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SOCIEDAD ESPAÑOLA DE NUTRICIÓN CLÍNICA Y METABOLISMO

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La bioimpedancia como herramienta útil para el estudio de hidratación y composición corporal en pacientes con enfermedad renal crónica

Bioimpedance as a useful tool for the study of hydration and body composition in patients with chronic kidney disease

Existe una alta prevalencia de enfermedad renal crónica (ERC) a nivel mundial (1) y a medida que progresa la proporción de pacientes que presentan desgaste proteico energético aumenta. Conseguir prevenir su aparición solo puede conseguirse estableciéndose una monitorización adecuada del estado de nutrición, donde la composición corporal juega un papel determinante para su evaluación.

Dado que no existe una herramienta única para el diagnóstico del desgaste proteico energético (DPE), debemos aglutinar las más sencillas, reproducibles, no observador dependiente, con coste adecuado y que nos sean de utilidad para tomar decisiones en la práctica clínica (2).

Para el estudio de composición corporal el "gold standard" es el DXA para medir directamente los compartimentos graso, magro, muscular y mineral, pero no el agua corporal. Tiene el inconveniente de su coste elevado, que no es portátil y que lógicamente se suele tener en algún servicio centralizado y su accesibilidad no siempre es fácil (Fig. 1).

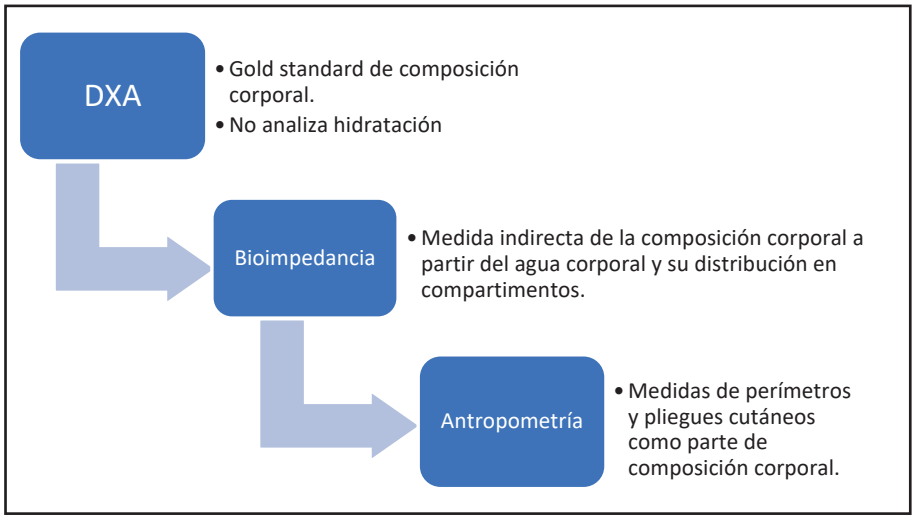

Figura 1.

Distintas herramientas para evaluar composición corporal.

editorial

El principio de la bioimpedancia es considerar el cuerpo como un condensador cilíndrico (único en total) y (5 en segmental), y, a través de unos electrodos, hacer pasar una corriente a voltaje único de 50 khz (monofrecuencia) o con distintas frecuencias (multifrecuencia) que nos darán los mismos parámetros que se unificarán para dar la composición corporal partiendo de la hidratación.

El desarrollo de la bioimpedancia en sus distintas versiones nos ha ofrecido una herramienta sencilla, de coste razonable, que fundamentalmente mide resistencia, reactancia y ángulo de fase, y con ello el estado de hidratación a través del agua corporal total y su distribución en los diferentes compartimentos; a partir de estas medidas, nos calcula la masa celular, masa magra, masa grasa y muscular a través de fórmulas desarrolladas. En la evolución de las diferentes versiones de los *softwares* se han ido incluyendo parámetros como medida de grasa visceral, contenido mineral óseo, tasa de filtrado glomerular o agua intravascular, intersticial o transcelular en los más desarrollados. Existen estudios en los que se han comparado las diferentes BIAS estableciendo concordancias entre ellas y con el "gold estándar" como en el artículo que se publica en este número de la revista *Nutrición Hospitalaria* (2-5).

Así pues, la primera condición para interpretar la BIA es ver el estado de hidratación para poder saber si se sobreestima o subestiman los parámetros calculados (6-8). En pacientes con ERC no en diálisis, conocer el agua corporal total y su distribución es básico para interpretar aparición de edemas, HTA volumen dependiente y cociente agua extracelular/intracelular que nos va a dar la respuesta a diuréticos. En pacientes en HD y DP también nos dará la tolerancia a ultrafiltración, completándola con parámetros bioquímicos de nutrición e inflamación (9-12).

Manteniendo al paciente próximo a la normohidratación y dado que cada paciente es control de sí mismo podemos ver la variación de la composición corporal y con ayuda de la antropometría (si tenemos personal entrenado para ello) corroborar el diagnóstico con la medida de pliegues y circunferencias.

Se debe de considerar la contribución de la BIA a la hora de analizar los compartimentos de masa magra, grasa y muscular ayudando a la detección de sarcopenia y DPE.

Cabe resaltar que existe evidencia de que algunos parámetros como el ángulo de fase o el cociente agua extracelular/intracelular, así como la hiperhidratación, como se refiere en uno de los artículos de este número, se consideran como parámetros predictores de mortalidad cuando aparecen alterados (10-13). En pacientes incidentes en hemodiálisis puede ayudar a conservar la función renal residual si su uso es optimizado, evitando ultrafiltración excesiva.

Por todo ello la BIA es una herramienta útil y de fácil manejo para detectar malnutrición a través de cambios en la composición corporal, siendo útil en el caso de pacientes con enfermedad renal crónica, tanto antes de entrar como en la etapa de terapia renal sustitutiva como muestra el estudio CRIC.

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ARÁN

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Trabajo Original

Nutrición artificial

Evaluación del uso de la brida nasal en la práctica habitual

Evaluation of the use of nasal bridle in clinical practice

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Resumen

Introducción: la brida nasal (BN) es una de las estrategias para evitar el desplazamiento de las sondas para nutrición enteral (NE) utilizadas en el curso de una intervención nutricional.

Objetivos: revisar la eficacia y la seguridad de la colocación de la BN en una población de pacientes que precisan NE por sonda. Analizar sus características clínicas e identificar las complicaciones relacionadas con este procedimiento.

Métodos: estudio observacional, retrospectivo en condiciones de práctica clínica habitual, incluyendo pacientes ingresados en un hospital de segundo nivel, portadores de sonda para NE, que hayan precisado la utilización de un sistema comercial CORGRIP NG/NI TFEEDING TUBE RETENTION SYSTEM de BN.

Resultados: se analizan 51 pacientes con una edad media de 73 años (37-96); el 64,7 % eran varones. La disfagia orofaringea (DOF) fue la indicación fundamental para la colocación de la sonda de NE (54,9 %), seguida del rechazo de la ingesta (17,6 %) y la intubación orotraqueal (7,8 %), entre otras. La BN fue retirada en el 7,8 % de los casos por cambio de acceso digestivo (gastrostomía), en el 21,6 % por paso a la vía oral y en el 9,8 % por desconocimiento de su manejo. Evidenciamos diferencias significativas entre los arrancamientos accidentales y las autorretiradas de las sondas antes y después de la colocación de la BN (2,59 ± 1,512 *vs.* 0,24 ± 0,596; $p < 0,05$). No se registraron complicaciones relacionadas salvo un caso de úlcera cutánea.

Conclusiones: la BN es un sistema de retención seguro y eficaz en la prevención de desplazamientos y retiradas de la sonda en los pacientes con amplia variedad de patologías. Formar a los profesionales sanitarios es imprescindible para su adecuada utilización.

Palabras clave:

Brida nasal. Nutrición enteral. Sonda de alimentación. Retirada inadvertida de la sonda de alimentación.

Abstract

Introduction: the nasal bridle (NB) is one of the strategies to avoid the displacement of tubes for enteral nutrition (EN) used during a nutritional intervention.

Objectives: to review the efficacy and safety of NB placement in a patient population requiring EN by tube feeding. To analyze their clinical characteristics and identify complications related to this procedure.

Methods: a retrospective observational study in usual clinical practice including patients admitted to a second-level hospital with EN catheters who required the use of a commercial NB—CORGRIP NG/NI TFEEDING TUBE RETENTION SYSTEM.

Results: 51 patients with a mean age of 73 years (37-96) were analyzed; 64.7 % were men. Oropharyngeal dysphagia (OPD) was the fundamental indication for placement of an EN tube (54.9 %) followed by refusal to ingest (17.6 %), and orotracheal intubation (7.8 %), among others. NB was withdrawn in 7.8 % of cases due to change in digestive access (gastrostomy), in 21.6 % because of transition to the oral route, and in 9.8 % due to ignorance on how to use it. We found significant differences between accidental removal and self-withdrawal of probes before and after BN placement (2.59 ± 1.512 vs 0.24 ± 0.596; $p < 0.05$). No related complications were recorded except for only one case of skin ulcer.

Conclusions: NB is a safe and effective retention system for the prevention of probe displacement and withdrawal in patients with a wide variety of pathologies. Training health professionals is essential for proper use.

Keywords:

Nasal bridle. Enteral nutrition. Tube feeding. Inadvertent feeding tube dislodgement.

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INTRODUCCIÓN

La intervención nutricional juega un papel fundamental en la prevención y tratamiento de la desnutrición relacionada con la enfermedad (DRE) y debe siempre formar parte del cuidado integral de todos los pacientes (1). La nutrición enteral (NE) administrada por sonda nasogástrica, sonda nasoentérica u ostomía (gastrostomía o yeyunostomía) resulta ser una de las estrategias más empleadas en el tratamiento médico nutricional (TMN).

La NE está indicada en los pacientes desnutridos o en riesgo de desnutrición que tienen un tubo digestivo funcionante pero que son incapaces de mantener un estado nutricional adecuado mediante la ingesta oral voluntaria. Los pacientes con pérdida de apetito y patologías crónicas que no pueden cubrir sus requerimientos con alimentación natural o artificial por via oral, las situaciones clínicas que cursan con disfagia orofaríngea (DOF) moderada o grave que condiciona alteraciones de la seguridad y eficacia de la alimentación e hidratación del individuo, y que no se pueden tratar con técnicas de compensación del bolo alimentario (modificaciones de la textura, la viscosidad y el volumen), y los pacientes quirúrgicos y críticos son los candidatos que más habitualmente se benefician de la utilización de esta técnica de nutrición artificial (2).

El aumento de la esperanza de vida y la elevada presencia de la DRE entre la población mayor, la creciente prevalencia de la patología oncológica y neurológica, y la mayor sensibilidad de los profesionales sanitarios en la lucha contra la DRE, entre otras razones, están condicionando un mayor uso de la nutrición enteral por sonda nasogástrica (SNG) o nasoenteral (SNE) como parte del TMN según la recomendación de las diferentes guías clínicas, tanto en el ámbito hospitalario como en el domiciliario (3-5). Además, otras circunstancias, como el reciente tsunami vivido por la pandemia de la COVID-19, han puesto en evidencia esta observación (7).

Se estima que alrededor del 6 % de los pacientes ingresados en un centro hospitalario requieren NE por SNG o SNE (8). Cada vez se hacen más evidentes los problemas asociados a su uso, como arrancamientos y salidas accidentales involuntarias de las mismas. Según diferentes estudios, entre un 40 % y un 62 % (9,10) de las sondas colocadas sin sistemas de retención se desplazan. En los casos de pacientes críticos, el porcentaje de salidas de la sonda oscila entre un 33 % y un 53 %, impactando en la evolución de estos pacientes en muchas ocasiones (11). Algunos autores llaman la atención sobre la necesidad de su reemplazamiento en un 30-50 % de los casos, con las implicaciones de cuidados de salud y costes que estos procedimientos tienen (12). Entre un 28 % y un 59 % de los pacientes requieren hasta tres reemplazos de sonda; además, el riesgo de una nueva pérdida aumenta entre el 2,1 % y el 32 % cuando ha habido una perdida anterior, y el riesgo de neumonía aumenta del 5 % al 36 % después de más de tres reemplazamientos (13,14).

La salida de la sonda de nutrición enteral implica riesgos para la salud del paciente y no solo los que acabamos de comentar; además, limita el poder alcanzar los objetivos terapéuticos nutricionales o los retrasa en el tiempo y aumenta el riesgo de broncoaspiraciones y de molestias durante su reemplazamiento. En muchas ocasiones expone a mayor cantidad de radiación a los pacientes tras las comprobaciones radiológicas necesarias de la colocación de la sonda, sin olvidar la situación de estrés a la que se ve sometido el paciente cada vez que se le recoloca una sonda (13). También, en ocasiones, supone un riesgo para la salud de los profesionales sanitarios, como hemos podido comprobar durante la pandemia de la COVID-19 por la exposición a los aerosoles que se generan durante el procedimiento. Y, por supuesto, no podemos olvidar el aumento de los costes directos (mayor número de radiografías de comprobación, incremento del número de ingresos en Urgencias, inversión de tiempo evitable en el trabajo de enfermería, etc.), los indirectos (disminución de la asistencia laboral del paciente o los familiares por incidencias, infranutrición y deterioro de la situación basal) y los intangibles en relación a la peor calidad de vida y al impacto emocional en los pacientes (13,15).

Se han descrito distintas estrategias para evitar el arrancamiento y la salida accidental de las SNG y SNE, que van desde la intervención directa de los equipos de enfermería con técnicas de vigilancia estrecha, distracciones y persuasión del paciente, pasando por la colocación de manoplas hasta el lazo o la brida nasal (13,15). La revisión sistemática realizada por Brugnolli y cols. (16) en 2014, sobre los sistemas de sujeción de sondas nasogástricas en adultos, concluyó que, si bien estas intervenciones se realizan en un número importante de pacientes, los datos son insuficientes para sugerir una técnica, dispositivo o método que sirva para evitar la salida accidental o el arrancamiento de las SNE frente a otro.

La colocación de una brida nasal es uno de los procedimientos más utilizados. Una brida es un material alargado que se introduce por una narina, gira en la pared posterior del *septum* nasal y se extrae por la narina contralateral, permitiendo sujetar la sonda (17). Su primera descripción fue realizada en 1980 por Armstrong y colaboradores (18). Estos autores definen la técnica por la que se coloca algún tipo de ancla (sonda de alimentación adicional, cinta umbilical o tubo de goma) alrededor del hueso del vómer o del tabique nasal. La brida se coloca mediante una variedad de métodos y el resultado final es un anclaje a través de una fosa nasal, alrededor del tabique nasal y saliendo por la otra fosa nasal. Ambos extremos de la brida se aseguran juntos al tubo nasoentérico cerca de las fosas nasales, sujetos con una abrazadera que coindice con los French de la sonda nasoentérica. Se han utilizado muchos tipos diferentes de anclajes con diversos grados de éxito. Sin cinta adhesiva en la nariz, la frente o las mejillas, es menos probable que la brida nasal interfiera con heridas, quemaduras, tubos orotraqueales o dispositivos de las vías respiratorias orales (11). En 2009, Gunn y cols. (19) describieron una nueva técnica de brida nasal utilizando un sistema comercial de recuperación magnética unido a una cinta umbilical de 1/8 pulgadas para asegurar las sondas nasoentéticas (Applied Medical Technology, Brecksville, OH, EE UU) con buenos resultados. Las bridas nasales redujeron la extracción accidental de la sonda de un 36 % a un 10 %.

Los sistemas de retención de sondas nasoyeyunales se han prodigado en los últimos años, especialmente en los pacientes pediátricos y en los adultos críticos. Seder y cols. (20), en un ensayo clínico controlado comparando la evolución de pacientes críticos adultos con sondaje nasoentérico con y sin brida nasal, demostraron que, en el grupo de los pacientes con brida, se desprendieron involuntariamente menos sondas que entre los que no tenían brida (18 % frente a 63 %, p < 0,001) y el porcentaje de calorías administradas fue mayor en el grupo de pacientes con brida (mediana del 78 % frente al 62 %, p < 0,016). Un metaanalisis publicado en 2014 (9), que revisa la seguridad de los sondajes con las bridas nasales frente a la simple fijación con sistemas adhesivos en la nariz u otras regiones de la cara, concluye que las bridas nasales parecen ser más efectivas para asegurar las SNE y prevenir sus desplazamientos que la utilización tradicional de la adhesión a la piel para su fijación *(odds ratio* [OR], 0,16; intervalo de confianza [IC] del 95 %, 0,10-0,27; $p <$ 0,01). El uso de bridas nasales se asociaba a una mayor ratio de complicaciones, comparada con las complicaciones en la piel provocadas por los sistemas adhesivos (OR, 4,27; IC 95 %, 1,79-10,23; $p < 0,01$). La incidencia de sinusitis no fue diferente en ambos grupos (OR, 0,26; IC 95 %, 0,03-2,28; $p = 0,22$). Se han descrito nuevos resultados positivos en estudios posteriores de pacientes críticos adultos, mostrando una asociación independiente de la utilización de la brida nasal con una reducción del 80 % en la pérdida inadvertida de la SNE *(odds ratio* (OR): intervalo de confianza (IC) del 95 %: 0,2: 0,12-0,33, p < 0,0001); mayor duración del uso de la sonda (2,2 días, IC del 95 %: 0,7-3,7, p = 0,004); y una probabilidad casi tres veces mayor de que se utilicen las sondas hasta que ya no se necesiten (OR: 2,8, IC del 95 %: 1,9-4,3, p < 0,0001) (11). La revisión de 3 meses de una unidad de críticos mostró que la colocación de la brida en el primer día de sondaje aseguraba una significativa reducción de las salidas involuntarias de las sondas y una mayor duración del uso de las sondas y la probabilidad de que la sonda alcance la redundancia cuando no requiere más tiempo, con las implicaciones que esto puede tener en la recuperación de los pacientes (11).

Un reciente estudio también ha demostrado los beneficios del sistema de sujeción de la brida nasal en una población pediátrica tras una laringotraqueoplastia, reduciendo significativamente los desplazamientos de las sondas de nutrición; registraron una incidencia de salidas accidentales de la sonda de 9,4 por 100 días en los pacientes sin brida nasal y de 0 en el grupo con brida (IC del 95 %: 6,0-14,0) y 0,0 (IC del 95 %: 0,0-1,9), y una menor exposición radiológica de los menores, así como una reducción de los días de estancia hospitalaria (21).

Como hemos comentado anteriormente, los pacientes que han sufrido un accidente cerebrovascular y presentan disfagia orofaríngea precisan una sonda nasogástrica para la hidratación y nutrición, y para asegurar la toma de la medicación. Brazier y cols. (22) auditaron las extracciones involuntarias de sondas, los métodos utilizados para la sujeción (cinta adhesiva, manoplas, observación especial), las demoras incurridas en la administración de la medicación y la nutrición enteral y los costes. Concluyeron que el 75 % de los pacientes habían perdido la sonda nasogástrica con o sin los métodos de sujeción auditados y esto había contribuido a un retraso significativo de la administración de la medicación de entre 1 y 4 h, a una reducción de la vida útil para la administración de la NE y a un aumento de los costes directos, estimando que se podrían haber ahorrado un 55 % (5979 £) de estos si se hubieran utilizado bridas nasales.

Una revisión realizada para evaluar la efectividad y la aceptabilidad de las manoplas y la brida nasal por parte de pacientes que habían sufrido un ictus y sus familiares, mostró que mas allá de la necesidad de conseguir disponer de evidencia sobre este extremo, que en el momento actual no existe, se hace necesario elaborar protocolos y guías de actuación sobre su utilización, siendo necesario en el proceso de toma de decisiones alcanzar el consenso entre profesionales sanitarios, paciente y/o familiares sobre el mejor método en cada caso para evitar el arrancamiento involuntario o no de las sondas del paciente (23).

Sin embargo, y a pesar de estos buenos resultados comunicados, creemos que el subjetivo aumento percibido del riesgo asociado al uso de la brida nasal como mecanismo retenedor (epistaxis posterior, aparición de sinusitis, daño del septo) ha limitado probablemente su utilización por el personal sanitario en nuestro entorno.

OBJETIVOS

Objetivo principal: revisar la eficacia y la seguridad de este procedimiento en nuestro hospital en una población de pacientes que precisan TMN con NE.

Objetivos secundarios:

- Analizar las características clínicas de los pacientes subsidiarios de colocación de una brida nasal.
- Identificar las complicaciones relacionadas con este procedimiento.

MÉTODOS

Estudio observacional retrospectivo en condiciones de práctica clínica habitual en pacientes críticos y no críticos, mayores de 18 años, que precisan, por indicación de su médico responsable, recibir TMN con NE, portadores de sonda nasogástrica y nasoenteral, y que hayan acreditado en su historia el riesgo de arrancamiento accidental repetido, voluntario o fortuito, de la misma durante procesos de agitación o desorientación, o en los que la salida de la sonda implique necesidad de usar técnicas sofisticadas o invasivas para su recolocación (SNY, SNE), resultando estos pacientes subsidiarios de ser tratados con sistema de retención de brida nasal. Se evaluaron los pacientes ingresados en el Hospital Universitario Príncipe de Asturias (HUPA) del 1 de febrero de 2020 al 1 de febrero de 2021.

El equipo de enfermería de la Unidad de Nutrición Clínica y Dietética (UNCyD) del centro fue el encargado de la implantación del total de bridas que se colocaron en todo el centro. El tipo de brida nasal que se utilizó corresponde al sistema comercial COR-

GRIP NG/NI FEEDING TUBE RETENTION SYSTEM de recuperación magnética unido a una cinta umbilical de 1/8 pulgada (Fig. 1). Resulta ser el único disponible en nuestro país y está distribuido por la compañía Griffols.

La técnica de embridar con este sistema consiste en introducir la guía de la brida previamente lubricada por una narina y atravesar la cavidad nasal hasta aproximadamente 7-8 cm, pasando el *septum* e introduciéndose en la nasofaringe. Posteriormente, se introduce la combinación del catéter-fiador por la otra narina. Una vez introducido, se retira el fiador y los imanes de la guía y el catéter se unen, escuchándose un "clic". Entonces se puede retirar la guía (10).

Cada *set* lleva dos juegos de abrazadera que deben coincidir con los French de la sonda colocada y una púa que se utiliza para poder liberar la abrazadera sin necesidad de cortar la brida (Fig. 2). La colocación de esparadrapo alrededor de la sonda para evitar la movilización de la abrazadera se puede realizar de manera sistemática (Fig. 3). En esta dirección web, una de las firmantes de este trabajo realiza una simulación de cómo se debe realizar esta técnica de colocación en la práctica (https://youtu.be/dKDU4JBTqNI).

Figura 1.

Set comercial de la brida nasal: dos fiadores, uno de ellos con algodón enhebrado; púa (pieza triangular); dos juegos de abrazadera.

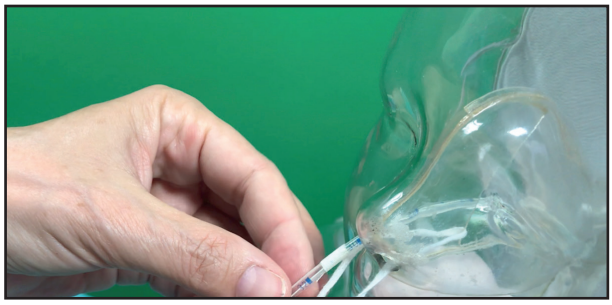

Figura 2.

Circular de esparadrapo de tela en el lugar de colocación de la abrazadera.

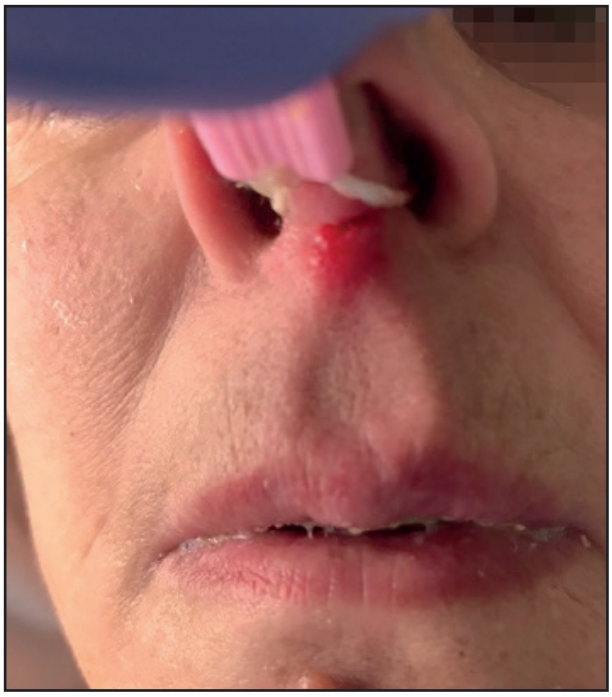

Figura 3.

Úlcera por presión provocada por la excesiva tensión del la brida nasal sobre el *septum.*

Se recogieron las siguientes variables de la historia clinica electrónica (sistema HCIS) de los pacientes incluidos: edad, sexo, patología por la que requirieron la SNG o SNE, motivo de colocación de la brida, número de salidas de sonda (accidentales o por arrancamiento) antes y después de la colocación de la brida y posibles complicaciones asociadas, durante las hospitalizaciones y en el periodo ambulatorio, hasta la finalización del soporte nutricional enteral o hasta el momento de la revisión si se mantenía el soporte con sonda. En el caso de que se mantuviese la nutrición por sonda al alta, se realizó un seguimiento en el sistema HCIS y HORUS (plataforma informática que permite a los profesionales sanitarios del Servicio Madrileño de Salud compartir información clínica de los pacientes que hayan sido atendidos en centros de nuestra red sanitaria, independientemente de donde se haya generado la información, de quien la haya generado y del lugar en que esté almacenada) para registrar posibles notificaciones de incidencias (complicaciones, salidas o retiradas de sonda).

