tras tres minutos de ejercicio aeróbico moderado, con mayores valores en el MG que en el SG.

En la tabla V se observan los valores de la FC en basal, máxima y recuperación, como el incremento y el descenso durante y posterior al test del escalón.

No hay diferencias significativas en ninguno de los grupos en comparación con el SG. Se obtuvieron diferencias significativas en el pulso tras recuperación, con un mayor descenso en la FC en el ANAEG ($p < 0,05$) y el MG ($p < 0,01$) con respecto al SG.

En la tabla VI se muestran los valores respiratorios obtenidos por los diferentes grupos.

Se observan diferencias significativas en el VEMS y en el CV ($p < 0,01$), con mayores valores en los grupos AEG y MG que en el SG, y en el PEF y MVV, con valores más elevados en los grupos AEG, ANAEG y MG en general que en el SG. Se observan también diferencias significativas en el VO_2máx, siendo mayor el valor del SG que del MG ($p < 0,01$).

Tabla III. Peso neto y porcentajes de masa grasa, muscular y ósea

Variables	Sedentarios (n = 50)	Deportistas (n = 175)		Sig.
Peso graso (kg)	8,15 ± 4,20	AEG (n = 38)	5,94 ± 1,80	*
		ANAEG (n = 66)	6,07 ± 2,54	*
		MG (n = 62)	10,17 ± 4,24	NS
Peso muscular (kg)	25,10 ± 5,50	AEG (n = 38)	29,49 ± 5,14	*
		ANAEG (n = 66)	28,11 ± 8,33	NS
		MG (n = 62)	29,17 ± 5,17	*
Peso óseo (kg)	9,93 ± 1,89	AEG (n = 38)	10,96 ± 1,28	NS
		ANAEG (n = 66)	10,13 ± 3,03	NS
		MG (n = 62)	11,54 ± 1,48	*
Peso magro (kg)	48,74 ± 10,37	AEG (n = 38)	55,18 ± 8,30	NS
		ANAEG (n = 66)	52,31 ± 12,02	NS
		MG (n = 62)	56,86 ± 9,04	†
Peso graso (%)	13,77 ± 4,04	AEG (n = 38)	9,61 ± 1,76	†
		ANAEG (n = 66)	10,30 ± 2,95	†
		MG (n = 62)	14,70 ± 4,09	NS
Peso muscular (%)	44,38 ± 3,28	AEG (n = 38)	48,13 ± 2,39	†
		ANAEG (n = 66)	47,82 ± 5,03	†
		MG (n = 62)	43,69 ± 3,22	NS
Peso óseo (%)	17,75 ± 1,75	AEG (n = 38)	18,15 ± 2,11	NS
		ANAEG (n = 66)	17,77 ± 4,21	NS
		MG (n = 62)	17,51 ± 2,17	NS
Peso magro (%)	86,23 ± 4,04	AEG (n = 38)	90,39 ± 1,76	†
		ANAEG (n = 66)	89,69 ± 2,95	†
		MG (n = 62)	85,30 ± 4,09	NS

*ANAEG: grupo anaeróbico; AEG: grupo aeróbico; MG: grupo de deportes mixtos; NS: no significación. **p < 0,05; †p < 0,01.*

Tabla IV. Presión arterial sistólica y diastólica en reposo, tras la prueba del escalón y tras tres minutos de recuperación e incrementos y diferencias tras esfuerzo con respecto a reposo

Variables	Sedentarios (n = 50)	Deportistas (n = 175)		Sig.
Presión arterial sistólica en reposo (mmHg)	121,96 ± 15,68	AEG (n = 39)	131,67 ± 14,61	NS
		ANAEG (n = 65)	121,33 ± 14,86	NS
		MG (n = 62)	130,85 ± 14,15	NS
Presión diastólica en reposo (mmHg)	68,20 ± 6,55	AEG (n = 39)	70,10 ± 8,25	NS
		ANAEG (n = 54)	68,00 ± 10,53	NS
		MG (n = 62)	75,45 ± 10,98	†
Presión arterial sistólica final (mmHg)	136,76 ± 18,74	AEG (n = 8)	122,63 ± 14,99	NS
		ANAEG (n = 15)	138,33 ± 18,59	NS
		MG (n = 62)	151,69 ± 20,03	†
Presión arterial diastólica final (mmHg)	72,16 ± 7,91	AEG (n = 8)	63,00 ± 9,35	NS
		ANAEG (n = 15)	73,40 ± 9,78	NS
		MG (n = 62)	80,37 ± 14,46	*
Presión arterial sistólica tras 3 min recuperación (mmHg)	119,52 ± 13,61	AEG (n = 8)	112,25 ± 10,52	NS
		ANAEG (n = 9)	119,56 ± 16,87	NS
		MG (n = 62)	128,66 ± 17,39	NS
Presión arterial diastólica tras 3 min recuperación (mmHg)	68,52 ± 8,51	AEG (n = 8)	59,50 ± 6,80	NS
		ANAEG (n = 9)	77,89 ± 14,37	NS
		MG (n = 62)	72,55 ± 10,19	NS
Incremento presión arterial sistólica tras esfuerzo (mmHg)	14,80 ± 13,29	AEG (n = 8)	5,12 ± 8,17	NS
		ANAEG (n = 15)	17,67 ± 12,80	NS
		MG (n = 62)	20,81 ± 14,30	NS
Incremento presión arterial diastólica tras esfuerzo (mmHg)	3,96 ± 7,20	AEG (n = 8)	-5,50 ± 8,96	NS
		ANAEG (n = 15)	3,93 ± 18,46	NS
		MG (n = 62)	4,92 ± 15,71	NS
Descenso presión arterial sistólica tras 1 min recuperación (mmHg)	17,24 ± 12,29	AEG (n = 8)	10,37 ± 8,93	NS
		ANAEG (n = 9)	25,33 ± 18,08	NS
		MG (n = 62)	23,03 ± 11,78	NS
Descenso presión arterial diastólica tras 3 min recuperación (mmHg)	3,64 ± 7,80	AEG (n = 8)	3,50 ± 4,07	NS
		ANAEG (n = 9)	-8,22 ± 12,09	NS
		MG (n = 62)	7,82 ± 14,36	NS

*ANAEG: grupo anaeróbico; AEG: grupo aeróbico; MG: grupo de deportes mixtos; NS: no significación. *p < 0,05; †p < 0,01.*

DISCUSIÓN

DIFERENCIAS EN LA COMPOSICIÓN CORPORAL

Es abundante la bibliografía científica que recoge estudios comparativos de valores de composición corporal y salud entre jóvenes sedentarios y practicantes de actividad física con los que se puede comparar el presente estudio.

En un estudio comparativo entre jóvenes deportistas y no deportistas de edades comprendidas entre los 15 y los 18 años en Ciudad de México, se encontró que en lo que se refiere a la estatura total, a la estatura sentado y a la longitud de las piernas, los deportistas masculinos presentan dimensiones algo mayores que los no deportistas, es decir, los que practican algún ejercicio físico organizado son de talla ligeramente más alta que los no practicantes (12).

En la línea de este hallazgo se encuentran los resultados obtenidos en el presente estudio con respecto a las diferencias en estatura entre los grupos SG y DG en la comunidad de Extremadura, sabiendo que en el MG son más altos que en el SG. Sin embargo, en otros estudios se afirma que la estatura no es un

Tabla V. FC por minuto en reposo, tras la prueba del escalón y tras un minuto de recuperación, incremento de la FC y descenso de la FC tras un minuto de recuperación

Variables	Sedentarios (n = 50)	Deportistas (n = 175)		Sig.
FC en reposo (ppm)	79,92 ± 17,37	AEG (n = 39)	71,26 ± 13,72	NS
		ANAEG (n = 30)	76,27 ± 12,24	NS
		MG (n = 62)	83,26 ± 17,53	NS
FC máxima (ppm)	106,40 ± 25,30	AEG (n = 10)	104,80 ± 27,82	NS
		ANAEG (n = 22)	123,27 ± 37,17	NS
		MG (n = 62)	118,63 ± 19,91	NS
FC recuperación (ppm)	95,88 ± 20,69	AEG (n = 10)	87,40 ± 12,78	NS
		ANAEG (n = 22)	96,14 ± 24,71	NS
		MG (n = 62)	91,05 ± 23,22	NS
Incremento de FC tras esfuerzo (ppm)	30,48 ± 17,13	AEG (n = 10)	21,80 ± 24,32	NS
		ANAEG (n = 22)	44,18 ± 33,60	NS
		MG (n = 62)	35,37 ± 18,96	NS
Descenso de FC tras 1 min recuperación (ppm)	10,52 ± 8,27	AEG (n = 10)	17,40 ± 20,50	NS
		ANAEG (n = 22)	27,14 ± 35,04	*
		MG (n = 62)	27,58 ± 18,69	†

ANAEG: grupo anaeróbico; AEG: grupo aeróbico; MG: grupo de deportes mixtos; NS: no significación.

Tabla VI. Valores respiratorios

Variables	Sedentarios (n = 50)	Deportistas (n = 175)		Sig.
VEMS (L/s)	3,23 ± 0,88	AEG (n = 40)	4,36 ± 0,82	†
		ANAEG (n = 71)	3,59 ± 0,87	NS
		MG (n = 62)	4,19 ± 0,86	†
CV (L/s)	3,58 ± 0,97	AEG (n = 40)	4,96 ± 1,01	†
		ANAEG (n = 71)	4,21 ± 1,35	NS
		MG (n = 62)	4,72 ± 0,98	†
PEF (L/s)	5,33 ± 1,88	AEG (n = 40)	8,52 ± 1,74	†
		ANAEG (n = 71)	6,89 ± 1,89	†
		MG (n = 62)	7,85 ± 1,77	†
MVV (L/m)	112,08 ± 37,53	AEG (n = 40)	167,95 ± 33,95	†
		ANAEG (n = 71)	136,44 ± 34,56	*
		MG (n = 62)	146,52 ± 42,92	†
VO_2máx (ml/kg/min)	56,65 ± 8,91	AEG (n = 8)	59,67 ± 10,59	NS
		ANAEG (n = 15)	51,51 ± 11,80	NS
		MG (n = 60)	45,63 ± 5,96	†

*ANAEG: grupo anaeróbico; AEG: grupo aeróbico; MG: grupo de deportes mixtos; NS: no significación. *p < 0,05; **p < 0,01.*

indicador relevante con el que se pueda diferenciar a grupos en función del nivel de actividad física-deportiva realizada (13).

Con respecto al peso corporal, en el presente estudio, encontramos que el DG tiene un mayor peso que el SG, siendo mayor la diferencia especialmente significativa en el MG, aunque puede ser debido a la diferencia significativa hallada en la altura.

Así, se observa que los sujetos de este estudio, por lo general, no presentan sobrepeso y que no hay diferencias en este índice

entre sedentarios y deportistas, en contrapunto a los numerosos estudios donde se han hallado relaciones entre sedentarismo y obesidad (5,14,15). Por lo cual, la inactividad puede estar injustamente implicada en la evolución epidemiológica reciente del sobrepeso y la obesidad entre los niños y jóvenes, como ya señalan Biddle y cols. (2017) en su revisión reciente, en la cual afirman que las asociaciones entre el comportamiento sedentario y la adiposidad en niños y adolescentes son pequeñas o muy pequeñas, con poca o nula evidencia de que esta asociación sea causal (16).

Aunque en el SG no se hallaron parámetros de obesidad, sí se hallaron diferencias significativas tanto en porcentaje como en el peso graso entre los grupos de actividad física y el grupo sedentario, en línea con lo establecido en recientes estudios en donde se asocian mayores niveles de adiposidad, tanto en el porcentaje como en el peso absoluto, con niveles bajos de actividad física (15,17,18).

Los niños deportistas presentan una masa ósea superior, pues la actividad está asociada positivamente con la densidad mineral ósea (19). La American Society for Bone and Mineral Research halló, en 2009, que la actividad deportiva en la infancia y la adolescencia se asocia con un aumento del tamaño cortical de los huesos, lo que sugiere que la actividad deportiva durante el crecimiento confiere efectos positivos en la geometría del hueso. En la misma línea, una reciente revisión llevada a cabo por Weaver y cols. (2015) concluye que hay evidencia sobre los beneficios de la actividad física en la acumulación de masa ósea (20). Los resultados del presente estudio revelan, en concordancia con lo anterior, que el grupo MG tiene mayor proporción que el sedentario en valores absolutos de peso óseo. Sin embrago, en comparación con los grupos AEG y ANAEG no se hallan diferencias. La causalidad de que el MG tenga mayor densidad ósea puede hallarse en la práctica del balonmano, deporte en el cual hay una gran carga de saltos. Todos los exitosos ensayos controlados aleatorios que evalúan el ejercicio como un factor causal para la resistencia ósea han utilizado el salto como actividad física primaria. Saltar impone un mayor estímulo anabólico en el hueso que las comúnmente prescritas actividades de carga metabólica como caminar o correr. Esta habilidad motora carga mecánicamente el sitio clínicamente importante de la cadera a través de la carga muscular durante el despegue y mediante la carga de impacto durante el aterrizaje (21).

Los valores que se obtuvieron sobre el componente muscular son favorables al AEG y al ANAEG con respecto a los sedentarios, coincidiendo con las conclusiones halladas por un estudio de Miranda, en 2007, donde un grupo de jugadores de voleibol mostró un mayor porcentaje muscular que el grupo de sedentarios (13).

El componente magro también es superior en el ANAEG y el AEG, con valores acordes a lo establecido por Jiménez y cols. en 2001, que afirman que los niños deportistas presentan mayor masa magra. Dos estudios recientes relacionan una mayor masa magra con masa ósea (22,23). Por otro lado, en el presente estudio, no se observa en los sujetos que presentan mayor masa magra una mayor masa ósea que en el grupo control.

CARDIORRESPIRATORIO

En valores relacionados con la presión arterial, encontramos que el MG obtiene valores más desfavorables en la presión arterial diastólica en reposo que el SG, en la línea de otros estudios que no han hallado en adolescentes relación entre presión arterial y actividad física (24-26). Esto contradice algunos estudios epidemiológicos que sugieren una relación dosis-respuesta entre el nivel de actividad física habitual, o de aptitud y capacidad física, y la presión arterial de reposo (27), así como estudios que reportan que una actividad física de alta intensidad puede mejorar el sistema cardiovascular en niños adolescentes, pues el ejercicio físico produce una vasodilatación que tiende a disminuir las resistencias vasculares periféricas y, en consecuencia, a disminuir la presión arterial diastólica durante el ejercicio (18,28). Tras el test submáximo, el SG obtiene mejores valores de presión arterial, tanto sistólica como diastólica, que el MG. Al comparar el grupo SG con los grupos AEG y ANAEG, no se hallan diferencias estadísticamente significativas en cuanto a la presión arterial en reposo, tras ejercicio y después de la recuperación, lo que contradice la afirmación de que los ejercicios físicos pueden reducir la presión arterial en reposo, durante un esfuerzo con carga de trabajo submáxima y después del ejercicio físico (29). Los resultados obtenidos podrían carecer de significación considerando que todos los valores sedentarios se encuentran dentro de los parámetros establecidos como saludables.

Se ha establecido que los individuos que poseen una mayor resistencia aeróbica suelen tener un ritmo cardiaco lento en reposo. El entrenamiento habitual logra un aumento del volumen cardiaco en reposo, del mismo modo que durante el ejercicio, con una FC baja y un gran volumen sistólico. Entre las modificaciones cardiovasculares, se observa un descenso de la FC en reposo y también durante la realización de un ejercicio físico (30). El ejercicio aeróbico ejerce efectos beneficiosos en el ritmo circadiano de la FC, especialmente en el horario matutino (31). Sin embargo, en la presente investigación no se hallaron diferencias en las FC en reposo, tras un esfuerzo y tras la recuperación, en contrapunto a los estudios que sugieren que mayores niveles de adiposidad se relacionan con elevados niveles de FC (32). Por otro lado, sí se observa un mayor descenso de la FC en los grupos ANAEG y MG tras un minuto de recuperación después de un esfuerzo, pudiendo ser debido a una mejor recuperación tras esfuerzo en deportes interválicos, ya que la variabilidad de la FC se ve asociada con la actividad moderada-vigorosa (33).

Da Silva y cols. (2016) observaron que los niños que eran activos (tiempo de ocio y actividad física total) a las edades de 11 y 15 años tenían mayores ganancias en FEV1, FVC y PEF que los que estaban inactivos. Por lo tanto, el presente estudio obtiene resultados acordes a los últimos estudios relacionados con actividad física y función pulmonar.

En relación a los parámetros respiratorios, se observa que todos los grupos se encuentran dentro de los valores espirométricos saludables (34), en concordancia con estudios que sugieren que la función pulmonar no se ve afectada por el comportamiento sedentario (35). Sin embargo, se observaron mejores valores

espirométricos en el DG en comparación con el SG, especialmente en el caso del AEG, pues tal y como ha sido reportado, el ejercicio aeróbico aumenta la capacidad pulmonar (36). Bae y cols. (2015) observaron que la estatura, el peso, el IMC y la grasa corporal se correlacionaban significativamente con los parámetros espirométricos, así como la fuerza de la mano derecha, la fuerza de agarre de la mano izquierda y el salto de Sargent también se correlacionaron significativamente con la CVF y el FEV1 (37).

En cuanto al VO_2máx, los sujetos evaluados en el presente estudio, están dentro del umbral de salud cardiovascular fijado por Ortega y cols. (2005) en 42 ml/kg/min para toda la adolescencia en el caso de los varones (38). No se encontraron diferencias significativas, sin embargo, entre el SG y los grupos AEG y ANAE estos resultados parecen contradictorios, teniendo en cuenta la mejor función pulmonar obtenida en los valores espirométricos y la gran cantidad de estudios que sugieren que unos mayores niveles de actividad física y menor masa grasa se relacionan con un aumento del VO_2max (39,40). Sorprendentemente, se puede apreciar que los practicantes de deportes mixtos y anaeróbicos tienen un menor VO_2max que los que no practican ningún deporte, pudiendo ser debido a que el VO_2max estimado no se considera un buen indicador de la capacidad de rendimiento aeróbica.

Las limitaciones del presente estudio residen en el tamaño de la muestra, donde un mayor número de participantes ayudaría a obtener resultados más concluyentes. Además, otra limitación de la presente investigación fue la obtención del VO_2máx de forma estimada, siendo más precisa la obtención de sus resultados a través del análisis de gases, lo cual permite, en ese caso, comparar datos de mayor fiabilidad.

CONCLUSIONES

A través de los resultados obtenidos en esta investigación podemos extraer una serie de conclusiones con respecto a las diferencias en parámetros de salud medidos entre jóvenes varones sedentarios y deportistas:

- Los sujetos evaluados en este estudio, tanto sedentarios como deportistas, en general se encuentran dentro de los parámetros de normalidad de IMC.
- Los deportistas mixtos tienen mayor peso y estatura que los sedentarios.
- Los practicantes de deportes aeróbicos y anaeróbicos tienen una menor cantidad de grasa cutánea que los sujetos sedentarios.
- Los deportistas tienen mayor cantidad de masa muscular y masa libre de grasa, y menor cantidad de grasa que los sedentarios.
- En valores de presión arterial, los deportistas mixtos tienden a tener valores más elevados que el resto de los evaluados.
- Los deportistas recuperan antes los valores cardiacos de reposo tras un esfuerzo.
- Los deportistas tienen una mayor capacidad pulmonar que los sedentarios.
- El VO_2máx estimado no es un buen indicador para establecer diferencias entre distintos grupos de actividad física y sedentarismo.

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ARÁN

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Trabajo Original

Otros

Hyperlipidemia during gestational diabetes and its relation with maternal and offspring complications

Hiperlipidemia durante la diabetes gestacional, complicaciones maternas y para la descendencia

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Abstract

Introduction: lipid profile suffers adaptive changes during pregnancy due to estrogen stimulation and insulin resistance. Several relations have been suggested between maternal lipid profile, glucose tolerance, endothelial cell dysfunction and long-term cardiovascular risk; the effects of maternal lipid profile metabolism in fetal growth are also inconclusive. Since a regular evaluation and follow-up of lipid profile during pregnancy has not been established yet, we aimed to evaluate the incidence of dyslipidemia in patients with gestational diabetes (GDM) and analyze some putative relations with pregnancy, offspring complications and maternal metabolic syndrome parameters determined three and twelve months after delivery.

Patients and methods: two hundred and fifty patients with GDM were included. Full medical history, offspring characteristics, lipid profile and maternal variables of metabolic syndrome were evaluated during pregnancy and three- and twelve-months after delivery. The incidence of dyslipidemia during pregnancy was determined using two different classifications.

Results: lower plasma HDL and hypertriglyceridemia were the most current disorders; prematurity or birth weight were not correlated with dyslipidemia. During pregnancy, the lipid-related parameter that better predicted the risk of offspring macrosomia was triglycerides (TG). High TG three months after delivery were correlated to macrosomia and metabolic syndrome variables before and after pregnancy (three and twelve months).

Conclusions: TG during pregnancy is the parameter that best predicts the risk of macrosomia and is related to increased metabolic risk after delivery. The evaluation of lipid profile and other metabolic variables during pregnancy and after delivery is required to early diagnose cardiovascular risk factors, especially in high risk population.

Key words:

Lipid profile. Triglycerides. Gestational diabetes. Offspring complications.

Resumen

Introducción: los cambios del perfil lipídico durante el embarazo se relacionan probablemente con la estimulación estrogénica y la resistencia a la insulina. Diversas relaciones se han planteado entre el perfil lipídico gestacional, la intolerancia a la glucosa, la disfunción endotelial y el riesgo cardiovascular a largo plazo; sus efectos sobre el crecimiento fetal no son concluyentes. Dado que no existe un protocolo de diagnóstico y seguimiento de la dislipemia durante el embarazo, el objetivo del presente estudio fue evaluar la incidencia de dislipemia en pacientes con diabetes gestacional (DMG) y analizar su relación con complicaciones maternas, fetales y variables de síndrome metabólico 3 y 12 meses tras el parto.

Pacientes y métodos: fueron incluidos 250 pacientes con DMG. Se analizaron variables clínicas maternas y del recién nacido y se determinó el perfil lipídico durante el embarazo, 3 y 12 meses tras el parto. La incidencia de dislipemia se realizó utilizando dos clasificaciones diferentes.

Resultados: las alteraciones más frecuentes fueron bajos niveles de HDL y altos de triglicéridos (TG). La prematuridad o el peso al nacer no se relacionaron con la presencia de dislipemia. El parámetro lipídico que mejor predijo el riesgo de macrosomía fueron los TG. Altos niveles de TG tres meses después del parto se relacionaron con macrosomía y variables de síndrome metabólico pregestacional, así como 3 y 12 meses después del parto.

Conclusiones: los niveles de TG durante el embarazo representan el parámetro que mejor predice el riesgo de macrosomía y se relacionan con un mayor riesgo metabólico después del parto. La evaluación del perfil lipídico durante el embarazo y después del parto permite un diagnóstico precoz de factores de riesgo cardiovascular, especialmente en poblaciones de alto riesgo.

Palabras clave:

Perfil lipídico. Triglicéridos. Diabetes gestacional. Complicaciones fetales.

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INTRODUCTION

Several adaptive mechanisms occur during pregnancy. Changes in the energetic metabolism are related to estrogen stimulation and insulin resistance. Physiologically, a 2-3 fold increase in plasma triglycerides (TG) is observed in the second and third trimester of pregnancy, accompanied by lower increases in total cholesterol (TC), high density lipoprotein (HDL) and low density lipoprotein (LDL). After delivery, TC, HDL and TG decrease while LDL tends to remain constant (1-3).

During the first two-thirds of gestation, hyperphagia, increased lipid synthesis and fat accumulation are characteristic (4,5), followed by a decrease in fat storage in the last third of gestation, related to enhanced lipolytic activity and decreased lipoprotein lipase activity in the adipose tissue (6).

Maternal serum TC and LDL are transported across the placenta, and this exchange provides cholesterol to the fetus, especially during early pregnancy (7,8). Cholesterol is required for cell proliferation and development of the fetus. Maternal hypertriglyceridemia also serves as an energy depot for maternal dietary fatty acids (9). TG do not cross the placental barrier, but the presence of lipoprotein receptors in the placenta, lipoprotein lipase, phospholipoproteins A2 and intracellular lipase activities allow the release of polyunsaturated fatty acids (transported as TG in maternal plasma lipoproteins) to the fetus (10,11). In addition, it has been suggested that serum TG values measured during the first third of gestation have predictive value for glucose tolerance during pregnancy (2). During pregnancy, an increased production of oxidisable particles and inoxidative damage are observed; these effects may be related to long-term cardiovascular risk, especially in those patients with other risk factors for cardiovascular disease (12). An association between the atherogenic lipid profile of gestation and the endothelial cell dysfunction during preeclampsia has been also described (13). Some other effects related to the offspring have been also published. Maternal cholesterol seems to affect fetal sterol metabolism and the metabolic functions of extra embryonic fetal tissues (14,15); for this reason, some studies have proposed clinical relations between maternal TG and increased birth weight (BW), especially in those pregnancies complicated with gestational diabetes (GDM) (16). However, the influence of maternal lipid metabolism on fetal growth and complications of pregnancy is still inconclusive. Although changes in lipid profile are expected, its regular evaluation during pregnancy has not been established yet, probably related to the lack of consensus regarding reference values per trimester and the diagnostic criteria for dyslipidemia (DLP).

Thus, considering the importance of maternal complications during/after pregnancy, the fetal development and BW, the aim of this study was to evaluate the presence of dyslipidemia in a high risk Spanish population with GDM using two different classification methods, and to analyze some putative associations between lipid profile, delivery, offspring characteristics and maternal metabolic syndrome parameters determined three and twelve months after delivery.

MATERIALS AND METHODS

PATIENTS

This study was conducted in accordance with the Declaration of Helsinki and with national and international guidelines. Two hundred and fifty patients with GDM who underwent endocrinological evaluation from 2013 to 2015 were included. Clinical records were used to collect full medical history; gestational age (GA) was obtained from estimates of gestational age during the first ultrasound (USG) when available or by the date of the last menstrual period; prematurity was defined as gestational age at birth between 24 and 36 weeks of gestation. A screening test for GDM with 50 g of glucose was performed in the first or second quarter of pregnancy, according to the clinical risk of patients following the current clinical guidelines (17). The diagnosis of GDM was performed according to a three-hour curve after the oral administration of 100 g of glucose (Supp. Table I) or a screening test with a plasma glucose > 200 mg/dl (18). In addition, blood samples including HbA1c, total cholesterol, LDL, HDL, triglycerides, TSH and kidney function were obtained during pregnancy and three months after delivery; the last one included a 75 g oral glucose tolerance test (OGTT). Fifty patients of the initial sample were also followed with the same biochemical analysis one year after delivery.

BIOCHEMICAL ANALYSIS

Blood samples were collected after 12-hour fasting. In pregnant women with more than one lipidogram collected during pregnancy, the first examination was considered for analysis. Glucose was determined using the glucose oxidase method, and kidney and lipid profile, using mass spectrophotometry; HDL and LDL were calculated.

DYSLIPIDEMIA DURING PREGNANCY

The prevalence of dyslipidemia was evaluated considering two definitions: a) classical dyslipidemia according to Fahraeus et al., where TC, LDL, HDL and TG concentrations are classified in early or late pregnancy (19) (Table 2.1); and b) percentile criteria according to Piechota and Staszekski (when there is elevation

Supplemental Table I. Diabetes gestational diagnosis criteria using a 100 mg oral glucose tolerance test according the Spanish Group of Diabetes and Pregnancy

Fasting PG (mg/dl)	1-hour PG (mg/dl)	2-hour PG (mg/dl)	3-hour PG (mg/dl)
105	190	165	145

PG: plasma glucose.

of TC, LDL and TG concentrations above the 95th percentile and HDL levels below the 5th percentile for gestational age) (20) (Supp. Table 2.2).