ANÁLISIS ESTADÍSTICO

El tamaño muestral de este estudio está constituido por todos los pacientes evaluados en el centro que hayan tenido colocada una brida nasal durante el periodo de estudio establecido.

El análisis de los datos se realizó utilizando el programa de análisis estadístico IBM SPSS Statistics 27.0. Se realizó un análisis descriptivo de las variables recogidas en el estudio.

Para describir las variables cualitativas se calcularon las frecuencias relativas y absolutas. En el caso de las variables cuantitativas se calcularon las medidas de centralidad y dispersión (media, mediana, desviación estándar, error estándar, cuartiles, rango, mínimo y máximo). Se evaluó la distribución normal de los datos cuantitativos. Para ambos tipos de variables, las estadísticas descriptivas se calcularon en base a datos válidos, es decir, no habrá procesamiento de datos faltantes. Para el contraste de hipótesis, las pruebas univariadas empleadas fueron la del chi cuadrado para variables cualitativas y las pruebas t de Student y ANOVA para variables cualitativas dicotómicas y no dicotómicas, respectivamente. Se estableció un intervalo de confianza del 95 % para determinar la significación estadística.

ASPECTOS ÉTICOS Y LEGALES

El estudio se ha llevado a cabo de acuerdo con las normas de buena práctica clínica, descritas en las directrices tripartitas armonizadas de GCP (Conferencia Internacional sobre Armonización, ICH, 1996). Con el fin de preservar la confidencialidad de los datos de cada participante del estudio, todas las herramientas electrónicas, así como los documentos impresos utilizados, fueron codificados de tal forma que no puedan vincularse a ningún participante, disponiendo de un formulario de trazabilidad para el seguimiento adecuado del paciente. Este formulario de trazabilidad fue guardado y protegido mediante contraseña por dos miembros del equipo investigador. Además, se ajustó la gestión de estos datos al Reglamento del Parlamento Europeo y del Consejo, de 27 de abril de 2016, relativo a la protección de las personas físicas en lo que respecta al tratamiento de datos personales y la libre circulación de dichos datos, y en aquellos aspectos que no estén estipulados se siguió la vigente Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos de Carácter Personal y garantía de los derechos digitales.

El estudio fue aprobado por el CEIM (Comité de Ética de la Investigación con Medicamentos) del Hospital Universitario Príncipe de Asturias.

RESULTADOS

Durante el periodo de estudio se colocó a 51 pacientes una sonda nasogástrica o nasoenteral con el sistema de sujeción de brida nasal, de los cuales 18 eran mujeres y 33 hombres. La mediana de edad de los sujetos estudiados fue de 73 años (37-96) (la media es 72 ± 14,828). La patología de base de los pacientes queda recogida en la figura 4, siendo en nuestra muestra el grupo más numeroso los pacientes que presentaban un accidente cerebrovascular agudo (ACVA) (29,4 %) y los que tenían deterioro cognitivo en distintos grados de evolución (21,6 %). La indicación de la utilización de la sonda nasogástrica o nasoenteral para la administración de la NE se estableció en un 54,9 0% de la muestra por la presencia de DOF de origen neurológico, en el 17,6 % por rechazo de la ingesta; la disfagia mecánica en neoplasias de cabeza y cuello con progresión tumoral o parálisis de cuerdas vocales fue la causa de indicación de nutrición enteral por SNG en un 7,9 %. Por último, 4 pacientes (7,8 %) eran casos críticos con intubación orotraqueal.

La indicación de colocación de la brida fue consensuada por el equipo de enfermería, los médicos responsables y el paciente o la familia, según la situación individual de cada uno. Se evaluó el motivo de indicación de la brida nasal, siendo las repetidas salidas accidentales o por autorretirada la causa más frecuente de indicación (88,2 %). En los pacientes con esta indicación, la mediana de salidas de la sonda por paciente hasta la colocación de la brida fue de 3 ± 1,15 (0-8). Tras la colocación de la brida, la mediana de salidas de la sonda fue de 0,00 ± 0,596 (0-3) salidas por paciente hasta la finalización del soporte nutricional con sonda o hasta el periodo de tiempo incluido en el estudio (Fig. 5).

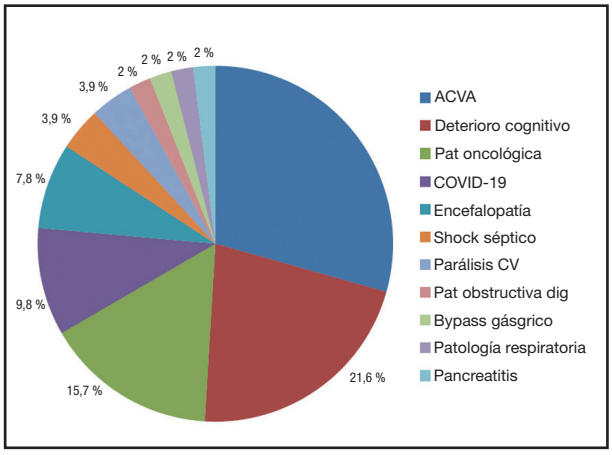

Figura 4.
Patología de base de los pacientes.

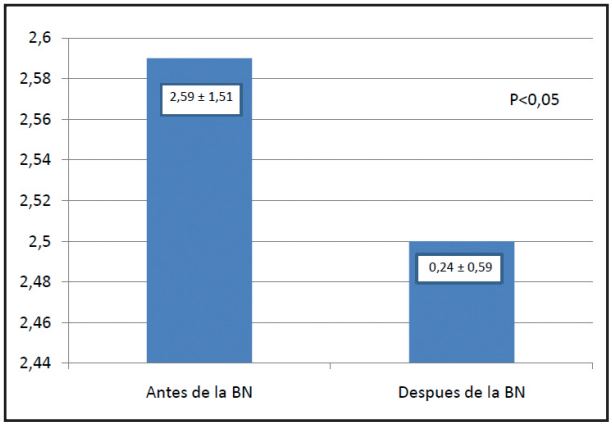

Figura 5.
Número de salidas de sonda por paciente antes y después de la colocación de la brida nasal.

La segunda causa más frecuente de indicación (11,8 %) fue la prevención de la salida de la sonda para evitar recolocaciones de sonda dificultosas (sonda nasoyeyunal, necesidad de colocación de sonda por radiología intervencionista o apoyo de fibroscopio, así como patología tumoral estenosante que comprometa la luz digestiva). Evidenciamos diferencias significativas entre los arrancamientos accidentales y las autorretiradas de las SNG y SNE antes y después de la colocación de la BN (2,59 ± 1,512 *vs.* 0,24 ± 0,596; $p < 0,05$).

La sonda con brida nasal tuvo un tiempo de uso medio de 59,7 días y una mediana de 35 días (3-221). Los motivos de finalización de la nutrición enteral fueron la resolución del motivo de indicación de la misma, la realización de una gastrostomía por indicación de nutrición enteral a largo plazo o el fallecimiento del paciente. En los casos en los que la sonda no se había retirado, se contabilizó el periodo desde la colocación de SNE con brida hasta la finalización de la inclusión de pacientes en el estudio.

Solo en un caso de los 51 pacientes incluidos en el estudio se produjo una complicación cutánea, con el diagnóstico de úlcera por presión en el tabique nasal. La aparición de la úlcera, a los 9 días de la colocación de la brida, se relacionó con un posible exceso de tensión en la implantación (Fig. 3). Se realizaron curas locales de la úlcera con undecilenamidopropil betaína y polihexanida al 0,1 %, y se utilizaron un protector de piel y cobertura de silicona, sin observarse más incidencias relacionadas o complicaciones posteriores de la úlcera. No se registraron epistaxis ni cuadros de sinusitis, ni se notificaron complicaciones relacionadas con la presencia de cuerpo extraño.

En uno de los casos en que el paciente era consumidor activo de cocaína inhalada se realizó una exploración con fibroscopio por parte del Servicio de Otorrinolaringología para comprobar la integridad de las estructuras nasales antes y después de la colocación de la brida, no observándose daños en las mismas.

Ocho pacientes (15,7 %) fallecieron en el curso de su enfermedad siendo portadores de SNG y BN. A 11 pacientes (15,7 %) se les retiró la BN y la SNG porque pasaron a recibir alimentación natural oral y suplementos nutricionales por vía oral, y a 4 pacientes (7,8 %) se les retiró porque precisaron gastrostomía percutánea. En 5 de estos sujetos de la muestra (9,8 %) se retiró la brida por desconocimiento del sistema en el centro sociosanitario o en el servicio de urgencias. En los pacientes que se mantuvieron ingresados no hubo retiradas no justificadas del sistema de brida.

DISCUSIÓN

La brida nasal resulta una técnica de sujeción de sondas nasogástricas y nasoenterales de gran utilidad para evitar la retirada accidental y el arrancamiento en pacientes que precisan TMN con nutrición enteral, especialmente utilizada en población infantil y adultos críticos. Como hemos visto anteriormente, existen dos tipos de brida, con diferencia en la técnica de aplicación. En uno de los tipos, las puntas distales de la brida son desplazadas a través de cada narina, retornando hacia la orofaringe y atándose para forma un nudo. Después se tira del nudo de una de las narinas, acortando, y las puntas distales se tensan para formar la brida. La otra técnica se basa en el uso del CORGRIP NG/FEEDING TUBE RETETNION SYSTEM, un dispositivo que utiliza un sistema magnético para facilitar la formación de la brida alrededor del *septum* nasal. El uso de la brida nasal en el Hospital Universitario Príncipe de Asturias tiene un corto tiempo de trayectoria. El equipo de enfermería de la UNCyD del centro se ha entrenado en la segunda técnica comentada, utilizando el dispositivo de CORGRIP NG.

En nuestro estudio se numeraron las salidas de sonda en el periodo pre y poscolocación de la brida nasal, con una media de 2,59 ± 1,51 salidas previas, y un 81,63 % de los pacientes no tuvieron movilizaciones tras la colocación de la brida. En un estudio con 26 pacientes, la media de salidas fue de 3,6 antes de la colocación de la sonda y este índice se redujo tras la colocación de la brida al 14,2 % de los pacientes (2). Dos de nuestros pacientes fueron capaces de autorretirarse la sonda a pesar de la brida por la posibilidad de introducir el dedo en el espacio de la brida, por lo que una técnica de implantación de la abrazadera más cerca del orificio nasal podría haber evitado la retirada de la sonda (Figs. 6 y 7). La resistencia de este sistema de brida nasal a la fuerza imprimida para un arrancamiento ha sido estudiada por un grupo de investigadores en una cabeza de oveja, resultando ser la brida capaz de resistir hasta 15,5 kg sin producir lesiones en el septo. En este estudio, el sistema de brida pudo fijar la sonda nasogástrica sin deslizamiento o daño a pesos mas altos que la sutura en el tabique anterior, siendo este

Figura 6.
Excesiva distancia de la abrazadera al *septum* nasal.

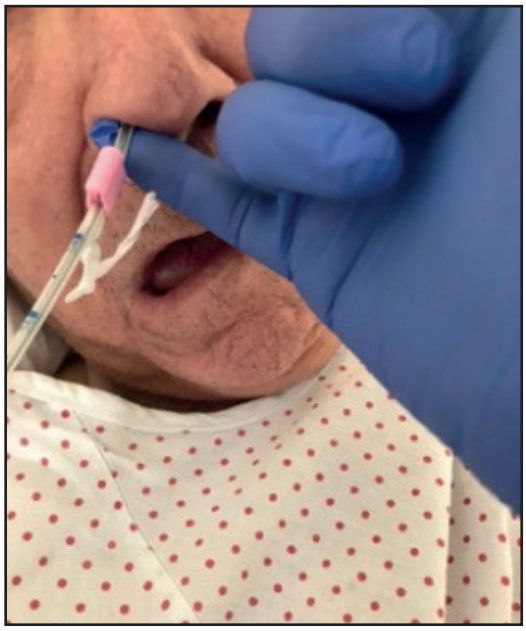

Figura 7.
Comprobación de la excesiva distancia de la abrazadera al *septum* nasal.

sistema utilizado ocasionalmente por los expertos en otorrinolaringología para cirugías complejas. Aunque se requiere profundizar más, investigando este punto, este hecho lo convierte en una estrategia terapéutica adecuada para algunas cirugías de cabeza y cuello (24).

En nuestra muestra se registraron pocas complicaciones y todas de índole menor. La epistaxis menor ha sido una de las principales complicaciones descritas en las series, notificándose hasta en un 21,4 % de los sujetos incluidos en un estudio prospectivo de 28 pacientes (9). Este porcentaje es superior al observado en nuestra muestra, a pesar de que el 35 % de nuestros pacientes habían sufrido un ACVA y en su mayoría se encontraban antiagregados. En la mayoría de las publicaciones se ha relacionado la epistaxis con la técnica de implantación de la brida. Con esta información se podría inferir que una adecuada selección de los pacientes subsidiarios y un entrenamiento adecuado en la técnica de implantación lograrían reducir el riesgo de epistaxis.

Por otro lado, la úlcera por presión en el septo nasal ha tenido una prevalencia de hasta el 13 % en una muestra de 438 pacientes, encontrándose una diferencia estadísticamente significativa con respecto al grupo de control, de pacientes con SNE sin brida (9). En otros estudios no se halló ninguna diferencia estadísticamente significativa (25). Se sugiere que la técnica de colocación puede disminuir el riesgo de aparición de complicaciones cutáneas. La excesiva tensión en la brida puede causar necrosis por presión en el tejido, con consiguiente ulceración. Además, a mayor tiempo de mantenimiento de la sonda, más riesgo de complicación cutánea. En nuestra serie, solo un paciente presento una lesión cutánea.

No se produjeron episodios de sinusitis en nuestra muestra. Tampoco en 57 de los pacientes de dos estudios incluidos en uno de los metaanálisis revisados frente a un 5 % de casos con sondas fijadas con adhesivo, sin encontrarse diferencias estadísticamente significativas entre los dos grupos (9). En nuestra opinión, el entrenamiento para realizar el procedimiento de embridamiento con el dispositivo elegido resulta fundamental para evitar también otras complicaciones no advertidas en el momento de la colocación. Se han descrito casos de lesiones por cuerpo extraño por permanencia del estilete como parte del sistema de la brida (26) o de pérdida y desplazamiento de la pieza magnética (27). Ninguna de estas complicaciones fue advertida en la muestra estudiada.

Nuestro estudio contribuye a aumentar el conocimiento de la utilización de la brida nasal como sistema de sujeción de sondas gástricas y enterales en colectivos de pacientes menos estudiados, ya que la mayoría de los estudios de la literatura se centran en los pacientes críticos adultos y en los pacientes pediátricos. Los sujetos incluidos en el estudio son pacientes adultos en riesgo de desnutrición o desnutridos con patología neurológica (ACVA y/o deterioro cognitivo por enfermedad neurodegenerativa) u oncológica que condicionaba su ingesta. Muchos de estos pacientes sufren salidas accidentales de las sondas por las que reciben medicación, hidratación y nutrición, condicionando menores aportes y un impacto negativo en los tiempos terapéuticos, el estado nutricional y la evolución clínica (20,28).

La falta de conocimiento de este tipo de dispositivos puede condicionar mala praxis, como ocurre cuando se corta el sistema de brida ante problemas locales no relacionados, siendo evitable la retirada de la brida con el uso de la púa (Fig. 8). Se necesitan programas formativos que actualicen esta información a todo el equipo de enfermería y que permitan entrenar a los profesionales de enfermería en la técnica de embridar las SNG y SNE. Así mismo, resulta imprescindible incorporar en los protocolos de actuación de los TMN las consideraciones necesarias que definan la indicación de la colocación de la brida nasal para hacer un uso racional de los recursos y magnificar sus beneficios.

Figura 8.
Liberación de la abrazadera con la púa.

En nuestra muestra, una elevada proporción de pacientes mantuvieron su nutrición enteral con el sistema de retención con brida de forma ambulatoria, permitiéndoles alcanzar los objetivos terapéuticos. En la revisión bibliográfica realizada no se han encontrado muestras de pacientes ambulatorios. Son necesarios ulteriores estudios centrados en el paciente ambulatorio portador de SNE con brida nasal para adquirir más evidencias que nos permitan racionalizar su uso en este grupo poblacional.

CONCLUSIONES Y APLICABILIDAD EN LA PRÁCTICA CLINICA

A pesar de la corta trayectoria en el manejo de la brida nasal en el Hospital Universitario Príncipe de Asturias, consideramos que el beneficio del uso de este dispositivo de sujeción de las sondas es superior al riesgo. La ausencia de complicaciones frecuentes o graves es un fundamento para apoyar el uso de la brida nasal. La disminución de las salidas accidentales o autorretiradas de la sonda puede suponer un beneficio a nivel de la salud física y mental del paciente, evitando sujeciones mecánicas y sobreexposición radiológica, disminuyendo el riesgo de broncoaspiración y optimizando su bienestar. Además, puede suponer beneficios a nivel económico para el sistema porque permite optimizar el uso de recursos.

Un valor añadido de este estudio es la inclusión en nuestra muestra de pacientes hospitalizados agudos no críticos con diferentes patologías, si comparamos con la literatura disponible centrada en paciente críticos adultos y niños. Esta circunstancia nos permite proponer un mayor número de indicaciones para la aplicación de este sistema de retención.

Por otro lado, el conocimiento de la existencia de la brida ofrece una posibilidad de uso como opción intermedia entre la sonda enteral y la decisión definitiva de realización de una gastrostomía para los pacientes cuya evolución clínica y necesidad de nutrición enteral a medio/largo plazo no está clara o si no existe acuerdo entre el equipo sanitario y el paciente y sus familiares en la indicación.

Resulta evidente que la formación de los equipos de enfermería es necesaria para mantener una baja incidencia de complicaciones, realizar el procedimiento de forma adecuada y establecer un uso racional de esta medida.

LIMITACIONES DEL ESTUDIO Y ÁREAS A MEJORAR

El pequeño tamaño muestral del estudio resulta un factor limitante. Sin embargo, consideramos que la escasa información comunicada de pacientes no críticos hasta la fecha sobre la brida nasal hace que este dispositivo tenga una aplicación inferior a su potencial uso, contribuyendo este estudio a construir un cuerpo de evidencia.

De igual modo, al tratarse de un estudio retrospectivo en práctica clínica habitual, en el que se incluye el periodo ambulatorio y hospitalario, la ausencia de seguimiento directo de los pacientes portadores de brida hasta la finalización de la nutrición enteral que pasa a control por su médico de atención primaria, o geriatra en muchos casos, presumiblemente puede condicionar una pérdida de información en relación a las complicaciones que puedan no haber sido recogidas en la historia clínica electrónica a pesar de todos nuestros esfuerzos en encontrarlas a través de la plataforma HORUS.

Dada la falta de conocimiento del sistema observado entre los profesionales sanitarios, se hace imprescindible la implantación de métodos de información y formación para otros servicios como Urgencias y centros sociosanitarios, para evitar perder la brida por desconocimiento del sistema si se requiere un cambio de sonda.

Las enfermeras de la UNCyD del HUPA, aprovechando el interés en las nuevas tecnologías de los programas formativos, han realizado un video de corta duración, explicando las indicaciones, inserción y cuidados enfermeros de la brida nasal, que se ha colgado en la intranet del hospital para poder llegar de forma eficaz y sencilla a todo el personal de enfermería del hospital. Este video también se ha compartido en redes sociales en la dirección https://youtu.be/dKDU4JBTqNI, como hemos comentado al explicar la metodología del estudio en esta publicación.

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Nutrición Hospitalaria

Trabajo Original

Nutrición artificial

Pharmaceutical care at discharge for patients with feeding tubes

Atención farmacéutica al alta para pacientes con sondas de alimentación

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Abstract

Objective: to assess and analyse a medication adaptation pathway for feeding tube administration followed by clinical pharmacists for patients at discharge, and to analyse the level of physician acceptance of the recommendations issued by pharmacists in pharmaceutical care reports to improve patient therapy.

Methods: a multidisciplinary protocol for treatment adaptation to feeding tube administration at discharge was implemented in a 350-bed hospital during 2019, in which pharmacists prepared feeding tube medication-adaptation reports during pharmaceutical care visits. The number of recommendations related to adaptation of a drug to route of administration was recorded and classified as need for change of active substance or change of pharmaceutical form. Physician acceptance of pharmacist recommendations was analysed in a one-year retrospective observational study.

Results: a total of 66 pharmaceutical care visits were recorded for 57 patients (1.2 visits per patient). In 47 of these 66 visits (71.2 %), at least one drug modification was required in a patient prescription, and the median number of drugs per patient needing to be modified was 2. Overall, 93 of the 489 prescribed drugs (19.0 %) required some changes to be suitable for administration via feeding tube: change of active substance in 52.7 % (49/93) of cases, and change of pharmaceutical form in 47.3 % (44/93) of cases. The physicians' level of acceptance of recommendations was 43.0 % (40/93), and change of pharmaceutical form was less accepted than change of active substance.

Conclusion: the inclusion of clinical pharmacists in multidisciplinary teams leads to an improvement in adapting medication to feeding tube administration, but also shows a lack of communication or understanding of pharmacist recommendations by physicians resulting in a low rate of prescription changes.

Keywords:

Patient safety. Medication adaptation. Feeding tube.

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The authors confirm that the principal investigator for this paper is Carmen López Gómez and that she had direct clinical responsibility for the patients.

Accessibility to the data in this article is guaranteed. Please contact the author for correspondence to get them (mail: carmenlopezgomez25@gmail.com).

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Resumen

Objetivo: evaluar y analizar un circuito de adaptación de la medicación para la administración por sonda de alimentación llevado a cabo por farmacéuticos clínicos para pacientes al alta, y analizar el nivel de aceptación por parte de los médicos de las recomendaciones emitidas por los farmacéuticos en los informes de atención farmacéutica para mejorar la terapia de los pacientes.

Métodos: durante el año 2019 se implementó en un hospital de 350 camas un protocolo multidisciplinario de adaptación del tratamiento para la administración por sonda de alimentación al alta, en el cual los farmacéuticos elaboraron informes de adaptación de la medicación por sonda de alimentación durante las visitas de atención farmacéutica. Se registró el número de recomendaciones relacionadas con la adecuación del fármaco a la vía de administración y se clasificaron como necesidad de cambio de principio activo o cambio de forma farmacéutica. La aceptación de las recomendaciones de los farmacéuticos por parte de los médicos se analizó en un estudio observacional retrospectivo de un año.

Resultados: se registraron un total de 66 visitas de atención farmacéutica para 57 pacientes (1,2 visitas por paciente). En 47 de estas 66 visitas (71,2 %) se requirió al menos una modificación de medicamentos en la prescripción de los pacientes, y la mediana de medicamentos por paciente que necesitaban modificarse fue de 2. En total, 93 de los 489 medicamentos prescritos (19,0 %) requirió algunos cambios para ser aptos para la administración por sonda: cambio de principio activo en el 52,7 % (49/93) de los casos y cambio de forma farmacéutica en el 47,3 % (44/93) de los casos. El nivel de aceptación de las recomendaciones por parte de los médicos fue del 43,0 % (40/93), siendo menos aceptado el cambio de forma farmacéutica que el cambio de principio activo.

Conclusión: la inclusión de farmacéuticos clínicos en equipos multidisciplinarios conduce a una mejora en la adaptación de la medicación a la administración por sonda de alimentación, pero también muestra que existe una falta de comunicación o comprensión de las recomendaciones de los farmacéuticos por parte de los médicos, lo que resulta en una baja tasa de cambios en la prescripción.

Palabras clave:

Seguridad del paciente.
Adaptación de medicación.
Sonda de alimentación.

INTRODUCTION

Drug administration through a feeding tube (FT) —performed when oral feeding cannot take place— gives rise to various complications including gastrointestinal intolerance, metabolic or infectious complications, and mostly mechanical complications such as FT obstruction resulting from inappropriate drug administration (1).

Most patients receiving nutritional support through FT suffer from chronic diseases that require long-term pharmacological therapy. Administration of crushed medications is the most common cause of FT obstruction (2), resulting in the need to replace the tube and, in turn, increasing patient morbidity and associated health care costs (3). In addition, tablet crushing alters the mechanism of extended-release of enteric coating formulations, leading to a rapid increase in drug bioavailability (and a greater risk of side effects) (4) as well as to lower blood levels towards the end of the dosing interval (early reoccurrence of symptoms).

Factors affecting drug therapy via FT that should be considered include:

- *Pharmaceutical form:* current guidelines recommend, whenever possible, the use of liquid pharmaceutical forms as they hardly require any manipulation (5,6). Regarding the use of extended-release tablets, the way these pharmaceutical forms act is altered when crushed (5).
- *Administration techniques:* administration techniques may vary depending on the type of drug and its pharmaceutical form. Furthermore, the type of diluent used will differ according to drug bioavailability.
- *Tube access:* access site determines drug absorption and, as the pH in the jejunum becomes more alkaline, this may limit absorption of certain drugs (7). Changes in pH in the digestive tract also affect the degree of drug ionization and therefore the percentage that can be absorbed. Another important factor to consider is osmolarity as hyperosmolar formulations lead to faster transit rates if administered directly in the small intestine (8).

A study published by Givens et al. (9) showed that FT-related complications accounted for almost half of the visits to emergency departments in patients with advanced dementia. It is therefore necessary to review and adapt medications to this route of administration to avoid errors in drug administration (10). In addition, patient and/or caregiver education on how to administer medication, with appropriate monitoring and follow-up systems improving treatment management, are essential.

Regarding the pharmacist's role, a study by Sánchez et al. (11) on pharmaceutical care in patients with enteral nutrition shows that the inclusion of a pharmacist in nutritional support teams helps resolve problems derived from the administration of drugs through FT. Pharmacists have the required knowledge enabling them to assess both nursing staff and patients/caregivers on the availability of appropriate preparations for enteral administration, interactions between drug-enteral nutrition, and potential adverse effects and incompatibilities (12-14).

The aim of this study was to assess a medication adaptation pathway for FT administration followed by clinical pharmacists for patients at discharge. We also aimed to assess and analyse the level of physicians' acceptance of recommendations issued by the pharmacists in pharmaceutical care reports.

METHODS

We conducted a one-year retrospective, observational study at the 350-bed Costa del Sol Hospital in Spain, which provides care to a population of 410.022 inhabitants. The patient population consisted of all patients aged 18 years and older discharged from hospital during 2019 who had an FT inserted for the first time. These patients were monitored for six months following study inclusion, and patient follow-up visits for pharmaceutical care after inclusion were recorded.

A multidisciplinary protocol for treatment adaptation for FT administration at discharge was implemented (Fig. 1). As shown, the pharmacists issued a discharge medication report with recommendations for the prescribing physicians.

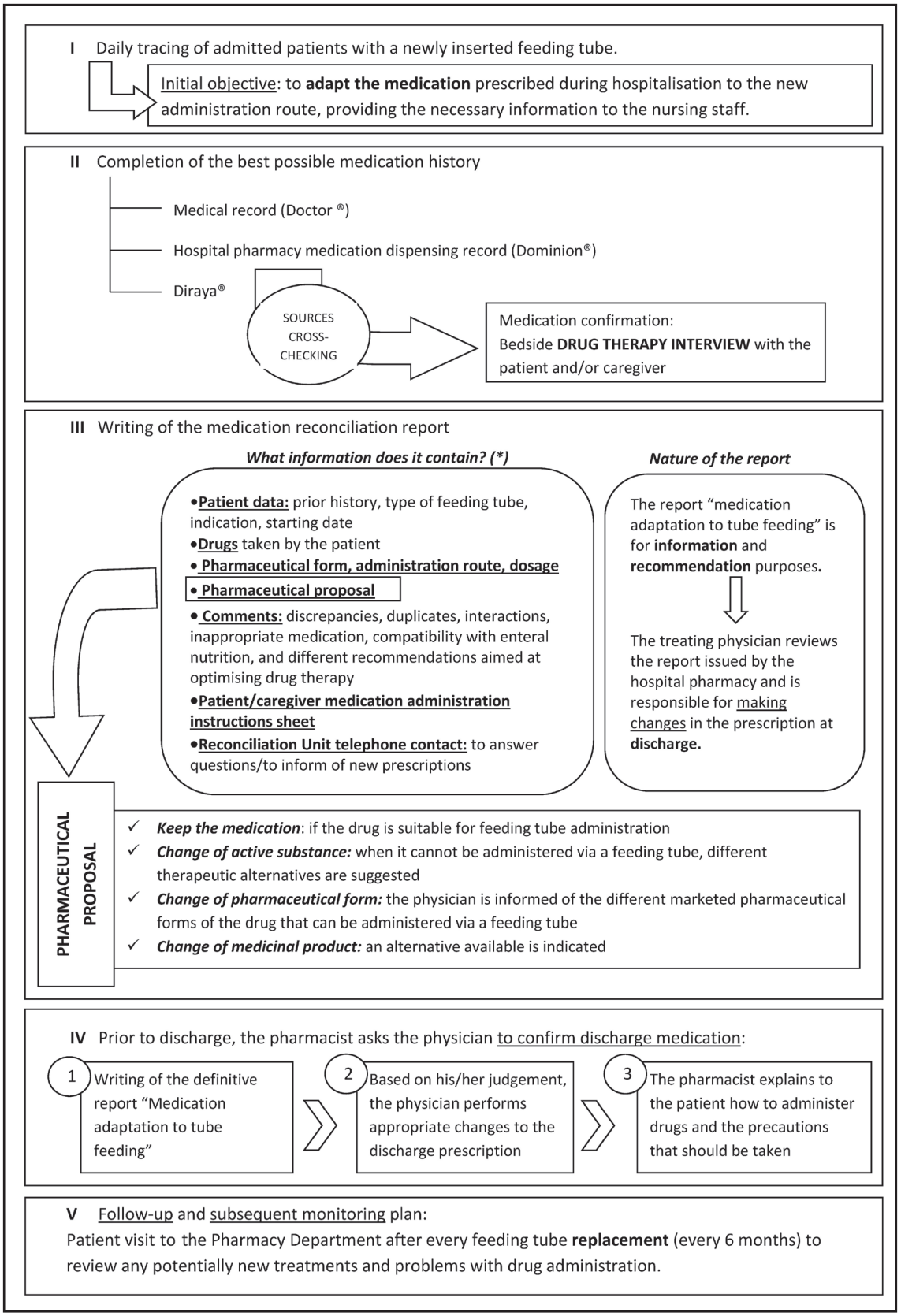

Figure 1.

Multidisciplinary protocol for treatment adaptation to FT administration at discharge.

Additionally, they explained the changes to the patients/caregivers at a pharmaceutical care visit.

All the recommendations issued regarding drug administration via FT were based on published literature (5,6). When no published recommendations for FT administration were available for a specific drug, recommendations were based on the pharmaceutical form and absorption site of the drug, and the prescriber was informed about the lack of published information. A pharmacist report was issued at the first visit and all the follow-up visits.

Demographics (Table I), number of pharmaceutical care visits (first visit and follow-up visits), number of patients requiring changes to at least one drug, and number of recommendations related to adaptation of the drug to the route of administration were recorded. Recommendations were classified as follows:

- *Change of active substance required due to:* tube obstruction problems, drug instability caused by crushing tablet coating, lack of drug compatibility or toxicity studies when manipulating the dosage form (5,6).
- *Change of pharmaceutical form required due to:* absorption alteration resulting from the modification of the release characteristics of extended-release pharmaceutical forms, prioritisation of liquid forms, lack of drug compatibility or toxicity studies when manipulating the dosage form (5,15).

Subsequently, acceptance of the recommendations by the prescribing physicians was recorded.

The statistical analysis was performed using absolute frequencies (percentages) for qualitative variables and central measures (mean) with dispersion measures (SD, range) for quantitative variables.

The study was conducted pursuant to the Spanish Organic Law 3/2018, of 5 December, on Personal Data Protection and Guarantee of Digital Rights and the Declaration of Helsinki. Patient privacy and confidential processing of the personal data were ensured.

Table I. General characteristics of the study population

General characteristics	
n	57
Age at feeding tube placement (mean ± SD)	71.4 ± 16.1
Sex (woman/man)	35.1 %/64.9 %
Reason for feeding tube placement - Cerebrovascular accident - Head-neck cancer - Neurodegenerative disorder-dementia	 28.1 % 33.3 % 38.6 %
Type of FT - NGT - PEG - NJT	 54.3 % 43.9 % 1.8 %

FT: feeding tube; NGT: nasogastric tube; NJT: nasojejunal tube; PEG: percutaneous endoscopic gastrostomy; SD: standard deviation.

RESULTS

A total of 57 patients were included in the study. Demographics, FT type, and reasons for FT placement are shown in table I.

A total of 66 pharmaceutical care visits were recorded, amounting to 1.2 visits per patient (nine were follow-up visits). Following treatment review, in 47 of these 66 visits (71.2 %), at least one drug modification was required in the patient's prescription. The median number of drugs to be modified per patient was 2 (Interquartile Range [IQR], 1-3).

In the 66 visits performed, of the 489 drugs reviewed, a total of 93 had to be modified for FT administration (19.0 %). The primary change required was switching to a different active substance, representing 52.7 % (49/93) of the cases, followed by changes of pharmaceutical form in 47.3 % (44/93) of the cases (Table II).

The level of acceptance of the recommendations by physicians was 43.0 %. Acceptance by type of change suggested is shown in table II.

The recommendations to adapt a drug for FT administration that were not accepted by physicians were analysed. A change of active substance was recommended when no other medicinal product or pharmaceutical form compatible with FT administration was available. Twenty-six (53.1 %) of these recommendations from a total of 49 were not accepted. They were based on: FT obstruction problems caused by the drug (omeprazole, 11 prescriptions); drug instability resulting from crushing coated tablets (pantoprazole, 2 prescriptions; tamsulosin, 7 prescriptions); lack of compatibility studies (5 prescriptions); or drug toxicity following dosage form manipulation (dutasteride, 1 prescription).

For the recommendations to change the pharmaceutical form, 27 (61.4 %) of a total of 44 were not accepted. These recommendations were issued based on: alteration of drug absorption; changes to the drug release characteristics for extended-release pharmaceutical forms or forms with enteric coating (14 prescriptions); availability of a more suitable pharmaceutical form for tube administration requiring less manipulation (7 prescriptions); potential toxicity for the person manipulating the drug resulting from aerosols formed when crushing tablets (coated valproic acid tablets, 3 prescriptions); or lack of compatibility studies (3 prescriptions).

DISCUSSION

Our study reveals that approximately three in four patients receiving a FT for the first time require at least one change in their treatment at discharge because of incompatibility issues of the prescribed drugs with the administration route. This is in line with the findings of a study by Van Dem Bemt et al., in which errors were identified in 76 % of medication administrations during hospitalization in patients with FT (1).

Our findings reveal that every patient with recommendations to adapt a drug for FT administration had been prescribed a median of two drugs requiring changes, a figure slightly higher compared

Table II. Prescriber acceptance of changes suggested following medication reconciliation

Type of recommendation	n	Accepted	Not accepted	% acceptance
Change of active substance	49 (52.7 %)	23	26	46.9 %
Change of pharmaceutical form	44 (47.3 %)	17	27	38.6 %
Total	93 (100 %)	40	53	43.0 %

to other studies where the median number of drugs inappropriately administered through an FT was 1.34 (16).

Overall, 19 % of all the drugs studied had to be modified. This figure is similar to the one found in a study performed in an Intensive Care Unit (ICU) where 20 % of the drugs prescribed were found to be inappropriate for FT administration (10).

The recommendations issued were classified in two types (Table II). The most common one was switching to a different active substance. For example, omeprazole can cause mechanical problems leading to tube obstruction because it has to be administered as whole microgranules, which cannot be crushed as this could result in changes in drug bioavailability (5,17). Given the greater complexities of omeprazole administration compared to other proton pump inhibitors (PPIs), we recommended replacing it with other pharmacotherapeutically equivalent active substances that did not present the same problems, such as esomeprazole. In the case of pantoprazole, this drug is only marketed in a gastro-resistant oral tablet form and therefore cannot be crushed because of the instability of the active substance in an acid environment (18). Another drug that had to be changed was tamsulosin, which is exclusively marketed as extended-release tablets or capsules. Crushing the tablets or opening the capsules would have an impact on the drug's pharmacokinetic characteristics (18). Recommendations were also given for cytotoxic drugs such as dutasteride because it can irritate the oropharyngeal mucosa when it is released from soft capsules and it can also cause foetal harm in pregnant women handling the substance as it is absorbed through the skin (5).

The second type of recommendation issued was changing a drug's pharmaceutical form. One of the most common reasons for this type of adaptation was the availability of a more appropriate pharmaceutical form for FT administration. It is important to note that the bioavailability of coated tablets is altered when crushed. This was the case with the proprietary medicinal product Adiro® (acetylsalicylic acid) which has a gastro-resistant coating allowing the drug not to be released immediately in the stomach but in the duodenum in a delayed fashion (19). This type of coating can cause obstruction problems in FTs and therefore it is advisable to replace it with tablets that do not have an enteric coating (5,20).

Less than half of the pharmacists' recommendations to switch to another active substance or to make changes to the pharmaceutical form were accepted by the physicians. This finding is in contrast to results from other studies showing a much higher degree of acceptance (between 82 % and 98 %) (21,22), although these studies focused on general medication reconciliation (MR) at discharge and not specifically on adaptation of the medication to FT administration.

The non-acceptance of recommendations by the prescribing physicians could stem from a lack of training on the compatibility of certain drugs with FT administration, leading them not to trust the recommendations issued. It may also result from a lack of knowledge of the different pharmaceutical forms available and the pharmaceutical characteristics of each one of them. Another potential factor is the lack of patient follow-up after discharge to Primary Care where medication adaptation to FT administration needs to be performed by primary care physicians, but the lack of contact with hospital pharmacists makes it a difficult process.

The low levels of physicians' acceptance should be considered internally as a lack of understanding of the recommendations and show that the in-hospital pathway and prescribers' training need improving.

The single-centre nature of the study and its small sample size resulting in a limited statistical power were the main study limitations. Moreover, research on medication adaptation for FT administration is scarce and further studies are necessary to draw more definitive conclusions.

We would like to conclude by highlighting that this study emphasises the importance of adapting medication to tube feeding and confirms that the inclusion of clinical pharmacists in multidisciplinary teams leads to improvements in patient drug therapy, as shown in multiple MR studies (21,23). In fact, specialised pharmacists have been shown to be more efficient in the reconciliation process than other healthcare professionals (24).

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Nutrición Hospitalaria

Trabajo Original

Pediatría

The leptin/adiponectin ratio as prognostic marker for dyslipidemia during 1 year of follow-up in pediatric patients receiving kidney replacement therapy

Índice leptina/adiponectina como indicador pronóstico de dislipidemia durante 1 año de seguimiento en pacientes pediátricos que reciben terapia de reemplazo renal

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Abstract

Background: leptin and adiponectin are associated with cardiovascular disease in chronic kidney disease (CKD) patients and could be useful prognostic factors.

Objectives: to explore the usefulness of the leptin/adiponectin ratio (LAR) to predict the presence or worsening of dyslipidemia during 1 year of follow-up in children receiving kidney replacement therapy (KRT).

Material and methods: a prospective cohort study was performed. Pediatric KRT patients aged between 8 and 17 years who were undergoing hemodialysis or peritoneal dialysis were included. At enrollment, the lipid profile, adiponectin and leptin levels, and somatometric measurements, including body fat percentage, were determined. At the one-year follow-up, the lipid profile was reassessed.

Results: of the 70 patients included, the median age was 13 years, and there was no sex predominance (52.8 % males). At the end of follow-up, the patients were divided into three groups: those without dyslipidemia (WOD), those who developed or experienced worsening of their dyslipidemia (DWD) and those with persistent dyslipidemia (PD). A LAR > 0.85 (OR, 16.7) and body fat percentage (OR, 1.46) were associated with an increased risk of PD and DWD at 12 months, independently of urea level, BMI Z-score, benzafibrate treatment, CKD progression time, and replacement treatment.

Conclusions: a LAR > 0.85 and fat body percentage at the beginning of follow-up were strongly associated with the presence, persistence or worsening of dyslipidemia at the 12-month follow-up in children with KRT.

Keywords:

Chronic kidney disease. Dyslipidemia. Leptin. Adiponectin. Leptin/adiponectin ratio. Body fat. Pediatric.

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Resumen

Antecedentes: la leptina y la adiponectina se asocian con enfermedad cardiovascular en los pacientes con enfermedad renal crónica (ERC) y podrían ser factores pronósticos útiles.

Objetivos: explorar la utilidad del cociente leptina/adiponectina (LAR) para predecir la presencia o empeoramiento de la dislipidemia durante 1 año de seguimiento en niños que reciben terapia de reemplazo renal (TRR).

Material y métodos: se realizó un estudio de cohortes prospectivo. Se incluyeron pacientes pediátricos con TRR de entre 8 y 17 años que estaban en hemodiálisis o diálisis peritoneal. Al inicio del estudio se determinaron el perfil lipídico, los niveles de adiponectina y leptina, y las mediciones somatométricas, incluido el porcentaje de grasa corporal. En el seguimiento de un año, se reevaluó el perfil de lípidos.

Resultados: de los 70 pacientes incluidos, la mediana de edad fue de 13 años y no hubo predominio de sexo (52,8 % de varones). Al final del seguimiento, los pacientes se dividieron en tres grupos: aquellos sin dislipidemia (SD), aquellos que desarrollaron o experimentaron un empeoramiento de su dislipidemia (ED) y aquellos con dislipidemia persistente (PD). Un LAR > 0,85 (OR: 16,7) y el porcentaje de grasa corporal (OR: 1,46) se asociaron con un mayor riesgo de ED y PD a los 12 meses, independientemente del nivel de urea, la puntuación Z del IMC, el tratamiento con benzafibrato, el tiempo de progresión de la ERC y el tratamiento de reemplazo.

Conclusiones: un LAR > 0,85 y el porcentaje de grasa corporal al inicio del seguimiento se asociaron fuertemente con la presencia, persistencia o empeoramiento de la dislipidemia a los 12 meses de seguimiento en niños con TRR.

Palabras clave:

Enfermedad renal crónica. Dislipidemia. Leptina. Adiponectina. Cociente leptina/adiponectina. Grasa corporal. Pediátrico.

INTRODUCTION

Chronic kidney disease (CKD) has a high prevalence among children, with an increase in incidence in recent years (1). Cardiovascular risk factors (CRFs), including dyslipidemia, are the main causes of morbidity and mortality in patients with CKD. This elevated cardiovascular risk begins in the early stages of CKD and is independent of age, ethnicity and sex (2).

CRFs are defined as factors that increase the risk for the development of atherosclerotic cardiovascular disease and diabetes *mellitus* (3). Patients receiving kidney replacement therapy (KRT) have an increased risk of CKD due to high prevalence rates of hypertension, dyslipidemia, obesity and sedentary lifestyle, in addition to factors related to uremia such as hypervolemia, anemia, alterations in calcium-phosphorus metabolism, hyperparathyroidism and accumulation of endogenous inhibitors of nitric oxide synthesis, among others (2,4).

As the deterioration of glomerular filtration progresses in patients, the lipid profile is altered, and the atherogenic risk index increases (5). This increase is due to the increased activity of cholesterol ester transfer protein, whose function is to transfer cholesterol esters from high-density lipoprotein cholesterol (HDLc) to low-density lipoprotein cholesterol (LDLc); to inhibit certain mediators that promote a decrease in HDLc; and to downregulate the action of lipoprotein lipase (LPL), which causes an elevation of very low-density cholesterol lipoprotein (VLDLc) and triglycerides (TGLs) (6,7).

Adipose tissue is considered an endocrine organ that produces multiple adipocytokines, and in recent years, two circulating adipokines, leptin and adiponectin, have been identified as mediators of inflammation and may be important markers of chronic systemic inflammation (8,9). Leptin is a peptide hormone produced by adipocytes that is correlated with the proportion of body fat stores (10). Additionally, leptin exhibits proinflammatory actions, including upregulating the phagocytic function of macrophages, increasing the production of proinflammatory cytokines, and stimulating reactive oxygen species (11). Adiponectin is produced by the mitochondria of adipocytes and acts as an anti-inflammatory factor, inhibiting the production of proinflammatory cytokines, especially with regard to atherosclerosis (12). Measuring the level of leptin or adiponectin in the peripheral circulation is useful in identifying the state of systemic inflammation; however, it has been shown that the leptin/adiponectin ratio (LAR) may be more valuable because high values of this index indicate an imbalance in pro- and anti-inflammatory conditions (13).

Since patients with KRT have high cardiovascular risk, the early identification and treatment of some risk factors, such as dyslipidemia, may reduce cardiovascular complications (14). In developing countries, such as Mexico, kidney transplantation is performed at a lower rate than in developed countries, and several years may pass before a pediatric patient undergoes kidney transplantation. Therefore, in these patients, strategies to keep long-term metabolic conditions under control are required, and it is important to identify cases that require greater vigilance and probably more aggressive treatment. The objective of our study was to determine the predictive value of the leptin/adiponectin index for the development of dyslipidemia after 1 year of follow-up in children with KRT.

METHODS

SUBJECTS

A prospective cohort study was carried out from January 2018 to December 2019 at two tertiary pediatric care centers in Mexico City: Hospital de Pediatría (Mexican Institute of Social Security) and Hospital Infantil de México Federico Gómez (Mexico Ministry of Health). In both centers, all pediatric KRT patients are usually cared for by a multidisciplinary team that includes pediatric nephrologists, pediatric endocrinologists, psychologists, and nutritionists.

Children aged between 8 and 17 years with stage V CKD according to the Kidney Disease: Improving Global Outcomes (KDIGO) staging scale (15) who were receiving peritoneal dialysis or

hemodialysis prior to the start of follow-up were considered eligible to participate in the study. All patients included were selected using the consecutive sampling technique. Patients who were scheduled for kidney transplantation in the next 12 months, were diagnosed with diabetes *mellitus*, did not agree to participate or had incomplete clinical and biochemical evaluation data were excluded. The cohort follow-up duration was 12 months.

Of the 137 potential candidates, 59 were excluded (38 were scheduled for kidney transplantation, six were less than 8 years old, five had secondary diabetes *mellitus* and ten refused to participate in the study). An analysis of 70 patients is presented. The causes for dropout during follow-up were deaths (2 patients, secondary to heart failure), and loss of medical insurance (6 patients); accordingly, these patients did not attend hospital follow-up.

According to the Declaration of Helsinki, the protocol was evaluated and approved by the ethics and research committee of the hospital under registry number R-2018-3603-075 & HIM-2017-117. A parent or legal guardian signed an informed consent form, and each child provided written assent according to the recommendations of the Declaration of Helsinki.

PROCEDURES

1. *At the beginning of follow-up, for all patients:* the lipid profile, adiponectin and leptin levels, and somatometry measurements, including body fat percentage, were determined. A serum TGL level higher than 250 mg/dl was an indication for treatment with benzafibrate.
2. *Nutritional assessment and indications:* the calorie requirements of each participant were estimated based on resting energy expenditure (calculated using the equation from the Institute of Medicine to predict dietary reference intake) and physical activity levels. Nutritionists designed patient diets according to daily calorie dietary requirements. The diets consisted of 50 % carbohydrates, 20 % protein and 30 % total fat. The protein intake differed according to replacement treatment and age (hemodialysis: 4-13 years, 1.05 g/kg/day and 14-18 years, 0.95 g/kg/day; peritoneal dialysis: 4-13 years, 1.1 g/kg/day and 14-18 years, 1.0 g/kg/day) (16). Additionally, consumption of low-fat dairy products was encouraged, and low consumption of high-cholesterol foods and refined grains was recommended. In addition, nutritionists provided nutrition lectures, and participants were given manuals with examples of serving sizes for the 7 food groups (fruits, vegetables, legumes, cereals/tubers, foods of animal origin, oils/fats, and dairy) so that the patients and their caregivers could identify the appropriate serving size of each food (16,17). All patients included were recommended physical activity for at least 30 minutes daily.
3. *Follow-up visits:* the patients were followed biweekly for the first 3 months and then once a month until completion of the one-year follow-up to evaluate nutritional indications.
4. *Final assessment:* the lipid profile was reassessed at the one-year follow-up. The presence of dyslipidemia was evaluated among the participants; in the case of patients who already had dyslipidemia, those who maintained their dyslipidemia status and who experienced exacerbation of their dyslipidemia were identified. Considering these data, at the 12-month follow-up, the patients were divided into three groups: those without dyslipidemia (WOD), those who developed or experienced worsening of their dyslipidemia (DWD) and those with persistent dyslipidemia (PD).

ANTHROPOMETRY

The anthropometric indicators of each patient were recorded by a certified nutritionist. Height was measured to the nearest 0.1 cm with a SECA model 769 stadiometer (SECA 769, SECA Corp. Oakland Center Columbia, MD, USA). Weight and body fat percentage measurements were conducted using the bioimpedance method (Tanita BC-568 Segmental Body Composition Monitor, Tokyo, Japan) with the patients barefoot and wearing only underwear.

SERUM HORMONES AND CHEMISTRY LEVELS

Blood samples were obtained from the forearm of each subject via the antecubital vein between 7:00 and 8:00 a.m. after a minimum of 12 hours of fasting during the baseline visit. Serum aliquots were separated (centrifuged at 4 °C; 3000 rpm; 15 min) and frozen at -80 °C until biochemical analysis.

Insulin was measured by chemiluminescence (Roche-Hitachi Modular P and D). Leptin and adiponectin levels were measured using an enzyme-linked immunosorbent assay (ELISA) (Human Leptin DuoSet (DY398) and Human Adiponectin DuoSet (DY1065), R&D Systems, Minneapolis, MN, USA). Plates were read using an ELISA microplate reader (Labsystems Multiskan EX, MTX Labsystems Inc., Vienna, VA, USA) and were determined in duplicate according to the manufacturer's instructions. The LAR was obtained by dividing the serum concentrations of leptin by those of adiponectin.

Hemoglobin, urea, creatinine and parathyroid hormone levels were measured by a colorimetric enzymatic method (IN-REACT, SPIM120). All electrochemiluminescence immunoassays (ECLIAs) were performed using a COBAS 6000 e601 (Roche Diagnostics GmbH, Indianapolis, IN, USA) in duplicate according to the manufacturer's recommendations. Glucose, TGLs, and HDLc were determined by colorimetric enzymatic methods (Bayer Diagnostics, Puteaux, France). Intra- and interassay coefficients of variation < 7 % were considered acceptable. A standard curve was also generated for each assay. The homeostatic model assessment for insulin resistance (HOMA-IR) was calculated according to the formula: HOMA-IR = fasting glucose (mg/dl) x fasting insulin (μU/ml) / 405 (18).

DEFINITIONS

Dyslipidemia was defined as the presence of one or more of the following criteria: a) hypertriglyceridemia (for children < 10 years old: TGLs ≥ 90th percentile for age and sex and for children 10 years old: TGLs ≥ 150 mg/dl (3); b) low HDLc (for children < 10 years old HDLc < 10th percentile for age and sex and for children > 10 years old HDLc < 40 mg/dl in males and < 50 mg/dl in females); c) elevated LDLc (LDLc > 130 mg/dl according to the International Diabetes Federation (IDF) definition) (3,19).