STATISTICAL ANALYSIS

Normality distribution of the data was determined using the Kolmogorov-Smirnov test. Continuous variables were presented as mean ± standard deviation. Categorical variables were reported in absolute and percentage values. Subjects were categorized as having dyslipidemia for each of the two criteria. Statistical differences between continuous variables with normal and non-parametric distribution were obtained using the unpaired Student's t-test and the Mann-Whitney U test, respectively. The Chi-squared and Spearman's correlation tests were used to compare categorical data. ROC curves were also performed; the area under the curve and the 95% confidence interval were also calculated. Statistical analyses were performed using SPSS statistical software v.20 and GraphPad Prism v.6. Data in graphs are expressed as mean ± SEM. p-values < 0.05 were considered as statistically significant.

RESULTS

PATIENT POPULATION AND CLINICAL CORRELATIONS

A total of 250 pregnant women with GDM were included. Demographic and clinical features of the general evaluated populations and their characteristics according to the presence of dyslipidemia are summarized in table I. The presence of dyslipidemia ranged from 27% to 86% using the Fahraeus et al. or the Piechota and Staszewski criteria respectively (Fig. 1). In both classifications, lower plasma HDL levels were the most current lipid disorder (9.9% and 61.9%, respectively) followed by hypertriglyceridemia (9.6% and 36.5%, respectively) (Fig. 1). Demographic and clinical characteristics were similar between patients with and without dyslipidemia according to both classification criteria. Insulin requirements tended to be increased in patients with dyslipidemia according to both classifications. Basal insulin requirements were statistically increased in dyslipemic patients according to the 3-quartile method (Piechota and Staszekski; $p = 0.015$). Prematurity and birth weight $< 2,500$ g or $> 3,500$ g were not correlated with the presence of dyslipidemia according to the classifications used (Table I).

Patients who required insulin for controlling their blood glucose exhibited significantly decreased plasma HDL levels compared to those who did not require insulin (59 ± 5 *vs* 67 ± 3 mg/dl), and they also exhibited decreased plasma LDL levels (133 ± 7 *vs* 137 ± 11 mg/dl). Those patients requiring insulin had also lower plasma TC values (234 ± 12 *vs* 251 ± 9 mg/dl) (Fig. 2). Interestingly, elevated TC and LDL levels during pregnancy were related to vaginal delivery and normal OGTT 3-month after delivery ($p < 0.05$) (Fig. 3).

The lipid profile three months and one year after delivery is shown in table II. Concerning the lipid profile three months after delivery, importantly, decreased HDL levels were correlated to pre-pregnancy overweight, insulin requirement and obesity after delivery ($p < 0.01$). LDL and TC plasma values 3-month after delivery were lower in those patients that required basal insulin (175 ± 5 mg/dl and 107 ± 4 mg/dl, respectively). Women with pre-pregnancy overweight and newborns affected with macrosomia and obesity after delivery had increased TG values 3-month after delivery. On the other side, the presence of abnormal fasting glucose (plasma glucose > 100 mg/dl), abnormal OGTT (plasma glucose > 140 mg/dl) and abnormal HbA1c ($> 5.7\%$) 3-months after delivery were correlated to increased TG levels in the same analysis ($p < 0.05$). Interestingly, those patients who breastfed their newborns exhibited decreased TG levels 3-month after delivery compared to those who used only artificial feeding (92 ± 10 *vs* 117 ± 14 mg/dl) (Fig. 3).

Supplemental Table II. Diagnosis criteria for dyslipidemia during pregnancy

2.1 Diagnosis criteria using TC, LDL-C and TG and HDL according Fahraeus et al. (19)			
Variable		**Early pregnancy**	**Late pregnancy**
Total cholesterol (mg/dl)		200	250
LDL (mg/dl)		125	150
HDL (mg/dl)		75	65
Triglycerides (mg/dl)		100	210
2.2 Percentiles 95 for TC, LDL and TG and 5 for HDL in mg/dl per quartile according to Piechota and Staszekski (18)			
Variable	**1st quarter**	**2nd quarter**	**3rd quarter**
Total cholesterol (mg/dl)	277	319	380
LDL (mg/dl)	186	217	250
HDL (mg/dl)	35	42	40
Triglycerides (mg/dl)	175	254	414

Table I. Clinical and demographic characteristics of the evaluated population categorized according to the presence of any lipid alteration according to the classical criteria and the percentiles criteria

Characteristic	Total 100% (n = 250)	Dyslipidemia: classical criteria (n = 99) (19)	p1	Dyslipidemia: percentile per quartile criteria (n = 31) (20)	p2
Age (years old)	33.08 ± 4,78				
Age over 35 years	38% (92)	40.4% (40)	0.17	38.7% (12)	0.38
Family history of T2DM	76.1% (150)	78% (71)	0.58	80.8% (21)	0.48
Previous GD	24.2% (24)	30.4% (14)	0.57	30% (6)	0.58
Active smoke habit	21.4% (43)	18.1% (17)	0.36	23.3% (7)	0.45
Primigravida	43.5% (94)	43.6% (41)	0-60	37.9% (11)	0.30
Previous aborts	37.1% (50)	47.4% (7)	0.14	45% (9)	0.56
Hypertension	2.3% (5)	3.1% (3)	0.62	0% (0)	0.38
Pre-pregnancy BMI (kg/m^2)	27.67 ± 6.47		0.14		0.36
Pre-pregnancy overweight	37.8% (45)	35% (21)	0.54	25% (4)	0.34
Pre-pregnancy obesity	30.4% (52)	28.6% (24)		33.3% (8)	
Insulin requirement during pregnancy	59.4% (71)	37.9% (36)	0.052	48.3% (14)	0.058
Basal insulin requirement during pregnancy	59.4% (41)	55.9% (19)	0.33	30.8% (4)	0.015
Prandial insulin requirement during pregnancy	85.3% (58)	84.8% (28)	0.73	81.8% (9)	0.51
Prematurity	5.8% (9)	6.9% (5)	0.66	4.5% (1)	0.51
Vaginal delivery	72.4 (123)	74.7% (56)	0.15	79.2% (12)	0.25
Complications during delivery	28.9 (26)	23.8% (10)	0.66	16.7% (3)	0.31
Offspring weight at birth (g)	3314 ± 511				
Low weight at birth	6.5% (11)	6.7% (5)	0.30	4.2% (1)	0.38
Weight at birth > 3,500 g (%)	40.2% (68)	44% (33)	0.09	50% (12)	0.19
Weight at birth > 4,000 g (%)	10.1 (17)	10.7% (8)	0.23	16.7% (4)	0.13
3-month after delivery overweight (%)	27.8% (20)	29.3% (12)	0.47	7.1% (1)	0.26
3-month after delivery obesity (%)	55.6% (50)	34.1% (14)	0.47	42.9% (6)	0.26

T2DM: type 2 diabetes mellitus; BMI: body mass index. p1 refers to relation with the presence of dyslipidemia according the classical definition; p2 refers to relation with the presence of dyslipidemia according the 3-quartile definition.

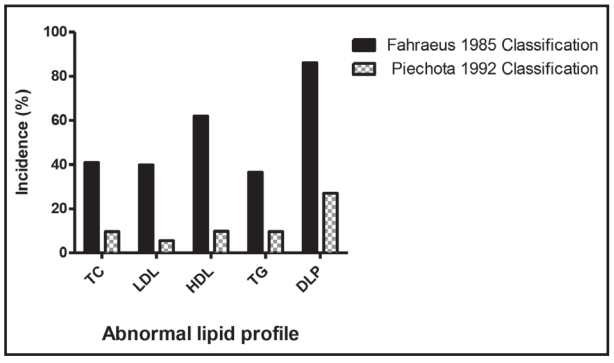


Figure 1.

Incidence of dyslipidemia during pregnancy according classical criteria (Fafreus et al., 1985) and 3-quartile classification (Piechota et al. 1992). TC: total cholesterol; LDL: low density lipoprotein cholesterol; HDL: high density lipoprotein cholesterol; TG: triglycerides; DLP: dyslipidemia.

Furthermore, when patients were evaluated one year after delivery, those patients with pre-pregnancy overweight still had higher TG and lower HDL values. Decreased HDL values were also related to offspring weight > 4,000 g, abnormal fasting glucose and OGTT three months after delivery. TG > 100 mg/dl were observed in obese mothers and in those with abnormal fasting glucose 3-months after delivery. Breastfeeding was also related to decreased TG serum levels one year after delivery (Fig. 4). During pregnancy, the lipid-related parameter that better predicted the risk of offspring macrosomia was TG (AUC 0.655) (Fig. 5). This parameter was compared not only to other lipid profile serum parameters but also with other parameters related to metabolic syndrome including fasting glucose, OGTT, HbA1c and weight gain (data not shown).

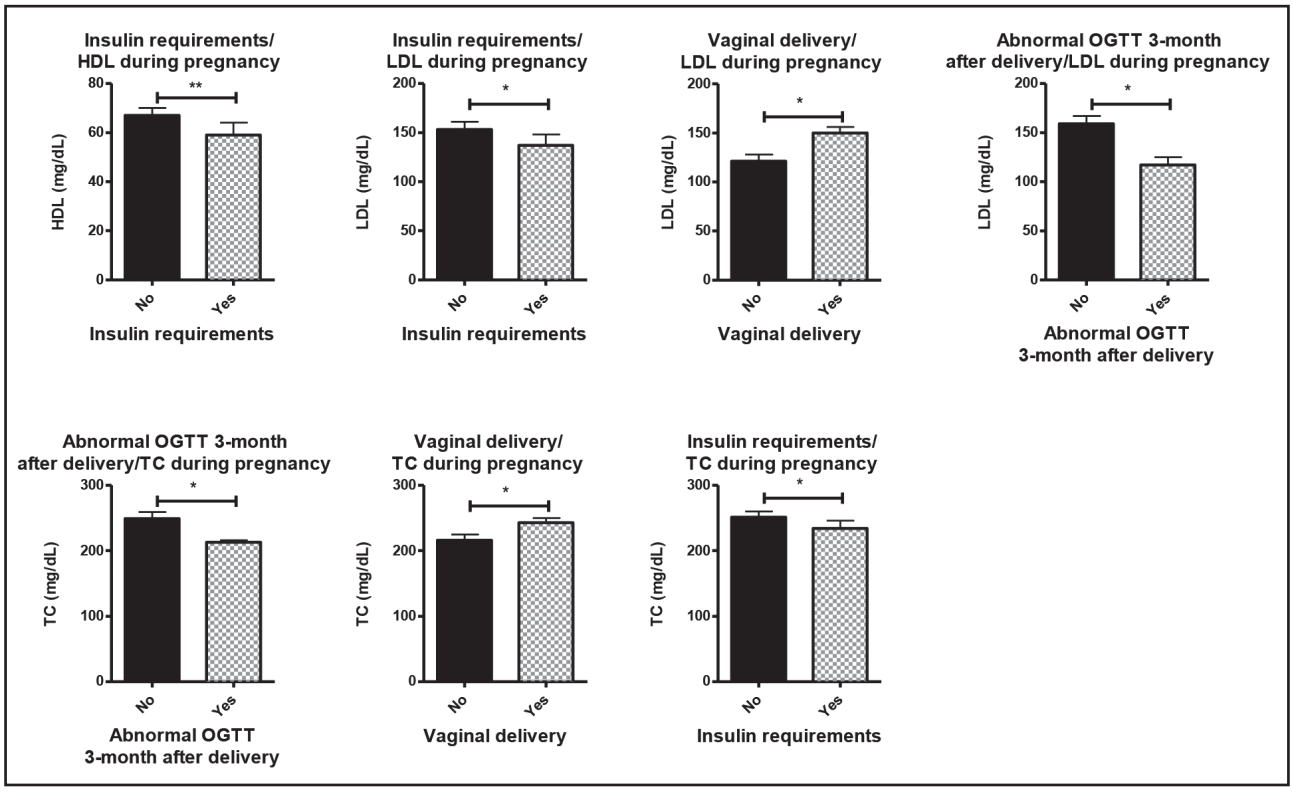


Figure 2.

Clinical relations concerning pregnancy, metabolic syndrome characteristics and lipid profile during pregnancy. Asterisks (*$p < 0.05$; **$p < 0.01$).

DISCUSSION

During pregnancy, although a physiological increase in TC, HDL, LDL and TG is expected, it is difficult to determine the cut-off level for diagnosing dyslipidemia (DLP) in pregnant women. It is important to early diagnose and identify those patients requiring intensive non-pharmaceutical intervention during and after pregnancy. This study shows the lipid profile behavior in Caucasian patients with gestational diabetes, and describes the presence of DLP according to two different classification methods, evaluating their utility to identify risk factors among patients with gestational diabetes.

The presence of dyslipidemia was significantly different according to the criteria used. However, the lack of association between the presence of DLP using these methods and the maternal/fetal outcomes raises questions about the clinical significance of measuring lipid profile during pregnancy. In the absence of evidence of cut-off points that early identify the risk population, probably the percentiles definition seems to better adjust to the lipid distribution during pregnancy. TG is apparently the best lipid parameter for identifying metabolic risk in pregnant women with GDM, while the evaluation of lipid profile after delivery provides useful information about the future risk of metabolic syndrome and cardiovascular complications.

There is debate over the lipid patterns in gestational diabetes and whether they are potential markers on preexisting insulin resistance (21). In our study group, hypertriglyceridemia was one of the most prevalent modifications, as it has been described in pregnant women without GDM (16,22). One study in Spain reported an increased lipid profile in patients with GDM compared to pregnant women without GDM, which seemed to precede the diagnosis of GDM (23). Comparing our results to those of that study, in our group, similar TC values but increased serum TG are observed, suggesting an increased proinflammatory condition in our study population.

When pregnancy complications are considered, epidemiologic data suggest that women with proinflammatory phenotype tend to deliver preterm infants (24), and have a consequent increased risk for cardiovascular diseases (25). Some other studies have proposed that maternal hyperlipidemia could increase the oxidative stress in the fetus, resulting in vessel wall damage and disruption of normal placentation (26). In our study, no relation between lipid profile and birth date was observed.

The precise biological mechanism by which maternal cholesterol affects BW is still unknown. It has been suggested that altered sterol hormone metabolism and impaired cell cycle/signaling of growth factors including insulin could affect placental transport of nutrients influencing fetal growth (14,27). Some studies have described a relation between variations in maternal TG/weight and BW (28). In this sense, it has been suggested that not only BMI before pregnancy is related to BW (16), but also maternal adiposity and weight gain during pregnancy (28-30).

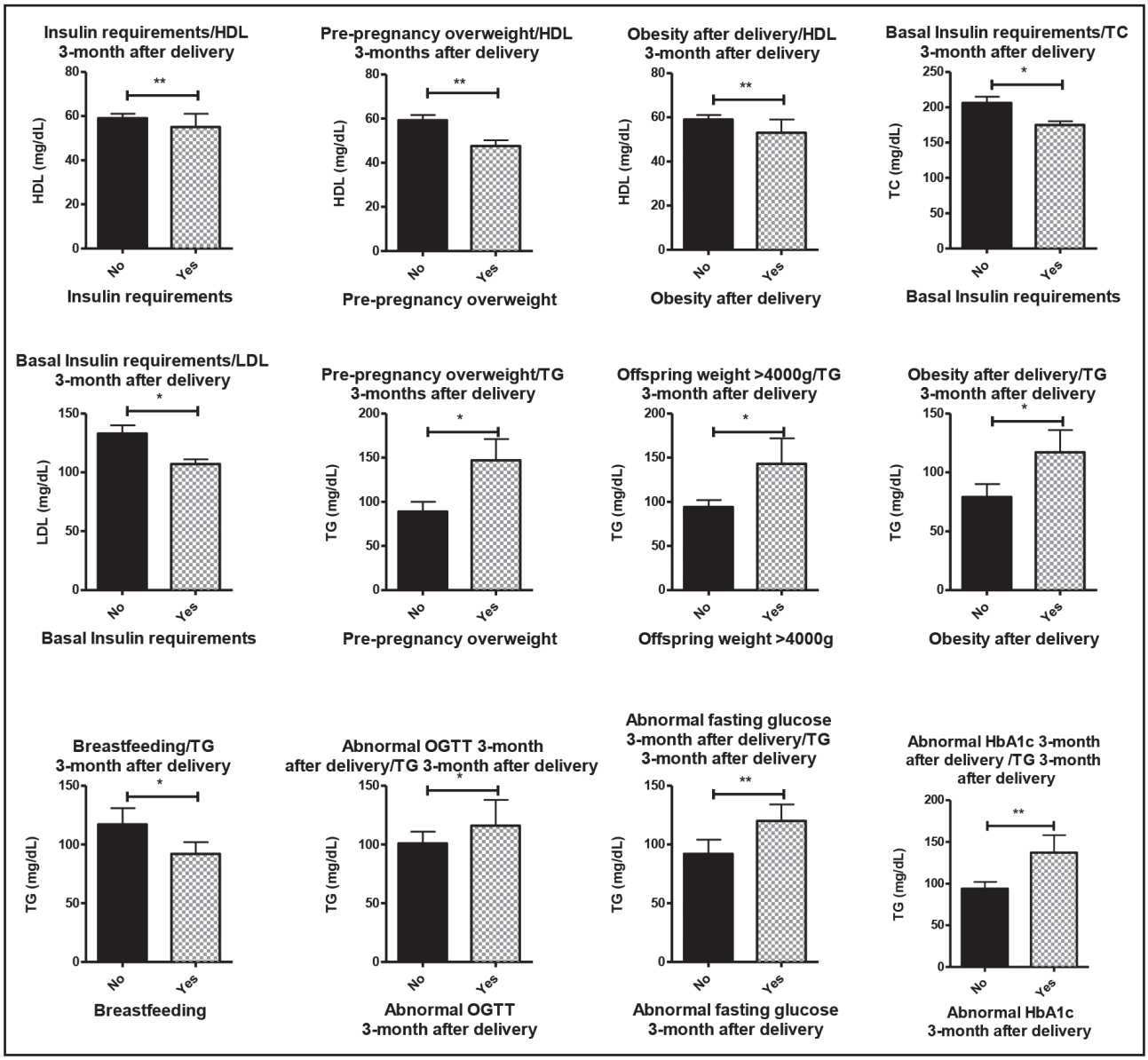


Figure 3.

Clinical relations concerning metabolic syndrome characteristics and lipid profile 3-months after delivery. *p < 0.05; **p < 0.01).

Table II. Lipid profile during pregnancy, 3-month after delivery and 1-year after delivery

Variable	Pregnancy	3-month after delivery	p1	1-year after delivery	p2
TC (mg/dl)	240 ± 56	195 ± 40	< 0.001	189 ± 33	< 0.01
LDL (mg/dl)	144 ± 47	118 ± 31	< 0.001	116 ± 30	< 0.01
HDL (mg/dl)	61 ± 19	56 ± 18	< 0.05	57 ± 18	0.13
TG (mg/dl)	182 ± 95	101 ± 66	< 0.001	88 ± 43	< 0.001

TC: total cholesterol; LDL: low density lipoprotein cholesterol; HDL: high density lipoprotein cholesterol; TG: triglycerides. p1 refers to the comparison between pregnancy and 3-months after delivery plasma analyses; p2 refers to the comparison between pregnancy and 1-year after delivery plasma analyses.

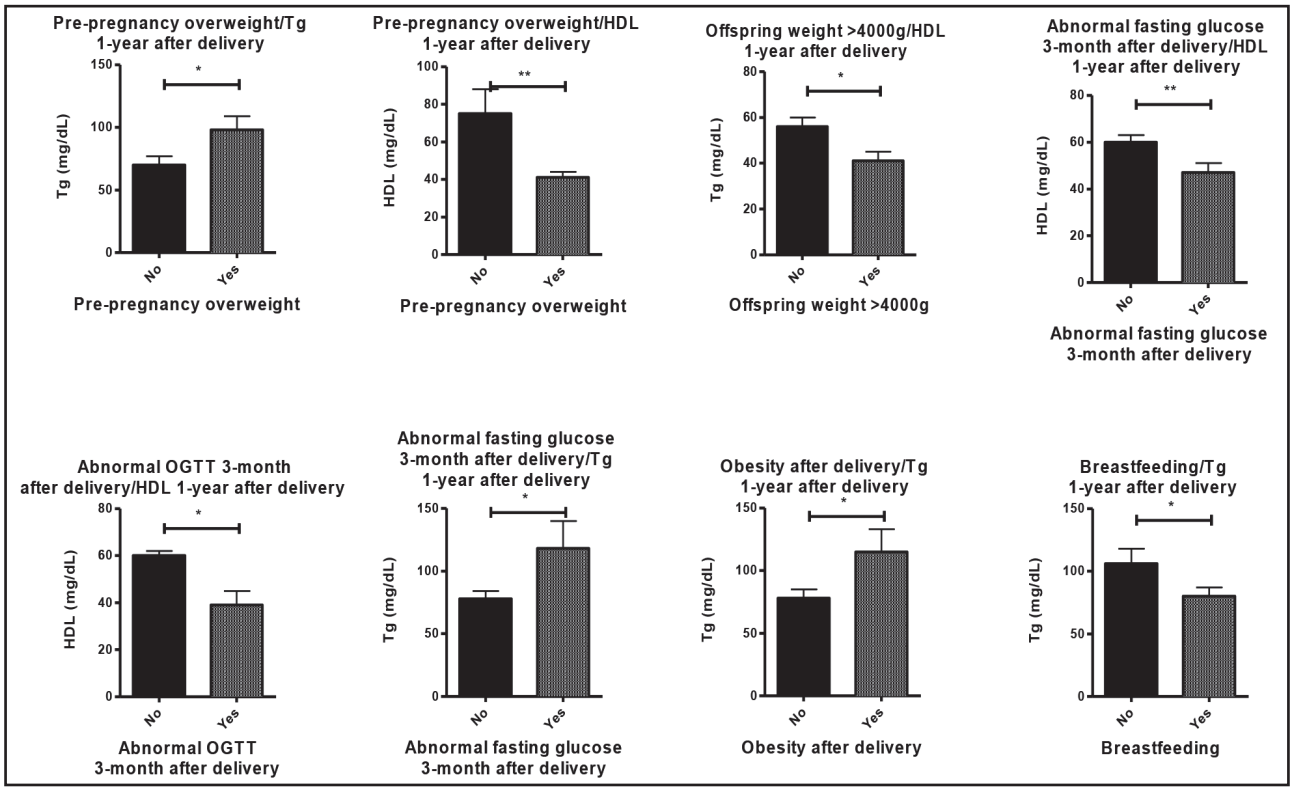
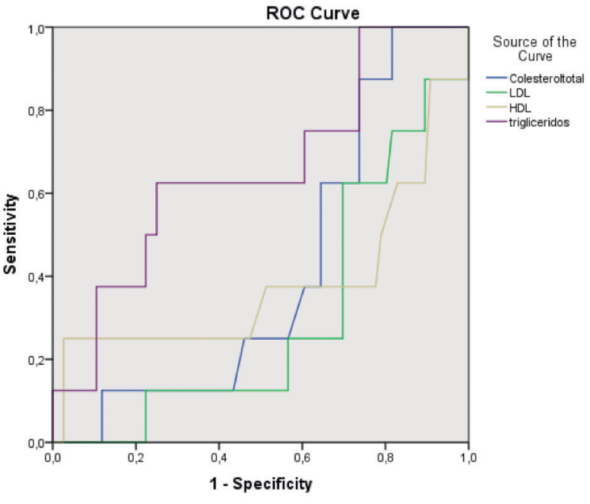


Figure 4.

Clinical relations concerning metabolic syndrome characteristics and lipid profile 1-year after delivery. *p < 0.05; **p < 0.01).



Parameter	AUC	
TC	0.409	IC 95% (0.24-0.58)
LDL	0.302	IC 95% (0.13-0.47)
HDL	0.382	IC 95% (0.12-0.64)
Tg	0.655	IC 95% (0.45-0.86)

Figure 5.

ROC curves of fetal weight and lipid profile during pregnancy.

A meta-analysis found that women with gestational diabetes have elevated triglyceride concentrations compared to women without gestational diabetes (21), and these values, even the lipid profile, could be also influenced by lifestyle factors during pregnancy (31). In our group, triglycerides represented the best parameter to predict the presence of macrosomia, compared not only to lipid profile but also to the other metabolic syndrome parameters. At the same time, these mothers had significantly higher TG values three months after delivery.

There is limited knowledge on the relationship between maternal HDL and fetal development. HDL does not cross the placenta but it seems to influence cholesterol metabolism in the placenta, which could affect the size of the fetus (14). Related to this, HDL has been negatively associated to BW in some studies (30,32), including its rate of change among pregnancy (30). On the contrary, some others have reported no relations between HDL change during pregnancy and the BW adjusted by BMI (33). In our group, mothers with neonates > 4,000 g had decreased HDL levels one year after delivery, but not during pregnancy. Interestingly, the most prevalent lipid modification during pregnancy in our group was a decreased HDL value.

In our study, no relation between lipid profile and preeclampsia was found, as previously reported (16), but data concerning this cardiovascular risk factor is contradictory. Other publications, in contrast, suggest an association between hyperlipidemia, espe-

cially hypertriglyceridemia and preeclampsia (34). Concerning other complications, no relation between lipid profile and malformations was observed in our group. It has been reported that pregnancies complicated by both GDM and obesity have been associated with an increased rate of congenital malformations (23). A relation between congenital malformations and the oral administration of lipid peroxides generated from heated culinary oils has been described in animal models (35).

Pre-pregnancy BMI has been reported as the main factor related to changes in TC and LDL during pregnancy (36). In our cohort, patients with pre-pregnancy overweight had worse lipid profile (higher TG, lower HDL) even one-year after delivery, suggesting that the lipid profile during pregnancy obeys not only physiological changes but also the metabolic condition of the patient. Interestingly, there are contradictory publications about the effects of breastfeeding and lipid profile in young adults. It has been published that breastfed babies have better HDL/LDL ratio at six months compared to mix-fed babies (37). In our cohort, the lipid profile was not evaluated in the offspring, but breastfeeding was associated with healthier lipid profile in those mothers who breastfeed their children during the first three months of life, suggesting that breastfeeding may have benefits not only to the neonates but also to the mothers.

The association between impaired glucose tests 3-month after pregnancy and the HDL and TG levels one year after delivery confirms the close relation between glucose and lipid profile, and the importance of their parallel study in order to early identify and treat high-risk patients. This study adds to the current knowledge of associations between maternal blood lipid concentrations during pregnancy and outcomes for the baby.

This study had many strengths, including a prospective cohort evaluated 3-month and 1-year after delivery; anthropometric measurements were collected by trained healthcare professionals, and blood samples were analyzed according to a systematized protocol in our hospital. This task presents, however, some limitations. It is a unicentric study with pregnant women with GDM, the lipid profile is not compared to that of normal pregnant women, and the number of patients evaluated one-year after delivery was low. The results of the present study therefore do not allow national or international generalization and the absence of association with clinical outcomes. It would be interesting to follow up the metabolic behavior of the offspring, as well as the presence of cardiovascular complications in women with dyslipidemia during pregnancy. At the same time, future research should examine whether lipid abnormalities in the first trimester are useful to identify patients who will develop GDM.