Insulin resistance was defined as a HOMA-IR score higher than 3.16 (20). Obesity was indicated by a BMI ≥ the 95th percentile, and overweight was indicated by a BMI ≥ the 85th percentile for age and sex according to the 2000 CDC Growth Charts (21). For patients with < 2 standard deviations of height for age, BMI was calculated considering the age that corresponds to the 50th percentile of actual height. Hyperglycemia or elevated fasting plasma glucose was considered a fasting glucose level ≥ 100 mg/ dl (3).

STATISTICAL ANALYSES

The Shapiro-Wilk test was used for quantitative variables, and a nonparametric distribution was observed. We calculated the medians and ranges of quantitative variables.

To determine differences in quantitative basal variables among the three groups (WOD, DWD and PD), the Kruskal-Wallis test was used. To detect differences between serum glucose and lipid profiles at the baseline visit and the 12-month follow-up, the Mann-Whitney U-test was performed. Changes in HDLc, LDLc, TGLs, BMI Z-score, and body fat (ΔHDLc, ΔLDLc, ΔTGLs, ΔBMI Z-score, Δbody fat) were calculated by subtracting the HDLc, LDLc, TGLs, BMI Z-score, and body fat at 12 months from those at baseline. The correlation of the LAR with ΔHDLc, ΔLDLc, ΔTGLs and body fat percentage were determined using Pearson's correlation coefficient.

In the multivariate analysis, the DWD and PD groups were combined to produce 2 groups: the WOD group and the present, persistent or worsened dyslipidemia (PPWD) group. Logistic regression analysis was performed to determine the relationship between LAR and PPWD at the 12-month follow-up; the analysis was adjusted for body fat percentage, BMI Z-score, ΔBMI Z-score, Δbody fat, replacement therapy, age at study onset, serum urea and bezafibrate use.

A receiver operating characteristic (ROC) curve was generated for the LAR to identify the cutoff point with the best sensitivity and specificity that allowed the correct classification and a positive likelihood ratio (LR+) to predict PPWD at the 12-month follow-up. With the results of the ROC curve, considering a cutoff point of 0.85, logistic regression analysis was performed to determine the relationship between a LAR > 0.85 and PPWD.

Differences were considered significant at $p < 0.05$. STATA v.11.0 was used for the statistical analyses.

RESULTS

BASELINE

The general characteristics of the patients are shown in table I. Seventy patients with KRT (37 male, 33 female) were included. The median age was 13 years (range, 8-17 years). The most frequent CKD etiology was congenital anomalies of the kidney and urinary tract (CAKUT) (45.7 %), followed by glomerulopathy (27.1 %) and indeterminate etiologies (21.4 %). At the time of evaluation, 35 pa-

Table I. General characteristics of patients receiving kidney replacement therapy at the beginning of follow-up

		n = 70
		Median *(minimum-maximum)*
Age (years)		13 (8-17)
Sex: male		37 (52.8)
Body mass index (kg/m^2)		17.2 (12.7-24.7)
Z score body mass index		-0.3 (-3.3 to 2.9)
Body fat (%)		23.6 (12.3-41.3)
Chronic kidney disease etiology	Glomerulopathy	19 (27.1)
	CAKUT	32 (45.7)
	Immunological	2 (2.9)
	Tubulopathy	2 (2.9)
	Indeterminate	15 (21.4)
Replacement therapy	Peritoneal dialysis	35 (50)
	Hemodialysis	35 (50)
Time of CKD evolution (months)		24 (1-180)
Hemoglobin (g/dl)		10.6 (5.2-15.3)
Urea (mg/dl)		106 (24-364)
Parathormone (pg/dl)		449 (22-2500)
Leptin (ng/ml)		4.3 (0.7-7.0)
Adiponectin (µg/ml)		6.1 (1.4-7.3)
Leptin/adiponectin index		0.84 (0.11-4.44)
Insulin (mU/L)		12.2 (2.0-73.1)
HOMA-RI		2.75 (0.39-18.0)

CAKUT: congenital anomalies of the kidney and urinary tract; CKD chronic kidney disease; HOMA-IR: insulin resistance index.

tients (50 %) were receiving hemodialysis as a replacement therapy, and the remaining patients were receiving peritoneal dialysis with a median of 16 months of substitution treatment.

At enrollment, 80 % (n = 56) of the children were classified as having a normal nutritional status, eleven (15.7 %) were overweight, and three (4.3 %) were obese. In addition, 40 patients (57.1 %) had dyslipidemia, and 41.4 % (n = 29) had insulin resistance. Among the dyslipidemia patients, hypertriglyceridemia was most common (40.7 %), followed by decreased HDLc (27.1 %) and increased LDLc (7.1 %); of the 40 patients, 27 had combined dyslipidemia.

FOLLOW-UP

During the follow-up, among all the children, there were important changes in dyslipidemia status (Fig. 1). Of the 30 patients who did not present with dyslipidemia at the beginning of follow-up, only 13 remained without dyslipidemia (43.3 %); among the 17 who developed dyslipidemia, the most frequent types of dyslipidemia were reduced HDL and hypertriglyceridemia (n = 11). Of the 40 patients who had dyslipidemia at baseline, 14 (35 %) had normal lipids at the end of follow-up. In 11 patients (27.5 %), dyslipidemia worsened, with hypertriglyceridemia (n = 8) being the most frequent type, followed by increased LDLc (n = 7) and reduced HDLc (n = 6). It is worth mentioning that nine patients were indicated benzafibrate and only 2 improved dyslipidemia, in 4 cases they maintained hypertriglyceridemia and 3 patients, another dyslipidemia was added.

At the end of follow-up, 27 patients did not have dyslipidemia (WOD), 15 patients maintained their dyslipidemia status (persistent dyslipidemia [PD]), and 28 patients experienced worsening of their dyslipidemia or developed another type of dyslipidemia (DWD). At the end of the follow-up period, in the PD and DWD groups, there were significant increases in LDLc and TGs and a significant decrease in HDLc, while in the woD group, there were statistically significant improvements in serum concentrations of total cholesterol, HDLc, and TGs (Table II).

Regarding physical activity, at the interrogation, only 10 % (n = 7) of the included patients followed the indication (WOD n = 3 and PPWD n = 4).

COMPARISONS AMONG CKD PATIENTS WITHOUT DYSLIPIDEMIA (WOD), WITH PERSISTENT DYSLIPIDEMIA (PD), AND WITH WORSENED DYSLIPIDEMIA (DWD) AT THE END OF FOLLOW-UP

When comparing age, CKD progression time, renal replacement time, and replacement treatment, no differences were identified among the WOD, PD and DWD groups; however, a low-

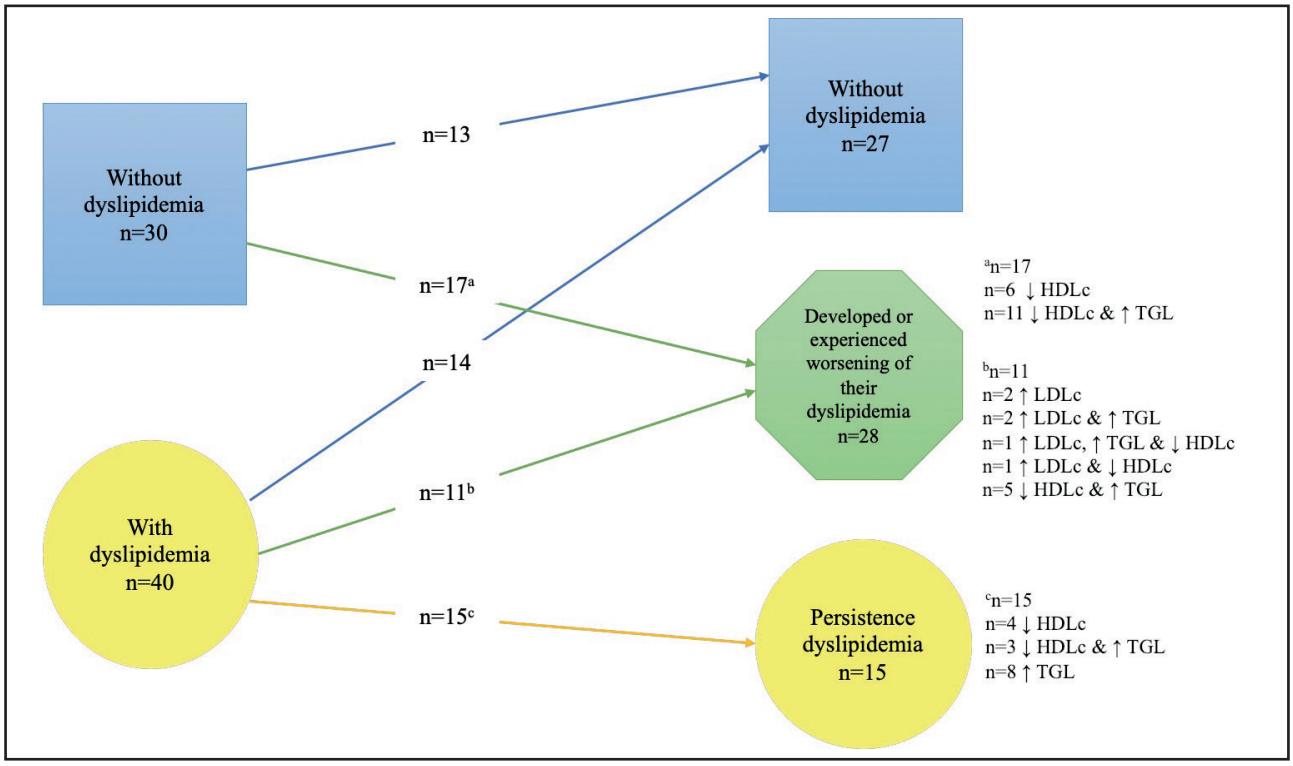

Figure 1.
Flow diagram of changes in dyslipidemia status.

Table II. Comparison of the biochemical profile of all patients, and by groups at 12 months of follow-up

	All n = 70			Without dyslipidemia n = 27			Persistence, developed or experienced worsening of their dyslipidemia n = 43		
	Median *(minimum-maximum)*								
	Baseline	**12 months**	**p**	**Baseline**	**12 months**	**p**	**Baseline**	**12 months**	**p**
BMI z	-0.3 (-3.3 to 2.9)	-0.9 (-3.8 to 1.5)	0.53	-0.4 (-2.4 to 1.4)	-0.3 (-2.5 to 1.4)	0.12	-0.2 (-3.3 to 2.9)	-0.2 (-2.8 to 3.1)	0.73
Fat body (%)	23.6 (12.3-41.3)	24.2 (12.0-42.1)	0.01	20 (12.3-25.6)	20.8 (12.0 to 26.7)	0.01	28.1 (14.3-41.3)	27.8 (14.0-42.1)	0.01
Glucose (mg/dl)	89 (65-99)	88 (60-131)	0.06	88 (67-99)	84 (60-99)	0.16	89 (65-99)	90 (60-131)	0.11
Total cholesterol (mg/dl)	147.2 (99-374)	149.3 (92.3-301)	0.37	146 (110-234)	134 (92.3-177)	0.01	148 (99-374)	154 (109-301)	0.29
HDL-c (mg/dl)	45.8 (16-95.1)	44.1 (20-87)	0.34	43.9 (16-95.1)	53 (40-87)	0.002	46 (24-84.4)	39 (20-87)	0.02
LDL-c (mg/dl)	72.5 (45.4-226)	82.8 (42.2-250)	0.13	76 (48.5-120)	76 (36.8-113)	0.13	71.9 (35-226)	85 (43-250)	0.02
Triglycerides (mg/dl)	138 (78-531)	131 (48-369)	0.19	139 (73-319)	100 (48-149)	0.001	137 (70-531)	165 (67-369)	0.07

LDL-c: low density cholesterol; HDL-c: high density cholesterol.

er body fat percentage was observed in the WOD group (WOD 19.5 % vs PD 25.3 vs DWD 28 %, $p < 0.001$). Regarding biochemical studies, no differences were identified among the three groups, but when the leptin, adiponectin, insulin, and HOMA-IR measurements were compared, serum leptin concentrations (median 5.6 ng/ml vs 5.8 ng/dl vs 3.6 ng/ml $p < 0.001$) and the leptin/adiponectin index (median 0.95 vs 0.95 vs 0.67 $p < 0.001$) were higher in the PD and DWD group than in the woD group (Table I). There was also no difference in the proportion of insulin resistance among the groups.

On the other hand, LAR was correlated with serum ΔHDLc, ΔLDLc and ΔTGs, and a positive correlation of LAR with ΔLDLc was identified ($r = 0.306$, $p = 0.013$). Likewise, a positive correlation of percentage of body fat with the LAR was observed ($r = 0.438$, $p < 0.001$) (Fig. 2).

Considering that the LAR levels were significantly different between the groups, multivariate logistic regression analysis was performed to identify the factors related to PPWD in patients with KRT, and it was determined that LAR (OR, 15.36; 95 % CI, 1.05 to 224.3; $p = 0.046$) and body fat (OR, 1.30; 95 % CI, 1.11 to 1.53; $p < 0.001$) were independent risk factors for PPWD, while the level of urea, BMI Z-score, treatment with benzafibrate, CKD progression time, delta BMI Z-score, delta body fat, and replacement treatment were not (Table IV). Other logistic regression models were constructed, and leptin and adiponectin were included in the independent models; there was no statistical significance for the risk of PPWD in patients with KRT (Tables V and VI).

A ROC curve analysis was performed to identify the best LAR cutoff value for the prediction of PPWD in patients with KRT; the best LAR cutoff value was 0.85 (sensitivity of 72.09 %, specificity of 85.19 %, correct classification: 77.14 %, LR+, 4.8) (Fig. 3). Using this cutoff point, a multivariate logistic regression analysis was performed to identify the factors related to PPWD in patients with KRT, and it was determined that a LAR > 0.85 (OR, 16.7; 95% CI, 2.8 to 99.9; $p = 0.002$) and body fat percentage (OR, 1.46; 95 % CI, 1.16 to 1.84; $p = 0.001$) were independent risk factors associated with PPWD in patients with KRT.

DISCUSSION

In the present study, in pediatric patients with KRT, the body fat percentage and LAR were associated with worsened or persistent dyslipidemia at the 12-month follow-up. Our findings suggest an imbalance between leptin and adiponectin and that the percentage of fat plays an important role in dyslipidemia, considering that these factors are markers of metabolic risk (22,23).

Currently, it is recognized that regardless of the characteristics of the patient, renal failure produces changes in the lipid profile (14).

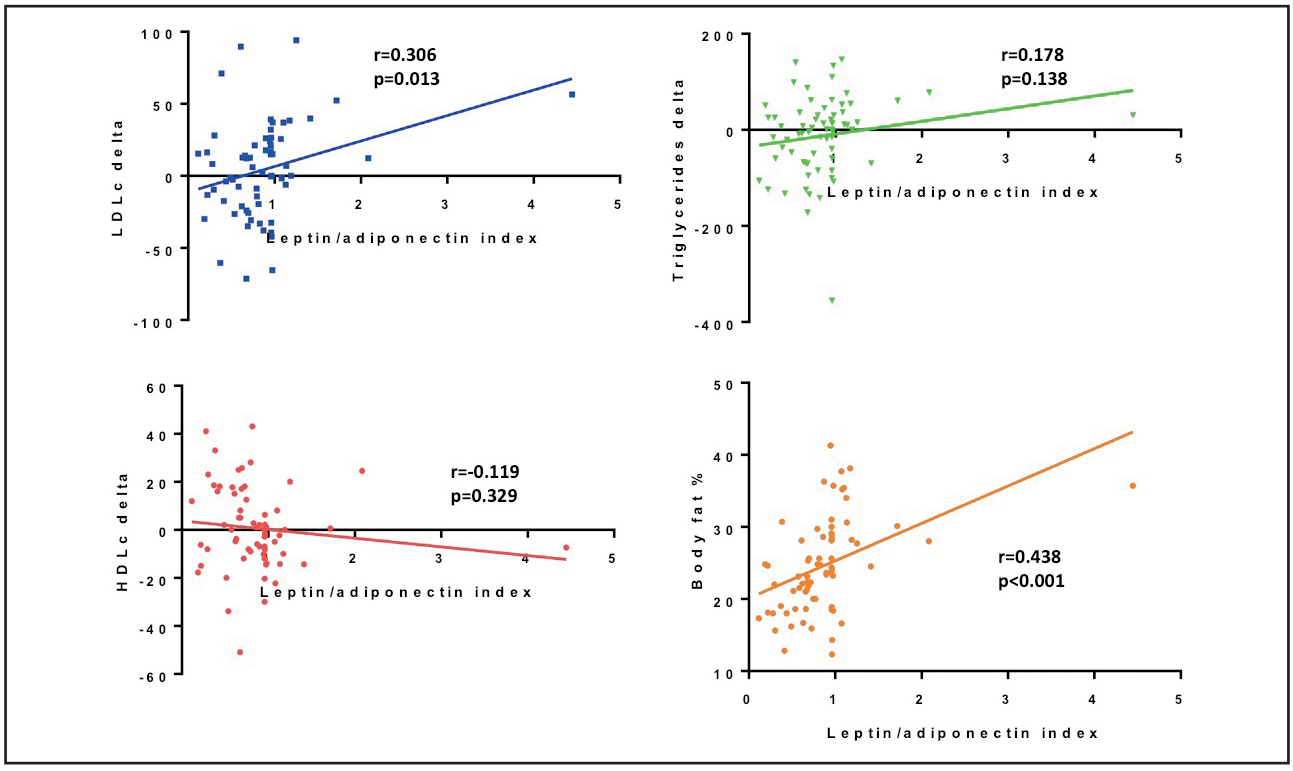

Figure 2.

Leptin/adiponectin ratio correlation with serum low-density lipoprotein cholesterol delta, triglycerides delta, high-density lipoprotein cholesterol delta, and body fat percentage.

Table III. Comparison of general characteristics of patients receiving kidney replacement therapy at the beginning of follow-up according to the study groups

		Without dyslipidemia n = 27	Persistence dyslipidemia n = 15	Developed or experienced worsening of their dyslipidemia n = 28	
		Median *(minimum–maximum)*			p
Age (years)		13 (8-16)	14 (8-17)	14 (8-17)	0.821
Sex: male		15 (55.6)	4 (26.6)	18 (64.3)	0.066
BMI (kg/m^2)		16.8 (13.2 -22.9)	17.4 (12.7-23.7)	18 (13.1-24.7)	0.299
Z-score BMI		-0.96 (-3.12 to 0.81)	-0.92 (-3 to 1.16)	-0.73 (-2.53 to 1.56)	0.591
Body fat (%)		19.5 (12.3-25.6)	25.3 (14.3-25.4)	28.0 (14.3-41.3)	< 0.001
CKD etiology	Glomerulopathy	6 (22.2)	7 (46.7)	4 (14.3)	0.381
	CAKUT	13 (48.1)	6 (40.0)	15 (53.6)	
	Immunological	-	0 (0)	2 (7.1)	
	Tubulopathy	1 (3.7)	0 (0)	1 (3.6)	
	Indeterminate	7 (25.9)	2 (13.3)	6 (21.4)	

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Table III (Cont.). Comparison of general characteristics of patients receiving kidney replacement therapy at the beginning of follow-up according to the study groups

		Without dyslipidemia n = 27	Persistence dyslipidemia n = 15	Developed or experienced worsening of their dyslipidemia n = 28	
		Median *(minimum–maximum)*			p
Replacement therapy	Peritoneal dialysis	10 (37)	11 (73.3)	14 (50.0)	0.084
	Hemodialysis	17 (63)	4 (26.7)	14 (50.0)	
Time of CKD evolution (months)		24 (1-180)	36 (6-168)	24 (1-120)	0.402
Hemoglobin (g/dl)		11.2 (6.3-14)	9.2 (5.2-13.1)	11.1 (8-15.3)	0.072
Urea (mg/dl)		94 (48-266)	122 (45.7-238)	107 (24-364)	0.187
Parathormone (pg/dl)		407 (22-2010)	523 (44-2080)	470 (44-2500)	0.605
Leptin (ng/ml)		3.6 (0.7-5.3)	5.6 (1.8-6.2)	5.8 (1.2-7.0)	< 0.001
Adiponectin (µg/ml)		5.9 (1.7-6.8)	5.9 (1.9-6.5)	6.1 (1.3-7.1)	0.194
Leptin/adiponectin index		0.67 (0.11-0.97)	0.95 (0.49-1.71)	0.95 (0.18-4.44)	< 0.001
Insulin (mU/L)		11.5 (2.2-73.1)	12.9 (5.1-48.3)	12.2 (2.0-34.6)	0.323
HOMA-RI		2.43 (0.42-18.0)	3.40 (1.12-17.0)	2.75 (0.39-9.73)	0.295

CAKUT: congenital anomalies of the kidney and urinary tract; CKD: chronic kidney disease; HOMA-IR: insulin resistance index; BMI: body mass index.

Table IV. Logistic regression to identify factors that affect persistence, development or worsening of dyslipidemia in pediatric patients receiving kidney replacement therapy at one year of follow-up

	OR	95 % CI	p
Leptin/adiponectin ratio	16.72	1.40 to 345.4	0.028
BMI Z-score	0.72	0.37 to 1.41	0.352
Body fat (%)	1.42	1.16 to 1.75	0.001
Treatment with benzafibrate	2.48	0.36 to 17.39	0.778
Urea (mg/dl)	1.01	0.99 to 1.02	0.164
Replacement therapy	1.40	0.66 to 2.96	0.370
Time of CKD evolution (months)	1.01	0.99 to 1.03	0.092
Delta BMI Z-score	2.42	0.23 to 25.1	0.459
Delta body fat (%)	0.35	0.09 to 1.26	0.111

Table V. Logistic regression to identify factors that affect persistence, development or worsening of dyslipidemia in pediatric patients receiving kidney replacement therapy at one year of follow-up

	OR	95 % CI	p
Leptin (ng/ml)	1.41	0.84 to 2.36	0.192
BMI Z-score	0.82	0.44 to 1.54	0.550
Body fat (%)	1.39	1.12 to 1.71	0.002
Treatment with benzafibrate	1.95	0.24 to 15.59	0.537
Urea (mg/dl)	1.00	0.99 to 1.02	0.368
Replacement therapy	1.56	0.76 to 3.18	0.218
Time of CKD evolution (months)	1.01	0.99 to 1.03	0.095
Delta BMI Z-score	3.68	0.33 to 40.13	0.284
Delta body fat (%)	0.36	0.10 to 1.25	0.109

Table VI. Logistic regression to identify factors that affect persistence, development or worsening of dyslipidemia in pediatric patients receiving kidney replacement therapy at one year of follow-up

	OR	95 % CI	p
Adiponectin (µg/ml)	0.78	0.40 to 1.50	0.467
BMI Z-score	0.85	0.45 to 1.59	0.615
Body fat (%)	1.49	1.20 to 1.85	< 0.001
Treatment with benzafibrate	1.99	0.25 to 15.38	0.509
Urea (mg/dl)	1.00	0.99 to 1.01	0.362
Replacement therapy	1.36	0.68 to 2.72	0.379
Time of CKD evolution (months)	1.01	0.99 to 1.02	0.089
Delta BMI Z-score	4.42	0.45 to 43.36	0.202
Delta body fat (%)	0.36	0.10 to 1.28	0.117

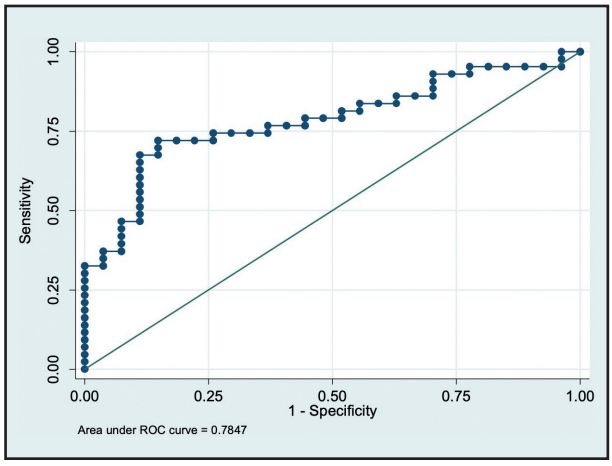

Figure 3.

ROC curve analysis to identify the best leptin/adiponectin ratio cutoff value for the prediction of present, persistent or worsened dyslipidemia in patients with kidney replacement therapy.

These modifications in the lipid profile during the evolution of CKD are characterized by normal or slightly elevated LDLc levels, decreased HDLc levels, elevated TGLs and increased lipoproteins that are mainly related to the degree of kidney damage, age, the presence of proteinuria, the replacement therapy used and obesity (24-26). In our study, 68.5 % of the patients had dyslipidemia at the beginning of follow-up, which is similar to that reported by Bonthius M et al., who identified a 68 % dyslipidemia rate in 917 pediatric patients (27).

In general, the usual recommendations for the management of dyslipidemia in patients with KRT are based on lifestyle modification interventions (17). However, despite appropriate implementation of lifestyle changes, there is a high rate of dyslipidemia reduction failure, which is observed several months after initiating the interventions (28). At present, there is no marker that can help initially identify patients who have a high probability of failure to initiate more intensive treatment.

In CKD patients, the accumulation of TGs is caused by both the excess production of lipoparticles rich in TGs and a decrease in their catabolism due to a decrease in the activity of LPL and liver lipase. This outcome is due to an increase in apoC-III levels, which causes an increase in the apoC-III/apoC-II ratio, and a decrease in LPL synthesis, secondary to the presence of hyperparathyroidism, or a decrease in insulin levels. Alterations in the HDLc level in CKD patients decrease its atheroprotective properties and may contribute to excess cardiovascular mortality in such patients, although the effect of advanced CKD on the composition and function of HDLc has not been completely clarified (14). These conditions explain the high prevalence of dyslipidemia and indicate that lifestyle modifications, which in these patients were indirectly analyzed by delta body fat percentage and BMI Z-score, are not sufficient to improve dyslipidemia in patients with CKD.

Adipose tissue is metabolically active and secretes adipokines, such as leptin, which cause vascular inflammation and insulin resistance, and adiponectin inhibits adherence molecules and increases the production of anti-inflammatory cytokines, such as IL-10 (29-31). Analyzing the impacts of leptin and adiponectin on inflammatory conditions independently can give us an incomplete picture, as happened in this study; no statistical significance was shown for the prediction of PPWD at the 12-month follow-up when leptin and adiponectin were analyzed independently (ANNEX); however, the LAR was significant. This indicates that the imbalance of these adipokines is a prognostic factor in pediatric patients with KRT. The LAR in adults with CKD has been associated with the presence of cardiometabolic factors (32) and is considered a prognostic factor the presence of cardiometabolic factors (33). Although the LAR has not been evaluated as a prognostic factor for cardiometabolic factors in pediatric patients with KRT, this concept has been explored in another group of pediatric patients, showing that an elevated LAR is associated with the risk of metabolic syndrome (34) or the development of systemic arterial hypertension at the 2-year follow-up (35). The elevated LAR reflects an increased risk due to the proatherogenic effect of leptin; at the endothelial cell level, leptin induces oxidative stress, increases the production of endothelin-1, and enhances proliferation, while at the vascular smooth muscle level, leptin favors proliferation, migration and hypertrophy in addition to facilitating thrombosis by increasing platelet aggregation (36); low levels of adiponectin prevent this adipocin from performing cardioprotective functions (37,38) such as inhibiting C-reactive protein mRNA and stimulating nuclear factor-κB signaling and tumor necrosis factor-alpha secretion (39). Hence, it is important to measure the LAR, as LAR elevation reflects an increase in proatherogenic conditions and a decrease in cardioprotective conditions that counteract it.

With regard to body fat, in pediatric patients with KRT, at the one-year follow-up, it was shown that changes in abdominal fat were associated with changes in circulating levels of adipokines and an increase in serum cholesterol (40). However, as indirect causes, a decrease in the volume of muscle mass and an increase in fat mass have been reported in patients with KRT (30,31), with large impacts on cardiometabolic factors and mortality; this was supported by the association of leptin levels with lower muscle mass in subjects with KRT (32).

We recognize that there are some limitations in the study. The sample size was small and the follow-up time was relatively short; it is possible that during a longer follow-up period, the LAR might behave differently. In addition, we did not objectively measure the adolescents' lifestyle modifications, and only 10 % performed physical activity for 30 minutes daily, so it is possible that the LAR and body fat percentage are more useful in those who follow the recommendations more closely.

According to the results obtained, we consider that a LAR > 0.85 and fat body percentage can serve as a prognostic indicator for persistent or worsened dyslipidemia in patients with KRT.

CONCLUSION

LAR and fat body percentage were strongly associated with development or worsening of dyslipidemia at the 12-month follow-up in children with KRT.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Pediatría

Riesgo cardiovascular y resistencia insulínica en supervivientes de leucemia infantil

Cardiovascular risk and insulin resistance in childhood leukemia survivors

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Resumen

Material y métodos: estudio retrospectivo de supervivientes de leucemia aguda en edad infantil. Se seleccionaron aquellos supervivientes con diagnóstico de leucemia antes de los 16 años de edad, en un hospital de tercer nivel y durante el período 1998-2018, que hubieran finalizado su tratamiento como mínimo dos años antes. Se analizaron: niveles de adipokinas y metabolismo hidrocarbonado en sangre, composición corporal mediante bioimpedancia y evaluación ecográfica carotídea. Se tomaron además datos somatométricos.

Resultados: de 82 niños con diagnóstico de leucemia aguda, con edades comprendidas entre 6 y 16 años, incluidos en el registro, solamente 22 cumplieron los criterios para ser incluídos en el estudio. Entre los resultados destaca que el 32 % de la muestra cumplían los criterios de sobrepeso-obesidad y el 36 % presentaban índices de resistencia insulínica (RI) elevados. Los niveles de leptina fueron más elevados en las mujeres (15,45 *vs.* 3,25; p = 0,044) y en los individuos con obesidad o sobrepeso, así como la ratio leptina/adiponectina, que se eleva en presencia de RI (2,52 *vs.* 0,45; p = 0,037). Se observó un incremento del grosor mediointimal carotídeo en relación con el IMC (0,008; IC: -0,002 a 0,013; p = 0,007) sin asociarse a un aumento de masa grasa en estos pacientes (0,204; IC: -0,043 a 0,451; p = 0,101).

Conclusiones: los pacientes supervivientes de leucemia en la edad infantil tienen un riesgo cardiovascular elevado, caracterizado por un aumento de la RI no asociado a aumento de la masa grasa. Este riesgo podría justificar la implementación de medidas preventivas en estos pacientes, cada vez más longevos.

Palabras clave:

Riesgo cardiovascular. Leptina. Adiponectina. cIMT. Resistencia insulínica. Leucemia.

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Aspectos éticos: este estudio ha sido aprobado por el Comité de Ética de la Investigación del Principado de Asturias (CEINPA). Todo participante ha sido informado con detalle del objeto y las particularidades del estudio, según la medida de su comprensión, y se ha obtenido su consentimiento informado o el de sus padres o tutores legales en caso de pacientes pediátricos.

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Abstract

Material and methods: a retrospective study of childhood acute leukemia survivors. Survivors with a diagnosis of leukemia before 16 years of age in a tertiary hospital, during the period of 1998-2018, were selected, who had completed their treatment at least two years earlier. We examined: blood adipokine levels and carbohydrate metabolism, body composition by bioimpedance, and carotid status by ultrasound. Somatometric measures were also taken.

Results: the registry showed 82 children diagnosed with acute leukemia, aged between 6 and 16 years. Only 22 met the criteria to be included in the study. Results reveled that 32 % of the sample met the criteria for overweight-obesity, and 36 % had high insulin resistance indexes (IR). Leptin levels were higher in women (15.45 vs. 3.25; p = 0.044) and in obese and overweight subjects, as was the leptin/adiponectin ratio, which rises in the presence of IR (2.52 vs. 0.45; p = 0.037). We observed an increase in carotid intima-media thickness in relation to BMI (0.008; CI, -0.002 to 0.013; p = 0.007) without any association with an increase in fat mass in these patients (0.204; CI, -0.043 to 0.451; p = 0.101).

Conclusions: childhood leukemia survivors have a high cardiovascular risk, characterized by an increase in IR, not associated with an increase in fat mass. This risk could justify the implementation of preventive actions in these long-lived patients

Keywords:

Cardiovascular risk. Leptin. Adiponectin. cIMT. Insulin resistance. Leukemia.

INTRODUCCIÓN

La leucemia linfoide aguda (LLA) constituye el 25 % de los tumores y el 75-80 % de las leucemias en la edad pediátrica, con un pico de incidencia máximo entre los 1 y 4 años de edad (1). La evidencia actual describe un ligero predominio en los varones, sobre todo en la edad puberal, y en cuanto a la raza, la incidencia de la LLA es mayor en los individuos de raza blanca. Existen diferencias geográficas: en los países industrializados, la LLA de estirpe B es con diferencia la más frecuente de las hemopatías malignas, lo que se ha relacionado con la mayor exposición en estos países a determinados agentes medioambientales leucemógenos (principalmente, radiaciones ionizantes [1]). Gracias a la mejora de los tratamientos de la leucemia, la supervivencia de estos pacientes se ha incrementado notablemente en las últimas décadas, pasando de una supervivencia de menos del 10 % en los años sesenta a una supervivencia libre de enfermedad a 3 años que con los tratamientos actuales se aproxima, e incluso supera, el 90 % en los países más desarrollados (2).

El sobrepeso y la obesidad son condiciones frecuentes en los supervivientes de cáncer infantil, lo que está relacionado tanto con los tratamientos del cáncer como con la adquisición de factores de riesgo cardiovascular a lo largo de los años de supervivencia, al igual que los adquiere la población general (3,4). En los supervivientes de LLA infantil se asocian diferentes factores a dicho riesgo cardiovascular. Factores bioquímicos, como leptina, adiponectina y la existencia de resistencia periférica a la insulina (RI), se han analizado en estos pacientes, aunque sin encontrar asociaciones definitivas (5-8). Asimismo, la existencia de un aumento del grosor miointimal carotídeo (cIMT), que se considera un importante marcador estructural de riesgo cardiovascular, también se ha estudiado en esta población, sin encontrarse una relación significativa (9,10). Por otro lado, el desarrollo de un mayor número de eventos cardiovasculares es la consecuencia a largo plazo más frecuente en los supervivientes de LLA. A los 35 años, esta población tiene 10,9 veces más riesgo de presentar un evento cardiovascular que aquellos que no han padecido cáncer en la infancia (11). El objetivo de nuestro estudio es conocer los factores de riesgo cardiovascular, tanto bioquímicos como funcionales y estructurales, presentes en los supervivientes de la leucemia infantil, así como establecer las posibles relaciones entre estos y el tratamiento recibido.

MATERIAL Y MÉTODOS

La muestra se obtuvo a partir del registro de pacientes con enfermedades hematológicas del Servicio de Hematología del Hospital Universitario Central de Asturias. Se seleccionaron aquellos con diagnóstico de leucemia aguda entre los 6 y los 16 años de edad, desde 1998 a 2018, que habían superado la enfermedad y finalizado el tratamiento al menos en los dos años anteriores. Como criterios de exclusión se establecieron: 1) negación del consentimiento informado; 2) presentación de eventos cardiovasculares (fallo cardiaco, necesidad de oxigenación por membrana extracorpórea o transplante, etc.) durante el tratamiento de la enfermedad; 3) presencia de cualquier enfermedad previa al diagnóstico de leucemia aguda que afectase a los sistemas cardiovascular, renal y hepático.

A cada paciente se le realizó una evaluación somatométrica, una extracción analítica, una medición del cIMT mediante ecografía y estudio de composición corporal mediante bioimpedancia eléctrica. Se revisó en su historial el tipo de tratamiento recibido, incidiendo en la recepción de radioterapia y corticoterapia.

EVALUACIÓN SOMATOMÉTRICA

Se midieron el peso y la talla, con el paciente descalzo y vistiendo ropa ligera, mediante una báscula marca TANITA con precisión de 0,1 kg, y un estadiómetro de pared marca SECA, modelo 264, con precisión de 0,1 cm. Se calcularon los valores de la puntuación z para cada caso individual según los estándares de referencia nacionales. A partir de las mediciones obtenidas se calculó el índice de masa corporal (IMC), el cual se estandarizó también según las referencias poblacionales de España en 2010. Nos servimos de estos datos para la definición de sobrepeso y obesidad, según se muestra en la tabla I. Se midieron los perímetros de cintura y cadera con el paciente de pie, con los pies juntos y los miembros superiores al costado del tronco, con el abdomen desnudo y relajado, en bipedestación y durante la espiración, con una cinta métrica flexible a nivel de la porción media existente entre la última costilla y la cresta ilíaca, así como a nivel de los trocánteres mayores de la cabeza del fémur, respectivamente. A partir de estas mediciones se calcularon los índices cintura/altura (ICA) y cintura/cadera (ICC), los cuales

Tabla I. Criterios para la definición de sobrepeso y obesidad según las recomendaciones de la Guía de Práctica Clínica para la Prevención y Tratamiento de la Obesidad Infanto-juvenil (actualmente en revisión) para los menores de 16 años, y según los criterios de la OMS para mayores de 16 años

	Menores 16 años	Mayores 16 años
Sobrepeso	IMC Pc > 90-96	IMC ≥ 25-30
Obesidad	IMC > Pc 97	IMC > 30

son indicativos de riesgo cardiovascular en caso de valores superiores a 0,5 para ICA, y valores superiorres o iguales a 0,9 en hombres, y 0,85 en mujeres para ICC.

NIVELES SANGUÍNEOS DE LEPTINA Y ADIPONECTINA

Se realizó una extracción sanguínea por vía periférica tras 12 horas de ayuno, y un análisis por técnicas de ELISA a partir de las muestras de suero. A posteriori se calculó el cociente leptina/adinonectina.

RESISTENCIA INSULÍNICA

Definida en nuestra población por un índice *Homeostasis Model Assesment* (HOMA) > 3, calculado a partir de la fórmula: RI = (glucemia basal en ayunas x insulina) / 405, donde la glucemia se expresa en mg/dL y la insulina en mU/L.

EVALUACIÓN ECOGRÁFICA

Realizada con un ecógrafo Philips modelo EPIQ 7 con sondas lineales para la evaluación del cIMT. Con el paciente en decúbito supino y la cabeza en ligera extensón, se tomaron tres mediciones de ambas carótidas comunes, a 1 cm de la bifurcación carotídea, reflejándose como valor del estudio la media de los valores obtenidos.

ESTUDIO DE COMPOSICIÓN CORPORAL

Se realizó mediante análisis de bioimpedancia eléctrica (BIA) con un monitor modelo AKERN 101 (Akern, Monachiello, Pisa). El estudio se efectuó en una camilla con el participante en decúbito supino, con los brazos separados del tronco aproximadamente 30° y las piernas separadas 45°. Se colocaron 4 electrodos (Biatrodes, Akern) en las extremidades, dos en la mano derecha y otros dos en el pie derecho, con una separación entre ambos de 4-5 centímetros. Estos adhesivos, conectados por cables al aparato, proporcionan los datos de resistencia (Rz) y reactancia (Xc). Estos, junto con peso, talla, edad, género, etnia y actividad física del paciente, se introdujeronn en el programa informático del dispositivo (Bodygram plus), registrándose los valores de masa grasa y masa magra obtenidos.

ANÁLISIS ESTADÍSTICO

A partir de los datos obtenidos se realizó un análisis descriptivo, proporcionando distribuciones de frecuencias relativas y absolutas para las variables cualitativas, y medidas de posición y dispersión para las cuantitativas. Las diferencias de variables cuantitativas entre dos grupos se estudiaron con el test de la t de Student o el de Wilcoxon para muestras independientes, en función del cumplimiento de la hipótesis de normalidad. Si los grupos eran 3 o más, se aplicó el test ANOVA previa verificación de la normalidad y homocedasticidad. El estudio de correlación entre dos variables cuantitativas se valoró con el coeficiente y test de correlación de Pearson o de Spearman, en función de que las variables se ajustasen o no a una distribución normal. Se contruyeron de forma univariante y multivariante modelos lineales para identificar los factores asociados a leptina, adiponectina, cIMT y homocisteína. El nivel de significación empleado fue de 0,05. El análisis estadístico se efectuó mediante el programa R (R Development Core Team), versión 3.6.3.

RESULTADOS

En los últimos 20 años, en el Hospital Universitario Central de Asturias se registraron 82 niños con diagnóstico de leucemia aguda a una edad entre los 6 y 16 años. De esta muestra, únicamente 22 pacientes pudieron ser evaluados, distribuyéndose los 60 pacientes restantes según se reproduce en el siguiente diagrama de flujo (Fig. 1).

Los sujetos de nuestro estudio tenían, en el momento de la evaluación, una edad media de 19 años y 5 meses (rango: 12,5 a 30 años). La edad media a la que los pacientes finalizaron el tratamiento fue de 9 años y dos meses (DE: 4 años) y el tiempo medio que había pasado desde entonces hasta el momento del estudio fue de 7,05 años (DE: 4,65 años). Distribuídos por sexos, nuestro estudio está conformado por 14 hombres y 8 mujeres.

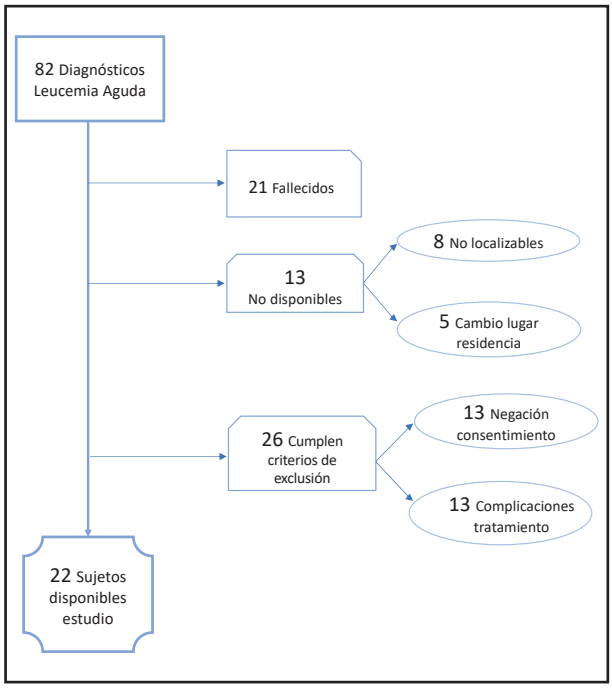

Figura 1.
Diagrama de flujo de pacientes.

Con respecto al diagnóstico de la enfermedad, prácticamente todos los casos fueron diagnosticados de LLA. Únicamente un paciente había padecido leucemia mieloide aguda (LMA) y tres pertenecían al grupo de las leucemias promielocíticas (LPM). Cabe destacar un caso de LLA con cromosoma Philadelphia positivo. El 45 % de los casos se incluyeron en protocolos de riesgo intermedio y el 18 % en protocolos de alto riesgo, correspondiendo el resto a un bajo riesgo.

Tras su evaluación somatométrica, el 16 % de los sujetos que conforman la muestra se etiquetaron de sobrepeso y otro 16 % alcanzaban criterios de obesidad; dos tercios de los sujetos estudiados presentaban normopeso.

Se encontraron ocho individuos (el 36 % de la muestra) con RI, de los cuales solamente dos eran mujeres, y todos menos uno eran menores de 18 años al momento de la evaluación. En nuestra muestra, el valor de HOMA-IR en el p75 fue de 3,76. Más de la mitad (5/8) tenían normopeso. Aquellos supervivientes con RI presentaban una ratio leptina/adiponectina significativamente más alta que la de aquellos sin RI (2,52 *vs.* 0,45; p = 0,037), situándose el p75 en 1,43.

Con respecto a los niveles de leptina, se ha analizado si su comportamiento difiere en función de otras variables, encontrándose diferencias significativas según el sexo, de forma que las mujeres presentan valores significativamente más altos (Tabla II). También con la presencia de obesidad y sobrepeso. Aunque se encuentran valores de leptina marcadamente superiores en los sujetos con RI, esta relación no alcanza la significación estadística. No se han encontrado tampoco diferencias estadísticamente significativas con respecto al tratamiento recibido con radiotera-

Tabla II. Variables somatométricas y clínico-analíticas

	Media	DS	Mínimo	Máximo
Z Peso	0,38	1,32	-215	3,06
Z Talla	-0,19	1,16	-2,61	1,76
Z IMC	0,73	1,47	-0,9	4,07
ICC	0,84	0,05	0,73	0,95
ICA	0,47	0,07	0,40	0,64
% MG	0,22	0,12	0,54	0,93
% MM	0,78	0,12	0,54	0,93
Leptina (ng/mL)	13,54	17,31	1,11	67,2
Adiponectina (µg/mL)	12,85	5,64	3,8	25,2
Ratio L/A	1,80	3,45	0,06	13,50
HOMA	2,77	1,35	0,94	5,75
cIMT (mm)	0,53	0,07	0,4	0,7

Estadísticos descriptivos. Z Peso: puntuación estandarizada segun sexo y edad para la variable peso; Z Talla: puntuación estandarizada segun sexo y edad para la variable talla; Z IMC: puntuación estandarizada segun sexo y edad para la variable índice de masa corporal; % MG: masa grasa corporal en porcentaje; % MM: masa magra corporal en porcentaje; Ratio L/A: ratio leptina/adiponectina; HOMA: índice Homeostasis Model Assesment; cIMT: espesor mediointimal carotídeo.

pia craneal o corticoterapia. Se construyeron modelos lineales con el fin de identificar variables asociadas a la leptina. Se aplica un método de selección paso a paso, resultando en el modelo final que, a mayor IMC, aumenta el valor de leptina (Tabla III).

En relación a los niveles de adiponectina, no se han encontrado diferencias estadísticamente significativas con respecto a la RI, el haber recibido tratamiento con radioterapia craneal o la corticoterapia. A diferencia de la leptina, tampoco se han encontrado diferencias con respecto al sexo y la presencia de obesidad. Solo el IMC parece asociarse de forma significativa a la adiponectina (Tabla III), aunque dicha significación desaparece al ajustar por el resto de variables en el modelo multivariante (Tabla IV).

Aplicado el mismo estudio con el cIMT, únicamente se han encontrado diferencias significativas con respecto a la presencia de obesidad (Tabla III). Se ha analizado si su comportamiento difiere en función de otras variables, encontrándose diferencias significativas según la presencia de obesidad y sobrepeso. Se construyeron modelos lineales con el fin de identificar variables asociadas al cIMT. Se aplica un método de selección paso a paso, resultando en el modelo final que al aumentar la proporción de masa grasa corporal aumenta el valor de cIMT, al igual que ocurre con la toma de corticoides, mientras que ser mujer se asocia con una disminución de dicho índice. Se incluyen otras variables en el modelo final sin alcanzar significación estadística (Tabla IV).

DISCUSIÓN

Nuestro estudio aporta nuevas evidencias de las alteraciones del metabolismo hidrocarbonado, así como de la disfunción secretora del tejido adiposo y las células endoteliales en individuos supervivientes de leucemia en edad pediátrica. Su interés radica en ser una fuente de datos de una población escasamente estudiada, como es la edad infantojuvenil, sin claros valores de referencia establecidos en cuanto a adipokinas, RI o cIMT. Todo esto ayuda a entender el elevado riesgo cardiovascular de este tipo de pacientes y pretende enfatizar el mantenimiento de estrategias de control y vigilancia de la salud que ayuden a contener la evolución de dicho riesgo en accidentes cardíacos y cerebrovasculares.

Sobrepeso y obesidad son ya condiciones habituales en nuestro entorno pediátrico (12) y se han asumido por parte de la ciudadanía como normales, a pesar del alto riesgo que entrañan. Sin embargo, no está tan asumido que los niños con normopeso puedan tener factores de riesgo cardiovascular ya presentes a edades muy tempranas y capaces de deteminar un futuro adverso (13,14). Esto se acentúa en el caso de determinadas patologías, como en el caso que nos ocupa: los supervivientes de leucemia aguda infantil. Factores como la exposición a corticoides, la radioterapia, la predisposición genética o el sexo femenino favorecen la acumulación en exceso de grasa corporal (15).

Tabla III. Análisis del comportamiento de adipokinas y cIMT entre los distintos grupos de una misma variable para HOMA, sexo, tratamiento corticoideo, presencia de radioterapia y peso. Se detallan para los grupos definidos por variables cualitativas la media (desviación típica) en la aplicación de test paramétricos y la mediana (recorrido intercuartílico) en el supuesto no paramétrico

	Leptina		cIMT		Adiponectina	
	Mediana (p25-p75)	**Valor p**	**Media (DS)**	**Valor p**	**Media (DS)**	**Valor p**
HOMA						
< 3	3,28 (2,41-5,47)	0,096	0,51 (0,08)	0,247	14,45 (5,92)	0,212
> 3	15,35 (8,70-23,62)		0,55 (0,05)		11,37 (4,05)	
Sexo						
Hombre	3,25 (2,41-9,29)	0,044	0,54 (0,06)	0,571	12,46 (4,70)	0,68
Mujer	15,45 (6,56-32,78)		0,52 (0,08)		13,53 (7,32)	
Corticoides						
No	16,50 (13,65-21,55)	0,18	0,48 (0,08)	0,2	13,31 (10,41)	0,883
Sí	12,84 (2,41-15,45)		0,54 (0,07)		12,77 (9,38)	
Radioterapia						
No	4,76 (2,41-21)	0,695	0,54 (0,07)	0,288	12,82 (5,81)	0,973
Sí	6,93 (3,23-10,8)		0,5 (0,04)		12,93 (5,66)	
Obesidad						
Normopeso	3,23 (2,29-6,20)[a]	0,004	0,51 (0,04)	0,001	13,40 (5,14)	0,104
Sobrepeso	21,00 (18,85-23,80)[b]		0,63 (0,06)		7,98 (3,75)	
Obesidad	41,40 (24,82-55,27)[b]		0,48 (0,09)		16,60 (7,54)	

cIMT: grosor mediointimal carotideo. [a-b]Diferente letra indica diferencia significativa (p < 0,05).

Tabla IV. Modelos de regresión, univariantes y multivariante, tanto para leptina como para grosor mediointimal carotídeo y adinopectina

	Leptina						cIMT						Adiponectina					
	Modelos univariantes			Modelo multivariante			Modelos univariantes			Modelo multivariante			Modelos univariantes			Modelo multivariante		
	Coef.	IC 95 %	Valor p	Coef.	IC 95 %	Valor p	Coef.	IC 95 %	Valor p	Coef.	IC 95 %	Valor p	Coef.	IC 95 %	Valor p	Coef.	IC 95 %	Valor p
HOMA < 3 > 3	14,47	1,24 a 27,71	0,034				0,036	-0,027 a 0,099	0,247				-3,08	-8,07 a 1,91	0,212			
Sexo Hombre Mujer	16,13	1,56 a 30,70	0,032				-0,018	-0,083 a 0,047	0,571	-0,077	-0,152 a -0,002	0,045	1,07	-4,25 a 6,38	0,68			
Corticoides No Sí	-5,13	-27,99 a 17,74	0,645				0,056	-0,032 a 0,143	0,2	0,1	0,032 a 0,168	0,007	-0,54	-8,02 a 6,95	0,883			
Radioterapia No Sí	-7,54	-26,03 a 10,95	0,405				0,038	-0,111 a 0,035	0,288				0,1	-6,03 a 6,23	0,973			
Edad	1,41	0,18 a 3,00	0,079	0,64	0,14 a 1,43	0,102	0,005	-0,001 a 0,012	0,105				-0,28	-0,82 a 0,27	0,303			
IMC	2,64	1,58 a 3,69	< 0,001	3,3	2,60 a 4,01	< 0,001	0,008	-0,002 a 0,013	0,007	0,413	0,136 a 0,690	0,006	-0,5	-0,97 a -0,02	0,04			
% MG	125,52	93,62 a 157,43	< 0,001				0,204	-0,043 a 0,451	0,101				-11,43	-32,48 a 9,62	0,271			

Coef.: coeficiente; cIMT: grosor mediointimal carotídeo; IMC: índice de masa corporal; % MG: masa grasa en porcentaje.