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ARÁN

Nutrición Hospitalaria

Revisión

Validez del perímetro del cuello como marcador de adiposidad en niños, adolescentes y adultos: una revisión sistemática

Validity of neck circumference as a marker of adiposity in children and adolescents, and in adults: a systematic review

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Resumen

El objetivo de la presente revisión sistemática fue realizar una búsqueda acerca de la validez del perímetro de cuello como marcador de adiposidad en niños y adolescentes así como en población adulta. Se realizó una búsqueda sistemática de artículos publicados antes del 30 de junio de 2017, utilizando las bases de datos PubMed y Web of Science. Se buscaron estudios originales, en idioma español o inglés, que analizaran la asociación entre el perímetro del cuello y al menos un marcador de adiposidad. En PubMed se usaron las categorías MeSH *(medical subject heading).* El criterio de búsqueda utilizado fue: *((“neck circumference” or “neck diameter”) AND (“Body Composition”[Mesh] OR “Anthropometry”[Mesh])).* Se repitió la búsqueda en Web of Science. Se identificó un total de 494 estudios, de los cuales 47 fueron finalmente seleccionados para esta revisión. El 66% de los estudios (16 en niños y adolescentes y 15 en adultos) solo especifican que existe relación entre perímetro del cuello e indicadores doblemente-indirectos tales como el índice de masa corporal, la circunferencia de cintura o ratio circunferencia cintura/cadera en niños y adultos. Además, se observó que el perímetro del cuello se asocia de forma directa con marcadores de adiposidad indirectos, medidos mediante métodos de referencia tales como la tomografía axial computarizada (TAC) o la absorciometría dual de rayos X (DXA) en adultos, mientras que no se encontraron estudios en niños. En conclusión, el perímetro del cuello se asocia a marcadores indirectos de masa grasa total y central en niños y adolescentes, mientras que en adultos el perímetro del cuello se asocia a parámetros de adiposidad medidos tanto con métodos indirectos como doblemente-indirectos. Se requieren nuevos estudios con métodos que analicen la asociación entre el perímetro del cuello y la composición corporal analizada mediante métodos de referencia, principalmente en niños y adolescentes.

Palabras clave:

Diámetro de cuello. Validez. Obesidad. Masa grasa.

Abstract

The objective of this systematic review was doing a search of the validity of neck perimeter as a marker of adiposity in children and adolescents as well as in adults. A systematic search for articles published before June 30, 2017 was conducted using the PubMed and Web of Science databases. Original studies, in Spanish or English, were searched to analyze the association between neck circumference and any other marker of adiposity. MeSH (Medical Subject Heading) categories were used in PubMed. The search criteria used were: ((“neck circumference” or “neck diameter”) AND (“Body Composition” [Mesh] OR “Anthropometry” [Mesh])). This search was repeated in Web of Science. We identified 494 studies, of which 47 were finally selected for this review. From the total, 66% of studies (16 in children and adolescents and 15 in adults) only specify that there is a relationship between neck circumference and body mass index or waist circumference, waist/hip circumference ratio in children and adults. We also observed that neck circumference was directly associated with adiposity markers indirectly measured by reference methods such as computed tomography (CT) or dual-energy x-ray absorptiometry (DXA) in adults. Conversely, no studies were found in children and adolescents. In conclusion, neck circumference is associated with doubly-indirect markers of total and central fat mass in children and adolescents, while in adults it is associated with adiposity parameters measured with indirect and doubly-indirect methods. Further studies including methods that address the association between neck circumference and body composition analyzed using reference methods are required, especially in children and adolescents.

Key words:

Neck diameter. Validity. Obesity. Fat mass.

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INTRODUCCIÓN

La obesidad es un problema de salud pública (1) porque es uno de los factores de riesgo más importantes para desarrollar enfermedad cardiovascular, diabetes tipo 2 y ciertos tipos de cáncer (2). A la obesidad se le atribuyen más de cuatro millones de muertes al año (1). Datos del European Health Interview Surveys (Eurostat) indican que más de la mitad de la población europea tiene sobrepeso u obesidad (3).

El índice de masa corporal (IMC) es el marcador de adiposidad (4,5) más utilizado para categorizar a las personas en base a la relación de su estatura con el peso corporal en bajo-peso, normo-peso, sobrepeso y obesidad (6). Además del IMC, se están utilizando otros marcadores como la circunferencia de cintura, la circunferencia de cadera y el índice cintura/cadera para determinar el grado de adiposidad central y total. Más recientemente, se ha propuesto el perímetro de cuello como un marcador antropométrico sencillo que se asocia significativamente a marcadores convencionales relacionados con la adiposidad total y central tales como el IMC (7) o la circunferencia de cintura, respectivamente (8). Además, el perímetro de cuello también se asocia a factores de riesgo cardiovascular tales como triglicéridos, colesterol total, c-LDL (9), glucosa (10) y andrógenos en mujeres premenopáusicas con sobrepeso y obesidad (11).

Dentro de las ventajas comparativas que tiene el perímetro de cuello sobre otros marcadores de adiposidad, destaca que es fácil de medir, no cambia en el transcurso del día, no se ve influenciado por la distensión abdominal ocasionada por los alimentos ingeridos, no se altera con la inhalación o exhalación y es práctico, ya que puede medirse fácilmente incluso en invierno cuando las personas utilizan una mayor cantidad de prendas de vestir (12). Esto es especialmente útil sobre todo en aquellas personas que están estigmatizadas por su peso corporal, tienen fobia de pesarse, y en circunstancias en las que retirar la ropa para medir la circunferencia de cintura no es viable.

El objetivo de esta revisión es realizar una búsqueda sistematizada acerca de la validez del perímetro de cuello como marcador de adiposidad en niños y adolescentes, así como en adultos.

MÉTODOS

ESTRATEGIA DE BÚSQUEDA

Se realizó una búsqueda sistemática de los artículos publicados con anterioridad al 30 de junio de 2017 en PubMed y Web of Science. Se buscaron estudios que analizaran la relación entre el perímetro de cuello y un indicador de adiposidad tanto en niños y adolescentes como en población adulta. Se optó por utilizar términos muy genéricos para intentar identificar todos los estudios que analicen perímetro de cuello y al menos un marcador de adiposidad. Por lo tanto, en PubMed se usaron los términos MeSH *(Medical Subject Heading).* El criterio de búsqueda utilizado fue: *((“neck circumference” or “neck diameter”) AND (“Body Composition”[Mesh] OR “Anthropometry”[Mesh])).* Se repitió la misma estrategia de búsqueda y combinación de términos en Web of Science, aunque sin usar los términos MeSH, ya que esta opción no existe en dicho buscador.

CRITERIOS DE INCLUSIÓN

Los criterios de inclusión fueron: a) estudios originales, incluidos estudios clínicos; b) estar escrito en inglés o español; c) estudio realizado en humanos mayores de dos años de edad, sanos o con alguna patología; d) que incluyan medidas de perímetro de cuello y algún otro marcador de adiposidad (ver abajo), y que estas sean relacionadas entre sí (analizando su concurrencia o validez); y e) estar disponibles como texto completo desde los accesos de los que disponían los autores. Un investigador (MJAT) revisó en detalle si los artículos cumplían los criterios de inclusión establecidos en dos fases: a) lectura de título y resumen; y b) lectura de texto completo de los artículos incluidos en la fase anterior.

Marcadores de adiposidad

En esta revisión se consideraron dos niveles de marcadores de adiposidad: a) aquellos medidos mediante métodos indirectos o de referencia tales como la resonancia magnética nuclear, la tomografía axial computarizada (TAC), la absorciometría dual de rayos X (DXA), o la pletismografía; y b) aquellos medidos con métodos doblemente-indirectos tales como la bioimpedanciometría (BIA, deriva de la medición de agua corporal total), antropometría bicompartimental (comprende mediciones para el cálculo de densidad corporal, las cuales provienen de regresiones lineales en base al método de peso hidrostático), y marcadores como el peso, el IMC, la circunferencia de cintura o el índice cintura/cadera. Se considera validez de criterio a lo estudiado en aquellos estudios que analizan la asociación entre perímetro de cuello y un marcador de adiposidad medido mediante un método de referencia mientras que se considera un estudio que analiza la validez concurrente cuando el método utilizado para determinar la adiposidad es un método doblemente-indirecto.

RESULTADOS

Se identificaron un total de 551 estudios, de los cuales el 10% (n = 57) estaban duplicados en PubMed y Web of Science. En una primera fase de lectura de título y resumen se eliminaron un total de 423 artículos. Finalmente, se seleccionaron un total de 47 estudios. La figura 1 muestra el diagrama de búsqueda de la literatura y proceso de selección de artículos.

Las tablas I y II resumen la totalidad de artículos seleccionados en niños y adolescentes, así como en adultos, respectivamente. De los estudios incluidos en esta revisión, un 38% incluyeron niños o adolescentes (cuatro estudios en niños, diez en adolescentes y cuatro en ambos grupos de edad) (Tabla I), mientras que el 62% (n = 29) se realizó en población adulta o adulta mayor (Tabla II).

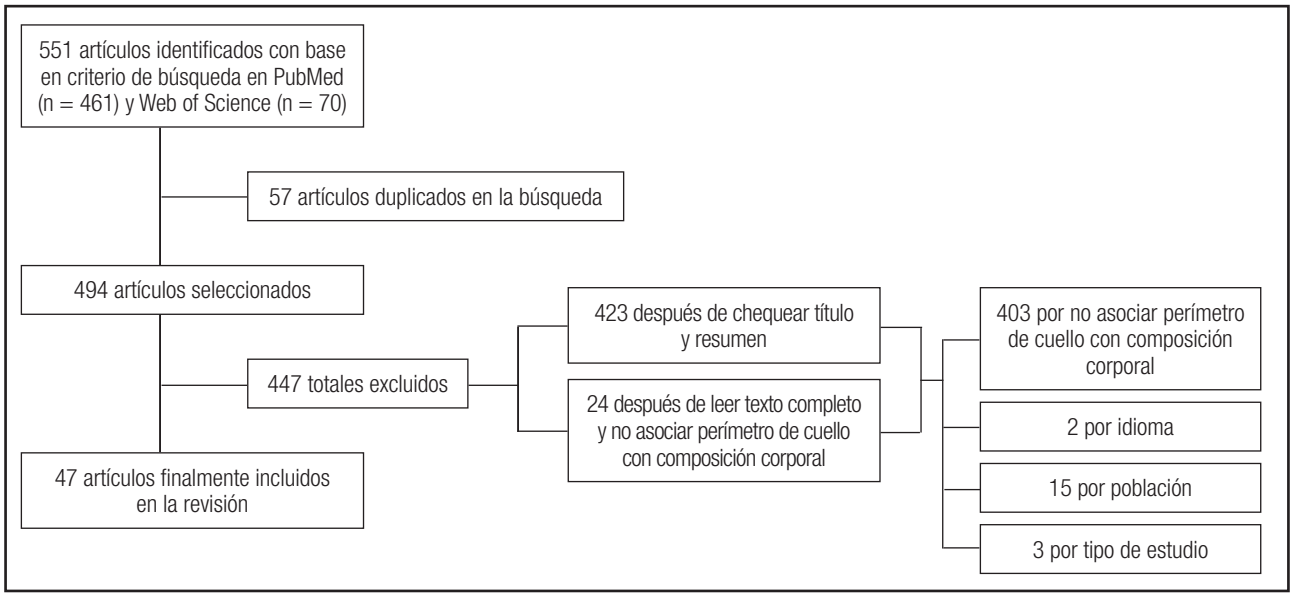

Figura 1.

Diagrama de búsqueda de literatura y proceso de selección de artículos.

Los protocolos de medición de perímetro de cuello varían entre estudios. El 51% de los estudios reportan el uso de una cinta métrica plástica no distensible, mientras que el 49% no lo específica. En niños y adolescentes, la medición del perímetro del cuello que predominó fue aquella realizada en la porción más prominente del cuello (23,4%, n = 11), mientras que un 12,8% (n = 6) la realizó en el punto medio o sobre o bajo la prominencia laríngea y un 2,1% (n = 1) no especificó la metodología utilizada.

En la población adulta, el 21,3% (n = 10) de los estudios miden el perímetro de cuello en el punto medio del cuello, un 36,2% (n = 17) lo miden sobre o bajo la prominencia laríngea (cartílago cricotiroideo), mientras que solo el 2,1% (n = 1) de estudios realizó esta medición en la circunferencia mínima y 2,1% (n = 1) no reportó la forma de medición.

Con respecto a los puntos de corte de perímetro de cuello para diagnosticar sobrepeso y obesidad, Ben-Noun y cols. (13) fueron los primeros en establecer puntos de corte para identificar sobrepeso (37 y 34 cm en hombres y mujeres respectivamente) y obesidad (39,5 y 36,5 cm en hombres y mujeres adultos respectivamente). Posteriormente, se han propuesto puntos de corte similares (14-16), aunque con ligeras modificaciones en el punto anatómico de medición. En el caso de la población pediátrica, el punto de corte del perímetro de cuello asociado a sobrepeso u obesidad depende de la edad y del grado de maduración sexual, pudiendo fluctuar entre 28 y 38 cm en niños y de 27 a 34,5 en niñas (17-21). Más recientemente, Castro-Piñeiro y cols. (22) han propuesto puntos de corte de perímetro de cuello para niños y niñas de 6 a 18 años asociado a sobrepeso u obesidad así como asociado a circunferencia de cintura de riesgo (Tabla I).

Todos los estudios incluidos en esta revisión mostraron relaciones estadísticamente significativas entre perímetro de cuello y los marcadores de adiposidad total y central, así como con otros marcadores de composición corporal tales como masa libre de grasa, o el índice de masa grasa tanto en niños (Tabla I) como en adultos (Tabla II).

VALIDEZ DE CRITERIO: ASOCIACIÓN DEL PERÍMETRO DE CUELLO CON MARCADORES DE ADIPOSIDAD DETERMINADOS CON MÉTODOS INDIRECTOS O DE REFERENCIA

Niños y adolescentes

No se encontraron estudios que analicen la asociación del perímetro de cuello con un marcador de composición corporal determinado mediante métodos de referencia, por lo que no se puede establecer la validez de criterio del perímetro del cuello en esta población.

Adultos

Un total de cinco estudios mostraron asociación del perímetro de cuello con masa grasa de cuerpo completo determinada mediante TAC en participantes de ambos sexos de nacionalidad estadounidense (n = 3) (23-25), china (n = 1) (26) e inglesa (n = 1) (27) (Tabla II). En los cinco estudios, esta técnica permitió estimar la cantidad de tejido adiposo visceral, que también se asoció de forma positiva y significativa con el perímetro de cuello en la totalidad de los casos.

Tabla I. Estudios que analizan la asociación entre perímetro de cuello y marcadores de adiposidad en niños

Autor	Sujetos	Edad (años)	Protocolo medición perímetro de cuello	Método de evaluación de la variable de adiposidad	Principales resultados y conclusiones
Hatipoglu y cols. 2010 (17)	969 turcos sanos: 271 niños y 284 niñas normopeso, 204 niños y 208 niñas con sobrepeso/obesidad	6-18	CMplas, Promcue	IMC y Cc	IMC: Niños prepúberes ($r = 0,70$, $p < 0,001$) y púberes ($r = 0,82$, $p < 0,001$) Niñas prepúberes ($r = 0,72$, $p < 0,001$) y púberes ($r = 0,84$, $p < 0,001$) Cc: Niños prepúberes ($r = 0,73$, $p < 0,001$) y púberes ($r = 0,83$, $p < 0,001$) Niñas prepúberes ($r = 0,77$, $p < 0,001$) y púberes ($r = 0,85$, $p < 0,001$)
Mazicioglu y cols. 2010 (19)	5.481 niños/as y adolescentes turcos sanos: 2.026 niños y 2.519 niñas	6-18	CMplas, Promcue	IMC	IMC, independiente del rango de edad y sexo ($p < 0,001$)
Nafiu y cols. 2010 (18)	1.102 estadounidenses sanos (62% normopeso): 573 niños y 529 niñas	6- 18	CMplas, Promcue	IMC, Cc	IMC: niños ($r = 0,71$, $p < 0,001$); niñas ($r = 0,78$, $p < 0,001$) Cc: niños ($r = 0,77$, $p < 0,001$; niñas ($r = 0,83$, $p < 0,001$) Al analizar los datos, por rango de edad (6-18 años) y sexo, esta asociación se mantiene ($p < 0,001$)
Guo y cols. 2012 (50)	6.802 chinos sanos (15% prehipertensos, 16% sobrepeso, 7% obesidad): 3.631 niños y 3.171 niñas	5-18	CMplas, Promcue	IMC, Cc	IMC: normopeso ($r = 0,68$, $p < 0,001$), sobrepeso ($r = 0,77$, $p < 0,001$) y obesidad ($r = 0,29$, $p < 0,001$) Cc: normopeso ($r = 0,75$, $p < 0,001$), sobrepeso ($r = 0,77$, $p < 0,001$) y obesidad ($r = 0,83$, $p < 0,001$) Covariables: edad, genero, IMC o Cc según corresponda, disminuyendo intensidad de correlación con mantención de la significación Solo en el grupo de obesos el IMC no es correlacionado al ser ajustado ($r = -0,004$, $p = 0,932$)
Lou y cols. 2012 (20)	2.847 chinos sanos: 1.475 niños (44% sobrepeso/obesidad) y 1.372 niñas (27% sobrepeso/obesidad)	7-12	CMplas, SCtir	IMC y Cc	IMC: niños ($r = 0,80$, $p < 0,001$); niñas ($r = 0,73$, $p < 0,001$) Cc: niños ($r = 0,80$, $p < 0,001$); niñas ($r = 0,73$, $p < 0,001$) Al analizar los datos, por rango de edad (7-12 años) y sexo, esta asociación se mantiene ($p < 0,001$)

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Tabla I (Cont.). Estudios que analizan la asociación entre perímetro de cuello y marcadores de adiposidad en niños

Autor	Sujetos	Edad (años)	Protocolo medición perímetro de cuello	Método de evaluación de la variable de adiposidad	Principales resultados y conclusiones
Kurtoglu y cols. 2012 (12)	581 turcos sanos (21% normopeso, 79% sobrepeso/obesidad): 199 niños y 262 niñas	5 y 18	CMplas, Promcue	IMC, Cc	IMC: Niños prepúberes: ($r = 0,75$, $p < 0,001$) y púberes ($r = 0,77$, $p < 0,001$) Niñas prepúberes: ($r = 0,78$, $p < 0,001$) y púberes ($r = 0,77$, $p < 0,001$) Cc: Niños prepúberes: ($r = 0,82$, $p < 0,001$) y púberes ($r = 0,83$, $p < 0,001$). Niñas prepúberes: ($r = 0,85$, $p < 0,001$) y púberes ($r = 0,78$, $p < 0,001$)
Phan y cols. 2012 (30)	152 obesos estadounidenses sanos: 76 niños y 76 niñas	13	Promcue	Porcentaje de grasa (BIA)	Porcentaje de grasa corporal total (medido en cada visita, en ambos sexos y según raza; existiendo mayor relación de esta medición antropométrica en niñas y niños/as no blancos [$p < 0,05$])
Bammann y cols. 2013 (31)	78 niños sanos de 4 países de la Unión Europea (3 bajo peso, 47 normopeso, 28 sobrepeso/obesidad): 35 niños y 43 niñas	4-10	CMmet, SCtir	Porcentaje de grasa (BIA)	Masa grasa ($r^2 = 0,48$, $p < 0,001$) Covariables: edad y sexo
Nafiu y cols. 2013 (51)	1.058 estadounidenses (62% normopeso, 10% prehipertensos, 19% hipertensos): 561 niños y 497 niñas	6-18	CMplas, Promcue	IMC, Cc	IMC: niños ($r = 0,72$, $p < 0,001$); niñas ($r = 0,71$, $p < 0,001$) Cc: niños ($r = 0,78$, $p < 0,001$); niñas ($r = 0,83$, $p < 0,001$)
Sacco y cols. 2013 (48)	98 brasileros recién nacidos de término sanos: 43 niños y 55 niñas	5	NR	Peso corporal, IMC y Cc	A un mayor peso de nacimiento (≥ 0,67 DS, $p = 0,01$) Rápida ganancia de peso hasta los 2 (≥ 1 DS, $p = 0,03$) Obesidad materna (≥ 2 DS, $p < 0,001$)
Coutinho y cols. 2014 (32)	2.794 brasileros sanos (1% bajo peso, 64% normopeso, 35% sobrepeso/obesidad): 1.394 niños y 1.400 niñas	6-18	Promcue	IMC, Cc y porcentaje grasa corporal (BIA)	El perímetro de cuello fue correlacionado en ambos sexos (6-15 años) con IMC, Cc y porcentaje de grasa corporal total $p < 0,001$ para todas las condiciones

(Continúa en la página siguiente)

Tabla I (Cont.). Estudios que analizan la asociación entre perímetro de cuello y marcadores de adiposidad en niños

Autor	Sujetos	Edad (años)	Protocolo medición perímetro de cuello	Método de evaluación de la variable de adiposidad	Principales resultados y conclusiones
Da Silva y cols. 2014 (49)	388 brasileros sanos (46% normopeso, 52% sobrepeso/obesidad): 169 niños y 219 niñas	10-19	PMcue	IMC y Cc	IMC: Niños prepúberes: ($r = 0,57$, $p < 0,001$) y púberes ($r = 0,58$, $p < 0,001$) Niñas prepúberes: ($r = 0,39$, $p < 0,01$) y púberes ($r = 0,53$, $p < 0,001$) Cc: Niños prepúberes: ($r = 0,82$, $p < 0,001$) y púberes ($r = 0,78$, $p < 0,001$) Niñas prepúberes: ($r = 0,51$, $p < 0,001$) y púberes ($r = 0,71$, $p < 0,001$) Covariables: porcentaje de grasa corporal
Katz y cols. 2014 (52)	1.913 canadienses sanos (74% normopeso, 26% sobrepeso/obesidad): 977 niños y 936 niñas	6-17	CMplas, Promcue	IMC y Cc	IMC (al categorizar la muestra como estado nutricional normal *vs.* exceso de peso) y a Cc en niños y niñas, p (beta) < 0,0001, para todas las condiciones Covariables: estado nutricional (peso normal, sobrepeso y obesidad)
Ferretti y cols. 2015 (53)	1.668 brasileros sanos: 794 niños (30% sobrepeso/obesidad) y 916 niñas (29% sobrepeso/obesidad)	10-17	CMplas, PMcue	IMC, Cc, porcentaje de grasa (antropometría bicompartimental)	IMC (OR crudo: 3,83, $p < 0,001$; OR ajustado: 1,21, $p = 0,019$) Cc (OR crudo: 1,13, $p < 0,001$; OR ajustado: 1,02, $p = 0,024$) Porcentaje de grasa corporal total (OR crudo: 1,03, $p < 0,001$; OR ajustado: 0,96, $p < 0,001$) El punto de corte de perímetro de cuello para obesidad fue asociado a: IMC (OR crudo: 23,5, $p < 0,001$) Cc (OR crudo: 1,10, $p < 0,001$) Porcentaje de grasa corporal total (OR crudo: 1,05, $p < 0,001$; OR ajustado: 0,97, $p = 0,048$) Covariables: no reportadas
Formisano y cols. 2016 (54)	15.673 europeos sanos: 7.962 niños y 7.711 niñas	3-10	CMplas, Promcue	Cc	*z-score* de Cc: niños ($r = 0,31$, $p < 0,001$); niñas ($r = 0,35$, $p < 0,001$)

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Tabla I (Cont.). Estudios que analizan la asociación entre perímetro de cuello y marcadores de adiposidad en niños

Autor	Sujetos	Edad (años)	Protocolo medición perímetro de cuello	Método de evaluación de la variable de adiposidad	Principales resultados y conclusiones
Kelishadi y cols. 2016 (55)	23.043 iraníes sanos: 13.549 niños y 9.494 niñas	6-18	CMplas, BCtir	IMC, Cc, IC/cad, Cc/talla, Ccad	IMC ($r = 0,38$, $p < 0,001$) Cc ($r = 0,47$, $p < 0,001$) IC/cad ($r = 0,023$, $p < 0,001$) Cc/talla ($r = 0,18$, $p < 0,001$) Ccad ($r = 0,47$, $p < 0,001$) Al analizar los datos, por rango de edad (6-18 años) y sexo, esta asociación se mantiene ($p < 0,001$) Covariables: edad, sexo, área geográfica de residencia (asociación entre NC, sobrepeso y obesidad abdominal), modelo estadísticamente no difiere del ajustado
Castro-Piñeiro y cols. 2017 (22)	2.198 españoles sanos: 1.277 niños y 921 niñas	6-18	CMplas BCtir,	IMC, Cc, Cc/talla, porcentaje de grasa corporal total (antropometría)	IMC: niños ($r = 0,75$, $p < 0,001$); niñas ($r = 0,79$, $p < 0,001$) Cc: niños ($r = 0,86$, $p < 0,001$); niñas ($r = 0,85$, $p < 0,001$) Cc/talla: niños ($r = 0,61$, $p < 0,001$); niñas ($r = 0,62$, $p < 0,001$) Porcentaje de grasa corporal total: niños ($r = 0,55$, $p < 0,001$); niñas ($r = 0,64$, $p < 0,001$) Índice de masa grasa total: niños ($r = 0,49$, $p < 0,001$); niñas ($r = 0,47$, $p < 0,001$)
Kondolot y cols. 2017 (21)	1.766 turcos sanos: 874 niños y 892 niñas	2-6	CMplas, Promcue	IMC clasificado en percentiles	El perímetro de cuello se incrementa con la edad, siendo estadísticamente mayor en niños(as) con obesidad, definida según IMC ≥ p95

Protocolo de medición: CMplas: cinta métrica plástica; CMmet: cinta métrica metálica; PMcue: punto medio del cuello; CMcue: circunferencia mínima del cuello: Promcue: porción más prominente del cuello; SCtir: sobre cartílago tiroideo; BCtir: bajo cartílago tiroideo; NR: no reporta. Método/indicador de adiposidad: IMC: índice masa corporal; Cc: circunferencia de cintura; Ccad: circunferencia de cadera; IC/cad: índice cintura/cadera; TAC: tomografía axial computarizada; BIA: bioimpedanciometría; DXA: absorciometría dual de rayos X.

Tabla II. Estudios que analizan la asociación entre perímetro de cuello y marcadores de adiposidad en adultos

Autor	Participantes	Edad (años)	Protocolo medición perímetro de cuello	Método/indicador de evaluación de adiposidad	Principales resultados y conclusiones
Yang y cols. 2009 (27)	18 pacientes obesos (IMC > 40 kg/m^2) no diabéticos ingleses	22- 66	CMplas, PMcue	TAC (estimación de tejido adiposo visceral en L4)	Tejido adiposo visceral (r^2 = 0,67, p = 0,0001)
Preis y cols. 2010 (23)	3.307 estadounidenses pertenecientes a la cohorte Framingham (media IMC 27,8 kg/m^2): 1.718 hombres y 1.589 mujeres	51	CMplas, BCtir	IMC, Cc, TAC	IMC (hombres r = 0,79, p ≤ 0,0001; mujeres r = 0,80, p ≤ 0,0001) Cc (hombres r = 0,75, p ≤ 0,0001; mujeres r = 0,78, p ≤ 0,0001) Tejido adiposo visceral (hombres r = 0,63, p ≤ 0,0001; mujeres r = 0,74, p ≤ 0,0001) Covariables: edad
Li HX y cols. 2014 (26)	Datos recolectados 177 chinos sanos: 87 hombres y 90 mujeres	35-75	CMplas, SCtir	TAC, IMC, Cc, IC/cad	Tejido adiposo visceral: hombres (r = 0,49, p > 0,001), mujeres (r = 0,25, p > 0,05) Tejido adiposo subcutáneo hombres (r = 0,59, p > 0,001), mujeres (r = 0,41, p > 0,001)
Rosenquist y cols. 2014 (24)	91 adultos pertenecientes a la cohorte Framingham: 46 hombres (media IMC 27,8 kg/m^2) y 45 mujeres (media IMC 27,1 kg/m^2)	58,5	BCtir	IMC, Cc, TAC	IMC (r = 0,73, p < 0,001) Cc (r = 0,65, p < 0,001) Tejido adiposo visceral (r = 0,71, p < 0,001) Tejido adiposo subcutáneo (r = 0,56, p < 0,001) Covariables: edad y sexo
Torriani y cols. 2014 (25)	303 estadounidenses sanos (media IMC: 28kg/m^2): 152 hombres y 151 mujeres	55 ± 17	NR	TAC, IMC y Cc	IMC (hombres r = 0,70, p < 0,001; mujeres r = 0,75, p < 0,001) Cc (hombres r = 0,71, p < 0,001; mujeres r = 0,69, p < 0,001) Tejido adiposo visceral (hombres r = 0,61, p < 0,001; mujeres r = 0,70, p < 0,001) Tejido adiposo subcutáneo (hombres r = 0,64, p < 0,001; mujeres r = 0,63, p < 0,001) Covariables: edad, estado de enfermedad y sexo
Cizza y cols. 2014 (28)	120 estadounidenses obesos (media IMC 38,6 kg/m^2, 40% con síndrome metabólico): 28 hombres y 92 mujeres	18-50	CMcue	Porcentaje de grasa corporal (DXA)	Porcentaje de grasa abdominal total, porcentaje de grasa visceral y porcentaje de grasa subcutánea (r = 0,482, p < 0,001)
Ravensbergen y cols. 2014 (29)	27 canadienses con lesión en la medula espinal	40	PMcue	Porcentaje grasa corporal total, grasa abdominal (DXA)	Gramos de grasa corporal total (r = 0,62, p = 0,003) Gramos de grasa abdominal (r = 0,63, p = 0,002)

(Continúa en la página siguiente)

Tabla II (Cont.). Estudios que analizan la asociación entre perímetro de cuello y marcadores de adiposidad en adultos

Autor	Participantes	Edad (años)	Protocolo medición perímetro de cuello	Método/indicador de evaluación de adiposidad	Principales resultados y conclusiones
Ben-Noun y cols. 2001 (13)	724 israelíes sanos (31% normopeso, 68% sobrepeso/ obesidad): 353 hombres y 371 mujeres	35 -65	CMplas, PMcue	IMC, Cc, Ccad, IC/cad	IMC (hombres r = 0,83, mujeres r = 0,71, p < 0,0001) Peso (hombres r = 0,70, mujeres r = 0,81, p < 0,0001) Cc (hombres r = 0,86, mujeres r = 0,85, p < 0,0001) Ccad (hombres r = 0,62, mujeres r = 0,56, p < 0,0001) IC/cad (hombres r = 0,66, mujeres r = 0,87, p < 0,0001)
Ben-Noun y cols. 2003 (9)	561 israelís sanos: 231 hombres y 330 mujeres	18 o más	CMplas, PMcue	IMC, Cc, IC/cad	IMC (hombres r = 0,71; mujeres r = 0,81, p < 0,0001) Cc (hombres r = 0,75; mujeres r = 0,79, p < 0,0001) IC/cad (hombres r = 0,56; mujeres r = 0,63, p < 0,0001)
Feet y cols. 2005 (33)	55 mujeres brasileñas sanas sedentarias con sobrepeso u obesidad (IMC > 25 kg/m^2)	36 ± 10	CMplas, PMcue	IMC, Cc, IC/cad, porcentaje de grasa (antropometría, BIA)	El perímetro de cintura se asoció pre y postintervención (ejercicio y dieta) con: IMC (pre r = 0,71, post r = 0,68, p = 0,0001) Cc (pre r = 0,67, p = 0,0001; post r = 0,62, p = 0,0006) IC/cad (pre r = 0,48, p = 0,0004; post r = 0,41, p = 0,03) Porcentaje de grasa según antropometría (pre r = 0,61, p = 0,0001; post r = 0,60, p = 0,001) Porcentaje de grasa según bioimpedancia (pre r = 0,64, p = 0,0001; post r = 0,74, p = 0,0002)
Ben-Noun y cols. 2006 (10)	364 israelíes sanos: 155 hombres y 209 mujeres	18 o más	CMplas, PMcue	IMC, Cc, IC/cad	Los cambios de perímetro de cuello se asociaban con: IMC (hombres r = 0,79, p < 0,001; mujeres r = 0,74, p < 0,001) Cc (hombres r = 0,75, p < 0,001; mujeres r = 0,71, p < 0,001) IC/cad (hombres r = 0,47, p < 0,001; mujeres r = 0,61, p < 0,0001) Covariables: edad
Davidson y cols. 2008 (39)	598 estadounidenses sanos con antecedentes de trastornos de la respiración durante el sueño: 424 hombres y 174 mujeres	48	PMcue	IMC, Cc, IC/cad	IMC (hombres r = 0,66, p ≤ 0,001; mujeres r = 0,69, p ≤ 0,001) Cc (hombres r = 0,61, p ≤ 0,001; mujeres r = 0,82, p ≤ 0,001) IC/cad (hombres r = 0,35, p ≤ 0,001; mujeres r = 0,54, p ≤ 0,001)
Onat y cols. 2009 (40)	1.912 turcos sanos: 934 hombres y 978 mujeres	55,1 ± 12	PMcue	IMC, Cc, IC/cad	IMC (hombres r = 0,69, p ≤ 0,001; mujeres r = 0,60, p ≤ 0,001) Cc (hombres r = 0,70, p ≤ 0,001; mujeres r = 0,60, p ≤ 0,001) IC/cad (hombres r = 0,42, p ≤ 0,001; mujeres r = 0,22, p ≤ 0,001)

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Tabla II (Cont.). Estudios que analizan la asociación entre perímetro de cuello y marcadores de adiposidad en adultos

Autor	Participantes	Edad (años)	Protocolo medición perímetro de cuello	Método/indicador de evaluación de adiposidad	Principales resultados y conclusiones
Kawaguchi y cols. 2010 (34)	219 japoneses sanos con sospecha de síndrome de apnea obstructiva del sueño: 170 hombres y 49 mujeres	52,8 ± 15,0	PMcue	Porcentaje de grasa corporal (BIA)	Porcentaje de grasa visceral ($r = 0,731$, $p < 0,0001$) Al realizar el análisis del perímetro de cuello/ talla, esta relación se incrementa ($r = 0,819$, $p < 0,0001$)
Yang y cols. 2010 (14)	3.182 diabéticos chinos: 1.294 hombres y 1.888 mujeres	20-80	SCtir	IMC, Cc	IMC (hombres $r = 0,41$, $p \leq 0,0001$; mujeres $r = 0,84$, $p \leq 0,0001$) Cc (hombres $r = 0,47$, $p \leq 0,0001$; mujeres $r = 0,47$, $p \leq 0,0001$)
Hingorjo y cols. 2012 (41)	150 pakistaníes sanos: 41 hombres y 109 mujeres	18-20	CMplas, SCtir	IMC, Cc, Cad, IC/cad	IMC (hombres $r = 0,86$, $p \leq 0,001$; mujeres $r = 0,70$, $p \leq 0,001$) Cc (hombres $r = 0,85$, $p \leq 0,001$; mujeres $r = 0,62$, $p \leq 0,001$) Ccad (hombres $r = 0,82$, $p \leq 0,001$; mujeres $r = 0,58$, $p \leq 0,001$) IC/cad (hombres $r = 0,69$, $p \leq 0,001$; mujeres $r = 0,22$, $p \leq 0,05$)
Akin y cols. 2013 (42)	92 hombres turcos sanos (47 de ellos con disfunción eréctil)	40-60	CMplas, SCtir	IMC, Cc	IMC ($r = 0,7$, $p < 0,001$) Cc ($r = 0,6$, $p < 0,001$)
Stabe y cols. 2013 (43)	1.053 brasileros (32% con síndrome metabólico, 24% con insulino-resistencia y 29% con DM2): 301 hombres y 752 mujeres	18-60	BCtir	IMC, Cc, IC/cad	IMC: hombres ($r = 0,67$, $p \leq 0,001$); mujeres ($r = 0,62$, $p \leq 0,001$) Cc: hombres ($r = 0,71$, $p \leq 0,001$); mujeres ($r = 0,64$, $p \leq 0,001$) IC/cad (hombres $r = 0,33$, $p \leq 0,001$; mujeres $r = -0,02$, $p = 0,56$) Covariables: edad
Aoi y cols. 2014 (35)	63 mujeres posmenopáusicas japonesas sanas	63.6 ± 7.1	BCtir	IMC, Cc, porcentaje de grasa (BIA)	IMC ($r = 0,74$, $p = 0,001$) Cc ($r = 0,72$, $p = 0,001$) Porcentaje de grasa ($r = 0,71$, $p = 0,001$)
Saka y cols. 2014 (15)	411 turcos sanos (40% con sobrepeso/obesidad): 174 hombres y 237 mujeres	20 -60	CMplas, BCtir	IMC, peso corporal, Cc, Ccad y IC/cad	Peso corporal (hombres $r = 0,57$, $p < 0,001$; mujeres $r = 0,70$, $p < 0,001$) IMC (hombres $r = 0,58$, $p < 0,0001$; mujeres $r = 0,68$, $p < 0,0001$) Cc (hombres $r = 0,59$, $p < 0,0001$; mujeres $r = 0,66$, $p < 0,0001$) Ccad (hombres $r = 0,56$, $p < 0,0001$; mujeres $r = 0,61$, $p < 0,0001$) IC/cad (hombres $r = 0,27$, $p < 0,0001$; mujeres $r = 0,45$, $p < 0,0001$)

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Tabla II (Cont.). Estudios que analizan la asociación entre perímetro de cuello y marcadores de adiposidad en adultos

Autor	Participantes	Edad (años)	Protocolo medición perímetro de cuello	Método/indicador de evaluación de adiposidad	Principales resultados y conclusiones
Yan y cols. 2014 (44)	2.092 chinos: 971 hombres (25,5% síndrome metabólico, 32,4% obesidad) y 1.121 mujeres (30,1% síndrome metabólico y 35,9% obesidad)	65	SCtir	IMC, Cc	IMC (hombres r = 0,70, p < 0,01; mujeres r = 0,7, p < 0,01) Cc (hombres r = 0,73, p < 0,01; mujeres r = 0,72, p < 0,01)
Cho y cols. 2015 (36)	3.521 datos de no diabéticos coreanos: 1.784 hombres y 1.737 mujeres	42-71	BCtir	IMC, Cc, porcentaje de grasa (BIA)	IMC (hombres r = 0,80, p < 0,001; mujeres r = 0,74, p < 0,001) Cc (hombres r = 0,74, p < 0,001; mujeres r = 0,70, p < 0,001) Porcentaje de grasa total (hombres r = 0,54, p < 0,001; mujeres r = 0,51, p < 0,001)
Özkaya y cols. 2016 (45)	1.157 turcos sanos (media IMC 15,3-49,4 kg/m^2): 319 hombres y 838 mujeres	18-24	CMplas, PMcue	IMC, Cc, Ccad, IC/cad	IMC (hombres r = 0,68, p < 0,01; mujeres r = 0,48, p < 0,01) Cc (hombres r = 0,68, p < 0,01; mujeres r = 0,47, p < 0,01) Ccad (hombres r = 0,64, p < 0,01; mujeres r = 0,55, p < 0,01) IC/cad (hombres r = 0,64, p < 0,01; mujeres r = 0,24, p < 0,01)
Aoi y cols. 2016 (37)	63 mujeres posmenopáusicas japonesas sanos	NR	BCtir	IMC, Cc, porcentaje de grasa (BIA)	IMC (r = 0,74, p = 0,001) Cc (r = 0,73, p = 0,001) Porcentaje de grasa (r = 0,74, p = 0,001) Tras 3 años de seguimiento, los cambios de perímetro de cuello también fueron asociados a IMC (r = 0,3, p = 0,002), CC (r = 0,2, p = 0,045) y porcentaje de grasa (r = 0,2, p = 0,027) Covariables: edad
Assyov y cols. 2016 (16)	255 búlgaros con IMC ≥ 30 kg/m^2: 102 hombres y 153 mujeres	49 ± 12	BCtir	IMC, porcentaje de grasa (BIA)	IMC (hombres r = 0,29, p < 0,05; mujeres r = 0,52, p < 0,01) Porcentaje de grasa corporal (hombres r = 0,52, p < 0,01; mujeres r = 0,46, p < 0,01) Covariables: edad
Baena y cols. 2016 (46)	15.105 brasileros sanos de la cohorte ELSA-Brasil: 3.810 hombres y 4.916 mujeres	35-74	SCtir	IMC, Cc	IMC (hombres r = 0,72, p < 0,001; mujeres r = 0,68, p < 0,001) Cc (hombres r = 0,72, p < 0,001; mujeres r = 0,72, p < 0,001) Covariables: edad
Coelho y cols. 2016 (47)	435 adultos mayores brasileros sanos (sin obesidad mórbida, IMC ≥ 40 kg/m^2): 64 hombres y 371 mujeres	> 60	SCtir	IMC, Cc, IC/cad	IMC, Cc y IC/cad: *valores de r y su significancia, no reportados en el artículo

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Tabla II (Cont.). Estudios que analizan la asociación entre perímetro de cuello y marcadores de adiposidad en adultos

Autor	Participantes	Edad (años)	Protocolo medición perímetro de cuello	Método/indicador de evaluación de adiposidad	Principales resultados y conclusiones
Joshipura y cols. 2016 (7)	Datos de 1.206 adultos con sobrepeso u obesidad, no diabéticos portorriqueños	40-65	CMplas, BCtir	IMC, Cc y porcentaje de grasa corporal (BIA)	IMC ($r = 0,66$, $p < 0,001$) Cc ($r = 0,64$, $p < 0,001$) Porcentaje de grasa corporal ($r = 0,45$, $p < 0,001$) Covariables: edad, sexo, tabaquismo y nivel de actividad física
Limpawattana y cols. 2016 (8)	587 tailandeses pertenecientes a un estudio de cohorte de enfermedades ateroscleróticas: 201 hombres y 386 mujeres	≥ 50	SCtir	Cc	Cc (hombres: $r = 0,7$, $p < 0,001$; mujeres: $r = 0,6$, $p < 0,001$)

Protocolo de medición: CMplas: cinta métrica plástica; CMmet: cinta métrica metálico; PMcue: punto medio del cuello: CMcue: circunferencia mínima del cuello; Promcue: porción más prominente del cuello; SCtir: sobre cartílago tiroideo; BCtir: bajo cartílago tiroideo: NR: no reporta. Método/indicador de adiposidad IMC: índice masa corporal; Cc: Circunferencia de cintura; Ccad: circunferencia de cadera; RC/cad: índice cintura/cadera; TAC: tomografía axial computarizada; BIA: bioimpedanciometría; DXA: absorciometría dual de rayos X.

Además, tres de los estudios (24-26) encontraron relación directa y significativa entre perímetro de cuello y tejido adiposo subcutáneo y uno de ellos (25) incluye la medición de los compartimientos del tejido adiposo del cuello subdividido en subcutáneo (ubicado entre la piel y la fascia cervical profunda), posterior (entre esternocleidomastoideo, escaleno y trapecio) y perivertebral (entre los músculos que rodean las cervicales).

Dos artículos realizaron el análisis de composición corporal mediante DXA, calculando la cantidad de grasa corporal total y abdominal en ambos casos. La población estudiada fue estadounidense (28) y canadiense (29) y los resultados muestran una asociación directa y significativa con el perímetro de cuello (Tabla II).

VALIDEZ CONCURRENTE: ASOCIACIÓN DEL PERÍMETRO DE CUELLO CON MARCADORES DE ADIPOSIDAD DETERMINADOS CON MÉTODOS DOBLEMENTE-INDIRECTOS

Niños y adolescentes

Se identificaron tres estudios que analizaron la asociación entre perímetro de cuello y marcadores de adiposidad mediante bioimpedanciometría (30-32) (Tabla I). La población estudiada (estadounidense, europea y brasileña) incluyó a niños y/o adolescentes de ambos sexos, mayores de cuatro años. Es importante destacar que la raza fue una variable considerada en uno (30) de los tres estudios. Finalmente, en este grupo de edad, un 34% (n = 16) de los 47 estudios seleccionados en esta revisión muestran asociación directa y significativa entre perímetro de cuello con IMC, circunferencia de cintura y/o índice cintura/cadera, independiente del sexo y la edad. Además, Castro-Piñeiro y cols. (22) mostraron una asociación positiva entre el perímetro del cuello e IMC, circunferencia de cintura, la ratio circunferencia de cintura y altura, porcentaje de masa grasa estimado mediante pliegues cutáneos e índice de masa grasa estimado también mediante pliegues cutáneos en niños y adolescentes españoles (Tabla I). Este estudio aporta puntos de corte de perímetro de cuello asociado a IMC y circunferencia de cintura para niños y niñas de 6 a 18 años que oscilan entre 25 y 37 cm.

Adultos

Se identificaron siete estudios que mostraban una asociación directa del perímetro de cuello con el porcentaje de masa grasa total, medido con bioimpedanciometría (7,16,33-37). El 42% (n = 3) de los estudios realizaron el análisis en población japonesa (dos de ellos incluyendo solo a mujeres postmenopáusicas) (35,37) y el 58% restante, en población búlgara (n = 1) (16), coreana (n = 1) (36), brasileña (n = 1) (33) y puertorriqueña (n = 1) (7). En relación a la asociación de perímetro de cuello solo con marcadores convencionales tales como el IMC, circunferencia de cintura y/o índice cintura/cadera, un 32% (n = 15) (8,10,13-15,38-47) de los estudios incluidos en esta revisión establece relación directa en ambos sexos y todos los grupos de edad.

DISCUSIÓN

Los resultados de la presente revisión sistemática muestran que el perímetro del cuello se asocia de forma directa con marcadores de adiposidad medidos mediante métodos de referencia tales como el TAC o el DXA en adultos, sin embargo, no se encontraron estudios en niños. Además, el perímetro del cuello se asocia consistentemente en todos los estudios con marcadores de adiposidad total y central tales como el IMC, perímetro de cintura e índice cintura/cadera tanto en población adulta como en niños. El perímetro de cuello es un método sencillo, inocuo, rápido, de bajo coste y no influenciable por el ayuno-saciedad, vestimenta, temperatura ambiente o limitaciones socioculturales. Además, la existencia de puntos de corte para el diagnóstico de sobrepeso y obesidad apunta a una gran utilidad de este marcador tanto en investigación como en clínica. Sin embargo, el reducido número de estudios de validación frente a métodos de referencia "*gold standard*" en adultos, y la ausencia de estudios con métodos de referencia "*gold standard*" en niños y adolescentes ponen de manifiesto la necesidad de realizar nuevos estudios que confirmen la validez de criterio del perímetro de cuello como indicador de adiposidad total, central y visceral.

En el caso de la población infantil, no se encontraron estudios que analicen la relación entre el perímetro de cuello y otros indicadores de adiposidad en base a métodos considerados de referencia; sin embargo, todos los resultados obtenidos en base a la asociación de esta medición antropométrica con marcadores convencionales son positivos y estadísticamente significativos. En relación a los estudios que utilizaron bioimpedancia en población infantil (30-32), el perímetro de cuello fue correlacionado con el porcentaje de masa grasa en niños estadounidenses, europeos y brasileños. Cabe destacar que un hallazgo novedoso es encontrado en 76 adolescentes obesos estadounidenses de 13 años (30), en los cuales se observó que, en etnias no caucásicas, la relación entre perímetro de cuello y porcentaje de masa grasa es más fuerte ($p < 0,05$), resultado que hasta la fecha no ha sido reportado en población adulta.

El crecimiento del cuello durante la etapa escolar podría estar influenciando directamente el punto anatómico de medición más utilizado en la mayoría de los estudios que trabajaron con este grupo de edad. El 56% de los estudios identificados midieron el cuello en la porción más prominente. Por otro lado, es posible que el perímetro de cuello pueda ser una medición muy útil desde los primeros años de vida. De hecho, un estudio en una cohorte de 98 niños brasileros concluyó que un mayor perímetro de cuello a los cinco años de edad estaría directamente vinculado a una mayor ganancia de peso hasta los dos años de edad (48). Estos resultados indican que el perímetro del cuello se puede utilizar como un marcador predictor de sobrepeso y obesidad. Aunque hacen faltan más estudios para confirmar esta hipótesis.

Todos los estudios que analizaron la validez de criterio en adultos y adultos mayores reportaron asociación positiva entre perímetro de cuello y adiposidad total, abdominal, visceral o subcutánea. El primer estudio que utilizó la técnica TAC para estudiar la asociación entre perímetro de cuello y masa grasa visceral fue realizado por Yang y cols. (27) en 18 obesos no diabéticos ingleses de entre 22 y 66 años de edad. Los estudios realizados por Preis y cols. (23), Li y cols. (26), Rosenquist y cols. (24) y Torriani y cols. (25) refuerzan los mismos resultados. Torriani y cols. (25), en una muestra de 303 sujetos de ambos sexos, examinaron además la relación entre el perímetro y la masa grasa posterior, subcutánea y perivertebral del cuello, describiendo que el perímetro de cuello aumentaría en un 30% (mujeres) y 24% (hombres) al comparar los grupos normopeso *vs.* obesos, y que los compartimentos adiposos del cuello se expandirían de diferente manera al incrementarse el IMC. Además, mostraron que el tejido adiposo perivertebral tendría una menor capacidad de almacenamiento de masa grasa, lo cual repercutiría en los depósitos de los compartimientos posterior y subcutáneo, que estarían relacionados con factores de riesgo cardiovascular en el grupo de mujeres ($p < 0,001$). Además, los dos estudios que realizaron el análisis de composición corporal mediante DXA también encontraron asociación positiva con perímetro de cuello. Cizza y cols. (28), en una muestra de 120 estadounidenses de entre 18 y 50 años, mostraron que el perímetro de cuello se relaciona con el porcentaje de grasa abdominal total, visceral y subcutánea. Resultados similares se describen en el estudio de Ravensbergen y cols. (29), el mismo año, en 27 participantes canadienses de 40 años, en los cuales se encontró correlación entre perímetro de cuello y porcentaje de grasa corporal total y abdominal ($r = 0,6$, $p = 0,003$ y $r = 0,63$, $p = 0,002$, respectivamente). En relación a los estudios que utilizan métodos de composición corporal indirectos, estos se caracterizaron por considerar diversidad de raza, edad e incluir población saludable. La excepción a la regla con respecto al tipo de condición fisiopatológica de población investigada fue publicada el año 2010 por Yang y cols. (14) en 3.182 diabéticos chinos de entre 20 y 80 años, con resultados similares de relación de perímetro de cuello con IMC y circunferencia de cintura a los hallazgos anteriormente mencionados.

Por último, la ausencia de estudios que ajusten el análisis por posibles variables confusoras tales como el sexo, la edad y el porcentaje de adiposidad total, junto con el hecho de que Da Silva y cols. (49) encontraron, en un reciente estudio en 388 brasileros de entre diez y 19 años, que la asociación entre perímetro de cuello e IMC podría ser independiente de masa magra, sugieren que las futuras líneas de investigación deberían analizar la relación de este indicador también con masa magra, en diferentes edades, etnias, condiciones fisiológicas y/o patológicas.

CONCLUSIONES

El perímetro de cuello se asocia a marcadores doblemente-indirectos de masa grasa total y central en niños y adolescentes. En adultos, no hay duda de que el perímetro del cuello es un marcador válido para medir adiposidad total y central. Se requieren más estudios que analicen la asociación entre el perímetro del cuello y la adiposidad analizada mediante métodos de referencia en niños y adolescentes. También es necesario analizar si el pe-

rímetro del cuello se asocia a otros parámetros de composición corporal tales como la masa magra tanto en niños y adolescentes como en adultos.

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Revisión

Modulation of intestinal microbiota, control of nitrogen products and inflammation by pre/probiotics in chronic kidney disease: a systematic review

Modulación de microbiota intestinal, control de productos de nitrógeno e inflamación por pre/probióticos en la enfermedad renal crónica: una revisión sistemática

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Abstract

Dysbiosis may favor the occurrence of inflammation and oxidative stress in chronic kidney disease (CKD). It has been suggested that the intake of pre/probiotics may control the progression of chronic kidney disease. Thus, the objective of this study was to systematically review the literature on the effects of pre/probiotic intake on the intestinal microbiota, control of nitrogen products, oxidative stress, and inflammation in CKD patients. The literature search was conducted on MEDLINE, LILACS, Cochrane Library of Clinical Trials, and Science Direct. After careful evaluation by the reviewers, ten potentially relevant articles were selected for this study. Based on previous studies, intake of prebiotics appears to have the following effects: increased bifidobacteria and lactobacillus counts; reduced formation of uremic toxin, p-cresol, and its serum concentrations; improved lipid profiles; reduced systemic inflammatory state and concentrations of oxidative stress markers. Similarly, consumption of probiotics can reduce blood urea and serum phosphate concentrations. Furthermore, an increase in fecal volume and intestinal *Bifidobacterium* and a reduction in p-cresol serum and blood urea concentrations were observed in response to symbiotic intake. These results suggest that consumption of pre/probiotics may modulate the intestinal microbiota, and promote the growth and metabolism of anaerobic bacteria by decreasing the production of uremic solutes, further causing oxidative stress and systemic inflammation in CKD patients.

Key words:

Hemodialysis. Oxidative stress. Symbiotic. Uremia. Uremic toxins.

Resumen

La disbiosis puede favorecer la incidencia de inflamación y de estrés oxidativo en enfermedades renales crónicas. Se ha sugerido que el consumo de prebióticos y probióticos puede controlar la progresión de enfermedades renales crónicas. De este modo, el objetivo de este estudio es revisar sistemáticamente la literatura sobre los efectos del consumo de prebióticos y probióticos en la microbiota intestinal, el control de los productos de nitrógeno, el estrés oxidativo y la inflamación en enfermedades renales crónicas. La búsqueda bibliográfica fue realizada por medio de MEDLINE, LILACS, Cochrane Library of Clinical Trials y Science Direct. Diez artículos fueron incluidos en este estudio. Los prebióticos parecen aumentar las bifidobacterias y el recuento de lactobacillus, reducir la formación de toxina urémica, p-cresol y su concentración sérica; mejorar los perfiles lipídicos y reducir el estado de inflamación sistémica y la concentración de indicadores de estrés oxidativo. El consumo de probióticos puede reducir la urea en sangre y la concentración de fosfato sérico. Se verificó el aumento del volumen fecal y de las bifidobacterias intestinales y la reducción de la concentración sérica de p-cresol y de urea en sangre en respuesta a la ingesta de simbióticos. Estos resultados indican que los prebióticos y probióticos modulan la microbiota intestinal y promueven el crecimiento del metabolismo de bacterias anaerobias, disminuyendo la producción de solutos urémicos y la incidencia de estrés oxidativo e inflamación sistémica en pacientes portadores de enfermedades renales crónicas.

Palabras clave:

Hemodiálisis. Estrés oxidativo. Simbiótico. Uremia. Toxinas urémicas.

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INTRODUCTION

Chronic kidney disease (CKD) is a global public health problem. In countries, such as the United States of America and Australia, it affects 10-13% of the population (1,2). Over the last decade, there has been an increase in the incidence and prevalence of this disease, with a significant increase in the number of patients requiring dialysis therapy (3). Studies conducted in Brazil have shown a gradual increase in the prevalence of CKD, with a high proportion of patients in need of dialysis treatment. In 2016, 122.825 CKD patients were recorded to be on dialysis, and 92.3% of patients were on hemodialysis (HD) (4,5).

Uremia is a serious complication of CKD, and it is associated with renal injury, food restriction, and hydration status. Besides activating the renin-angiotensin-aldosterone system and favoring the occurrence of vascular calcifications, uremia also changes the microbiota (known as dysbiosis) and increases intestinal permeability (6-8). It results in an increased flow of urea into the intestinal lumen, which is then hydrolyzed by microbial urease. Bacterial urease catalyzes the hydrolysis of urea to produce ammonium hydroxide; this reaction leads to an increase in the local pH, facilitating the growth of pathogenic bacteria and promoting mucosal irritation and damage (9-10). These changes allow entry of endotoxins and other harmful luminal contents into the underlying tissues and systemic circulation, favoring the manifestation of other diseases (6,7,11,12).

Patients with CKD demonstrate significant quantitative and qualitative changes in intestinal microbiota, related to the overgrowth of aerobic and anaerobic pathogenic bacterial species (7,11). These bacteria can use nitrogen products, thus increasing the production of uremic toxins, such as indoxyl sulfate and p-cresyl sulfate. Such toxins induce inflammation, oxidative stress, and cause a pathophysiological impact, resulting in structural and functional changes that indirectly influence patient morbidity and mortality (13,14).