Otros factores relacionados con la obesidad en estos pacientes son el descenso de los niveles de somatotropina y el aumento de la resistencia a la leptina (16). En nuestra muestra, un tercio de los evaluados se etiquetaron de sobrepeso/obesidad y un 36 % presentaban resistencia insulínica. Entre los individuos con RI, más de la mitad tenían normopeso y no se encontraron diferencias entre sexos.

Entre los supervivientes de LA infantil, la evidencia disponible revela datos de RI en parte independientes del índice de masa corporal (6), encontrándose un índice HOMA elevado en pacientes sin sobrepeso ni obesidad. Hay estudios que demuestran una correlación positiva entre el índice HOMA y la ratio leptina/adiponectina (L/A) (19-21), y algunos autores defienden que obtienen valores más elevados en aquellos pacientes que habían sido expuestos a radioterapia craneal (6,21,22). Los resultados de nuestro estudio están alineados con los mostrados por la publicación de Tonorezos y cols. (6), de forma que podemos decir que también observamos datos de RI en parte independientes del IMC, sugiriendo en estos pacientes sin sobrepeso ni obesidad la implicación de otros mecanismos en la generación de la misma. Además, encontramos una correlación positiva entre la ratio L/A y la elevación del índice HOMA, aunque en nuestro estudio no conseguimos alcanzar la significación estadística, quizás por lo limitado de la muestra. En esta relación no encontramos diferencias en función de la historia de radioterapia craneal y tampoco entre los sexos.

La adiponectina es una adipokina implicada en la regulación del metabolismo de los hidratos de carbono de forma independiente del grado de adiposidad (14). Su deficiencia genética se asocia al desarrollo de RI, mientras que su administración a modelos experimentales aumenta la sensibilidad a la acción de la insulina. Cifras inferiores a 7 ng/mL se relacionan con la presencia de síndrome metabólico (23). Cuando hay un diagnóstico de leucemia se observa que los niveles de adiponectina son bajos, y son numerosos los estudios que han planteado el rol que esto puede tener en el desarrollo de la misma (24,25). Entre los supervivientes, los niveles de adiponectina se encuentran generalmente descendidos, lo cual se relaciona más con la presencia de resistencia insulínica y obesidad que con las secuelas de la propia enfermedad. En nuestro estudio no hemos logrado encontrar asociación significativa alguna en relación a la sensibilidad a la insulina, el sexo, la composición corporal o el tratamiento recibido. La relación entre niveles de adiponectina a largo plazo y el tratamiento con radioterapia craneal (CRT) es controvertida; mientras unos estudios muestran niveles bajos de adiponectina en relación con la CRT (6), otros los descartan (5).

La leptina es una adipokina proinflamatoria sintetizada y secretada casi de forma exclusiva por el tejido adiposo. Presenta secreción pulsátil y acción sobre el hipotálamo, determina nuestro comportamiento alimentario, regula el gasto energético y la termogénesis, y tiene un papel importante en la homeostasis del metabolismo de la glucosa y los lípidos (17). Sus niveles (ajustado el IMC) son mayores en mujeres que en hombres y se elevan exponencialmente en los estados de obesidad (26). En la población adulta española, los valores medios de leptina en el año 2010, en el p75, fueron de 14,3 ng/ml en los varones y 37 ng/ml en las mujeres (27). Según la bibliografía consultada, cifras superiores a 14 ng/mL se relacionan con la presencia de síndrome metabólico (23). En relación a la leucemia, se ha observado que las mujeres supervivientes a esta patología presentan leptinemias más elevadas, incluso a largo plazo, tras finalizar el tratamiento; en esta población, el sexo femenino es factor de riesgo para la elevación de los niveles de leptina (8,29). Este hallazgo se ha atribuido en mayor medida a la elevación del IMC y al sexo femenino más que al tratamiento recibido (28). Resultados acordes encontramos en nuestro estudio, en el cual las mujeres presentan, con respecto a los varones, mayores valores de leptina; lo mismo ocurre en presencia de obesidad y sobrepeso con respecto a los individuos con normopeso. Se ha prestado especial atención a la radioterapia intracraneal, la cual se ha postulado como factor para la resistencia a la leptina debido al daño hipotalámico producido por la radiación (6,29,30). Sin embargo, otros estudios sugieren niveles elevados de leptina, incluso más de un año después del tratamiento, tanto en hombres como en mujeres, y tanto en aquellos que han recibido radioterapia intracraneal como en aquellos que no la han recibido (31). En nuestro estudio no hemos encontrado diferencias estadísticamente significativas con respecto a la presencia o no de resistencia insulínica, o a haber recibido tratamiento con radioterapia craneal, al contrario que lo descrito en los estudios de Karaman (29) o Jahnukainen (30). Nuestro modelo lineal predice un aumento de la leptina a mayor IMC, y un descenso de valores de la misma según aumenta el gasto energético en reposo. En el modelo univariante se aprecia relación entre la masa grasa corporal y los niveles de esta adipoquina, relación que se pierde al ajustar el resto de variables; esto estaría también en consonancia con la bibliografía consultada (21). Lo que parece estar claro es que, de alguna manera, la propia leucemia o su tratamiento parecen generar una resistencia central a la leptina, de forma que estos sujetos almacenan energía de forma inapropiada, ayudando a explicar los cambios de composición corporal y de RI que sufren a largo plazo los supervivientes de leucemia (6).

El cIMT, establecido en los últimos años como marcador de riesgo cardiovascular, evalúa la aterosclerosis subclínica de forma precoz y no invasiva. Estudios recientes no han encontrado diferencias en cuanto al cIMT entre pacientes jóvenes supervivientes de LLA y controles sanos (10,32). Esto se explica porque el cIMT demuestra alteraciones morfológicas mientras que la disfunción endotelial, que es uno de los primeros componentes de la aterosclerosis, precisa de un daño mantenido en el tiempo para que se materialice en alteraciones de la pared de los vasos. Los incrementos del cIMT en los primeros años de la edad adulta deben interpretarse con cautela, ya que se ha descrito un remodelado arterial en respuesta al aumento de la masa magra y la presión arterial correspondientes a la adolescencia y el crecimiento en adultos jóvenes. Además, la exposición continuada a dislipemias, inflamación y otros factores de riesgo cardiovascular podría ser crítica en el desarrollo de daño arterial en la edad adulta posterior (34,35). En nuestro

estudio, únicamente hemos encontrado diferencias significativas con respecto a la presencia de obesidad y sobrepeso. Ni el sexo ni la presencia de RI se han podido relacionar de forma significativa con valores aumentados de cIMT, lo que puede en parte explicarse por el limitado tamaño de la muestra. Con respecto al uso de radioterapia, esta no parece ser un factor influyente en el aumento del cIMT. En esta línea, nuestro estudio es uno más para intentar resolver la controversia existente en este momento (9,28,32).

Como fortaleza de este estudio destaca la amplia evaluación multifactorial de sus integrantes, la cual abarca aspectos bioquímicos, estructurales y de composición corporal que, integrados en conjunto en una misma muestra, no se han investigado hasta la fecha en esta población. La principal limitación es el tamaño muestral, así como la complejidad de su análisis debido a la diversidad de la muestra, lo cual puede disminuir su potencia por la presencia de pacientes en distintos tramos etarios y con particularidades propias. Cabe mencionar además las dificultades de interpretación por falta de estudios previos con datos de referencia en la población infantojuvenil y la escasa bibliografía disponible.

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ARÁN

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Trabajo Original

Pediatría

Concentración de vitamina D en niños diabéticos de tipo 1. Asociación con el control glucémico y el metabolismo óseo y lipídico

Vitamin D concentration in type 1 diabetic children. Association with glycemic control, lipidic and bone metabolism

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Resumen

Introducción: debido a que la vitamina D juega un papel primordial en la regulación de la secreción de insulina y su déficit parece conferir un mayor riesgo de desarrollar diabetes *mellitus*, se ha pretendido analizar la prevalencia del déficit de vitamina D en nuestra población de niños diabéticos de tipo 1 y si se relaciona con un peor control de la enfermedad, así como con el metabolismo lipídico y óseo.

Material y métodos: se trata de un estudio retrospectivo en el cual se disponía de los datos clínicos y analíticos de 124 niños diabéticos de tipo 1, controlados en la Unidad de Diabetes Pediátrica de nuestro hospital.

Resultados: la concentración mediana de vitamina D del total de la muestra fue de 25,41 (7,43) ng/mL, siendo más elevada en el sexo masculino que en el femenino (p = 0,006). Un 43,55 % de los niños presentaron buen control metabólico, con hemoglobina glicosilada inferior al 7,5 %, siendo la concentración de glucosa y la de colesterol ligeramente más bajas, y la de fosfatasa alcalina ósea más elevada, cuando la concentración de vitamina D era ≥ 20 ng/ml.

Conclusiones: no hemos encontrado diferencias significativas en el control metabólico de los niños con concentración suficiente o insuficiente de vitamina D. Los niños del estudio tenían concentraciones de vitamina D muy parecidas a las de un estudio similar en niños sanos, así como un buen control metabólico de su diabetes, siendo su perfil óseo y lipídico más favorable cuando presentaban buen control metabólico.

Palabras clave:

Vitamina D. Diabetes *mellitus* de tipo 1. Niños. Metabolismo óseo.

Abstract

Introduction: vitamin D plays a key role in regulating insulin secretion and its deficit seems to confer an increased risk of developing diabetes *mellitus*. In this study, we have tried to analyze the prevalence of vitamin D deficiency in our type 1 diabetic children population and if their deficiency is related to a worse control of the disease, as well as with their bone and lipid metabolism.

Material and methods: this is a retrospective study, in which both clinical and laboratory data were available for 124 children, who were controlled in the Pediatric Diabetes Unit of our Hospital.

Results: the median vitamin D concentration of the total sample was 25.41 (7.43) ng/ml, higher in males than in females (p = 0.006); 43.55 % of patients had good metabolic control, with glycosylated hemoglobin lower than 7.5 %. Slightly lower glucose and cholesterol concentrations and higher bone alkaline phosphatase concentrations were found, when vitamin D concentration was ≥ 20 ng/ml.

Conclusions: we have not found any significant differences in relation to metabolic control between children with sufficient and insufficient concentration of vitamin D. The children in the present study presented very similar vitamin D concentrations to those found in a study made in healthy children, and a good metabolic control of their diabetes, with bone and lipid profiles being more favorable when they had good metabolic control.

Keywords:

Vitamin D. Type 1 diabetes *mellitus*. Children. Bone metabolism.

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INTRODUCCIÓN

La vitamina D es una prohormona compleja (1) cuya principal función es mantener la concentración de calcio y fósforo dentro del rango fisiológico que permita el metabolismo normal, la transmisión neuromuscular y la mineralización ósea.

En los últimos años se han encontrado receptores de vitamina D o de sus metabolitos en diferentes células del organismo, lo cual sugiere que, además de estar implicada en el metabolismo fosfocálcico, puede estar implicada en numerosos procesos fisiológicos (2). Por ello, recientemente no solo se relaciona su déficit con el raquitismo y la osteomalacia, como clásicamente se pensaba. Por sus propiedades no calciotrópicas (3,4), no tan conocidas hasta ahora, se está asociando también con mayor riesgo de padecer diabetes *mellitus* (5), obesidad (6), enfermedades cardiovasculares (7), oncológicas (8) e infecciosas, enfermedades autoinmunes (3) e incluso enfermedades psiquiátricas (9).

Las interacciones con el sistema inmune son los más conocidos de sus efectos no clásicos (10-12). La vitamina D actúa en la mayoría de las células del sistema inmune a través de su receptor VDR, haciendo que aumente su efectividad de acción ante las infecciones e inhibiendo el desarrollo de la autoinmunidad, así como el rechazo de los trasplantes.

Asimismo, la vitamina D juega un papel primordial en la regulación de la secreción de insulina, pudiendo aumentar su secreción y la sensibilidad a la misma, por lo que su déficit confiere un mayor riesgo de sufrir diabetes *mellitus* de tipo 1 y 2 (13,14), habiéndose comprobado también que los niños, en su debut, tienen menores concentraciones de vitamina D, en comparación con los controles sanos (15).

Además, la vitamina D parece afectar a la homeostasis de la glucosa, mediante un efecto directo sobre las células β y, de forma indirecta, mediante la regulación del calcio, puesto que la secreción de insulina depende del calcio intracelular (16). Sin embargo, la relación entre la concentración de vitamina D y el control metabólico de la DM de tipo 1, así como el efecto de la suplementación con vitamina D, son dos aspectos que permanecen todavía sin aclarar (17,18).

El objetivo del presente estudio fue analizar la prevalencia de déficit de vitamina D en nuestra población de niños diabéticos de tipo 1 y estudiar si existe relación entre el déficit de vitamina D y un peor control de la enfermedad, así como con el metabolismo óseo y lipídico, dado que la DM1 puede inducir osteopenia y/o alteraciones en la homeostasis mineral, principalmente durante el crecimiento, y que la presencia de dislipidemia incrementa la frecuencia y la severidad de las complicaciones asociadas a la diabetes.

MATERIAL Y MÉTODOS

Se trata de un estudio retrospectivo en el cual se determinó la concentración de 25-hidroxivitamina D, aprovechando la analítica anual de control, en la revisión rutinaria trimestral de los niños afectos de DM1, que se controlan en la Unidad de Diabetes Pediátrica de nuestro hospital. En dicha Unidad se controlan 290 niños y, en el periodo analizado, se disponía de los datos de 124 niños con DM1, ya que se excluyeron los debuts que se produjeron en dicho periodo, por considerarse más adecuado que la muestra fuera homogénea y que todos los pacientes estuvieran ya en tratamiento con insulina. También se excluyeron los niños que tuvieran en ese momento una enfermedad aguda o estuvieran tomando alguna medicación que pudiera interferir con el metabolismo de la vitamina D o con el metabolismo óseo.

Las analíticas se realizaron tras la obtención del consentimiento informado de los pacientes, padres o tutores. El estudio fue aprobado por el Comité de Ética de nuestra comunidad autónoma y se han seguido los protocolos de nuestro hospital para poder acceder a los datos de las historias clínicas.

Debido a que la concentración de vitamina D se asocia con la exposición solar, variable que cambia con la estación del año, se anotó la estación del año en que se extrajo la muestra de la analítica, de acuerdo con las siguientes categorías: invierno (22 de diciembre a 21 de marzo), primavera (22 de marzo a 21 de junio), verano (22 de junio a 21 de septiembre) y otoño (22 de septiembre a 21 de diciembre).

Ninguno de los niños con DM1 estaba tomando suplementos de vitamina D y se analizaron también, en el suero, otros parámetros del metabolismo fosfocálcico, como calcio, fósforo, parathormona intacta (PTHi), osteocalcina y fosfatasa alcalina ósea, así como el perfil lipídico completo: colesterol total (CT), colesterol LDL (C-LDL), colesterol HDL (C-HDL) y triglicéridos (TG). La clasificación en cuanto a suficiencia o deficiencia de vitamina D se ha llevado a cabo basándonos en las recomendaciones de la OMS y de las guías de práctica clínica publicadas en el año 2011, considerándose como deficientes aquellas concentraciones de vitamina D < 20 ng/ml y como suficientes aquellas ≥ 20 ng/ml (19).

Para determinar la concentración de 25-hidroxivitamina D en el suero, el laboratorio utiliza el analizador IDS-iSYS. El ensayo emplea una técnica de quimioluminiscencia, totalmente automatizada. Dicha técnica se encuentra estandarizada como garantía de calidad de los resultados.

La isoenzima ósea de la fosfatasa alcalina (FAO) en suero se midió mediante un enzimoinmunoensayo manual (Microvue BAP EIA, Quidel Corporation, San Diego, CA, EE. UU.), así como la osteocalcina (N-MID Osteocalcin ELISA, Inmunodiagnostic Systems Ltd, Boldon, Reino Unido). El rango de referencia de la FAO es de 12-43 U/L y el de osteocalcina de 5,8-39,8 ng/ml. Tanto la PTHi como los parámetros lipídicos se determinaron mediante técnicas totalmente automatizadas en un AU 5420 Analyzer, (Beckman Coulter Inc, Brea, EE. UU.). Para el análisis estadístico se utilizó el programa IBM SPSS® Statistics 21.0 (IBM Corporation, Armonk, NY). En primer lugar se empleó el test de Kolmogorov-Smirnov (K-S) para estudiar la distribución de las variables cuantitativas. En el caso de que siguieran una distribución normal (K-S, $p > 0,05$) se emplearon para su descripción la media (M) y la desviación estándar (DS) y para el análisis, respecto a una variable cualitativa de 2 categorías, el test de la t de Student (*t-test*).

En el caso de que las variables cuantitativas no siguieran una distribución normal (K-S, $p \leq 0,05$), se emplearon para su descripción la mediana (Me) y el rango intercuartílico (RQ) y, para el análisis respecto a una variable cualitativa de 2 categorías, el test de la U de Mann Whitney (W). Respecto a una variable cualitativa de más de 2 categorías, se usó el test de Kruskal-Wallis (H) con la corrección de Bonferroni. El test del chi cuadrado (χ^2) se empleó para el análisis entre variables cualitativas.

Además, se analizaron las correlaciones entre las variables cuantitativas, empleando el test de Pearson (r) y el test de Spearman (rs), según siguieran o no una distribución normal, respectivamente.

Los resultados más relevantes y significativos se describen en el apartado de resultados. El nivel de significación estadística, para todos los test estadísticos empleados, se estableció a partir de un valor $p \leq 0,05$.

RESULTADOS

La muestra estaba formada por 124 niños con DM1, existiendo una distribución homogénea entre niños (43,5 %) y niñas (56,5 %). La edad mediana de los niños fue de 13,92 (RQ: 7) y la edad media de debut de 7,50 (DS: 3,90 años). El porcentaje de prepúberes fue del 33,1 %.

La enfermedad autoinmune más frecuente de los niños incluidos en la serie fue la enfermedad tiroidea autoinmune (11,3 %), seguida de la celiaquía (7,3 %). Como tratamiento, al 78,2 % de los niños se les aplicaba terapia convencional con múltiples dosis de insulina (MDI) y, al resto, infusión continua de insulina subcutánea (ICIS).

Alrededor de la mitad (43,55 %) de los niños con DM1 presentaban un buen control metabólico (HbA1c < 7,5 %). La mediana de tiempo de evolución de la enfermedad de la población de estudio fue de 4,32 años (RQ: 4,81).

Las características del grupo con respecto a edad, años de evolución, índice de masa corporal (IMC), necesidad de insulina total y bolos de insulina rápida al día se muestran en la tabla I y los resultados bioquímicos en las tablas II y III.

La concentración media de vitamina D del total de la muestra fue de 25,41 (DS: 7,43). El presente estudio mostró que la prevalencia del déficit de vitamina D en estos niños, entendida como aquellas concentraciones por debajo de 20 ng/mL, era del 24,79 %. Un 54,55 % del total presentaban concentraciones de vitamina D entre 20 y 29 ng/mL, y el 20,66 % las tenían iguales o superiores a 30 ng/ml. La mayoría de los sujetos presentaban, por tanto, concentraciones iguales o superiores a 20 ng/ mL (79,84 0%).

Tabla I. Características antropométricas y tratamiento recibido por los niños con diabetes *mellitus* de tipo 1

Variable	Valores*	Prueba de normalidad†
Porcentaje de varones	43,5 %	
Edad en años	13,92 (7)[1]	0,118 (p = 0,001)
Años evolución	4,32 (4,81)[1]	0,143 (p < 0,001)
IMC (kg/m^2)	19,62 (3,23)[2]	0,063 (p = 0,200)
Número bolos insulina/día	4 (1)[1]	0,266 (p < 0,001)
Insulina en UI/kg/día	0,79 (0,38)[1]	0,087 (p = 0.038)

**En las variables cuantitativas se muestran las medidas de tendencia central y desviación típica en relación a los resultados de las pruebas de normalidad. †Test de prueba de normalidad realizado: Kolmogorov-Smirnov. [1]Mediana y rango intercuartílico. [2]Media y desviación típica.*

Tabla II. Parámetros del metabolismo glucídico y óseo

Variable	Total	Pruebas de normalidad*	Niños	Pruebas de normalidad*	Niñas	Pruebas de normalidad*
Glucosa (mg/dl)	178,74 (67,35)[2]	0,083 (p = 0,060)	174,74 (62,71)[2]	0,086 (p = 0,200)	183,62 (71,05)[2]	0,096 (p = 0,200)
HbA1c (%)	7,84 (18,60)[2]	0,080 (p = 0,074)	7,8 (1,2)[1]	0,087 (p = 0,200)	7,75 (1,4)[1]	0,135 (p = 0,024)
Vitamina D (ng/ml)	25,41 (7,44)[2]	0,069 (p = 0,200)	26,8 (7,4)[2]	0,092 (p = 0,200)	23,42 (8,8)[2]	0,080 (p = 0,200)
PTHi (pg/ml)	26 (9,5)[1]	0,148 (p < 0,001)	37,67 (16,05)[1]	0,132 (p = 0,010)	40,52 (17,38)[1]	0,199 (p < 0,001)
Calcio (mg/dl)	9,90 (0,4)[1]	0,119 (p = 0,001)	9,84 (0,34)[1]	0,113(p = 0,052)	9,77 (0,29)[1]	0,134 (p = 0,026)
Fósforo (mg/dl)	4,65 (0,68)[2]	0,064 (p = 0,200)	4,69 (1)[2]	0,070 (p = 0,200)	4,60 (1)[2]	0,083 (p = 0,200)
Fosfatasa alcalina ósea (FAO) (U/L)	101,805 (48,56)[2]	0,072 (p = 0,200)	112,5 (76,2)[1]	0,082 (p = 0,200)	90,75 (95,6)[1]	0,137 (p = 0,019)
Osteocalcina (ng/ml)	62,48 (47,859)[1]	0,142 (p < 0,001)	55,5 (47)[1]	0,199 (p < 0,001)	48,75 (47)[1]	0,144 (p = 0,011)

**Test de prueba de normalidad realizado: Kolmogorov-Smirnov. [1]Mediana y rango intercuartílico. [2]Media y desviación típica.*

Tabla III. Parámetros del metabolismo lipídico

Variable	Total	Pruebas de normalidad*	Niños	Pruebas de normalidad*	Niñas	Pruebas de normalidad*
Colesterol total (mg/dl)	173 (37)[1]	0,102 (p = 0,007)	168 (36)[1]	0,115 (p = 0,042)	177 (35)[1]	0,096 (p = 0,200)
Colesterol HDL (mg/dl)	61,58 (12,46)[2]	0,064 (p = 0,200)	58,54 (11,15)[2]	0,068 (p = 0,200)	65,28 (13,06)[2]	0,083 (p = 0,200)
Colesterol LDL (mg/dl)	100 (27)[1]	0,087 (p = 0,037)	98 (26)[1]	0,129 (p = 0,013)	102 (28)[1]	0,085 (p = 0,200)
Triglicéridos (mg/dl)	59 (31)[1]	0,129 (p < 0,001)	62,5 (28)[1]	0,176 (p < 0,001)	55 (33)[1]	0,129 (p = 0,037)

**Test de prueba de normalidad realizado: Kolmogorov-Smirnov. [1]Mediana y rango intercuartílico. [2]Media y desviación típica.*

La concentración de vitamina D, tanto en el grupo de niños como en el de niñas sigue una distribución normal (niñas: vit. D: K-S, 0,08, p = 0,20; niños: vit. D: K-S, 0,092, p = 0,20) y se observó una media de concentración de vitamina D significativamente más elevada (t-test: -2,8, p = 0,006) en los niños (IC 95 %: 25,48-29,11) frente a las niñas (IC 95 %: 21,05-25,18). La HbA1c media de la muestra total, expresada en porcentaje (%), fue de 7,84 (DS: 1,010).

La vitamina D, la glucosa y la HbA1c de la muestra total siguieron una distribución normal (K-S, 0,069, p = 0,020; K-S, 0,083, p = 0,060 y K-S, 0,080, p = 0,074, respectivamente) y tanto la asociación entre vitamina D y glucosa como la asociación entre vitamina D y HbA1c no fueron estadísticamente significativas (r: 0,099, p = 0,281 y r: 0,020, p = 0,829, respectivamente).

Sin embargo, cuando se establecieron dos grupos de niños, en función de su concentración de vitamina D (≥ 20 ng/ml y < 20 ng/ml), se pudo observar que la concentración de glucosa en sangre de los niños con concentración < 20 ng/ml (K-S, 0,097, p = 0,20) era inferior, pero no de forma significativa (t-test: -1,818, p = 0,072) a la concentración de glucosa de los niños con concentración ≥ 20 ng/ml de vitamina D (K-S, 0,077, p = 0,20).