In uremic patients, oxidative stress and inflammation cause dysregulation of the immune system. This is evidenced by the presence of elevated oxidative biomarkers, such as lipid oxidation and protein oxidation products (15,16). A cross-sectional study involving patients with chronic renal failure demonstrated that the presence of indoxyl sulfate and p-cresyl sulfate was also associated with elevated concentrations of inflammatory markers and increased arterial stiffness, a key clinical finding associated with CKD (17). In the past decade, these toxins have been associated with the progression, cardiovascular morbidity and mortality of CKD patients (18). In addition to uremia and metabolic acidosis, routine therapeutic interventions for treating CKD, such as dietary restriction of fruits, vegetables, and foods with high fiber content, iron intake, phosphate binders, and antibiotics modify the colonic environment. These modifications negatively affect the intestinal microbiota and induce the production of uremic toxins and inflammatory markers (19).

Some interventions are being used to modulate the intestinal microbiota, block LPS or attenuate inflammation, or target adsorption of uremic toxin end products of microbial fermentation (20). Previously published review articles have described some of these interventions: administration of small intestine alpha-glycosidase inhibitor that increases the fermentation of carbohydrates in the colon and can reduce the colonic generation of p-cresol; utilization of essential oils as agents to treat dysbiosis; use of oral adsorbents to restore epithelial tight-junction proteins and reduce plasma endotoxin and markers of oxidative stress and inflammation; administration of synthetic TLR4 antagonists to inhibit LPS signaling; ingestion of prebiotics and/or probiotics that play an important role in the progression of CKD (12,20).

The results of a recent study suggest that the ingestion of prebiotics and probiotics can increase the production of short chain fatty acids, modulating the intestinal microbiota (17). They can also reduce intestinal permeability via blocking the entry of endotoxins into the bloodstream and suppressing inflammation (21); these events are believed to play an important role in the progression of CKD. Therefore, the objective of this study was to systematically review the literature on the effects of intake of prebiotic and/or probiotic products on the intestinal microbiota, oxidative stress, and inflammation in patients with CKD.

METHODS

This systematic review was conducted according to a pre-specified protocol and is described according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (22). This article is based on previously conducted studies, and it does not include studies conducted by any of the authors of this study.

SEARCH STRATEGY

A literature review was conducted in computerized databases MEDLINE (PubMed), Latin American and Caribbean Health Sciences (LILACS), Cochrane Library of Clinical Trials and Science Direct. Databases were searched using the key words: “chronic kidney disease,” “hemodialysis,” “intestinal permeability,” “intestinal/gut microbiota,” “inflammation,” “oxidative stress,” “uremic toxins,” “supplementation,” “probiotic,” “prebiotic,” and “symbiotic.” These terms were searched alone or in combinations with each other. The search was limited to articles published between 2005 and 2016.

First, a manual search on references of all selected articles was conducted. To ensure that no relevant data was missed, a survey of the gray literature was conducted using the databases of theses and dissertations from the following sources: the Coordination of Improvement of Higher Education Personnel (CAPES), the Digital Library of theses and dissertations of the Federal University of Viçosa, and the Brazilian digital library of theses and dissertations to ensure that no important studies were missed out. Next, the abstracts of these articles were analyzed to verify compliance with the inclusion criteria, and full-text articles were subsequently examined to confirm their eligibility.

SELECTION CRITERIA

In this review, we included randomized clinical studies that examined the efficacy of prebiotic, probiotic, or symbiotic supplementation in modulating intestinal microbiota and regulating nitrogen products and inflammation in CKD patients (both sexes) who had received the intervention for at least one day. Review articles, animal studies, articles not written in English, and those not related to the topic of interest were excluded.

DATA EXTRACTION AND SYNTHESIS

All relevant studies identified in the electronic databases were consolidated in a single database to remove all duplicates. After exclusion of the duplicates, two independent reviewers selected the references in three phases: analyses of titles, abstracts, and full texts. Any disagreements related to conflicting data or study eligibility were resolved by a third reviewer. Data including methodological quality, participant information, duration of intervention, and outcome type (changes in intestinal microbiota, nitrogen products, uremic toxins, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, and inflammatory markers) were extracted and collected in duplicates in a Microsoft Excel worksheet. The quality of the included trials was measured using the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials (23). Quality assessment was conducted by three independent reviewers, and disagreements were resolved by consensus.

RESULTS

SEARCH RESULTS

During the initial selection process, 1,679 articles were identified. Later, 781 duplicate articles were excluded, and 890 articles were removed after reading their titles and/or abstracts. Eight other articles were identified by reverse search and were considered as eligible; however, after reading their abstracts, six did not meet the inclusion criteria and were thus excluded from this study. Finally, we included and critically analyzed a total of ten articles (Fig. 1).

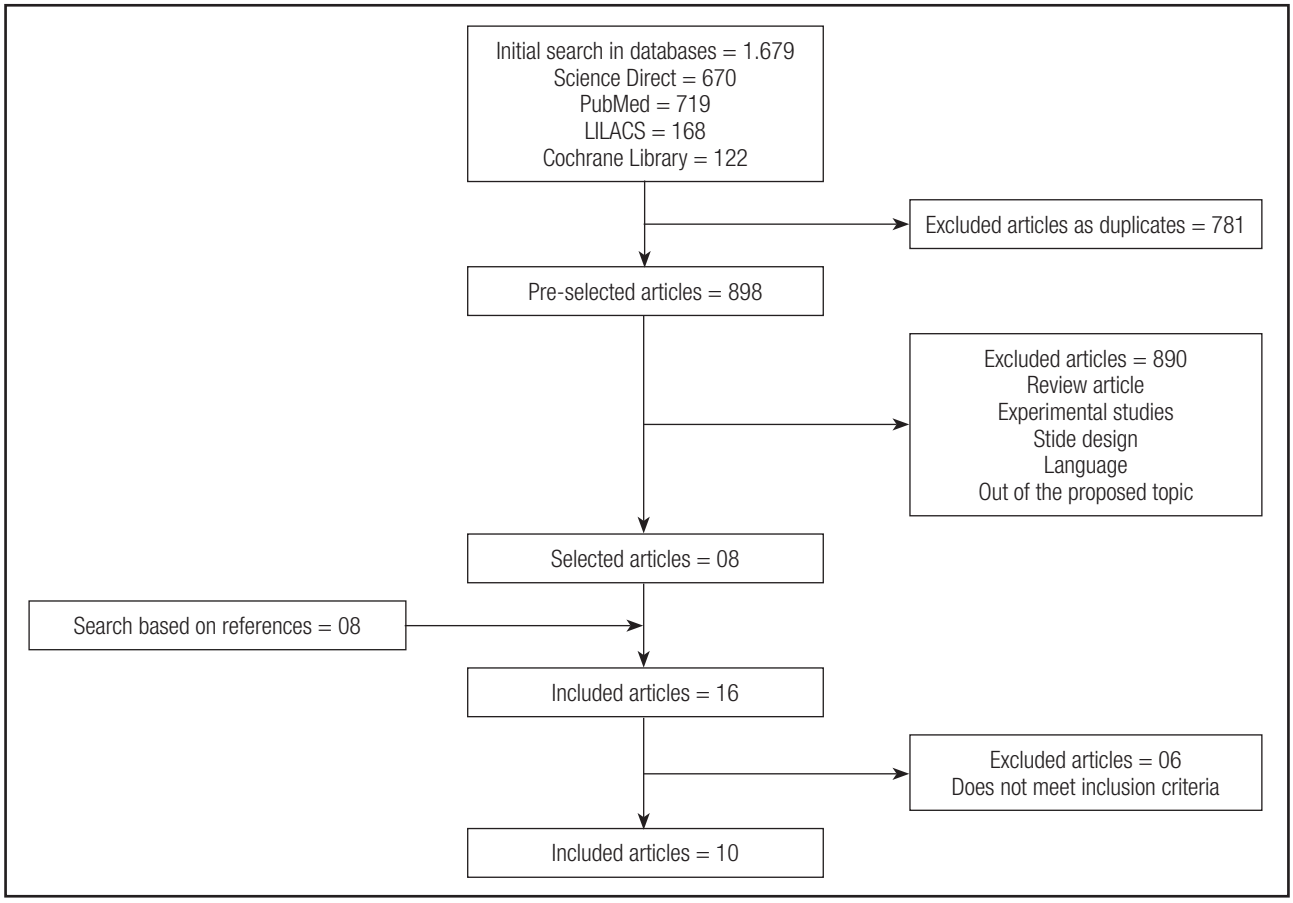

Figure 1.

Flowchart of the steps for obtaining the articles selected for this systematic review.

According to the Cochrane Collaboration's risk of bias tool for randomized trials, ten selected studies presented varying degrees of bias. All trials had a low or an unclear risk of bias for sequence generation, allocation concealment, blinding, selective outcome reporting, and other sources of bias.

STUDY CHARACTERISTICS

The selected articles described studies involving CKD outpatients who were either in stages 3-4 of the disease (five studies), stages 4-5 without dialysis (one study), or were receiving HD (four studies). These studies were further grouped based on the type of supplement that was used for treating the participating patients (Table I). While two studies tested the effectiveness of prebiotic products in patients with CKD, the remaining eight studies investigated the efficacy of either probiotics (four studies) or symbiotics (four studies) in these patients.

PARTICIPANT CHARACTERISTICS

A total of 423 subjects participated in the clinical trials, and the sample size ranged from 12 to 125. Their mean age ranged from 26 to 82 years and 64.18% of the participants were male. The sample sizes of three studies were similar, all of which involved patients with stages 3-4 of the disease (Table I).

INTERVENTIONS

Interventions with prebiotics in HD patients showed that the consumption of dietary fermentable fiber (10 g and 20 g for six weeks) and the consumption of lactulose (30 mm three times a day for eight weeks) improved lipid profiles (total cholesterol and LDL) and oxidative status (increased total antioxidant capacity and decreased malondialdehyde), suppressed the systemic inflammatory responses (TNF-α, IL-6, IL-8, and CRP), and increased bifidobacteria and lactobacillus counts (24,25).

Probiotic supplementation used in outpatient treatment (16×10^9 colony forming unit [CFU]/day of *Lactobacillus casei shirota* for two months; and 9×10^9 CFU/day of *Lactobacillus acidophilus [L. acidophilus]*, *Bifidobacterium longum [B. longum]*, and *Streptococcus thermophilus [S. thermophiles]* for three months) decreased the concentrations of blood urea and uremic toxins in treated patients. In addition, HD patients who received 2×10^9 CFU/day of *B. longum* demonstrated a reduction in their serum phosphate concentrations (26-28). However, probiotics had no effect on uremic toxin levels or inflammatory markers in HD patients who used 1.8×10^{11} CFU/day of *S. thermophilus*, *L. acidophilus, and B. longum* for two months (29).

Effects of symbiotics were studied in patients receiving outpatient treatment and those receiving HD. An increase in the *Bifidobacterium* population was observed in subjects who consumed a symbiotic containing *L. acidophilus*, *Bifidobacterium bifidum* (2×10^{12} CFU/day), and inulin (2.31 g) for two months. A reduction in serum p-cresol concentration and an increase in stool volume were observed in patients who received 5×10^9 CFU/day Probinul neutro® for four weeks. An intake of symbiotic supplement with seven strains of probiotics and fructooligosaccharides (500 mg twice a day for six weeks) reduced blood urea nitrogen in patients with CKD stages 3 and 4. The symbiotic intervention that used three different types of fibers (15 g) and a combination of probiotics (*Lactobacillus, Bifidobacterium,* and *Streptococcus* genus [9×10^{10} CFU] for six weeks [4-week washout]) also showed an increase in the *Bifidobacterium* population and a reduction in serum p-cresol concentration (30-33).

DISCUSSION

In CKD, oxidative stress and inflammation occurs at the onset of the disease and increases with its progression. HD individuals experience increased oxidative stress possibly due to loss of antioxidants during dialysis, interactions between blood and dialysis membrane, and malnutrition (34). However, despite the fact that HD patients present greater oxidative stress and inflammation than other outpatient-treated patients, the results of selected studies indicate that the consumption of prebiotic (24,25), probiotic (26-29), and symbiotic (30-33) supplementation causes positive changes in HD and CKD patients.

Prebiotics are non-digestible food compounds that stimulate the beneficial growth of microbiota conferring health benefits to the host. They decrease oxidative stress, systemic inflammation, and the production of uremic solutes in CKD patients (35,36). In a randomized placebo-controlled trial, prebiotic consumption for six weeks by individuals receiving HD was associated with the following changes: reduced levels of total cholesterol and LDL, increased oxidative stress through reduction of malondialdehyde and increase of total antioxidant capacity, and improvement in systemic inflammation (TNF-α, IL-6, IL-8 and CRP) (24). These effects may be due to the ability of dietary fibers to hinder the process of dietary fat digestion and absorption, and favor the production of short chain fatty acids. During micelle formation phase of the digestion process, dietary fibers bind to cholesterol or bile acids forming a gel. This binding reaction delays gastric emptying, decreases dietary fat absorption and bile acid reabsorption by the enterohepatic circulation, and drives the use of hepatic cholesterol for bile acid production (37). Dietary fibers are not digested by humans; they are rather fermented by the intestinal bacteria that release short chain fatty acids. These fatty acids are responsible for modulating the intestinal microbiota and exerting immunomodulatory effects (31,37). Such changes in the intestinal microbiota were observed in a randomized controlled clinical trial. In this study, 30 mm of lactulose supplement three times a day for eight weeks increased bifidobacteria and lactobacillus counts in HD patients (25).

Probiotics are live microorganisms that, when administered in appropriate amounts, may confer benefits to the host's health (27).

Table I. Characteristics of selected studies and their major results

Author Year	Study design	Patients n	Intervention	Duration	Major results	Conclusion
Xie et al. (2015) (24)	Randomized, placebo control	HD G1 n = 42 G2 n = 39 GC n = 44	Prebiotic - Soluble fiber with more than 75% of fermentability G1- 10 g G2 - 20 g GC - without fibers	6 weeks	↓ TC, LDL and TC/LDL relationship; ↓ MDA; ↓ TNF-α, IL-6, IL-8 e CRP; ↑ TAC	In patients on hemodialysis, fermentable fiber in the diet supplementation: – Improves the lipid profile and oxidative stress – Decreases the systemic inflammatory state
Tayebi-Khosroshahi et al. (2016) (25)	Randomized, placebo control	Outpatient on stage 3 and 4* GC n =16 GT n = 16	Lactulose 30 mm syrup three times a day	8 weeks	↑ Bifidobacteria and Lactobacillus	The prebiotic will increase Bifidobacteria and Lactobacillus counts in patients with CKD
Ranganathan et al. (2009) (27)	Randomized, placebo control, double-blind, crossover	Outpatient on stage 3 and 4* GC = 13 GT = 13	Probiotics L. acidophilus B. longum S. thermophiles 9×10^{10} CFU/day	3 months	↓ Urea nitrogen and uric acid	The probiotic intake was well tolerated, with a reduction in the concentrations of urea nitrogen and uric acid, being able to contribute to a better quality of life
Ogawa et al. (2012) (28)	Placebo control	HD GC = 15 GT = 15	Probiotics: B. longum in tablets JBL01/day 2×10^{9} CFU/day	4 weeks	↓ Phosphate	B. longum can be used to treat hyperphosphatemia in patients on hemodialysis
Alatriste et al. (2014) (26)	Randomized	Outpatient on stages 3 and 4 n = 15	Probiotic: L. casei shirota G1 - 8×10^{9} CFU/day G2 - 16×10^{9} CFU/day	2 months	G2: larger reduction urea	Dose of 16×10^{9} CFU resulted in a greater reduction in blood urea levels
Natarajan et al. (2014) (29)	Randomized, placebo control, double-blind, crossover	HD GC = 22 GT = 22	Probiotics: S. thermophilus L. acidophilus B. longum 1.8×10^{11} CFU/day	2 months	Trend to reduce CRP, total indoxil glucuronil and white blood cells	The use of probiotics seems to be safe and well tolerated
Cruz-Mora et al. (2014) (30)	Randomized, placebo control, double-blind	HD GT n = 8 GC n = 10	Synbiotic: L. acidophilus B. bifidum (2×10^{12} CFU/day) Inulin (2.31 g)	2 months	↑ Bifidobacterium	Synbiotics can increase the bifidobacterium population maintaining the balance of intestinal microflora

(Continue in the next page)

Table I (Cont.). Characteristics of selected studies and their major results

Author Year	Study design	Patients n	Intervention	Duration	Major results	Conclusion
Guida et al. (2014) (31)	Randomized, placebo control double-blind	Outpatient on stages 3 and 4 GT n = 18 GC n = 12	Synbiotic 5 x 10^9 CFU/day Probinul neutro®	4 Week	↓ p-cresol	Synbiotic lowers serum concentration of p-cresol in patients with CKD not subject to dialysis
Dehghani et al 2016 (32)	Randomized, placebo control double-blind	Outpatient on stages 3 and 4 GT n = 18 GC n = 12	Synbiotics: L. casei, L. acidophilus L. bulgarigus L. rhamnosus B. breve B. longum, S. thermophilus Fructo-oligosaccharides (1,000 mg/day)	6 weeks	↓ Blood urea nitrogen	The intake of synbiotic supplement could reduce blood urea nitrogen in patients with CKD in stages 3 and 4
Rossi et al. 2016 (33)	Randomized, placebo control double-blind crossover	Outpatient on stages 4 and 5 n = 31	Synbiotics: Lactobacillus, Bifidobacteria, Streptococcus (9 x 10^{10}) inulin fructo-oligosaccharides, galacto-oligosaccharides (15 g)	6 weeks (4-week washout)	↓ p-cresol ↓ Ruminococcaceae ↑ Bifidobacteria	In patients with CKD, synbiotics did decrease serum p-cresol and favorably modified the stool microbiome

*G1: group 1; G2: group 2; G3: group 3; GC: group control; GT: group test; IS: indoxyl sulfate; NF-kB: nuclear factor kappa beta; TC: triglycerides; CRP: C-reactive protein; TAC: total antioxidant capacity; MDA: malondialdehyde; TNF-α: tumor necrosis factor α; IL 6: interleukin 6; IL 8: interleukin 8. *Phases 3 and 4: phase of the chronic kidney disease preceding the hemodialysis phase.*

Their effect on the immune system is evidenced by an increased expression of anti-inflammatory cytokines (interleukin 10 and nuclear factor kappa b), and a decrease in proinflammatory cytokines (interleukin 6 and TNFα) and levels of systemic inflammation (38,39).

In a randomized clinical trial, the consumption of probiotics containing 16×10^9 CFU/day of *L. casei shirota* for two months reduced the levels of serum urea in uremic patients with moderate to severe CKD (stages 3-4) (26). Similar results were observed in a pilot study that tested the effects of a probiotic containing different bacterial strains (*L. acidophilus*, *B. longum*, and *S. thermophilus*) at a dose of 9×10^9 CFU/day. After three months, the majority of the participants who received probiotic had reduced concentrations of serum urea nitrogen and uric acid, contributing to a better quality of life for those individuals (27). Oral administration of *B. longum* capsules in a placebo-controlled clinical trial was shown to reduce serum phosphorus concentrations in HD patients (28). This suggests that the reduction of these metabolites in CKD patients may be associated with the ability of the microbiota to use the metabolic waste as a substrate. A possible explanation for the observed reduction in uremia is related to the ability of certain anaerobic bacteria to degrade urea and uric acid through the production of enzymes, such as uricase, allantoinase, and urease. In an *in vitro* study, *Lactobacillus* exposure to an urea-enriched environment induced the production of enzymes responsible for urea reduction (40). Following the intake of probiotics, an increase in *Lactobacillus* and *Streptococcus* populations in the feces can be explained by the conversion of urea to ammonia, a source of nitrogen for metabolic purposes (27). Probiotics can increase dietary fiber fermentation, reduce the intestinal pH, modulate the intestinal microbiota, and increase calcium ionization. Calcium, in turn, binds to phosphorus, reducing its absorption and leading to a reduction in serum phosphorus concentration (28). On the other hand, serum levels of uremic toxins and inflammatory markers were not affected in HD individuals who received a daily dose of 1.8×10^{11} CFU/day of a probiotic (containing *S. thermophilus*, *L. acidophilus*, and *B. longum*) for two months. However, the results showed a trend for the reduction of C-reactive protein ($p = 0.071$), indoxyl glucuronyl ($p = 0.058$), and white blood cell counts ($p = 0.057$) (29). We believe that if the probiotics were administered in combination with soluble fibers, the results would have been different; this is based on our knowledge that soluble fibers can potentiate the effects of probiotics, resulting in a reduction of these markers. A decrease in uremic toxin concentration may be associated with fermentation of soluble fiber by intestinal anaerobic bacteria. This process of fermentation increases the production of short chain fatty acids and reduces colonic pH. The modified environment favors the growth of beneficial bacteria, inhibits the enzymes involved in generation of p-cresyl sulfate and indoxyl sulfate, improves epithelial barrier function (via induction of mucin production, blocking epithelial binding receptors, and strengthening

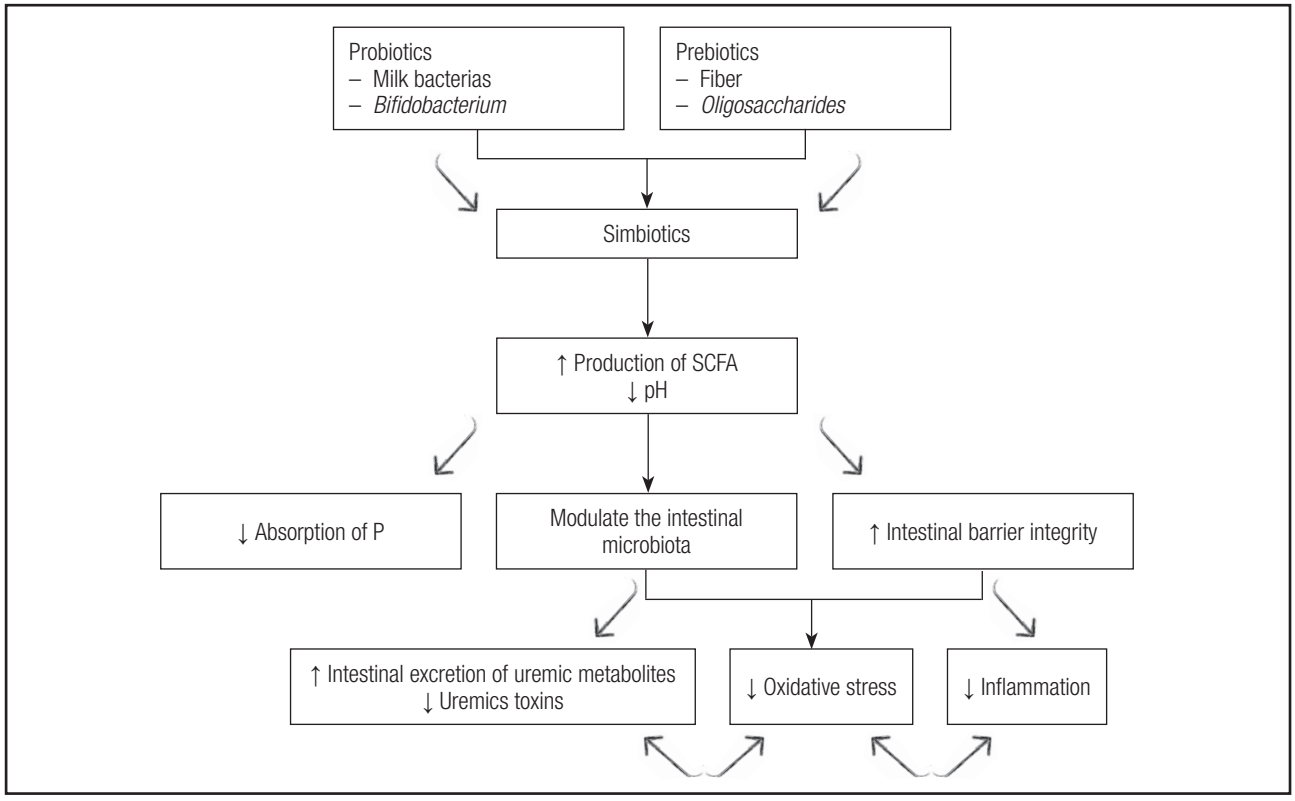

Figure 2.

Potential mechanisms involved in the modulation of intestinal microbiota and the reduction of oxidative stress and inflammation by pre- and/or probiotic products in chronic kidney disease. SCFA: short-chain fatty acids; P: phosphorous.

epithelial tight junctions), and reduces the influx of uremic toxins (41) (Fig. 2).

Supplementation of a symbiotic compound containing *L. acidophilus* and *B. bifidum* (2×10^{12} CFU/day) and inulin (2.31 g) for two months improved intestinal dysbiosis in individuals receiving HD, increasing the population of *Bifidobacterium* and preserving the numbers of *Lactobacillus* in the gut (30). Symbiotic intake in different stages of CKD decreased p-cresol serum concentration and normalized bowel habits (31,33). The symbiotic supplement (seven strains of probiotics and fructooligosaccharides), when consumed 500 mg twice a day for six weeks, can reduce blood urea nitrogen in patients with CKD at stages 3 and 4. One of the mechanisms by which this supplementation can potentially benefit the kidneys is by stimulating growth of gut microbial biomass by increased consumption of dietary fibers; this subsequently decreases ammonia production, increases the ratio of ionized ammonia, and facilitates the use of nitrogenous wastes by bacterial cells. Thus, more ammonia is excreted through the feces, and there is a low level production of potentially damaging forms of nitrogen, such as urea, uric acid, and creatinin (32). These results indicate the need to conduct a study to assess microbiota composition, uremic parameters, and inflammatory biomarkers in response to consumption of symbiotics.

In summary, the mechanism by which prebiotics and/or probiotics modulate the intestinal microbiota and decrease oxidative stress and inflammation may be due to increased intestinal anaerobic bacteria count and maintenance of intestinal barrier integrity (Fig. 2). Intestinal barrier integrity may be improved by the production of mucin, blocking of connection receptors, and strengthening of the epithelial junctions (17).

Due to the inclusion and exclusion criteria adopted in this study, we could include only ten studies in our review, and this limitation did not allow us to carry out a meta-analysis study. Our search for relevant studies was confined to the main databases; thus, it is possible that we might have limited our numbers by missing out some studies that fulfilled our inclusion criteria. Nonetheless, despite these limitations, the present study allowed us to identify "the gaps" in the literature in relation to the topic of interest, allowing us to propose future studies to unravel the mechanisms by which the prebiotics and/or probiotics can control progression of CKD.

CONCLUSIONS

Prebiotics and/or probiotics can modulate the intestinal microbiota by promoting the growth and metabolism of anaerobic bacteria, decreasing the production of uremic solutes, and resulting in oxidative stress and systemic inflammation. There is scarcity of studies that address the effects of prebiotics and/or probiotics on the intestinal microbiota, oxidative stress, and inflammation in CKD patients. Therefore, future studies are needed to provide clarification on topics, such as mechanisms that link regulation of dysbiosis and manifestation of diseases associated with CKD or its precursor diseases, such as diabetes mellitus, hypertension, and atherosclerosis.

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Revisión

Intestinal adaptation in short bowel syndrome. What is new?

Adaptación intestinal en el síndrome de intestino corto: ¿qué hay de nuevo?

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Key words:

Short bowel syndrome. Intestinal failure. Parenteral nutrition. GLP-2 analog. Intestinal adaptation.

Abstract

Short bowel syndrome (SBS) is a well-known cause of intestinal failure (IF) (1). SBS occurs after extensive resection of the small bowel (RSB) resulting in a bowel length of less than 150/200 cm. The colon may have been partially or completely removed. SBS patients experience severe water and nutrient malabsorption, so that they are often managed with parenteral nutrition (PN) to supplement their oral intake (2-4). A complete understanding of the pathophysiology of SBS and postoperative adaptations may allow identifying the spontaneous processes that compensate for the reduction in absorptive surface. A better knowledge of these adaptive mechanisms may help to improve the management of patient nutrition, to reduce the need for PN and to prevent D-encephalopathy episodes. This review focuses on the overall adaptations described in adult SBS patients but does not review pediatric cases.

Palabras clave:

Síndrome de intestino corto. Fallo intestinal. Nutrición parenteral. Adaptación intestinal. Agonista GLP2.

Resumen

El síndrome del intestino corto es la primera causa de fallo intestinal (que requiere suplementación intravenosa de fluidos, electrolitos y/o calorías). La adaptación fisiológica intestinal ocurre uno a dos años después de la resección quirúrgica. Esta adaptación incluye hiperfagia, cambios en la microbiota, cambios morfológicos intestinales (incluida la hiperplasia), adaptaciones hormonales y otros… El colon desempeña un papel importante y permite la recuperación hidroelectrolítica y energética. Es posible mejorar la adaptación fisiológica mediante la optimización de la intervención dietética, restaurando la continuidad y tratando con factores de crecimiento, como el análogo del GLP-2 *(glucagon-like peptide-2)*.

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INTRODUCTION

Short bowel syndrome (SBS) is a well-known cause of intestinal failure (IF) (1). SBS occurs after extensive resection of the small bowel (RSB) resulting in a bowel length of less than 150/200 cm. The colon may have been partially or completely removed. SBS patients experience severe water and nutrient malabsorption, so that they are often managed with parenteral nutrition (PN) to supplement their oral intake (2-4). A complete understanding of the pathophysiology of SBS and postoperative adaptations may allow identifying the spontaneous processes that compensate for the reduction in absorptive surface. A better knowledge of these adaptive mechanisms may help to improve the management of patient nutrition, to reduce the need for PN and to prevent D-encephalopathy episodes. This review focuses on the overall adaptations described in adult SBS patients but does not review pediatric cases.

INTESTINAL FAILURE AND SHORT BOWEL SYNDROME

Intestinal failure (IF) occurs in various gastrointestinal diseases such as gut motility disorders, mechanical obstruction, intestinal fistula, extensive small bowel mucosal disease, volvulus or systemic conditions such as mesenteric infarction and post-radiation enteritis. IF is defined as a reduction in gut function below the minimum needed for the absorption of macronutrients and/or water and electrolytes, resulting in intravenous (IV) supplementation to maintain health and/or growth (1).

Three different types of IF have been described based on duration: a) acute, short-term and usually self-limiting conditions; b) prolonged acute conditions, often in metabolically unstable patients, requiring complex multi-disciplinary care and IV supplementation over long periods; and c) chronic reversible or irreversible conditions in metabolically stable patients, requiring long-term intravenous supplementation. In adults, SBS appears after massive intestinal resection leaving patients with less than 200 cm of small bowel defines SBS, and a small bowel length of < 100 cm is highly predictive of permanent IF (5-7). While the actual prevalence of SBS in adults is unknown, the estimated prevalence is 1.4 cases per million people in Europe. It varies depending on the region, from 0.4 to approximately 30 cases per million in Poland and Denmark, respectively (8). The prevalence of SBS is lower in regions where there are no major intestinal rehabilitation centers and efficient home PN (HPN) or IV programs, likely because of under-reporting and the inability to adequately treat these patients.

Adaptive changes following resection explain why some patients can be weaned off PN. The degree of intestinal adaptation depends on the underlying pathology for which resection is needed, the unresected anatomic sections of the intestine and the length of the remaining bowel (6,9). Resection of the small bowel results in three different anatomic anastomoses: a) enterostomy; b) jejuno-colonic; and c) jejuno-ileo-colonic. In most cases, intestinal adaptation in adults is supposed to occur 1-2 years after resection, but no objective, clinically practical markers have been identified to determine the time course or extent of adaptation in humans (10). Preserving the colon is essential for reducing the need for PN in SBS patients (6,11). The probability of PN-independence is of 47% five years after surgery and is significantly associated with a remnant small bowel length greater than 75 cm, a large portion of remaining colon and a postoperative citrulline concentration greater than 20 µmol/l (12). The post-absorptive concentration has been shown to correlate with the small bowel length and to be a prognostic factor for HPN dependency (11,12).

ROLE OF THE COLON IN FLUID AND ELECTROLYTE ABSORPTION

The large intestine or colon measures about 1.5 m in length in adults and consists of four parts: the ascending colon, the transverse colon, the descending colon, and the sigmoid colon. Once the chyme has reached the colon, almost all nutrients and 80-90% of the water have been absorbed in the small intestine. At this point, some electrolytes such as sodium, magnesium and chloride are left as well as indigestible carbohydrates known as dietary fibers. Bacteria, by metabolizing dietary fibers, play a crucial role in the nourishment of the colon and in calorie sparing. Thus, the colon is involved in some clinical disorders such as SBS.

Immediately after extended ileal intestinal resection, gastric hypersecretion associated with hypergastrinemia may be observed (13). Both H2 antagonists and proton pump inhibitors aim to reduce gastric fluid secretion, and therefore, fluid losses (13-15). Intravenous delivery is usually needed. In patients without colon in continuity or who have a short residual jejunum or duodenum, fluid losses are especially high and a chronic control with antimotility agents such as loperamide or codeine sulphate may be needed. Therefore, in SBS patients, the rapid restoration of intestinal continuity not only helps to control fluid and electrolyte losses but also provides the metabolic benefits of the colon.

IMPORTANT ROLE OF THE COLON IN SBS PATIENTS

Metabolic role of the colon

Medium chain triglycerides (MCTs) (C8-C10) contain 8.3 kcal/g, are water-soluble and may be absorbed by the colon. Diets containing MCTs, long chain triglycerides (LCTs) and 50% of MCTs/50% of LCTs have been assessed in a randomized cross-over study comparing ten SBS patients with colon in continuity to nine SBS patients without residual colon (16). Patients with intact colon absorbed 96% of C8 and 87% of C10 from the mixed LCT/MCT diet, while energy absorption was significantly increased (500 kcal/day). Patients without residual colon absorbed 63% of C8 and 57% of C10 ($p = 0.007$ for C8 and $p = 0.004$ for C10). The LCT/MCT diet did not increase energy absorption in patients who underwent end-jejunostomy or ileostomy.

Some starches and soluble non-starch polysaccharides are not digested by the small intestine. They are fermented later in the colon by colonic bacteria into hydrogen, methane and short chain fatty acids (SCFAs) such as propionate, butyrate and acetate. In the colon, some SCFAs such as butyrate are metabolized and used as a source of fuel by colonic epithelial cells (17-20). It has been estimated that up to 1,000 kcal may be absorbed daily by the adult human colon in the form of SCFAs (21). In SBS animal models, adaptation of the small and large intestines may be improved by adding an elemental diet with pectin, which is also fermented into SCFAs in the colon (22). Supplementing PN with SCFAs or their intracecal administration reduces mucosal atrophy and intestinal immune dysfunction (23-25).

Animal studies have shown that systemic SCFAs may, in addition to their local effects, affect the motility of the stomach and the ileum through neuroendocrine mechanisms, probably by acting on intestinal secretion of proglucagon-derived peptides (GLP-1) and peptide YY (PYY). Systemic and enteral SCFAs exert trophic effects on the jejunal mucosa (17).

In patients with SBS, the colon becomes an important organ for energy salvage (26). About 75 mmol of SCFAs are produced from 10 g of unabsorbed carbohydrates. In SBS patients with intact colon in continuity, the fecal energy loss has been shown to be decreased by 310-740 kcal when they were fed with a diet consisting of 60% carbohydrates (19) and the colonic metabolism of unabsorbed carbohydrates was confirmed by a decrease in fecal carbohydrate losses in patients with colon in continuity. An intact colon may absorb up to 525-1,170 kcal daily from dietary fibers (19,27,28). Colonic energy absorption may also slightly increase during the post-resection adaptation phase, due to an increase in colonic bacterial carbohydrate fermentation (29). This may be due to changes in colonic microbiota in SBS patients as well as an increased concentration or activity of various enzymes such as galactosidase over time during the adaptation phase (29). Since bacterial metabolites such as SCFAs stimulate sodium and water absorption, patients are likely to experience a decrease in fecal fluid and sodium loss (19).

Morphological adaptation occurs in the colon of SBS patients. Both hyperphagia and adaptation of the remaining colon improve patient outcome. A study has assessed the morphology, proliferation status, and expression level of transporters in the epithelium of the remaining colon of SBS adult patients compared to controls (30). The authors have demonstrated the appearance of colonic hyperplasia with an increase in crypt depth compared to a control group. This increase in crypt depth and colonic epithelial cell number could participate in the decrease in PN dependency within two years after restoration of intestinal continuity in SBS patients. Based on clinician experience, the presence of a colon in continuity in SBS patients may help to improve residual intestinal absorption capacity and to decrease PN. Nowadays, the time needed to achieve this physiological process of intestinal adaptation is not yet completely known. After two or three years, the proportion of patients with a decrease in or weaning off PN remains very low. We can assume that the adaptive processes of physiological intestinal adaptation take time after surgery. Oral/enteral feeding is essential to promote adaptation. Even in cases with very short bowel syndrome, oral feeding should be encouraged, especially when SBS is associated with jejunocolonic anastomosis.

TRANSPORTER ADAPTATION IN ADULT SBS PATIENTS

Functional absorptive adaptation of the gut has also been reported in SBS patients through the induction of glucose absorption by the intestinal mucosa, net protein intake (31) and calcium absorption (32,33). There are some discrepancies in the literature regarding colonic transporters. An increase in H+-coupled oligopeptide (PepT1) transporter and Na+/H+ exchanger (NHE2 and NHE3) mRNA levels has been reported in the colon of SBS patients (34) and in rodents (35). But these data have not been confirmed as part of a SBS human study since similar levels of NHE2, NHE3 and PepT1 have been found compared to controls (30). These differences may be due to various nutritional statuses of patients, the use of different animal models and different times between the surgery and the study. The use of the overexpression of some transporters as an indicator of intestinal adaptation is not yet validated.

ENDOCRINE FUNCTIONS IN ADULT SBS PATIENTS

In SBS patients, intestinal absorption depends on the intestinal resection site and transit time (36). The accelerated transit time observed in jejunostomy and ileum-resected SBS patients promotes nutrient malabsorption since a precise control of the transit time is required to maintain equilibrium of hydroelectric and energetic balances. Hormones play a key role in gastric emptying and small bowel transit time. The endocrine functional adaptation should be assessed in SBS patients. Elevated fasting plasma levels of GLP1 and GLP2 have been reported in extensive gut resection patients with preserved colon and they further increased after breakfast (37). These two hormones are produced by enteroendocrine L cells located in the ileum and colon. GLP2 increases the absorptive surface via its trophic action on mucosal epithelial cells and GLP1 slows down gastric emptying and intestinal transit (38,39). These effects (increased contact time and surface of nutrients) may potentially improve intestinal absorption (38,40).

HYPERPHAGIA IN ADULT SBS PATIENTS

Dietary intervention is essential to improve the outcome and reduce PN dependency in SBS patients. Post-surgery, continuous tube feeding (exclusively or in conjunction with oral feeding) significantly increases the net absorption of lipids, proteins and energy compared to oral feeding (2). When oral feeding is possible, oral dietary intake and hyperphagia should be recommended. Specific dietary recommendations should be made depending on

intestinal anatomy. Based on the clinical experience, hyperphagia is reported in 70% of adult SBS patients and is defined as an oral intake > 1.5 times patient resting energy expenditure (REE) (41). Hyperphagia remains an essential mechanism to reduce the need for PN (42).

In hyperphagic patients, enterohormones play a key role. Increased secretions of glucagon-like peptide-1 (GLP-1) and GLP-2 have been reported in preclinical models and in SBS patients with colon in continuity. They orchestrate gastrointestinal functions, including intestinal trophicity, expression of intestinal nutrient transporters and gastro-intestinal motility. Ghrelin, an orexigenic gut hormone, increases food intake through the activation of orexigenic hypothalamic neurons (co-expressing neuropeptide Y and agouti-related peptide). Recently, a study has been conducted to better understand the hormonal mechanisms involved in the development of hyperphagia in an animal model of SBS and in SBS patients (59). An increase in plasma ghrelin concentrations, major changes in hypothalamic neuropeptide levels (increased levels of mRNA coding orexigenic hypothalamic NPY and AgRP) and a greater induction of PYY have been shown in SBS rats with jejunocolonic anastomosis. As hyperphagia leads to an increased amount of nutrients passing through the gastrointestinal tract, this adaptive mechanism may indirectly contribute to the structural and functional adaptations of the mucosa observed in the remaining gut (31,42).

COLONIC MICROBIOTA COMPOSITION AND METABOLIC FUNCTIONS IN ADULT SBS PATIENTS

The composition of the microbiota of SBS patients highly differs from the common profile observed in healthy humans with intact gastrointestinal tract. The fecal microbiota of healthy humans is mainly composed of a phylogenetic core containing Firmicutes, Bacteroidetes and Actinobacteria. The human gastrointestinal tract is colonized by a dense complex community of microorganisms, mainly composed of anaerobic bacteria in adults, and the dominant groups are *Clostridium leptum*, *Clostridium coccoides* and *Bacteroides-prevotella.* Gut microbiota composition and metabolic functions in SBS patients and healthy controls have been compared (44). The overall bacterial diversity is reduced in SBS patients. The composition of the fecal and colonic mucosa microbiota is unbalanced in SBS: *Lactobacillus* dominates and anaerobic bacteria (*C. leptum, C. coccoides* and Bacteroides) are under-represented (41,44). Lactobacillus overload should be considered massive, since this group contributes little (< 1%) to the complex microbiota population in healthy humans. For this reason, we proposed that the microbiota of SBS patients could be referred to as lactobiota. The essential role of the colon in SBS patients is related to its own absorptive capacity, the metabolic capacity of its specific lactobiota and the reciprocal cross-talk between the lactobiota and the colonic mucosa (43). After resection, the substrates that arrive in the colon are abundant and poorly digested. The fermentation of substrates by gut bacteria helps to maintain gut ecosystem diversity and to recover energy from nutrients in SBS patients (27). The bioconversion of macromolecules by the gut microbiota into metabolites is carried out by bacteria belonging to various functional groups (sharing similar and complementary activities) resulting in metabolic trophic chains and homeostasis with the colonic epithelium. In SBS, the trophic chains and fermentative end-products are produced by the lactobiota and are different from those produced by a healthy microbiota (44). Resection leads to deep lumen alterations that are favorable to the lactobiota. In SBS patients, due to the short length of the remnant small intestine and colon, the level of oxygen might be too high to promote the growth of anaerobic bacteria. In addition to the potential presence of O_2, the low fecal pH, rapid transit time, disruption of enterohepatic circulation and large amount of undigested nutrients arriving in the remaining colon may modify the luminal environment. This may create a niche favorable to the proliferation of lactic acid-producing bacteria.

In SBS, the biological signals arising from the microbiota need to be better understood as they are both beneficial (with a high ability to recover energy) and deleterious (with a potential to overproduce D-lactate, as explained in the next section). Fecal microbiota transfer from SBS rats to recipient germ-free (GF) rats triggers colonic changes through crypt deepening (45) and humanized SBS rats (SBS-H) had higher levels of some hormones than rats carrying a conventional microbiota. The microbiota from SBS rats may promote energy recovery since its transfer to GF rats is associated with high plasma levels of leptin. In summary, the microbiota from SBS rats seems to be a reservoir of multiple and complex signals that could modify the postresection adaptation. Several studies have described an increase in fasting plasma GLP-1 levels in SBS patients with jejunocolonic anastomosis or in resected rats (46). In the specific model of SBS-H rats, fecal transplantation resulted in higher plasma GLP-1 levels associated with a higher number of L cells. GLP-1 is a key mediator of the colonic-ileal brake (it inhibits gastro-intestinal motility) in response to nutrients. The increased fasting plasma GLP-1 levels in SBS-H rats may be an adaptive mechanism in response to a high demand of energy that slows down intestinal transit and consequently enables greater nutrient absorption. The higher level of GLP1 in the presence of the microbiota from SBS rats might promote energy recovery.

FECAL D- AND L-LACTATE AND CLINICAL RISK FOR D-ENCEPHALOPATHY IN ADULT SBS PATIENTS WITH COLON IN CONTINUITY

D-lactic acidosis is very rare in humans. This disease is mainly observed in SBS patients who have a part of or an intact colon in continuity (47). Metabolic acidosis seems to be due to D-lactic acid accumulation but the mechanisms involved in its toxicity are not well understood. D-lactic acid predominantly affects the central nervous system. As D-lactate is converted into pyruvate and the cerebellar level of pyruvate dehydrogenase (the enzyme required to convert pyruvate into acetyl co-A) is limited, the cerebellum may

potentially be damaged in D-lactic acidosis. Indeed, the cerebellar levels of pyruvate dehydrogenase are not sufficient to metabolize all of the additional pyruvate and this, in combination with thiamine deficiency, may result in neurological symptoms (48).

The symptoms of D-lactate acidosis are often transient, making its diagnosis difficult. Clinical suspicion is based on the presence of some symptoms such as slurred speech, ataxia, altered mental status, gait disturbance, weakness, aggressive behavior, explosive speech, feeling drunk, psychosis, or even coma and biological changes: elevated anion gap metabolic acidosis (48). Patients often present with a history of symptoms following consumption of a high-carbohydrate meal. The early identification and correction of metabolic abnormalities improves the neurological symptoms. The therapeutic strategy is based on the decrease of the offending agent (carbohydrates) and treatment to decrease the level of D-lactate-producing bacteria in the colon. Poorly absorbed oral antibiotics (clindamycin, vancomycin, neomycin and kanamycin) are the most effective and may be used. Strategies for preventing future occurrences must be implemented once the acute phase is controlled. The long-term management should focus on avoiding taking the substrates responsible for D-lactate production. A child with SBS and recurrent, debilitating D-lactic acidosis has recently been successfully treated with fecal transplantation (49). Understanding the pathophysiological mechanisms for the effects of D-lactate should help physicians to identify D-lactate acidosis and to improve preventive and therapeutic strategies (48). We have proposed that HCO32 amount in blood, total fecal lactate and the fecal D/L lactate ratio may become useful tools for identifying SBS patients at risk for D-encephalopathy (Mayeur 2013). However, further investigations are needed to diagnose patients with high risk of D-lactic encephalopathy using the most relevant combination of specific biomarker(s) and to propose a specific microbiota modulation in order to prevent acute episodes.

A PLACE FOR PHARMACOLOGICAL ADAPTATION

Some recombinant hormones are produced and used as a specific therapy in SBS patients. In controlled clinical trials, the administration of teduglutide, a GLP-2 analog, has reduced by more than 20% the intravenous needs in 63% of patients after a 6-month treatment (50). Teduglutide has been shown to significantly reduce stool wet weight and fecal energy excretion (51). It also significantly increased villus height, crypt depth and the mitotic index in the jejunum of SBS patients with end jejunostomy, whereas crypt depth and the mitotic index did not change in colonic biopsies of SBS patients with an intact colon (51). The purpose of these novel approaches using GLP-2 analogs is to enhance the natural adaptation process, and to reduce intravenous calorie needs. While some patients were weaned off PN, a greater number of patients were able to reduce the frequency of infusions. Patients who received teduglutide showed significant increases in plasma citrulline levels compared to patients receiving a placebo in two phase III studies (52).

While teduglutide is currently marketed and used in some countries with very good results in terms of efficacy in SBS patients, other hormones or combinations will probably be assessed in SBS in the future. In 2013, an open-label, sequential, placebo-controlled study assessing the acute effects of continuous infusions of GLP-1, GLP-2 and their combination (GLP-1 + GLP-2) on intestinal absorption in SBS patients has shown that GLP-1 decreased diarrhea and fecal excretions. Although GLP-1 reduced fecal wet weight, and sodium and potassium excretions, the absolute absorption was not significantly improved.

Recently, liraglutide (a GLP-1 analog) has been given subcutaneously once daily to eight end-jejunostomy patients in the context of an eight-week, open-label pilot study (53). Liraglutide reduced ostomy wet weight output by 474 ± 563 g/d from 3,249 ± 1,352 to 2,775 ± 1,187 g/d ($p = 0.049$).

In the last two decades, a hormonal treatment paradigm focusing on intestinal rehabilitation by promoting intestinal "hyperadaptation" has been proposed in patients with SBS who require PN. But, if we consider all aspects of physiological intestinal adaptation in SBS patients, especially in SBS patients with jejunocolonic anastomosis and a physiological increase of hormone levels such as GLP1, GLP2, PYY in the absence of treatment, conducting further studies assessing the response of new drugs and taking into account the levels of native hormones will be of interest.

CONCLUSIONS

The morphological and functional alterations described in SBS may contribute to improve nutrient and fluid absorption in the remnant bowel. A better understanding of the cellular, molecular and microbiological mechanisms involved in functional adaptation of the remnant bowel in SBS could help clinicians to optimize the overall nutritional absorption, and thus to reduce or wean patients off PN and to prevent D encephalopathy episodes. It would now be informative to identify molecular and functional links between the three levels of signal integration: control of food intake, remodeling of the intestinal mucosa and balancing of the microbiota. Important issues should be addressed in the future: a) study nutritional peripheral hormones and central hypothalamic neuropeptides that control food intake in SBS patients; b) determine whether mucosal adaptation of the remnant gut is involved in hyperphagia in SBS patients; c) investigate whether the lactobiota of SBS patients contributes to hyperphagia and mucosal hyperplasia; and d) assess the real impact of new drugs such as GLP2 agonist on intestinal adaptation and the specific benefits of these trophic agents in SBS treatment.

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ARÁN

Nutrición Hospitalaria

Artículo Especial

Difusión de la nutrición clínica a través de sociedades y revistas científicas. Un encuentro en la Real Academia Nacional de Farmacia

Dissemination of clinical nutrition through societies and scientific journals. A meeting at the Spanish Royal Academy of Pharmacy

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Resumen

Este artículo especial define muy brevemente algunos aspectos de importancia de la alimentación artificial como soporte nutricional en situaciones especiales en pacientes que no mantienen una función digestiva suficiente y adecuada para restablecer o mantener un estado nutricional óptimo o en aquellos malnutridos o en vías de estarlo. También revisa los aspectos centrales de una mesa redonda a la que acudieron directivos de revistas y entidades científicas en el campo de la salud y, en particular, de la nutrición. La mesa redonda se organizó al amparo de un homenaje al Dr. Jesús M. Culebras, en enero de 2018, en la sede de la Real Academia Nacional de Farmacia. El Prof. Culebras fue fundador de la revista *Nutrición Hospitalaria* y artífice de muchos logros e iniciativas de la Sociedad Española de Nutrición Enteral y Parenteral de gran importancia para la nutrición y para la alimentación artificial en España. Durante la mesa redonda se insistió en la conveniencia de incrementar la colaboración entre las revistas *Nutrición Hospitalaria, Farmacia Hospitalaria, Anales de la Real Academia Nacional de Farmacia* y *Journal of Negative and No Positive Results* y las entidades que representan, especialmente en lo que se refiere al marco de la nutrición y, particularmente, de la nutrición clínica y la alimentación artificial, insistiendo en la necesidad de iniciar una serie de reuniones en un futuro muy próximo con la finalidad de delimitar competencias y derechos, así como la toma de posiciones conjuntas en publicaciones y acuerdos de consenso que garantizarían la difusión y visibilidad de este tema de enorme importancia para la salud.

Palabras clave:

Alimentación artificial. Mesa redonda. Nutrición. Revistas científicas.

Abstract

This special article defines very briefly some central aspects of artificial nutrition as nutritional support in special situations in patients that are not able to maintain a sufficient and adequate digestive function to restore or maintain optimal nutritional status or in those who are malnourished or in the way to be. It also reviews the central aspects of a round table attended by executives of journals and scientific entities in the field of health and, in particular, of nutrition. The roundtable was organized under the auspices of a tribute to Dr. Jesus M. Culebras, in January 2018 at the headquarters of the Spanish Royal Academy of Pharmacy. Prof. Culebras was founder of the journal *Nutrición Hospitalaria* journal and architect of many achievements and initiatives of the Spanish Society of Enteral and Parenteral Nutrition of great importance for nutrition and artificial nutrition in Spain. During the workshop, the convenience of increasing collaboration between the scientific journals *Nutrición Hospitalaria, Farmacia Hospitalaria, Anales de la Real Academia Nacional de Farmacia* and *Journal of Negative and No Positive Results* and the entities they represent was highlighted, especially concerning the framework of clinical nutrition and, particularly, artificial feeding, insisting on the need to initiate a series of meetings in the very near future with the purpose of delimiting competencies and rights, and taking joint positions in publications, and consensus agreements that would guarantee the dissemination and visibility of this issue of enormous importance for health.

Key words:

Artificial nutrition. Workshop. Nutrition. Scientific journals.

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Hoy existe consenso unánime con respecto a que un estado nutricional correcto constituye el arma más poderosa disponible para conservar la salud e imprescindible, en muchos casos, para recuperarla. También existe acuerdo en que a través de la nutrición debemos cubrir las necesidades y los requerimientos diarios de energía, nutrientes y aspectos hedónicos y de bienestar relacionados, lo cual contribuye a garantizar una alimentación óptima y funcional que sintonice adecuadamente con nuestro genoma (1,2). Y la situación es aún más clara cuando nos movemos en el área de la nutrición clínica, un área pluridisciplinar que intenta asegurar la individualización y optimización nutricional de todos los pacientes de acuerdo con su enfermedad y evolución, y que este cuidado se extienda desde la dieta oral (junto con consejos dietéticos) hasta un soporte específico, administrado por vía parenteral, enteral o mixta (3). Es decir, en estas situaciones concretas debe hablarse específicamente de dietoterapia. Especial importancia adquiere la alimentación artificial o nutrición artificial como soporte nutricional en situaciones especiales en pacientes que no mantienen una función digestiva suficiente para restablecer o mantener el estado nutricional óptimo o en aquellos malnutridos o en vías de estarlo (3).

Con la finalidad de hacer palpable la importancia de la alimentación artificial, se incluye una tabla resumen (Tabla I) en la que se esquematiza en qué situaciones el soporte nutricional está

Tabla I. Trastornos que frecuentemente requieren soporte nutricional

Vía de alimentación o nutrición	Trastorno	Trastornos específicos
Nutrición enteral	Incapacidad para comer	Anomalías congénitas Insuficiencias respiratorias con ventilación asistida Disfagias y otros trastornos neurológicos relacionados Traumatismo facial, oral o esofágico Lesión cerebral por traumatismo Estado comatoso Cirugía digestiva (esófago)
	Incapacidad para comer adecuadamente	Retraso del desarrollo Anorexia nerviosa Estados hipermetabólicos Tumores Deterioro por cirugía o lesión bucofacial Insuficiencia cardiaca Cardiopatía congénita Fibrosis quística
	Deterioro de la digestión, absorción o metabolismo	Gatroparesia grave Errores metabólicos congénitos Enfermedad de Crohn Síndrome de intestino corto con mínima resección Pancreatitis
Nutrición parenteral	Incompetencia digestiva	Diarrea o vómitos no tratables, refractarios al tratamiento Fístulas distales de alto débito Síndrome de intestino corto o resección importante Enfermedad intestinal inflamatoria grave Isquemia del intestino delgado Atresia intestinal Insuficiencia hepática grave Hemorragia digestiva grave Ileo postoperatorio persistente Pancreatitis aguda grave con intolerancia a la alimentación enteral
	Enfermedad crítica con inadecuada tolerancia o accesibilidad enteral	Insuficiencia respiratoria aguda con dependencia de respiración asistida y disfunción digestiva Insuficiencia multiorgánica Grandes traumatismos o grandes quemados Emaciación grave en insuficiencia renal con diálisis Trasplante de intestino delgado tras la cirugía Trasplante de médula ósea

Modificado de McClave y cols. (6).

recomendado o es imprescindible. De ella se extrae claramente la importancia de un soporte nutricional adecuado, dada la incapacidad total o parcial de poder utilizar la vía de acceso normal de alimentos a nuestro cuerpo y, por tanto, de hacer llegar a nuestras células y órganos los nutrientes y sustancias bioactivas que contienen. No obstante, debe quedar claro que el espíritu de esta publicación no es realizar una revisión sobre alimentación enteral y parenteral, sino dar unas breves pinceladas de su relevancia. Múltiples factores son responsables del auge de la aplicación de la mal llamada alimentación artificial, pues en el caso de una alimentación enteral, lo único que la diferencia de una alimentación convencional es la aplicación del alimento mediante una sonda a diferentes partes de nuestro aparato digestivo, administrando en muchos casos alimentos o módulos nutricionales similares a los que convencionalmente comemos (4).