Al estudiar el colesterol total respecto a la concentración de vitamina D (< 20 ng/ml CT, K-S: 0,12, p = 0,20; ≥ 20 ng/ml CT, K-S: 0,11, p = 0,014) y el colesterol HDL (< 20 ng/ml HDL-C, K-S: 0,068, p = 0,20; ≥ 20 ng/ml HDL-C, K-S: 0,069, p = 0,20) se encontraron en ambos casos diferencias estadísticamente significativas (W: 9,435, p = 0,011 y t-test: -3,277, p = 0,001 respectivamente). En el caso de la FAO respecto a la concentración de vitamina D (< 20 ng/ml CT, K-S: 0,121, p = 0,20; ≥ 20 ng/ml CT, K-S: 0,083, p = 0,020), las diferencias no llegaron a ser estadísticamente significativas (t-test: 1,725, p = 0,087) (Tabla IV).

Es decir, los niños con una concentración adecuada de vitamina D (≥ 20 ng/ml) tenían a su vez menores concentraciones de colesterol total (≥ 20 ng/ml, Me: 170; < 20 ng/ml, Me: 186,5). Sin embargo, los niños con insuficiencia de vitamina D (< 20 ng/ml) tenían concentraciones más elevadas de colesterol HDL (< 20 ng/ml, C-HDL: 63,93-73,43; ≥ 20 ng/ml, C-HDL: 56,64-61,72).

Tampoco se encontraron diferencias significativas al analizar la relación de la concentración de vitamina D con el control metabólico de los niños con DM1 (χ^2: 1,13, p = 0,286), pues la concentración de vitamina D era muy similar entre los pacientes con buen y mal control metabólico.

Tabla IV. Parámetros bioquímicos según la concentración de vitamina D

Parámetros bioquímicos	Concentración de vitamina D	Media (IC 95 %)	Significación estadística (p)
Glucosa (mg/dl)	< 20 ng/ml	199,61 (172,15-227,06)	*t de Student -1,818 (p = 0,072)*
	≥ 20 ng/ml	171,70 (157,49-185,91)	
Colesterol total (mg/dl)	< 20 ng/ml	187,79 (177,43-198,14)	*U de MannWhitney 943,500 (p = 0,011)*
	≥ 20 ng/ml	174,05 (167,68-180,41)	
Colesterol HDL (mg/dl)	< 20 ng/ml	68,68 (63,93-73,43)	*t de Student -3.277 (p = 0,001)*
	≥ 20 ng/ml	59,18 (56,64-61,72)	
Fosfatasa alcalina ósea (U/l)	< 20 ng/ml ≥ 20 ng/ml	89,51 (68,04-110,99)	*t de Student -1,725 (p = 0,087)*

Cuando se analizó la concentración de vitamina D según la estación del año en la que se realizó la analítica (invierno, vit. D, K-S: 0,107, p = 0,20; primavera, vit. D, K-S: 0,128, p = 0,20; verano, vit. D, K-S: 0,136, p = 0,20; otoño, vit. D, K-S: 0,143; p = 0,048) se encontraron diferencias significativas (H: 15,07, p = 0,02). En invierno y primavera se obtuvieron concentraciones más bajas (20,65-24,40 y 19,91-27,66, respectivamente) mientras que en verano y otoño (23,15-35,80 y 25,89-29,78, respectivamente) se encontraron concentraciones más elevadas. Las diferencias intergrupos encontradas entre invierno y otoño e invierno y verano fueron estadísticamente significativas (corrección de Bonferroni, 0,003 y 0,025, respectivamente (Fig. 1).

Al analizar la concentración de vitamina D según la comorbilidad (no comorbilidad, vit. D, K-S: 0,075, p = 0,20; sí comorbilidad, vit. D, K-S: 0,118, p = 0,20) no se observaron diferencias estadísticamente significativas (t-test: 1,431, p = 0,155).

Por otra parte, al estudiar la correlación entre la concentración de vitamina D y la concentración de los marcadores óseos (fósforo, K-S: 0,064, p = 0,20; FAO, K-S: 0,072, p = 0,20; PTH, K-S: 0,148, p < 0,001; calcio, K-S: 0,119, p = 0,001; osteocalcina, K-S: 0,142, p < 0,001) no se encontró correlación estadísticamente significativa con ninguno de ellos (vitamina D y fósforo: r = 0,026, p = 0,779; vitamina D y FAO: r = -0,004, p = 0,967; vitamina D y PTHi: rs = -0,173, p = 0,062; vitamina D y calcio: rs = 0,031, p = 0,734; vitamina D y osteocalcina: rs = 0,005, p = 0,961).

Por otra parte, los niños que tenían buen control metabólico (HbA1c < 7,5) presentaban mayor concentración de colesterol HDL y de FAO de forma estadísticamente significativa (p = 0,015 y p = 0,005, respectivamente), al aplicar el test de la t de Student, por tratarse de muestras que siguen una distribución normal. Asimismo, se obtuvieron diferencias estadísticamente significativas al comparar los niveles de triglicéridos, colesterol LDL y osteocalcina (U de Mann Whitney, distribuciones no paramétricas) según el control metabólico. Tanto la concentración de triglicéridos como la de colesterol LDL fueron superiores en los niños con mal control metabólico (p = 0,006 y p = 0,010, respectivamente). Sin embargo, la concentración de osteocalcina fue inferior en los niños que presentaban mal control metabólico (p = 0,044).

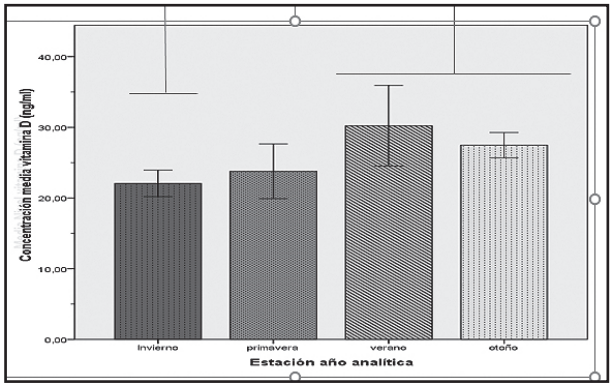

Figura 1.

Concentración de vitamina D en niños con DM1 según las distintas estaciones del año.

DISCUSIÓN

Los resultados del presente estudio muestran que no hay una relación entre la concentración adecuada o inadecuada de vitamina D y el control metabólico de la DM1. La concentración media de vitamina D obtenida en nuestra población está por encima del límite de 20 ng/ml, al igual que lo descrito en otro estudio realizado en una cohorte de 107 niños sanos (20). Sin embargo, el porcentaje de niños con concentraciones de vitamina D por debajo de 20 ng/ml es bastante más bajo que el que presentan otros estudios, también realizados en poblaciones de niños con DM1.

Aunque varios estudios muestran mayor prevalencia de déficit de vitamina D en los niños con DM1, en comparación con los controles sanos (21), nuestros resultados muestran concentraciones plasmáticas de vitamina D muy similares entre los niños con DM1 y los niños sanos, al igual que otros estudios (22-24).

El establecimiento como punto de corte de la concentración de 25(OH)D por debajo de 20 ng/mL para considerar que existe déficit de vitamina D se fundamenta en los estudios de Chapuy y cols. (25), que ya en 1997 observaron un claro aumento de la PTHi en sangre cuando la concentración de vitamina D era < 20 ng/ml y que la densidad mineral ósea no disminuye hasta alcanzar concentraciones de 25(OH)D < 20 ng/mL. No obstante, para maximizar el efecto de la vitamina D en otros tejidos, deberían conseguirse concentraciones por encima de 30 ng/mL, ya que la concentración de 25(OH)D, que precisa la 1-alfa-hidroxilasa para sintetizar 1,25(OH)D, varía según si la acción es endocrina o autocrina/paracrina (26,27). En nuestro estudio el porcentaje encontrado de niños con concentración de vitamina D igual o superior a 30 ng/ml solo fue del 20,16 %, por lo que sigue siendo necesario controlar y mejorar la concentración de vitamina D en estos niños.

Cuando analizamos la concentración de vitamina D según la estación del año en que se realizó la extracción, encontramos concentraciones más elevadas en verano y otoño (tras pasar el verano) y más bajas en invierno y primavera, resultados similares a los obtenidos por Hansen y cols. en una población formada por niños y adultos (28), y por Shen y cols. en un estudio llevado a cabo en población adulta (29).

Es importante destacar que, en condiciones normales, existe una variación importante en los niveles de vitamina D según la estación del año, debido a la diferente exposición solar. Sin embargo, Pozzilli y cols. (30) no encontraron esta variación estacional de la concentración de vitamina D en los niños con DM1.

Por otra parte, mientras que existe evidencia respecto a la asociación entre el déficit de vitamina D y el riesgo de padecer diabetes *mellitus*, hay mayor controversia en cuanto a la relación entre la concentración de vitamina D y el control metabólico de la enfermedad. En este estudio no hemos encontrado correlación estadísticamente significativas entre la concentración de vitamina D y el porcentaje de HbA1c, al igual que en los estudios de Carakushansky y cols. (24), Mutlu y cols. (31) y Brody y cols. (32), todos ellos realizados en niños diabéticos de tipo 1, lo cual, sin embargo, contrasta con los resultados aportados por otros autores como ALkharashi y cols. (33) y Savastio y cols. (34), los cuales encontraron una asociación inversa estadísticamente significativa.

Existe también bastante controversia en cuanto a la relación existente entre la presencia de dislipemia y los niveles bajos de vitamina D. Así, por ejemplo, en la *National Health and Nutrition Examination Survey* encontraron, al igual que nosotros, concentraciones de CT más elevadas en los niños que presentaban déficit de vitamina D (35), a diferencia de otros autores (36,37). En nuestro estudio, los niños con déficit de vitamina D también presentaban concentraciones más altas de C-HDL, al igual que en el estudio de Szternel y cols. (38). En la misma línea, Wang y cols. (39), en un metaanálisis acerca del efecto de la suplementación de vitamina D sobre los lípidos, encontraron que se producía una disminución del C-HDL y los TG al suplementar a los niños con vitamina D, aunque las diferencias no llegaron a ser estadísticamente significativas.

Cabe destacar también que en nuestro estudio no se ha encontrado ninguna asociación inversa ($p = 0,062$) entre la concentración de PTHi y vitamina D, lo cual difiere de la asociación inversa estadísticamente significativa que se encuentra habitualmente en los niños no diabéticos (21). En este sentido, algunos estudios, como el de Schwarz y cols. (40), llevado a cabo en una población adulta, sugieren que en los pacientes diabéticos existe una respuesta entorpecida de PTHi ante valores bajos de vitamina D, debido a la desregulación de la homeostasis del calcio.

Además, los niños incluidos en el presente estudio también presentaron una tendencia a una mayor concentración de fosfatasa alcalina ósea (marcador de formación ósea) cuando la concentración de vitamina D era ≥ 20 ng/ml. Es decir, cuando la concentración de vitamina D es suficiente, existe una mayor formación ósea, lo cual puede apoyar la idea de que una concentración adecuada de vitamina D en estos niños ayudará a prevenir la osteoporosis futura, comorbilidad bien conocida de los pacientes adultos con DM1.

Una de las limitaciones del estudio es el escaso número de niños incluidos en el mismo, aunque es bastante representativo de la totalidad de niños que se controlan en la Unidad de Diabetes Pediátrica de nuestro hospital. Además, el menor déficit de vitamina D encontrado en nuestra población de niños con DM1 en relación con otros estudios podría deberse en parte a que a los niños se les hace mucho hincapié para que mejoren los hábitos de vida saludable, tanto en lo que respecta a la alimentación como en lo referente a la práctica de ejercicio físico al aire libre, lo que puede contribuir a aumentar la concentración de vitamina D en la sangre.

La vida saludable al aire libre y el ejercicio son fundamentales en la consecución de unos niveles adecuados de vitamina D y, en consecuencia, en la obtención de un pico de masa ósea adecuado que permita contrarrestar otros efectos de la propia enfermedad.

CONCLUSIONES Y RECOMENDACIONES

Se trata de un estudio descriptivo transversal de los niveles de vitamina D en pacientes con DM de tipo 1 y de su asociación con el metabolismo óseo y lipídico en el que no hemos encontrado diferencias estadísticamente significativas de control metabólico entre los niños con concentración suficiente e insuficiente de vitamina D.

Los niños con DM1 del presente estudio presentan un buen control metabólico de su diabetes y su concentración de vitamina D es bastante parecida a la encontrada en un estudio similar en niños sanos. Aunque no hemos encontrado relación entre las concentraciones plasmáticas de vitamina D y la mayoría de los marcadores del metabolismo óseo analizados, sí hemos observado una tendencia a una mayor concentración de fosfatasa alcalina ósea (marcador formación ósea) cuando la concentración de vitamina D era ≥ 20 ng/ml, por lo que sigue siendo muy importante controlar y, a ser posible, mejorar la concentración de vitamina D de estos niños para prevenir una osteoporosis futura y garantizar una salud adecuada en todos los aspectos. El perfil óseo y lipídico de estos niños era más favorable cuando presentaban buen control metabólico.

Por otra parte, debido a la capacidad de la vitamina D para modular el sistema inmunológico, varios estudios han demostrado que concentraciones bajas de la misma se asocian de forma estadísticamente significativa a riesgo de contraer infección por coronavirus; a su vez, sabemos que la severidad de los debuts diabéticos de los niños ha aumentado durante la pandemia de COVID, por lo que es de vital importancia el mantenimiento de una concentración adecuada de vitamina D en estos niños, aportando suplementos de la misma si fuera necesario.

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Trabajo Original

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Association of physical activity, muscular strength, and obesity indicators with self-concept in Chilean children

Asociación de indicadores de actividad física, fuerza muscular y obesidad con el autoconcepto en niños chilenos

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Abstract

Objectives: the present study examined the association of physical activity, muscular strength, and obesity indicators with self-concept in Chilean children.

Methods: this cross-sectional study included 1078 Chilean children (mean age: 9.1 years [standard deviation: 1.1]; 598 boys). Physical activity was evaluated using the Physical Activity Questionnaire for Older Children. Upper and lower limb strength was evaluated using a digital dynamometer and standing long jump performance, respectively. The general strength index was calculated based on z-score values. Obesity indicators used were height, weight, body mass index, and body fat. The self-concept test was used to determine the academic, social, emotional, family, physical self-concept dimensions and total self-concept of children.

Results: the mean total self-concept was 3.3 (standard deviation: 0.5). Physical activity was associated with academic (β: 0.32; p = 0.03), social (β: 0.24; p = 0.04), family (β: 0.13; p = 0.01), physical (β: 0.46; p = 0.01) self-concept dimensions and total self-concept (β: 0.22; p = 0.01), regardless of sex and age. Upper limb strength and general strength index were negatively associated with academic self-concept dimensions (β: -0.02; p = 0.01 and β: -0.13; p = 0.02) and total self-concept (β: -0.04; p = 0.01). Body weight and body mass index were negatively associated with academic (β: -0.01; p = 0.01 and β: -0.01; p = 0.02) and physical self-concept dimensions (β: -0.03; p = 0.03).

Conclusions: these findings suggest that physical activity is positively related with self-concept. Thus, physical activity and self-percept must be considered as an essential social cognitive perspective to provide suitable mental health in children.

Keywords:

Physical activity. Physical fitness. Obesity. Self-concept. Schoolchildren.

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Resumen

Objetivos: el presente estudio examinó la asociación de indicadores de actividad física, fuerza muscular y obesidad con el autoconcepto en niños chilenos.

Métodos: este estudio transversal incluyó a 1078 niños chilenos (edad media: 9,1 años [desviación estándar: 1,1]; 598 niños). La actividad física se evaluó mediante el *Physical Activity Questionnaire for Older Children*. La fuerza de los miembros superiores e inferiores se evaluó utilizando un dinamómetro digital y el rendimiento en salto de longitud de pie. El índice de fuerza general se calculó en base a los valores de z-score. Los indicadores de obesidad utilizados fueron altura, peso, índice de masa corporal y grasa corporal. Se utilizó el test de autoconcepto para determinar las dimensiones académicas, social, emocional, familiar, físico y autoconcepto total.

Resultados: la muestra total presento un autoconcepto promedio de 3,3 (desviación estándar: 0,5). La actividad física se asocio con autoconcepto académico (β: 0,32; p = 0,03), social (β: 0,24; p = 0,04), familiar (β: 0,13; p = 0,01), físico (β: 0,46; p = 0,01) y total (β: 0,22; p = 0,01). La fuerza muscular de miembros superiores y el índice general de fuerza se asociaran negativamente con al autoconcepto académico (β: -0,02; p = 0,01 y β: -0,13; p = 0,02) y total (β: -0,04; p = 0,01). Mientras que el peso corporal e índice de masa corporal se asociaron negativamente con autoconcepto académico (β: -0,01; p = 0,01 y β: -0,01; p = 0,02) y físico (β: -0,03; p = 0,03).

Conclusiones: estos hallazgos sugieren que la actividad física se relaciona positivamente con el autoconcepto. Así, la actividad física y la autopercepción deben ser consideradas como una perspectiva cognitiva social imprescindible para proporcionar una adecuada salud mental en los niños.

Palabras clave:

Actividad física. Aptitud física. Obesidad. Autoconcepto. Escolares.

INTRODUCTION

Self-concept is a psychological construct that refers to the mental perception that an individual has of himself or herself. This mental perception begins to develop early and is critical for the future physical and mental balance (1). Self-concept during early ages is based on the relationship with others. It considers a multidimensional perspective including academic, emotional, social, family and physical dimensions (2). The academic dimension is the result of experiences, fails and successes in the school context; the emotional dimension relates to the feeling of wellbeing and personal satisfaction; the social dimension refers to the meaning a child's behavior has for others (family, friends, teachers); and the physical dimension includes the perception of the own appearance and physical skills (2). All of these dimensions form a global self-concept, which is considered an emotional resource for mental and physical health (3). Moreover, each dimension of self-concept can be related to different aspects of wellbeing in childhood. A positive academic self-concept would be associated with academic performance and motivation to learn in primary school children (4), and the emotional self-concept would be associated with higher feelings of satisfaction with life and better psychological wellbeing (5). The social self-concept has been positively related to psychosocial wellbeing and satisfactory relationships with peers, and negatively with bullying victimization (6). The family self-concept is negatively related to disruptive behaviors and victimization (7).

The physical self-concept is one of the most studied dimensions in relation to health indicators such as nutritional status, body composition, physical activity and fitness. Such health indicators are considered predictors of physical and mental health in childhood and in adulthood (8,9), so studying its relationship with self-concept is interesting for developing health promotion strategies at young ages.

Cross-sectional studies have shown associations of physical self-concept with obesity indicators. Raustorp et al. reported a negative correlation between physical self-concept and body mass index in Swedish schoolchildren (11-12 years), and this association was stronger in girls than in boys (10). Similar results have also been shown in Spanish children (10-12 years) (11). In addition, moderate relationships between physical self-concept and physical activity and fitness have been observed in Estonian schoolchildren (11-14 years). This study further showed that specific components of self-concept predict physical activity and fitness (12). This positive correlation between physical self-concept and fitness has been observed even in the absence of a correlation between fitness and global self-concept (11). There is also evidence for positive effects on physical activity and strength interventions on children's physical self-concept. Lubans et al., for example, showed that that girls increased their physical self-concept (specifically body attractiveness) after an 8-week strength training. There was also a significant but marginal effect on the body. However, among the boys who participated in the intervention, physical self-concept remained stable (13). In addition, 80 % of Chilean children do not meet the minimum recommendations for physical activity, and their eating habits are far from the healthy ideal (14). Chilean children increased their prevalence of overweight and obesity by 3.9 % from 2009 through 2018 (15). The results of the 2018 Nutritional Map of Chile showed that more than 50 % of children were overweight and obese (15). This suggests that improving physical activity and decrease the rate of obesity has the potential to influence psychological health in children positively.

A meta-analysis studied the effect of physical activity interventions on self-outcomes, including self-concept. Included studies consisted of supervised physical activity interventions in children and adolescents in different settings. The results showed that randomized controlled interventions that considered physical activity alone (not in conjunction with other interventions) are effective in improving self-concept (16). A systematic review on the mechanisms of the effect of physical activity on mental health reported similar results (17). Both increase the physical activity level and muscular strength, are important for healthy future levels, and consequently decrease overweight and obesity in childhood. Nonetheless, few studies have associated health indicators with self-concept in Chilean children (18). To enhance the understanding of the association between physical activity, physical fitness, and self-concept the present study examined the association of physical activity, muscular strength, and obesity indicators with self-concept in Chilean children.

METHODS

STUDY DESIGN AND SAMPLE

This cross-sectional study is part of the "Development, scaling and validation of an integrated system for school interventions on diet, physical activity, and community environment in the Metropolitan Region of Chile". Details have been previously published (18).

The target population of the study included all students enrolled in primary schools from the southern area of Santiago, which provides a total sample size of 6,308 students. The study population consists of second to fourth-grade students (mean age of 9 years) from seven schools in the the Metropolitan Region of Chile. Data collection occurred from October to December 2019. Stratification, proportionality, and randomization techniques were employed to establish a representative sample (sample error, 0.04; IC = 95.5 %). Random stratified sampling with proportional affixation was used to ensure a homogeneous representation of the sample. The strata considered were grade (second, third and fourth grades from primary school), and sex (men and women). The final sample was 1,078 participants (598 boys).

The research team was present during the application of the instruments to ensure their correct implementation. Students completed the questionnaire anonymously, ensuring confidentiality during regular class time. Physical condition tests were administered during their regular physical education classes. Assessments were applied by health professionals who were previously trained in applying the tests and supervised by the expert investigators during all the dimensions.

This project was approved by the Ethics Committee of the Universidad de Santiago de Chile (number 187-2019). In all aspects, this research has been conducted according to the Declaration of Helsinki. Written consent has been obtained before participation from the guardians of students and the school community, who were informed of the study's nature before obtaining informed consent.

PHYSICAL ACTIVITY

Physical activity was evaluated using the Physical Activity Questionnaire for Older Children (19-21), in its validated Spanish version (21). The Physical Activity Questionnaire for Older Children is appropriate for school-aged children (grades 4-8; approximately, ages 8-14) who are currently in the school system and have recess as a regular part of their school week (22). Measures of physical activity have been validated previously and showed acceptable levels of test-retest reliability for both males ($r = 0.75$) and females ($r = 0.82$) (19).

Questions related to the amount of physical activity carried out in the last 7 days through 10 questions about its type and frequency. From the answers, a score that ranged between 1 and 5 was obtained, with a higher score indicating a greater practice of physical activity. The overall Physical Activity Questionnaire for Older Children score is a composite value that calculates the mean of nine item scores.

MUSCULAR STRENGTH

A Jamar® PC-5030 hydraulic dynamometer was used to determine maximum voluntary grip force contraction with precision range of 5-100 kg to 100 g, through two alternated attempts per hand with participants maintaining a standardized position with arms parallel to the body without touching it. The average of the best attempt for each hand was used for further analyses. Children were instructed to stop squeezing if they felt pain or discomfort during measurement. A standing long jump was used as a measure of lower limb strength. Participants performed two trials, with the better attempt being used for further analyses. The participants were verbally encouraged by the examiner to do their best during the tests. A general strength index was calculated as the mean of the z-scores (Z = [value-mean] / standard deviation) for upper and lower limb strength, for example (23).

OBESITY INDICATORS

The data were collected by professionals during the school visit according to standardized procedures of the National Health and Nutrition Examination Survey (24). The children were weighed with a Seca 813 scale (Seca®, Hamburg, Germany), which has a precision of 100 g, in light clothing and barefoot. Height was measured with the participants in the Frankfurt position using a Seca 213 (Seca®, Hamburg, Germany) stadiometer with a precision of 1 mm. Body mass index (kg/m^2) was calculated and subsequently converted to z-scores based on the World Health Organization growth reference charts (25).

Body fat was estimated via skinfold measurements using a Lange® caliper with a precision of 0.2 mm, and a constant pressure of 10 g/mm^2. Specifically, the equation proposed by Slaughter was used, which estimates total body fat based on triceps and subscapular skinfold thickness (26).

SELF-CONCEPT ASSESSMENT

To determine the level of self-concept of the participants, the Five-Factor Self Concept Questionnaire was used (27). The Five-Factor Self-Concept Questionnaire (27) is based on the Shavelson et al. (28) model and is one of the self-concept questionnaires most utilized for Spanish-speaking samples (29,30). The Five-Factor Self Concept Questionnaire was developed, validated, and normed in Spain on a large sample of nearly 6,500 participants ranging in age from 10 to 62 years, providing national norms for sex and age (28). Furthermore, Five-Factor Self Concept Questionnaire has been shown to be a valid and reliable measure of self-concept and has been used

previously in health research (17,31,32). Specifically, the AF-5 was developed to evaluate a person's self-concept, including academic (e.g., "I do my homework well"), social (e.g., "I am a friendly person"), emotional (e.g., reversed item, "Many things make me nervous"), family (e.g., "I feel that my parents love me"), and physical dimensions (e.g., "I like the way I look"). The scale consists of 30 items, six for each dimension. The items are statements that the participant must rate using a continuous response on a 99-point scale (visualized as a thermometer), ranging from 1 (complete disagreement) to 99 (complete agreement).

All participants completed the questionnaire on one occasion. Participants were asked to complete the questionnaire independently and honestly, based upon their feelings at that precise moment. Questionnaires were completed inside the school environment in the presence of the researchers.

STATISTICAL ANALYSIS

Descriptive statistics included mean and standard deviation as summary measures. The normality of continuous variables was verified using the Kolmogorov-Smirnov test. Sex differences were assessed using Student's t-test for independent samples. The correlation between physical activity, muscular strength, obesity indicators, and self-concept were performed with Pearson's correlation coefficients (r). The correlation was classified as weak (< 0.40), moderate (between ≥ 0.40 and < 0.70), or high (≥ 0.70) (33).