Por un lado, la propia enfermedad puede comportar una ingesta inadecuada de nutrientes por anorexia, dificultad para la ingesta, problemas de masticación, disfagia y falta de autonomía para comer, pero también por dificultades en la digestión o en la absorción de alimentos o, incluso, por el aumento de los requerimientos nutricionales, por la existencia de estados hipermetabólicos o de pérdidas relevantes de nutrientes por vómitos o diarreas crónicas refractarias al tratamiento (Tabla I).

Además, existe evidencia científica de que la ausencia de nutrientes en la luz intestinal provoca la atrofia de las vellosidades intestinales y, por tanto, interfiere de forma neta sobre su papel fisiológico digestivo e inmunitario (3,4). También afecta negativamente a la microbiota intestinal y a los muchos aspectos fisiológicos que controla, tanto a nivel intestinal como sistémico (5).

Existe, además, consenso en que la aplicación de la nutrición parenteral durante largos periodos de tiempo produce la falta de la utilización del aparato gastrointestinal, lo que provoca efectos indeseados que refuerzan la idea de que la nutrición enteral debe mantenerse como primera opción en pacientes con ingesta oral inadecuada, reservando la nutrición parenteral para el fracaso o la contraindicación de la nutrición enteral (4,6,7).

Un aspecto de gran importancia en la nutrición clínica es considerar y potenciar la idea de que los equipos multidisciplinarios de soporte nutricional deben estar formados por profesionales sanitarios (médicos, farmacéuticos, enfermeros, dietistas, psicólogos, etc.) y ser los encargados de identificar a los pacientes en riesgo nutricional, proporcionar un soporte nutricional y un seguimiento clínico de forma individualizada y optimizada y elaborar protocolos para la identificación, el seguimiento y el tratamiento de los pacientes en nutrición artificial. Estos protocolos no solo se ceñirán a la nutrición, es decir, a la inclusión o exclusión en el hospital de diferentes tipos de productos o de alimentos para la nutrición parenteral o enteral (8,9), sino también a la administración de medicamentos, al estudio de las posibles interacciones entre ellos o con alimentos, así como al manejo de catéteres, la atención psicológica y física al paciente, e incluso a temas de bioética (10-12). Debe considerarse también que la nutrición artificial a nivel domiciliario está adquiriendo una dimensión impensable hace años, debido, entre otros aspectos, a la comodidad que implica para el paciente recibir en su propio domicilio el soporte nutricional y al abaratamiento del tratamiento, al no requerirse la hospitalización del paciente (4).

Es preceptivo señalar en este artículo que el pasado 25 de enero de 2018 tuvo lugar en la sede de la Real Academia Nacional de Farmacia (RANF) una mesa redonda titulada "Difusión de la nutrición artificial en España: sociedades médicas y revistas científicas". En el acto se hacía, además, reconocimiento y homenaje al Excmo. Sr. D. Jesús M. Culebras Fernández por su labor durante más de tres décadas como director de la revista *Nutrición Hospitalaria,* órgano de expresión de la Sociedad Española de Nutrición Parenteral y Enteral (SENPE).

La mesa redonda estuvo constituida por el Dr. Jesús Culebras Fernández, académico de número de la Real Academia de Medicina de Asturias y León y académico de número de la Real Academia de Medicina de Valladolid y fundador y director emérito de la revista *Nutrición Hospitalaria,* el cual habló de "La SENPE y la revista *Nutrición Hospitalaria.* Orígenes y desarrollo"; por la Dra. Teresa Bermejo Vicedo, jefa del Servicio de Farmacia del Hospital Universitario Ramón y Cajal y directora de la revista *Farmacia Hospitalaria,* que impartió sobre "La revista *Farmacia Hospitalaria,* afín a los intereses de *Nutrición Hospitalaria*"; por el Dr. José Manuel Moreno Villares, de la Unidad de Nutrición Clínica del Hospital 12 de Octubre y director de la revista *Nutrición Hospitalaria,* que disertó sobre "El futuro de *Nutrición Hospitalaria*"; y por el Dr. Jesús Pintor Just, catedrático de Bioquímica y Biología Molecular IV en la Facultad de Óptica de la Universidad Complutense de Madrid, editor ejecutivo de la revista *Anales de la Real Academia Nacional de Farmacia* y secretario de la RANF, cuya ponencia versó sobre "La revista *Anales de la Real Academia Nacional de Farmacia* y la nutrición". La mesa redonda fue presentada y coordinada por el Dr. Francisco José Sánchez Muniz, miembro de número de la Real Academia Nacional de Farmacia y catedrático de Nutrición y Ciencias de los Alimentos de la Facultad de Farmacia de la Universidad Complutense de Madrid.

El profesor Sánchez Muniz se dirigió a la mesa presidencial y a la audiencia y, tras hacer un merecido recuerdo a la labor realizada e iniciada por el académico de número, ya fallecido, el Dr. Víctor Jiménez Torres en el campo de la nutrición clínica y en la relación entre la RANF y la SENPE, destacó dos hechos fundamentales:

1. Que la mesa redonda nacía como homenaje al Excmo. Dr. Jesús Culebras, que estuvo al mando de la revista *Nutrición Hospitalaria* durante 36 años, el cual hablaría de un libro (su segunda tesis doctoral) donde recogía muchos detalles de los inicios y el establecimiento de la revista *Nutrición Hospitalaria* como órgano de expresión de la SENPE.
2. Que aquella reunión era un encuentro de revistas científicas (*Nutrición Hospitalaria, Farmacia Hospitalaria, Journal of Negative and No Positive Results* y *Anales de la Real Academia Nacional de Farmacia*) cuya finalidad es la publicación y difusión de diferentes temas científicos de actualidad y de relevancia en el campo de la salud, con la finalidad de abrir colaboraciones e interacciones, en particular en temas de nutrición y nutrición clínica, y hacerlas lo más visible posible.

Posteriormente, el coordinador fue presentando a cada uno de los ponentes haciendo un breve esbozo de sus currículos.

El Dr. Culebras comenzó agradeciendo vivamente su presencia en la mesa redonda y el homenaje que la RANF realizaba a su persona. Su discurso se centró en el desglose de las enormes dificultades en el inicio de la revista *Nutrición Hospitalaria* y los pasos que tuvo que dar para sacar a la revista de un ámbito local a otro, con reconocimiento internacional premiado por el *Journal Citation Report* (JCR) con un hecho relevante, la concesión a la revista *Nutrición Hospitalaria* de factor de impacto, que incrementó de forma notable la visibilidad y la calidad de las publicaciones y contribuciones que recogía. Señaló que *Nutrición Hospitalaria* había crecido y había llegado a convertirse en la segunda revista más citada de las revistas en español. También destacó la enorme colaboración, difusión y contribuciones que ha tenido desde diferentes instituciones hispanoamericanas y comentó sobre las contribuciones de algunos países como China. Destacó el número elevadísimo de artículos publicados en los dos últimos años de su gestión y también el número elevado de suplementos de calidad publicados por la revista, donde se recogen actividades y contribuciones de diferentes sociedades y congresos científicos, así como acuerdos consenso de los mismos. Además, destacó las publicaciones "Lecciones Dr. Culebras", donde han impartido magistralmente primerísimas personalidades en al campo de la nutrición en España, y terminó comentando algunas anécdotas y agradeciendo al Prof. Sánchez Muniz su iniciativa.

La sesión continuó con la Dra. Teresa Bermejo Vicedo, quien, después de agradecer su presencia en aquella mesa redonda y unirse a las felicitaciones al Dr. Culebras, mostró el enorme valor de lo realizado por el ponente anterior y reseñó lo que a su entender debía ser la revista *Farmacia Hospitalaria:* el resultado de una triada que se basa en excelencia científica, visibilidad y gestión. Señaló que el farmacéutico hospitalario debe ser un profesional fundamental tanto en el hospital como en el campo de la salud y que hoy no se entiende un trabajo profesional sin la colaboración de equipos multidisciplinares de soporte y de asesoramiento nutricional y farmacológico. La Dra. Bermejo desglosó algunos aspectos sobre la trayectoria de *Farmacia Hospitalaria* y las formas de incrementar la excelencia de la revista. También habló de una serie de índices que posibilitan la inclusión de la revista dentro de la lista de aquellas con factor de impacto y su esfuerzo y gestión para conseguirlo.

El Dr. José Manuel Moreno se unió a la felicitación al Dr. Culebras, anterior director de la revista *Nutrición Hospitalaria,* y agradeció su presencia en aquella mesa redonda. Esbozó la realidad actual de la investigación y de las publicaciones en revistas de impacto y cuál debía ser, en su opinión y en la del Comité Ejecutivo, el futuro de la revista *Nutrición Hospitalaria.* También señaló algunos aspectos sobre la nutrición clínica y las novedades que esta revista internacional ha incorporado para adaptarse a los nuevos tiempos. Tras un breve análisis comparativo con otras revistas nacionales e internacionales, señaló que en las directrices había que mirar más allá del conocido factor de impacto y comentó algunos aspectos del índice H y de otros índices que se aplican a las revistas para definir su excelencia. Asimismo, comentó sobre el papel y la importancia de las redes sociales en este campo, incrementando no solo la visibilidad de la revista sino también de quienes publican en ella. No obstante, también disertó sobre la dificultad de la inversión en personas y en medios.

El Dr. Jesús Pintor habló del objetivo de la mesa redonda y el número de contribuciones en el campo de la nutrición que la RANF, a través de las monografías del Instituto de España o de la revista *Anales de la Real Academia Nacional de Farmacia,* había realizado en la última década. Señaló que aquella mesa redonda era una forma ágil de crear un compromiso entre las revistas y que debía buscarse una relación biunívoca entre ellas como vía para incrementar la visibilidad de la nutrición y, en particular, de la nutrición artificial. No obstante, entendía que aquello era solo el principio y que en un futuro próximo debían fijarse aspectos sobre publicaciones comunes, archivos compartidos, DOI, derechos de autor, etc.

Terminadas las intervenciones, el Dr. Sánchez Muniz preguntó a los ponentes sobre cuál era la vía más ágil para fundamentar la relación y coordinación y qué criterios debían aplicarse. Los cuatros ponentes estuvieron de acuerdo en fijar a corto plazo una serie de reuniones donde se plantearan los aspectos más importantes de colaboración y los acuerdos en temas relacionados con la nutrición y la nutrición hospitalaria que beneficiaran a las revistas que participaban en la mesa redonda.

Algunos asistentes felicitaron al Dr. Culebras y a la iniciativa de la reunión y a los ponentes. Cerró el acto el presidente de la RANF, el Excmo. Dr. D. Mariano Esteban, con unas palabras de felicitación al Dr. Culebras por su empuje y labor bien hecha y deseando la puesta en marcha de futuras reuniones donde se fijen los parámetros de colaboración y el compromiso de una mayor permeabilidad e interacción entre revistas y entre entidades y sociedades en este tema de enorme importancia sanitaria.

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ARÁN

Nutrición Hospitalaria

Nota Clínica

Tratamiento de obesidad con liraglutida en un paciente con síndrome de Prader-Willi: reporte de un caso

Obesity treatment with liraglutide in a patient with Prader-Willi syndrome: a case report

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Resumen

Introducción: el síndrome de Prader-Willi (SPW) es una de las principales causas de obesidad sindrómica, causado por deleciones en el cromosoma 15q11-q13. Está caracterizado por hipotonía neonatal, dificultad para la alimentación con peso bajo al nacer y posterior desarrollo de hiperfagia, alteraciones de la conducta y obesidad. El tratamiento para la pérdida de peso en estos pacientes es complicado debido a la limitación para el uso de algunos medicamentos y la controversia en el uso de opciones quirúrgicas.

Caso clínico: presentamos el caso de un paciente con SPW que logró disminución y control de peso mediante el uso de liraglutida, terapia nutricional y actividad física.

Discusión: el tratamiento de la obesidad en los pacientes con SPW es complicado y requiere un adecuado manejo dietético aunado a terapia psicológica y, en caso de persistencia del descontrol del apetito, el uso de medicamentos como metformina o los análogos de GLP-1.

Palabras clave:

Síndrome de Prader-Willi. Obesidad. Liraglutida.

Abstract

Background: Prader-Willi syndrome (PWS) is a major cause of syndromic obesity, caused by deletions on chromosome 15q11-q13. It is characterized by neonatal hypotonia, difficulty in feeding with low birth-weight and subsequent development of hyperphagia, behavioral disorders and obesity. Treatment options for weight control in those patients is limited and there are controversies for a surgical approach.

Case report: we present the case of a patient with PWS who achieved weight loss and control through the use of liraglutide, nutritional therapy and physical activity.

Discussion: the treatment of obesity in patients with PWS is challenging and requires an adequate nutritional approach combined with psychological therapy. In those patients that persist with uncontrolled appetite, medications such as metformin or GLP-1 analogs can be used.

Key words:

Prader-Willi syndrome. Obesity. Liraglutide.

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INTRODUCCIÓN

El síndrome de Prader-Willi (SPW) es un desorden genético multisistémico, resultado de alteraciones en la expresión de genes paternos en la región 15q11-q13, que en la mayoría de los casos ocurre esporádicamente. Existen tres tipos de mutaciones identificadas que son la deleción, la disomia uniparental materna y el defecto de impronta, representando la deleción el 75% de los casos. Tiene una incidencia entre 1:16.000 y 1:25.000 nacidos vivos (1) de acuerdo a lo reportado en Estados Unidos, pero se desconoce su prevalencia en otros países. Su cuadro clínico varía desde la etapa de nacimiento, con hipotonía neonatal, dificultad de alimentación y bajo peso al nacer, progresando en la infancia a hiperfagia, afectación cognitiva variable, trastornos de la conducta y alteraciones psiquiátricas. Desde el punto de vista endocrinológico, los pacientes presentan deficiencia de hormona de crecimiento, hipogonadismo hipogonadotrópico y aumento de las concentraciones de ghrelina que provocan obesidad hipotalámica y, *a posteriori,* complicaciones secundarias a la obesidad.

Este síndrome es una de las principales causas de obesidad sindrómica y, debido a la hiperfagia generada por la hiperghrelinemia, así como a las alteraciones hormonales y conductuales, es una entidad de difícil control en cuanto a la pérdida de peso (2). En estos pacientes el tratamiento farmacológico está enfocado al control de la hiperfagia, pero existen pocos resultados favorables. Otras opciones, como el tratamiento quirúrgico con *bypass* o manga gástrica, han tenido eficacia variable y son controversiales (3). Desde el año 2014, la Food and Drug Administration (FDA) aprobó el uso de liraglutida 3,0 mg para el tratamiento de obesidad (4). Existen algunos reportes de casos en donde su uso en el paciente con SPW ha inducido disminución del apetito, pérdida de peso y mejoría en el control metabólico (5).

El objetivo de este caso clínico es describir el control de peso asociado al uso de liraglutida en un paciente con SPW.

CASO CLÍNICO

Presentamos el caso de un hombre de 21 años de edad, sin antecedentes heredofamiliares de importancia, con antecedente perinatal de asfixia severa, hiperbilirrubinemia e hipotonía y, desde los dos años, con hiperfagia e incremento de peso hasta alcanzar un percentil por encima del 95%. Asimismo, desde la infancia presenta retraso mental moderado manifestado con problemas de aprendizaje y comunicación, así como alteraciones del estado de ánimo con irritación fácil y conducta caprichosa. A los ocho años inició con trastorno de refracción ocular, por lo que requirió tratamiento con lentes de corrección. A los 14 años se detectó con atrofia testicular derecha e hipoplasia testicular izquierda severa con criptorquidia, por lo que requirió orquiectomía bilateral. Dos años después, presentó sintomatología de reflujo gastroesofágico, detectándose mediante endoscopia hernia hiatal que requirió manejo con funduplicatura de Nissen. Debido a la sospecha de SPW, se realizó estudio genético que demostró patrón de metilación positivo para la presencia del alelo materno de gen SNRNP 15q11-q13, con FISH positivo para dicha deleción, por lo cual se corroboró el diagnóstico.

Fue referido a la consulta externa de la Clínica de Obesidad por persistir con hiperfagia, irritabilidad, aumento gradual de peso, ronquido y somnolencia diurna. Su madre refería que la hiperfagia se incrementaba durante los periodos de ansiedad y que durante un atracón podía consumir dietas de hasta 3.000 kcal, por lo cual requirió lavados gástricos en el Servicio de Urgencias debido a la dificultad para la emesis generada por la cirugía esofágica. A la exploración física presentó presión arterial de 90/60 mmHg, frecuencia cardiaca (FC) de 90 lpm, peso de 64 kg, talla de 1,44 m e índice de masa corporal (IMC) de 33,7 kg/m^2, biotipo endomórfico, párpados con aspecto almendrado y exotropia en ojo derecho, cuello y áreas de flexión con acantosis nigricans, fibromas laxos y en algunas áreas acromia, con abdomen globoso a expensas de panículo adiposo y distribución de vello genital con Tanner 3. Como parte de su valoración inicial se realizó estudio de coeficiente intelectual (previo consentimiento informado con su familiar y asentimiento informado con el paciente) con IQ de 90 puntos. Además, se realizaron los laboratorios referidos en la tabla I.

Con base en los resultados, se inició tratamiento con levotiroxina 50 µg/día. Debido a la edad ósea radiológica de 16 años, se

Tabla I. Evaluación bioquímica y hormonal del caso presentado

Parámetro	Valor del paciente	Valores de referencia
Glucosa (mg/dl)	83	55-99
Insulina (µUI/ml)	18,8	1,9-23
HOMA-IR	3,86	< 2,5
Colesterol (mg/dl)	167	50-200
Triglicéridos (mg/dl)	155	50-150
c-HDL (mg/dl)	16	> 50
c-LDL (mg/dl)	120	< 100
HbA1c (%)	5,6	< 5,7
TSH (µUI/ml)	7,78	0,27-4,20
T4L (ng/ml)	1,18	0,93-1,27
Prolactina (ng/ml)	19,37	6,0-25,0
FSH (mUI/ml)	0,113	1,5-12,4
LH (mUI/ml)	0,1	1,4-8,6
Testosterona (ng/dl)	281	290-800
GH (ng/ml)	0,1	0,02-1,23
IGF-1 (ng/ml)*	79,4	172-432
Vitamina D (ng/ml)	14,3	3-100

*HOMA-IR: homeostatic model of assessment of insulin resistance; c-HDL: colesterol asociado a lipoproteínas de baja densidad; c-LDL: colesterol asociado a lipoproteínas de baja densidad; HbA1c: hemoglobina glucosilada; TSH: hormona estimulante de tiroides; T4L: tiroxina libre; FSH: hormona estimulante folicular; LH: hormona luteinizante; GH: hormona de crecimiento; IGF-1: factor de crecimiento similar a la insulina 1 (*específico para edad y sexo).*

decidió prescribir enantato de testosterona 250 mg cada 28 días. Para tratamiento de las comorbilidades metabólicas, se prescribió vitamina D3 1.600 unidades por día, metformina 425 mg c/12 h, plan de alimentación de 1.400 kcal y recomendaciones de actividad física.

Durante su seguimiento persistía con hiperfagia y, a pesar de que ya se encontraba realizando actividad física (natación y actividades aeróbicas tres veces por semana), incrementó su peso hasta 70 kg. Por este motivo, se decidió inicio de tratamiento con liraglutida 0,6 mg por semana, con incremento gradual hasta 1,8 mg por semana, y modificación de plan dietético de 1.200 kcal. No se logró aumentar la dosis hasta 3,0 mg debido a que el paciente refería incremento de la náusea. Con esta estrategia se refirió disminución del apetito, llegando a alcanzar peso de 62,2 kg, con IMC de 29,9 kg/m^2. Este tratamiento fue administrado durante seis meses, posterior a lo cual se suspendió a petición de sus familiares. Sin embargo, el paciente ha mantenido su mismo peso hasta el momento, mediante tratamiento dietético y control regular con psiquiatría.

DISCUSIÓN

La obesidad es una enfermedad compleja causada por diferentes factores ambientales y genéticos (poligénicas). Solo el 5% de los casos de obesidad se deben a alteraciones monogénicas, las cuales pueden ser no sindrómicas o sindrómicas. La causa de obesidad en los pacientes con SPW es multifactorial. Si bien tiene un contexto genético, la función de los genes que no se expresan en el SPW no se conoce con exactitud y la ganancia de peso se asocia a la hiperfagia y disminución de la saciedad, la deficiencia de hormona de crecimiento (GH), el hipogonadismo, las alteraciones en el fenotipo conductual y los trastornos del estado de ánimo.

Se ha observado que los pacientes con SPW tienen elevación en las concentraciones de ghrelina, con alteración en la relación entre su forma acilada/desacilada (6). Existen algunos estudios que han intentado disminuir las concentraciones de ghrelina con fármacos como análogos de la somatostatina; sin embargo, no han sido exitosos (7). Por otra parte, la deficiencia de GH característica del SPW se ha relacionado con un incremento en el tejido adiposo y alteraciones en el metabolismo de lípidos (8). Además, el hipogonadismo contribuye al exceso de peso debido al dimorfismo causado por la disminución de hormonas androgénicas que alteran la adipogénesis al inhibir la proliferación y diferenciación de las células madre mesenquimatosas y preadipocitos (9). Sin embargo, no existe disminución de peso con el reemplazo hormonal, aunque su uso está justificado para la prevención de alteraciones óseas.

El manejo de la obesidad en pacientes con SPW se basa en la restricción calórica y la actividad física. En cuanto a la dieta, se sugiere con 25% de proteínas, 25% de grasas y 50% de carbohidratos, entre 800 y 1.300 kcal, dependiendo de la estatura del sujeto (10). Además, se requiere una restricción estricta del acceso a los alimentos mediante barreras físicas y una estrecha supervisión.

El tratamiento farmacológico está enfocado al control de la hiperfagia, pero existen pocos resultados favorables. El fármaco más recomendable es la metformina, sobre todo cuando existe resistencia a la insulina o intolerancia a la glucosa. Su uso se ha asociado con mejoría en la angustia relacionada con los alimentos, la ansiedad y la capacidad para mostrar autocontrol y permanecer alejados de la comida (11). En el caso clínico presentado, el paciente no tuvo mejoría en cuanto al control de peso con el uso de metformina, por lo cual se decidió buscar otro tratamiento adyuvante.

La liraglutida es un análogo del péptido similar al glucagón (GLP-1). Tanto el GLP-1 como el polipéptido inhibidor gástrico (GIP) son péptidos llamados incretinas, los cuales se liberan tras la ingestión de alimentos, inducen la liberación de insulina y disminuyen la liberación del glucagón; sin embargo, su vida media es de minutos debido a que son degradados por las dipeptidil-peptidasas tipo 4 (DPPIV) intestinales (12). La liraglutida tiene una homología del 97% con el GLP-1 y una vida media de 13 horas (13). Debido a sus efectos sobre la insulina y el glucagón, fue utilizado en primer lugar como fármaco antidiabético, logrando una adecuada disminución de la hemoglobina glucosilada (HbA1c) y, de forma adicional, disminución del peso corporal (4,14). Este efecto se obtiene debido a que regula el apetito a nivel del sistema nervioso central, al actuar por medio de sus receptores en los núcleos arcuato, eminencia media y núcleos paraventricular y supraóptico (hipotálamo) (15) y retrasando el vaciamiento gástrico, lo cual causa saciedad (16).

Si bien este medicamento es ampliamente utilizado en el tratamiento de pacientes con obesidad exógena, solo existen algunos casos de su uso en pacientes con obesidad de tipo hipotalámico. Fintini y cols. describen una serie de seis casos en los cuales se utilizó exenatida o liraglutida a dosis variables, y en todos ellos se observó disminución del IMC y del perímetro de cintura (5).

No se han encontrado diferencias en las concentraciones de GLP-1 entre pacientes con obesidad exógena o SPW (17), por lo que se ha postulado que su efecto sobre el control de peso se debe a que disminuye la concentración sérica de ghrelina y aumenta el PYY (18). De hecho, Senda y cols. observaron disminución de las concentraciones de ghrelina en una paciente de 25 años con SPW con uso de liraglutida a dosis de 0,9 mg/día durante un año (19). Sin embargo, en un estudio reciente, Salehi y cols. utilizaron exenatide 10 µg durante seis meses en diez pacientes con SPW de 14,7 a 24,6 años (cuatro hombres y seis mujeres). A pesar de que se observó disminución del apetito valorado mediante un cuestionario en los meses 1, 3 y 6, no se observó disminución en el peso, z-score del IMC ni en la adiposidad evaluada mediante absorciometría dual de rayos X (DEXA). En esta serie no se observaron cambios en las concentraciones de ghrelina (20). Como mencionan los autores, se requieren ensayos clínicos controlados y aleatorizados que corroboren la eficacia y seguridad de los análogos de GLP-1/exendina en estos pacientes. Con respecto a los efectos adversos, entre los más importantes reportados se encuentran los gastrointestinales, principalmente náuseas, y pueden ser dosis-dependientes (4). En nuestro paciente, este efecto limitó el incremento de la dosis hasta la

recomendada de 3,0 mg. Finalmente, no consideramos el uso de medicamentos anorexigénicos como fentermina, fenfluramina, inhibidores selectivos de la recaptura de serotonina y topiramato, debido a que no han mostrado resultados favorables (21). De igual forma, no se ofreció tratamiento quirúrgico en este paciente por la diversidad de opiniones en cuanto a la relación riesgo/beneficio.

CONCLUSIÓN

El tratamiento de la obesidad en el paciente con SPW debe ser multidisciplinario y multimodal, engloba la vigilancia y el tratamiento de las complicaciones endocrinológicas relacionadas con el aumento de peso (diabetes mellitus, hipertensión, dislipidemia aterogénica) y requiere un adecuado seguimiento nutricional y psicológico que incluya a la familia del paciente. El tratamiento farmacológico aún se encuentra en investigación y solo se considera como coadyuvante. El mejor caracterizado es la metformina, pero otras medidas farmacológicas como los análogos de GLP-1/exendina pueden considerarse por sus efectos sobre la disminución del apetito, el incremento de la saciedad y la disminución del vaciamiento gástrico.

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ARÁN

Nutrición Hospitalaria

Nota Clínica

Manejo nutricional de la diarrea crónica funcional asociada a desnutrición con una dieta peptídica: un caso clínico

Nutritional management of functional chronic diarrhea associated to malnutrition with peptide diet: a case report

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Resumen

Introducción: los trastornos funcionales del intestino se caracterizan por una ausencia de daño estructural o bioquímico, pero pueden causar diarrea crónica y malabsorción intestinal. Sin tratamiento adecuado, predisponen a un estado de desnutrición que, dependiendo de las patologías de base, podría condicionar la evolución de otras enfermedades concomitantes.

Caso clínico: la relevancia de este caso se debe a que nuestra paciente pluripatológica, de 43 años de edad, con pérdida progresiva de peso y masa muscular, tras cinco años de ineficiencia en el tratamiento nutricional y soporte estándar de la diarrea crónica consigue, después de unos meses de tratamiento con dieta peptídica, un buen estado nutricional y calidad de vida, habiendo logrado controlar la diarrea crónica y la desnutrición.

Discusión: en la pérdida inintencionada de peso que causa una diarrea de perfil funcional de larga evolución, la elección de una dieta peptídica puede ser muy útil para que la evolución del paciente sea satisfactoria.

Palabras clave:

Diarrea funcional.
Dieta peptídica.
Malabsorción.
Malnutrición.

Abstract

Background: functional bowel disorders are characterized by an absence of structural or biochemical damage, but can lead to chronic diarrhea and intestinal malabsorption. If not properly treated, they predispose to a state of malnutrition that, depending on the underlying pathologies, could affect the evolution of other concomitant diseases.

Case report: the relevance of this case stems from the fact that our 43-year-old patient, with multiple comorbidities, with progressive weight and muscle mass loss, after five years of inefficiency in the treatment of chronic diarrhea, achieves, on a peptide enteral formula basis, a good nutritional status and quality of life, which finally leads to the control of the chronic diarrhea and malnutrition.

Discussion: in the unintentional weight loss caused by long-term functional diarrhea, the choice of a peptide diet may have a fundamental role for a satisfactory patient's progress.

Key words:

Functional diarrhea.
Peptide diet.
Malabsorption.
Malnutrition.

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INTRODUCCIÓN

La diarrea funcional se define como un síndrome continuo o recurrente caracterizado por el paso de heces sueltas (blandas) o acuosas sin dolor abdominal o malestar, que no se explica por anomalías estructurales o bioquímicas (1).

Acorde al diagnóstico y la clasificación de Roma IV, y a la espera de un término que sea diferencial para distinguirlo de otros trastornos similares, la diarrea funcional es considerada como un trastorno de interacción "intestino-cerebro". La diarrea funcional pertenece a un grupo de trastornos relacionados con cualquier combinación de alteraciones de la motilidad, hipersensibilidad visceral, procesamiento del sistema nervioso central, microbiota intestinal, alteración de la función de la mucosa y de la función inmune (2).

La diarrea se considera crónica cuando su duración es superior a cuatro semanas (3) y puede clasificarse por la frecuencia, el volumen, la consistencia y la localización, bien en intestino delgado o en intestino grueso. Cuando las deposiciones son de volumen pequeño y frecuentes, sugieren una alteración en la capacidad de almacenamiento del colon rectosigmoide, mientras que la diarrea acuosa de gran volumen es más sugerente de un proceso en el intestino delgado o, menos comúnmente, en el colon derecho. Las características de las heces son probablemente el esquema de clasificación más utilizado para determinar la etiología de la diarrea crónica (4).

La ausencia de una serie de síntomas, la normalidad de la analítica sanguínea y la negatividad de los exámenes en heces para agentes infecciosos sugieren que la diarrea crónica es de causa funcional. Además, hay una relación entre diarrea crónica y malabsorción, ya que la malabsorción se manifiesta con frecuencia como un cuadro de diarrea crónica (5).

CASO CLÍNICO

Presentamos el caso de una mujer de 43 años, sin tratamiento farmacológico, con antecedentes personales de síndrome de Reed (leiomiomatosis hereditaria y cáncer renal), osteopenia, hemangioma hepático, esofagitis leve y úlcera péptica, en seguimiento en las consultas de digestivo del Hospital Fundación Jiménez Díaz por diarrea crónica.

Se derivó al Servicio de Endocrinología y Nutrición con criterio de desnutrición leve, con una pérdida progresiva de peso de larga evolución y especialmente agresiva de 7 kg en el último año. Asimismo, inició seguimiento en la consulta específica de cáncer hereditario. Hasta el momento, carecía de diagnóstico y se desconocía la etiología de la diarrea.

En las pruebas realizadas se descartaron celiaquía, intolerancias a la lactosa y a la fructosa, parásitos intestinales y *Helicobacter pylori.* La ecografía abdominal no mostró hallazgos significativos y la biopsia intestinal y la bioquímica mostraron valores normales (Tabla I).

Tabla I. Parámetros bioquímicos iniciales

Glucosa mg/l	89
Hemoglobina	13,4
Albúmina g/dl	4,4
Prealbúmina mg/dl	21,33
Creatinina mg/dl	0,72
Proteínas totales g/dl	7,2
Linfocitos %	21,6
Colesterol total mg/dl	152
Proteína C-reactiva mg/dl	0,01
Sodio mmol/l	141
Potasio mmol/l	4,1
Cloro mmol/l	106
Transferrina mg/dl	253
Calprotectina mg/kg	16,00
Elastasa mcg/g	> 500
TSH µUI/ml	1,260
T4 libre ng/dl	1,00
ACTH pg/ml	15,60
Cortisol ug/dl	8,82

En la consulta describió pérdida de peso progresiva durante cinco años y más acusada en el último año. Su peso al inicio de este último año fue de 60 kg. Describió una diarrea crónica, diaria, sin urgencia defecatoria, de consistencia acuosa y sin dolor y mostró una evidente preocupación por astenia, problemas cognitivos leves (problemas de atención, pensamiento y memoria), taquicardias, sudoración, pérdida de la libido y especialmente pérdida de fuerza y peso muscular. No refirió meteorismo ni presentó dolor a la palpación abdominal. Sus medidas fueron: peso 52,8 kg, talla 170 cm, índice de masa corporal (IMC) 18,2 kg/m^2 (desnutrición leve), un 12% de pérdida de peso en el último año y 26 cm de circunferencia media braquial (CMB).

No asoció como elemento desencadenante de la diarrea el consumo de algún alimento específico. Había probado algunas modificaciones dietéticas (dieta baja en FODMAP y dieta sin lactosa y sin gluten) sin mejora en el control de la diarrea y del peso. Describía buen apetito y la cantidad de alimento era adecuada en cada ingesta. Su alimentación era saludable, dentro del patrón mediterráneo, con alimentos naturales y escaso consumo de alimentos envasados y procesados. No refería estrés en su vida cotidiana, a excepción del causado por su pérdida de peso y sintomatología asociada. La práctica de deporte era habitual; no fumaba ni consumía alcohol.

Se prescribió una dieta de 2.200 kcal (40 kcal/kg/día) con recomendaciones de enriquecimiento de platos y pautas específicas para evitar la estimulación del intestino e irritación de la mucosa. Adicionalmente, se pautaron ejercicios de relajación y se recomendó un probiótico diario (Vivomixx®) para tratar la probable disbiosis intestinal. Se citó revisión de seguimiento mensual para evolución de síntomas y peso.

En la revisión, y tras un mes de seguimiento estricto de las pautas indicadas, la paciente refirió que persistían las deposiciones diarreicas acuosas, diarias y sin urgencia defecatoria, presentó una mayor astenia y continuó perdiendo peso, hasta llegar a 52,4 kg y masa muscular CMB 24 cm.

Dada la incapacidad de aumentar cuantitativamente el consumo diario de alimentos, se decidió reajustar calorías a 1.400 kcal/d con alimentación oral y suplementar un aporte de 800 kcal/d con una dieta peptídica normocalórica e hiperproteica (Bi[1] Pepticare®) con el fin de lograr una mejora en la absorción intestinal.

La paciente acudió a la semana con una visible mejoría de los síntomas. Mostró una recuperación notable de peso de 1,5 kg (53,9 kg), describió mejora en el estado anímico, mejora en la fuerza (CMB 24.5) y mejora en la astenia y observó un cambio en la consistencia de las deposiciones, describiéndolas de apariencia más pastosas. Se decidió continuar con las mismas pautas de dieta y suplementación. De nuevo en la revisión semanal, se apreció ganancia de peso (54,5 kg), hasta alcanzar normopeso por IMC (18,8 kg/m^2), ausencia de astenia, progresión en la mejora de la fuerza muscular, mejora del estado anímico y mejora cognitiva.

Con el fin de un diagnóstico concluyente y a lo largo de este periodo se realizaron otras pruebas exploratorias. Para descartar una patología endocrinológica o un tumor neuroendocrino se solicitaron perfiles específicos y metanefrinas, obteniéndose valores normales (Tabla II). Además, mediante enterorresonancia no se observaron lesiones y a través de una cápsula endoscópica se hallaron lesiones petequiales aisladas y angiodisplasia de intestino delgado, cuyo diagnóstico no justificaba la causa de la disfunción intestinal. Finalmente, digestivo concluyó su diagnóstico como síndrome diarreico de perfil funcional (probable síndrome de intestino irritable [SII]).

Con base en el diagnóstico y dada la mejora de la diarrea y recuperación del peso, se llevó a cabo un refuerzo de las recomendaciones nutricionales para el manejo del SII y se mantuvo la elección del suplemento peptídico. Tras seis meses de evolución, la paciente fue capaz de controlar el peso y mantuvo la mejoría en la diarrea crónica, si bien las deposiciones no llegaron a ser completamente de consistencia normal. Actualmente, continúa con revisiones periódicas de control.

La relevancia de este caso se debe a que nuestra paciente, después de cinco años de pérdida inintencionada de peso a causa de diarrea crónica de perfil funcional, tiene un buen estado nutricional y una buena calidad de vida con ayuda de suplementación con dieta peptídica.

Tabla II. Determinación de metanefrinas y marcadores específicos de tumor neuroendocrino

Normetanefrina orina mcg/24 h	154
Metanefrina orina mcg/24 h	62,1
VIP pmol/l	4,7
CgA ng/ml	56,10

DISCUSIÓN

El cuadro en nuestra paciente se presentó con una sintomatología atípica de SII, ya que, normalmente, este trastorno funcional cursa con dolor o disconfort abdominal. No presentó dolor abdominal y tanto la distensión como el meteorismo no fueron significativos, síntomas también frecuentes en personas con trastornos digestivos de tipo funcional. Además, las deposiciones en el SII que cursa con diarrea suelen ser sueltas, acuosas y en ocasiones de urgencia y difíciles de controlar. La paciente no experimentaba urgencia defecatoria.

Respecto a la suplementación peptídica, la elección fue a expensas de completar las pruebas, anterior al diagnóstico definitivo y en base al algoritmo de desnutrición calórica-proteica (6). En nuestro caso, con una función gastrointestinal comprometida, optamos por una dieta peptídica dada su mayor facilidad absortiva (7) y elegimos una formulación normocalórica e hiperproteica de baja osmolaridad.

El tratamiento nutricional fue prescrito acorde con las guías para el soporte nutricional de los pacientes con síndrome de intestino irritable de la Sociedad Española de Gastroenterología (8), las guías NICE (9) y ESPEN (10).

En conclusión, este caso clínico muestra que algunas diarreas son calificadas de funcionales y asociadas a cualquier situación como síndrome de intestino irritable. Cuando son de larga evolución, pueden llevar a malnutrición que afecta sin duda a la propia mucosa intestinal y a los procesos digestivos y absortivos y, aun no constituyendo un síndrome de malabsorción en toda regla, se puede beneficiar de un periodo de tratamiento con dieta peptídica cuyas características favorecen una absorción mejor.

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Fe de erratas

En el artículo "Características antropométricas en jugadores chilenos de tenis de mesa de nivel competitivo", publicado en la revista *Nutrición Hospitalaria* 2015;32(4):1689-94, hubo un error en la filiación de los autores.
En el artículo figuraba lo siguiente:

Rodrigo Yáñez Sepúlveda[1], Fernando Barraza[2], Giovanni Rosales Soto[3], Eduardo Báez[4] y Marcelo Tuesta[5]

[1]Facultad de Filosofía y Educación, Pontificia Universidad Católica de Valparaíso. [2]Escuela de Educación. Pedagogía en Educación Física, Universidad Viña del Mar. [3]Facultad de Ciencias de la Actividad Física, Universidad San Sebastián. [4]Departamento de Deportes y Recreación, Universidad de Playa Ancha. [5]UDA Ciencias de la Salud. Facultad de Medicina, Pontificia Universidad Católica de Chile, Chile

Y lo correcto debería ser:

Cristián Fuenzalida Alvaréz[1], Cristián Sierra Barrera[1], Gerardo Díaz Hidalgo[1], Fernando Barraza[1], Rodrigo Yáñez Sepúlveda[2], Giovanni Rosales Soto[3], Eduardo Báez[4] y Marcelo Tuesta[5]

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La nueva referencia de artículo sería: Fuensalida Alvarez C, Sierra Barrera C, Diaz Hidalgo G, Barraza F, Yáñez Sepúlveda R, Rosales Soto G, Báez E, Tuesta M. Características antropométricas en jugadores chilenos de tenis de mesa de nivel competitivo. Nutr Hosp 2015;32(4):1689-94. Corrección en Nutrición Hospitalaria 2018;35(3):750

Nutrición Hospitalaria

Órgano Oficial

Sociedad Española de Nutrición Parenteral y Enteral ❙ Sociedad Española de Nutrición ❙ Federación Latino Americana de Nutrición Parenteral y Enteral ❙ Federación Española de Sociedades de Nutrición, Alimentación y Dietética

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SECCIONES

Fundamentalmente la revista consta de las siguientes secciones:

Originales. Trabajos preferentemente prospectivos, de investigación clínica, y otras contribuciones originales sobre etiología, fisiopatología, anatomía patológica, epidemiología, diagnóstico y tratamiento. La extensión debe ser de 4.000 palabras, excluyendo bibliografía y resumen, 7 tablas y/o figuras, y 40 citas bibliográficas como máximo. Es necesario incluir números de línea en todo el texto, comenzando por la página de título.

Notas clínicas. Descripción de uno o más casos clínicos de excepcional observación que supongan una aportación importante al conocimiento del proceso, realizando una revisión crítica de la literatura. La extensión máxima debe ser de 2.000 palabras, excluidos resumen, abstract y bibliografía. Se aceptarán de 2 a 4 figuras y/o tablas. La bibliografía no debe superar las 15 referencias.

Cartas al Editor. En esta sección se publicarán a la mayor brevedad objeciones o comentarios relativos a artículos publicados recientemente en la revista. La extensión máxima será de 500 palabras y el texto no se estructurará en apartados. La bibliografía no debe superar las 10 referencias. Sólo se admitirá una tabla o figura.

Revisiones. En la actualidad, salvo excepciones, la política de la revista es encargar las revisiones. No obstante, artículos con evaluaciones sistemáticas de la literatura con criterios de búsqueda prediseñados (y, si es posible, con gradación de la evidencia), y no solo revisiones narrativas, tienen mejor cabida en nuestra revista, especialmente si el autor de la revisión tiene publicaciones sobre el tema en cuestión.

Si finalmente decide enviar un artículo a esta sección, aunque no haya sido por encargo, debe conocer que los artículos para esta sección, al igual que el resto, deben ser gestionados a través de la plataforma de la revista; se le asignará a un editor y pasará la evaluación por pares, por lo que el artículo podrá ser rechazado directamente, aceptarse o solicitarse cambios mayores o menores.

La extensión no deberá superar las 5.000 palabras, excluyendo el resumen (250 palabras no estructurado) y la bibliografía (60 citas máximo). Se aceptarán un máximo de 7 entre figuras y/o tablas.

Otras secciones. La revista incluye otras secciones (Editorial, Artículos especiales, Guías de Práctica Clínica y Grupos de trabajo

de SENPE) cuyos trabajos son escritos por encargo del Comité de Redacción.

PRESENTACIÓN Y ESTRUCTURA DE LOS TRABAJOS

Los artículos pueden remitirse en español o inglés y deben ser presentados de la siguiente manera:

1. En la **primera página** del artículo se indicarán, en el orden que aquí se cita, los siguientes datos: título del artículo, nombre y apellidos de todos los autores, nombre y dirección completos del centro de trabajo y dirección para la correspondencia, y otras especificaciones cuando se considere necesario (conflicto de intereses, financiación, registro de ensayos clínicos, etc.). Desde esta primera página de título y hasta el final del manuscrito deben incluirse números de línea en todo el texto.

2. **Resumen y abstract.** Su extensión será para los artículos de la sección de Originales de 250 palabras. Se caracterizará por: a) poder ser comprendido sin necesidad de leer parcial o totalmente el artículo; b) estar redactado en términos concretos desarrollando los puntos esenciales del artículo; c) su ordenación observará el esquema general del artículo en miniatura; y d) no incluirá material o datos no citados en el texto. En los artículos para la sección de Originales irá estructurado en los siguientes apartados: introducción, objetivos, métodos, resultados y conclusiones.

   En los artículos para la sección de Notas Clínicas irá estructurado en: introducción, caso clínico y discusión y la extensión será de 150 palabras.

   Todos los artículos remitidos en español deben llevar el título traducido en inglés así como el resumen y las palabras clave igualmente en ambos idiomas. Lo mismo pasa con los artículos remitidos en inglés, que deberán contener el título, resumen y palabras clave también en español.

3. **Palabras clave.** Se asignarán de tres a seis palabras clave de acuerdo con el MeSH de Index Medicus/MEDLINE, disponible en: http://www.nlm.nih.gov/mesh/

4. **Texto**

   4.1. Originales: Introducción, Material y métodos, Resultados y Discusión
   - Introducción: será lo más breve posible y su regla básica consistirá en proporcionar solo la explicación necesaria para que el lector pueda comprender el texto que sigue a continuación.
   - Material y métodos: se indica el tipo de estudio, el criterio de selección empleado, las técnicas utilizadas, proporcionando los detalles suficientes para que una experiencia determinada pueda repetirse sobre la base de esta información.
   - Resultados: relatan, no interpretan, las observaciones efectuadas con el material y métodos empleados. Estos datos se pueden publicar en detalle en el texto o bien en forma de tablas y figuras.
   - Discusión: el autor o autores intentarán ofrecer sus propias opiniones sobre el tema. Destacan aquí: 1) el significado y la aplicación práctica de los resultados; 2) las consideraciones sobre una posible inconsistencia de la metodología y las razones por las cuales pueden ser válidos los resultados; 3) la relación con publicaciones similares y comparación entre las áreas de acuerdo y desacuerdo; y 4) las indicaciones y directrices para futuras investigaciones.
   - Agradecimiento. Cuando se considere necesario, se citará a las personas, centros o entidades que hayan colaborado o apoyado la realización del trabajo.

   Además de la versión completa del texto (con autores y centros), debe enviarse una versión "ciega" del artículo en la que no figuren los nombres de los autores ni los centros de trabajo, ni debajo del título ni dentro del texto. Esta versión será la que se envié a la evaluación por pares. En esta versión "ciega" no deben ir ni Agradecimientos ni Financiación, así como ningún otro dato que permita identificar la autoría del manuscrito.

   4.2. Notas clínicas: Introducción, Caso clínico y Discusión
   - Introducción: será lo más breve posible y su regla básica consistirá en proporcionar solo la explicación necesaria para que el lector pueda comprender el texto que sigue a continuación.
   - Caso clínico: se expondrá el caso o casos tratados en el artículo de forma concisa, exponiendo la relevancia del mismo.
   - Discusión: se expone la resolución del caso y breve comentario sobre la patología tratada.

   4.3. Cartas al director: se enviarán los manuscritos sin resumen y con texto no estructurado en apartados

   4.4. Editoriales: los editoriales serán encargados por el Comité Editorial. Podrán ser firmados como máximo por dos autores y tendrán una extensión aproximada de 1,5 a 2 folios (con interlineado 1,5) y 10 referencias bibliográficas como máximo.

   4.5. Revisiones: los artículos de revisión serán solicitados por los editores. Solo en casos excepcionales el Comité Editorial podrá valorar material no encargado previamente. En este caso los autores deberán enviar a (nutricion@grupoaran.com) una carta de motivación previa antes de escribir el artículo de revisión. En cualquier caso, todos los artículos de revisión se someten a la misma revisión por pares y proceso editorial que los artículos originales. Deberán constar de: un resumen,

los apartados que consideren los autores (en función de la temática) y unas conclusiones.

5. **Texto sin identificar.** Además de la versión completa con autores, **en los artículos para la sección de Originales y Revisiones** los autores deben remitir **una versión sin identificación**, que es la que se enviará a revisión por pares. Esta "versión sin identificar" debe contener el título del artículo, resumen y abstract, texto, bibliografía, figuras y tablas, pero se debe poner especial atención a que dentro del manuscrito no se mencione ningún nombre propio, ni de persona, ni centro, ni ciudad. Tampoco deben aparecer agradecimientos.

6. **Bibliografía.** Se presentará según el orden de aparición en el texto con la correspondiente numeración correlativa. En el texto constará siempre la numeración de la cita entre paréntesis. Los nombres de las revistas deben abreviarse de acuerdo con el estilo usado en el Index Medicus, disponible en: ftp://nlmpubs.nlm.nih.gov/online/journals/. En lo posible se evitará el uso de frases imprecisas como citas bibliográficas; no pueden emplearse como tales "observaciones no publicadas" ni "comunicación personal", pero sí pueden citarse entre paréntesis dentro del texto. Los originales aceptados, pero aún no publicados, se incluyen en las citas bibliográficas como [en prensa] (entre corchetes). Las citas bibliográficas deben comprobarse por comparación con los documentos originales. Debe incluirse el DOI en aquellas citas que lo tengan. A continuación se dan unos ejemplos de formatos de citas bibliográficas.
   – *Revista:*
     a) *Artículo de revista estándar:*
     Relacionar todos los autores si son seis o menos, si son siete o más, relacionar solo los seis primeros añadiendo la expresión et al. Solter NA, Wasserman SL, Auster KF. Cold urticaria: release into the circulation of histamine and eosinophilic chemotactic factor of anaphylaxis during cold challenge. N Engl J Med. 1976;294:687-90. DOI: xxxxxxxxxxxxxxx
     b) *Trabajo publicado por una Institución (autor no especificado):*
     The Committee on enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Psychology. Recommended method for the determination of gammaglutamyltransferase in blood. Scand J Clin Lab Invest. 1976;36:119-25.

   – *Libros y otras monografías:*
     a) *Autor(es) personal(es):* Osler AG. Complement: mechanisms and functions. Englewood Cliffs: Prentice-Hall; 1976.
     b) *Autor corporativo:* American Medical Association Department of Drugs. AMA Drug evaluations. 3rd ed. Littleton: Publishing Sciences Group; 1977.
     c) *Editor, compilador, director o autor:* Rhodes AJ, Van Rooyen CE, comps. Textbook of virology for Students and practitioners of medicine and other health sciences. 5th ed. Baltimore: Williams & Wilkins; 1968.
     d) *Capítulo de un libro:* Weinstein L, Swartz MN. Pathogenetic properties of invading microorganisms. En: Sodeman WA, Jr, Sodeman WA, editores. Pathologic Physiology: Mechanisms of disease. Philadelphia: WB Saunders; 1974. p. 457-72.
     e) *Conferencias:* Yalow RS. New insights with radioimmunoassay. Special Lecture. Western Association of Physicians, 1 Feb. 1978, Carmel, California. National Center for Health Statistics.
     f) *Artículos en periódicos ordinarios (no revistas médicas):* Shaffer RA. Advances in chemistry are starting to unlock mysteries of the brain: Discoveries could help cure alcoholism and insomnia, explain mental illness. The Wall Street Journal. 12 Agost 1977, 1 (col. 1), 10 (col. 1).

7. **Imágenes.** Las fotografías se seleccionarán cuidadosamente, procurando que sean de buena calidad (300 píxeles/pulgada y 8 cm de ancho como mínimo) y deben enviarse en un formato que se pueda modificar. Se omitirán las que no contribuyan a una mejor comprensión del texto. Las fotografías y las gráficas irán con números arábigos de manera correlativa y conjunta, como figuras.

   Si se reproducen fotografías o datos de pacientes, estos no deben ser identificativos del sujeto. En todos los casos, los autores deben haber obtenido el consentimiento informado escrito del paciente que autorice su publicación, reproducción y divulgación en soporte papel y en Internet en *Nutrición Hospitalaria*.

   Asimismo, los autores son responsables de obtener los oportunos permisos para reproducir en *Nutrición Hospitalaria*, material (texto, tablas o figuras) publicado previamente.

8. **Tablas.** Las tablas se presentarán al final del manuscrito, después de la bibliografía, en hojas aparte que incluirán: a) numeración de la tabla en números romanos; b) enunciado (título) correspondiente, y c) una sola tabla por página. Se procurará que sean claras y sin rectificaciones; las siglas y abreviaturas se acompañarán siempre de una nota explicativa al pie. Si una tabla ocupa más de una hoja se repetirán los encabezamientos en la hoja siguiente.

CONSIDERACIONES ÉTICAS

Autoría. En la lista de autores deben figurar únicamente aquellas personas que cumplan cada uno de los siguientes requisitos:

1. Haber participado en la concepción y realización del trabajo que ha dado como resultado el artículo en cuestión.
2. Haber participado en la redacción del texto y en sus posibles revisiones.

3. Haber aprobado la versión que finalmente va a ser publicada.

CONFLICTO DE INTERESES

Los autores deben describir cualquier relación financiera o personal que pudiera dar lugar a un conflicto de intereses en relación con el artículo publicado. Incluso si los autores consideran que no los hay, deberán indicarlo.

RESPONSABILIDADES ÉTICAS

Cuando se describen experimentos que se han realizado en seres humanos se debe indicar si los procedimientos seguidos se conformaron con las normas éticas del Comité Ético de Investigación Clínica (institucional o regional) y de acuerdo con la Asociación Médica Mundial y la Declaración de Helsinki (http://www.wma.net/en/30publications/10policies/b3/). No se deben utilizar nombres, iniciales o números de hospital, sobre todo en las figuras.

Cuando se describen experimentos en animales, se debe indicar si se han seguido las pautas de una institución o consejo de investigación internacional, o una ley nacional reguladora del cuidado y la utilización de animales de laboratorio.

CONSENTIMIENTO INFORMADO

Los autores deben mencionar en la sección de Métodos que los procedimientos utilizados en los pacientes y controles han sido realizados tras la obtención del consentimiento informado. Si se reproducen fotografías o datos de pacientes (incluyendo los nombres, iniciales, o nombre del hospital de los pacientes), éstos no deben ser identificativos del sujeto. En todos los casos, los autores deben haber obtenido el consentimiento informado escrito del paciente (o del padre o tutor en caso de pacientes menores) que autorice su publicación, reproducción y divulgación en soporte papel e Internet. Del mismo modo, los autores deberán declarar que se han seguido los protocolos establecidos por sus respectivos centros sanitarios para acceder a los datos de las historias clínicas a los fines de poder realizar este tipo de publicación con finalidad de investigación/divulgación para la comunidad científica.

PROCESO EDITORIAL

Los trabajos serán enviados a través de www.nutricionhospitalaria.org, asignándoles un número de referencia. Este número debe usarse en todas las comunicaciones con la Editorial. Una vez los artículos hayan sido validados (es necesario enviar todos los documentos requeridos y cumplimentar aquellos que sean necesarios) pasarán al proceso de evaluación que realiza el Comité de la revista. Las consultas referentes a los manuscritos y al proceso editorial en el que se encuentran pueden hacerlas a través de la web de la revista.

El Comité de Redacción podrá rechazar un artículo para su publicación en la revista sin ser necesario que pase el proceso de revisión por pares, si este es poco probable que se acepte. La evaluación será anónima y los nombres de los autores ni su procedencia deben aparecer en ninguno de los documentos ("artículo sin identificación"): el artículo será enviado a un mínimo de dos revisores que emitirán su dictamen en un plazo inferior a un mes. Después de la revisión, el artículo podrá ser aceptado, o se puede pedir que sea modificado, especificando los cambios que son necesarios en cada caso (plazo: 3 meses máximo). En este último caso, después de volver a evaluar el manuscrito modificado, el Comité emitirá una nueva respuesta. Para facilitar la labor del Comité, los autores marcarán mediante subrayado los cambios realizados solicitados en su manuscrito.

Una vez el artículo haya sido aceptado y previo a su publicación, se enviará al autor de correspondencia las pruebas de imprenta de su artículo. Esta debe revisarse detenidamente, señalar posibles erratas y devolverla corregida a través de la plataforma en un plazo máximo de 48 horas. Una vez transcurrido este plazo, y si no se ha recibido respuesta por parte del autor correspondiente a las galeradas, se considerará que se dan por válidas por parte del autor y la revista las publicará conforme a la prueba remitida para corrección.

Las correcciones solicitadas deben ser mínimas; solamente se admitirán modificaciones en relación con la sintaxis y la comprensión semántica del texto. El Comité Editorial se reserva el derecho de admitir o no las correcciones efectuadas por los autores en la prueba de impresión.

ABONO EN CONCEPTO DE FINANCIACIÓN PARCIAL DE LA PUBLICACIÓN

En el momento de aceptarse un artículo original o una revisión no solicitada, se facturará la cantidad que se haya estipulado en ese momento + impuestos para financiar en parte la publicación:

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