Multilevel linear regression models were used to determine physical activity, muscular strength, obesity indicators that best predicted self-concept. Our models were run individually for each variable adjusted for sex and age and allowed for clustering at the school level. The adjusted β and respective confidence interval (95 % CI) were obtained from multilevel linear regression models investigating the β of four different outcomes: academic, social, emotional, family, physical, and total self-concept. The statistical analyses presented in this study were conducted using the Statistical Package for the Social Sciences V26 software (SPSS Inc., IBM Corp., Armonk, New York, NY, USA)(34) and a p-value < 0.05 was adopted as significance level.

RESULTS

The children's characteristics are presented in table I. Of the 1,078 Chilean children (mean age: 9.1 years) in the sample 598 (55.5 %) were boys. Mean physical activity level, muscle strength (upper and lower limb strength, and general strength index), body weight, and body mass index were significantly higher in boys compared to girls. Girls had significantly higher body fat percentage values. Girls also displayed higher academic, physical, and total self-concept dimensions than boys. There were no significant differences between boys and girls for age, body height, and social, emotional, and family self-concept dimensions (Table I).

Table II presents the results of the correlation analysis describing associations between physical activity, muscular strength, and obesity indicators with self-concept dimensions. Correlation coefficients, generally, showed weak correlations with physical activity as the most prominent correlate with various dimensions of self-concept. Specifically, physical activity was positively associated with academic, social, family, and physical as well as total self-concept. On the other hand, muscle strength was negatively associated with academic and emotional self-concept dimensions as well as total self-concept. Obesity indicators were negatively associated with academic, social, emotional, physical self-concept dimensions, and total self-concept (with a greater correlation coefficient for body weight) (Table II).

Table III shows the results of the multilevel linear regression models for the effects of physical activity, muscular strength, and obesity indicators on self-concept dimensions in children. Physical activity was positively associated with academic, social, family, physical self-concept dimensions, and total self-concept regardless of sex and age. Upper limb strength and general strength index were negatively associated with academic self-concept dimensions and total self-concept, respectively. Furthermore, body weight and body mass index were negatively associated with academic and physical self-concept dimensions.

Table I. Descriptive analysis [mean (SD)] of physical activity, muscular strength, obesity indicators, and self-concept in Chilean children

Variables	Total (n = 1078)	Boys (n = 598)	Girls (n = 480)	p-value*
Age (years)	9.1 (1.1)	9.2 (1.2)	9.0 (1.1)	0.072
Physical activity	2.8 (0.6)	2.9 (0.6)	2.7 (0.5)	*0.041*
Upper limb strength (kg)	11.2 (4.0)	11.7 (4.0)	10.6 (3.9)	*< 0.001*
Lower limb strength (cm)	104.3 (20.5)	109.7 (21.1)	97.4 (17.5)	*< 0.001*
General strength index (z-score)	-0.04 (0.8)	0.19 (0.8)	-0.24 (0.7)	*< 0.001*
Body height (cm)	133.8 (9.1)	134.1 (9.0)	133.5 (9.3)	0.597

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Table I (Cont.). Descriptive analysis [mean (SD)] of physical activity, muscular strength, obesity indicators, and self-concept in Chilean children

Variables	Total (n = 1078)	Boys (n = 598)	Girls (n = 480)	p-value*
Body weight (kg)	35.4 (10.5)	35.7 (11.3)	35.1 (9.4)	*0.010*
Body mass index (kg/m^2)	19.5 (3.9)	19.5 (4.2)	19.4 (3.6)	*< 0.001*
Body fat (%)	27.2 (9.3)	25.3 (9.9)	29.5 (8.1)	*< 0.001*
Self-concept				
Academic	3.6 (0.9)	3.4 (0.9)	3.8 (0.9)	*0.049*
Social	3.4 (0.6)	3.4 (0.7)	3.5 (0.6)	0.069
Emotional	2.6 (0.9)	2.5 (0.9)	2.7 (0.8)	0.150
Family	3.5 (0.5)	3.4 (0.6)	3.5 (0.5)	0.134
Physical	3.4 (0.8)	3.4 (0.6)	3.5 (0.8)	*0.004*
Total	3.3 (0.5)	3.2 (0.5)	3.4 (0.5)	*0.042*

**Student's t-test for comparisons between boys and girls (p < 0.05).*

Table II. Correlation (r) between physical activity, muscular strength, obesity indicators, and self-concept in Chilean children

Variables	Academic	Social	Emotional	Family	Physical	Total
Physical activity	0.22 (p = 0.01)*	0.24 (p = 0.02)*	-0.01 (p = 0.06)	0.15 (p = 0.01)*	0.34 (p = 0.02)*	0.28 (p = 0.04)*
Upper limb strength (kg)	-0.11 (p = 0.02)*	-0.02 (p = 0.06)	-0.01 (p = 0.08)	-0.04 (p = 0.12)	0.01 (p = 0.09)	-0.05 (p = 0.06)
Lower limb strength (cm)	-0.09 (p = 0.02)*	-0.04 (p = 0.11)	-0.08 (p = 0.01)	-0.05 (p = 0.14)	0.05 (p = 0.17)	-0.06 (p = 0.02)*
General strength index (z-score)	-0.11 (p = 0.04)*	-0.03 (p = 0.13)	-0.06 (p = 0.17)	-0.06 (p = 0.11)	0.04 (p = 0.18)	-0.07 (p = 0.01)*
Body weight (kg)	-0.12 (p = 0.04)*	-0.07 (p = 0.02)*	0.02 (p = 0.09)	-0.05 (p = 0.11)	-0.14 (p = 0.01)*	-0.10 (p = 0.01)*
Body mass index (kg/m^2)	-0.06 (p = 0.02)*	-0.04 (p = 0.08)	-0.04 (p = 0.07)	-0.01 (p = 0.15)	-0.12 (p = 0.01)*	-0.06 (p = 0.03)*
Body fat (%)	-0.01 (p = 0.18)	-0.01 (p = 0.11)	-0.06 (p = 0.03)*	-0.02 (p = 0.12)	-0.07 (p = 0.04)*	-0.01 (p = 0.11)

**p < 0.05: Pearson's correlation (r).*

Table III. Multilevel linear analyses [β (95 % CI)] for physical activity, muscular strength, obesity indicators with self-concept in Chilean children

Variables	Academic	Social	Emotional	Family	Physical	Total
Physical activity	0.32 (0.23; 0.40) p = 0.01*	0.24 (0.18; 0.30) p = 0.02*	-0.02 (-0.10; 0.06) p = 0.06	0.13 (0.08; 0.18) p = 0.02*	0.46 (0.38; 0.53) p = 0.03*	0.22 (0.18; 0.27) p = 0.01*
Upper limb strength (kg)	-0.02 (-0.04; -0.01) p = 0.04*	-0.00 (-0.01; 0.00) p = 0.06	-0.00 (-0.01; 0.01) p = 0.09	-0.00 (-0.01; 0.00) p = 0.07	0.00 (-0.01; 0.01) p = 0.06	-0.01 (-0.01; 0.00) p = 0.11

(Continues on next page)

Table III (Cont.). Multilevel linear analyses [β (95 % CI)] for physical activity, muscular strength, obesity indicators with self-concept in Chilean children

Variables	Academic	Social	Emotional	Family	Physical	Total
Lower limb strength (cm)	-0.00 (-0.01; 0.01) p = 0.06	-0.01 (-0.00; 0.01) p = 0.08	-0.01 (-0.00; 0.01) p = 0.05	-0.01 (-0.01; 0.00) p = 0.09	0.01 (0.00; 0.01) p = 0.11	-0.00 (-0.00; 0.00) p = 0.08
General strength index (z-score)	-0.13 (-0.19; -0.06) p = 0.04*	-0.03 (-0.07; 0.02) p = 0.07	-0.06 (-0.13; 0.00) p = 0.12	-0.04 (-0.08; 0.00) p = 0.11	0.04 (-0.01; 0.10) p = 0.15	-0.04 (-0.08; -0.01) p = 0.04*
Body weight (kg)	-0.01 (-0.01; -0.02) p = 0.02*	0.01 (-0.01; -0.00) p = 0.09	0.01 (-0.01; 0.01) p = 0.11	0.01 (-0.01; 0.01) p = 0.14	0.01 (-0.01; 0.01) p = 0.17	0.01 (-0.01; 0.01) p = 0.09
Body mass index (kg/m^2)	-0.01 (-0.02; -0.01) p = 0.03*	0.01 (-0.01; -0.00) p = 0.08	0.01 (-0.01; -0.00) p = 0.12	0.01 (-0.01; -0.01) p = 0.14	-0.03 (-0.04; -0.01) p = 0.02*	0.01 (-0.01; 0.01) P = 0.16
Body fat (%)	0.00 (0.00; 0.00) p = 0.24	0.00 (0.00; 0.00) p = 0.26	0.00 (0.00; 0.00) p = 0.29	0.00 (0.00; 0.01) p = 0.22	0.00 (0.00; 0.001) p = 0.35	0.00 (0.00; 0.00) p = 0.29

*Multilevel general linear model controlling for sex, age, and type of school with school as a random effect, unstandardized beta coefficients are presented. *p < 0.05.*

DISCUSSION

The present study examined the association of physical activity, muscular strength, and obesity indicators with self-concept in Chilean children. We found that physical activity was positively associated with academic, social, family, physical self-concept dimensions and total self-concept, independently of sex and age. Upper limb strength and general strength index, on the other hand, were negatively associated with academic self-concept and total self-concept, respectively. Furthermore, body weight and body mass index were negatively associated with academic and physical self-concept dimensions.

A systematic review and meta-analysis suggested that children or adolescents with stronger beliefs about their physical features are more likely to engage in physical activity than those who report lower levels of self-concept (35). However, the authors propose that it is not clear if participation in physical activity leads to developments in self-concept or those with high levels of self-concept are concerned with physical activity (35). Particularly, the strength of the relationship between physical activity and self-concept (and dimensions) did not depend upon how the data were treated (i.e., whether self-concept was the dependent or independent variable). There is conflicting evidence in the literature regarding associations of this nature (35).

Although there is satisfactory evidence from previous studies to conclude that there is a bi-directional association between physical activity and self-concept, investigators working in this area are encouraged to conduct mediation analyses to assist in unravelling the nature of the association between self-concept and physical activity (16,35,36). Also, separate analyses that model the bidirectional nature of self-concept and its dimensions as both mediators and moderators of physical activity are necessary.

The observed associations between obesity indicators and self-concept in the present study are similar to those of other studies, with a higher body mass index being associated with a lower self-concept (37-39). García-Sánchez et al., (40), for example, found significant associations of body mass index and waist circumference with physical self-concept. However, the authors suggest that being in good physical shape counteracts low total self-concept associated with excess body weight, and overweight/obese children can reach similar levels as children of normal weight. Nevertheless, college girls with a higher body mass index also displayed a lower self-concept (41). Intervention studies using anthropometric measures and psychological tests comparable to the present study also found that people with a high body mass index obtain lower scores in self-concept, with stronger associations in the physical dimension than in other dimensions of self-concept (42-44).

It is necessary to mention that fitness or physical condition are currently assigned a protective value against cardio-metabolic diseases in obese subjects of different ages, which, added to this line of study of psychological factors in children and young people, is revealing a very interesting panorama regarding the role of physical fitness as a protective factor against overweight and obesity, controlling the associated psychosocial and pathophysiological alterations. Other authors point out a tendency to influence the elevated body mass index in all self-concept scores, this being more accentuated in the physical dimension than in the others (42,43).

This study has several strengths and limitations. The strengths of the present study include the study population, which consists of a representative group of the southern sector of Santiago, which allows for the generalization of the results. The limitations include the cross-sectional design and not being representative of all Chilean children. The work presented was restricted to children 9-11 years of age and, therefore, limits generalizability to other age groups, and we did not assess pubertal development. Questionnaires were used to determine physical activity and self-concept, which can lead to recall bias. Interventions with strategies that focus on the physical activity, muscular strength,

obesity indicators and self-concept should be planned and implemented, which may help understand which strategies should be implemented to promote self-concept dimension. This helps build evidence on the direct and indirect effects of physical activity, muscular strength, obesity indicators and self-concept at the population level.

The results of this study have demonstrated a significant association between physical activity, muscular strength, and obesity indicators with self-concept in children. Thus, physical activity and self-percept must be considered as an essential social cognitive perspective to provide suitable mental health in children. Accordingly, self-concept needs to be considered in the development of interventions targeting health behavior in children. A better understanding of various correlates contributing to health behaviors may also facilitate a more targeted approach towards health promotion in children. However, future studies with larger sample sizes and more heterogeneous populations are needed to clarify the association between lifestyle behaviors and self-concept in children and adolescents.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Prevalence of non-alcoholic fatty liver disease (NAFLD) in a cohort of patients with type 2 diabetes: the PHIGNA-DM2 study

Prevalencia de la hepatopatía grasa no alcohólica (HGNA) en una cohorte de pacientes con diabetes de tipo 2: el estudio PHIGNA-DM2

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Abstract

Background: type 2 diabetes (T2D) is a risk factor for nonalcoholic fatty liver disease (NAFLD). Objective: to evaluate the prevalence of NAFLD in a cohort of patients with T2D.

Methods: an observational, descriptive study performed between May 2018 and December 2019 at the Endocrinology and Nutrition Unit. The χ^2 test was performed for qualitative variables and a non-parametric test for the comparison of medians of quantitative variables. Steatosis degree was defined by the coefficient attenuated parameter (CAP): (S0: < 248 dB/m; S1: 248-268 dB/m; S2: 268-288 dB/m; S3: > 288 dB/m) or stiffness: F0-F1: < 8 kPa; F2: 8-10 kPa; F3: 10-15 kPa; F4: > 15 kPa, using transient elastography (TE) (FibroScan®). A univariate analysis was performed and subsequently a multivariate analysis with statistically significant variables used to study the predictive factors of intense steatosis and advanced fibrosis.

Results: n = 104 patients with T2D; 84 (80.7 %) were obese. TE demonstrated advanced fibrosis in 20 % and intense steatosis (S3) in more than 50 %. Lower total bilirubin (OR: 0.028; 95 % CI: [0.002-0.337]; p = 0.005) was found to be an independent factor for S3 steatosis in the multivariate analysis. BMI (OR: 1.497; 95 % CI: [1.102-2.034]; p = 0.01) was a predictive factor for advanced fibrosis in a multivariate analysis.

Conclusions: NAFLD-associated intense steatosis and NAFLD-associated fibrosis were commonly found in patients with T2DM and obesity. Diabetic patients should be screened for liver disease as one more target organ.

Keywords:

Type 2 diabetes. Diabetes *mellitus*. Nonalcoholic fatty liver disease. Liver fibrosis. Liver steatosis. Elastography. Risk factor.

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Institutional review board statement: the study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Ethics Committee of Virgen del Rocío Universitary Hospital.

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Resumen

Antecedentes: la diabetes de tipo 2 (DM2) es un factor de riesgo para la enfermedad del hígado graso no alcohólico (EHGNA).

Objetivo: evaluar la prevalencia de la EHGNA en una cohorte de pacientes con DM2.

Métodos: estudio descriptivo observacional realizado entre mayo de 2018 y diciembre de 2019 en la Unidad de Endocrinología y Nutrición. Se realizó una prueba de χ^2 para las variables cualitativas y una prueba no paramétrica para la comparación de medianas de variables cuantitativas. El grado de esteatosis se definió mediante el parámetro coeficiente atenuado (CAP): (S0: < 248 dB/m; S1: 248-288 dB/m; S2: 268-288 dB/m; S3: > 288 dB/m) o rigidez: F0-F1: < 8 kPa; F2: 8-10 kPa; F3: 10-15 kPa; F4: > 15 kPa, usando la elastografía transitoria (TE) (FibroScan®). Se realizó un análisis univariante y posteriormente un análisis multivariante con las variables estadísticamente significativas para estudiar los factores predictivos de esteatosis intensa y fibrosis avanzada.

Resultados: n = 104 pacientes con DM2; 84 (80,7 %) eran obesos. La TE demostró fibrosis avanzada en el 20 % y esteatosis intensa (S3) en más del 50 %. Los niveles disminuidos de bilirrubina total (OR: 0.028; 95 % CI: (0.002-0.337); p = 0.005) se encontraron como factores independientes para la esteatosis S3 en el analisis multivariable. El IMC (OR: 1.497; 95 % CI: (1.102-2.034); p = 0.01) fue un factor predictivo de fibrosis avanzada.

Conclusiones: la esteatosis intensa asociada a EHGNA y la fibrosis asociada a EHGNA se encontraron comúnmente en pacientes con DM2 y obesidad. Los pacientes diabéticos deben someterse a pruebas de detección de enfermedad hepática como un órgano diana más.

Palabras clave:

Diabetes de tipo 2.
Diabetes *mellitus*.
Enfermedad de hígado graso no alcohólico.
Fibrosis hepática.
Esteatosis hepática.
Elastografía.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in Western countries, and it is estimated that in 2030 it will be the most common indication for liver transplant (1). It is currently the cause of liver transplantation after hepatocellular carcinoma (2). NAFLD is more common in men, with an estimated prevalence of 30-40 % compared to 15-20 % in women (3). These incidences are challenging to measure due to the difficulty of having an accurate diagnosis, although data obtained show an incidence of 20/10000 people/year, with a peak in the sixth decade of life (4). Risk factors for NAFLD are age > 50 years, obesity, insulin resistance, type 2 diabetes, elevated ferritin levels, and polymorphism in the PNPLA35-7 gene (5-7).

This disease has been linked to other diseases, especially type 2 diabetes, cardiovascular disease and chronic kidney disease, but also sleep apnea, colorectal cancer, osteoporosis, psoriasis and other endocrinopathies such as metabolic syndrome, polycystic ovary syndrome, Cushing's syndrome, and acromegaly (8). Mortality in these patients increases by 57 % and is usually due to cardiovascular disease or complications of liver disease (9). It is estimated that 30-40 % of people with non-alcoholic fatty liver disease develop NASH (non-alcoholic steatohepatitis) (10), which increases the risk of liver disease-related mortality by 5- or 10-fold (9) depending on fibrosis degree. Since 40-50 % of patients with NASH develop liver fibrosis (10), this is the highest predictor of death from all causes and specially of liver disease in patients with NASH (11). FibroScan® is a method that has been used to assess the degree of liver steatosis and fibrosis in a non-invasive way. It has been proven to be accurate and accessible to measure liver tissue stiffness and consists of an ultrasound technique based on elastography which measures the speed propagation of low-frequency ultrasonic waves through the liver. This technique has also been proven to be useful for estimating the prognosis of patients with NAFLD (12). NAFLD does not cause signs or symptoms until advanced stages and may not alter the values of liver enzymes in blood.

Especially relevant is the relationship of this disease with type 2 diabetes, where the prevalence of NAFLD is higher than 70 % in some studies (13). Furthermore, NAFLD doubles the risk of diabetes incidence (8). In a study carried out in Italy it was found that people with diabetes have a three times higher risk of dying from chronic liver disease, mostly from non-viral or non-alcohol-related diseases, presumably from NAFLD (14). Currently, it is not clear whether type 2 diabetes and/or obesity are risk factors for this liver disease or if the pathological mechanisms involved are similar. Both are risk factors for developing cellular hepatocarcinoma (15-19).

The aim of this study was to measure the prevalence of NAFLD in a sample of patients with DM2 using FibroScan® to correlate these results with those of diagnostic screening tools, and to determine predictive factors for advanced steatosis and fibrosis in this sample.

MATERIAL AND METHODS

STUDY DESIGN AND POPULATION

An observational and descriptive study was carried out. The patients were recruited consecutively between May 2018 and December 2019 at the clinics of the Endocrinology and Nutrition Services of Virgen del Rocío University Hospital.

Inclusion criteria were: patients over 18 years of age capable of signing an informed consent, with a diagnosis of type 2 diabetes at least in the previous three months, and under monotherapy or combination treatment for diabetes.

Exclusion criteria included: patients with refusal of informed consent; type 1 diabetes; personal history of alcoholism defined according to WHO criteria (daily alcohol intake greater than 50 g in women and 70 g in men); personal history of hepatitis B, C, or autoimmune; personal history of malignancy (excluding cutaneous basal cell carcinoma) in the previous 5 years; personal history of liver surgery for any cause, personal history of use of potentially hepatotoxic treatments in the previous three months; personal history of Gilbert, Rotor, or Crigler-Najjar syndrome; a personal history of HIV infection; personal history of liver transplantation; any condition that could pose an unacceptable risk for the patient's participation in the study at the discretion of the investigator.

SAMPLE SIZE

A target population (N) of 2000 patients was assumed, with a margin of error D of 5 % and a Z-value of 1.96 (corresponding to a confidence level of 95 %), accepting a prevalence of NAFLD of 30 % and of NASH of 5 % (1-5). Assuming 20 % potential losses, the number of patients to be enrolled was n = 334 for NAFLD and 85 for NASH.

VARIABLES

Once patients agreed to participate in the study, they underwent a routine analysis and an elastographic assessment with FibroScan®. The parameters measured in the analysis were: fasting plasma glucose, HbA1c, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, GOT/AST, GPT/ALT, GGT, total bilirubin, platelets, and albumin. With these parameters the following indices were calculated: HSI (hepatic steatosis index), FIB-4 (liver fibrosis index), NFS (NAFLD fibrosis score) and Hepamet Fibrosis Score (HFS). The HSI index was calculated with the formula [8 x (GPT/ALT / GOT/AST) + BMI], to which two points were added if the patient had type 2 diabetes and also two points if the patient was female, considering a result < 30 as low risk, a result between 30 and 36 as intermediate-risk and a result > 36 as high risk. The FIB-4 index was calculated with the formula [age (years) x GOT/AST (IU/L)] / [Platelets (10^9/L) x √GPT/ALT (IU/L)], considering as low-risk a result < 1.3, intermediate risk a result between 1.3 and 2.67, and high risk a result > 2.67. The NFS index was calculated with the formula [-1.675 + 0.037 x age (years) + 0.094 x BMI (kg/m^2) + 1.13 x altered glucose/diabetes (1 = Yes, 0 = No) + 0.99 x (GOT/AST / GPT/ALT) - 0.013 x platelets (109/L) - 0.66 x albumin (g/dL)], considering a result of < -1.455 as low risk, a result between -1.455 and 0.676 as intermediate risk, and a result > 0.676 as high risk. The Hepamet Fibrosis Score was calculated using the online application freely available at https://www.hepamet-fibrosis-score.eu, considering < 0.12 as low risk, results from 0.12 to 0.47 as intermediate risk, and results above 0.47 as high risk. Steatosis by the coefficient attenuated parameter (CAP) was measured using FibroScan® as S0 (< 248 dB/m); S1 (248-267 dB/m); S2 (268-280 dB/m) and S3 (> 280 dB/m). Fibrosis was measured using FibroScan® as F0-F1: < 8 kPa; F2: 8-10 kPa; F3: 10-15 kPa; F4: > 15 kPa. Advanced fibrosis was considered when > 10 kPa (F3-F4).

Other variables collected were: date of birth, sex, weight, height, BMI, degree of obesity, presence of arterial hypertension, use of antihypertensive drugs, presence of dyslipidemia, use of lipid-lowering drugs, history of smoking, the presence of a family history of early cardiovascular disease, the presence of established cardiovascular disease (ischemic heart disease and/or cerebrovascular events), the time of evolution of diabetes (in years), the type of antidiabetic drugs used and the presence of diabetic microvascular complications (diabetic retinopathy, diabetic nephropathy and diabetic neuropathy).

The study was approved by the Ethics Committee of Virgen del Rocío University Hospital

DATA ANALYSIS

The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS®), version 25 for Windows (IBM Corporation, New York, USA). A descriptive analysis was performed, obtaining the median and quartiles for quantitative variables (expressed as P50 [P25-P75]) and frequency for qualitative variables (expressed as n [%]), both in the total sample and in the subgroups with and without intense steatosis. A χ^2 test was performed for qualitative variables and a non-parametric test for the comparison of medians of quantitative variables for the comparison between both groups. A univariate analysis was performed and subsequently a multivariate analysis with the statistically significant variables to study the predictive factors of intense steatosis and advanced fibrosis. Results of the univariate and multivariate analysis were expressed as odds ratio (OR) (95 % confidence interval [CI]). A p-value of less than 0.05 was considered statistically significant.

RESULTS

SAMPLE DESCRIPTION

A sample of 104 patients was included in the study; 59 (56.7 %) patients were male and the median age was 59 years, with a median time of diabetes evolution of 9 (4-15.75) years. The median glycemic control by HbA1 was 7.3 % (6.47-8.52); 17.5 % of patients presented microvascular complications; 51 (49 %) patients used oral antidiabetic treatment, and 50 % used insulin and oral antidiabetic drugs, while the remaining 1 % used only basal-bolus insulin therapy. Other baseline characteristics are described in table I.

LIVER STUDY RESULTS

Figure 1 shows the results for risk of fibrosis according to FIB-4, NFS, and HFS. The NFS and HFS indices could only be calculated in 67 patients due to lack of albumin values in 48 patients.

The results of steatosis risk according to the HSI index were 2.9 % low risk, 3.9 % intermediate risk, and 93.2 % high risk. Transient elastography using FibroScan® was carried out in all patients: F0-F1: 64.65 %, F2: 15.15 %, F3: 11.11 %, F4: 9.09 %. Regarding steatosis results, 24.24 % of patients had S1 degree, 17.17 % had S2 degree, and 58.59 % had S3 degree.

When evaluating noninvasive scores as predictors of intense steatosis only HSI was statistically significant in the univariate analysis (OR: 1.099; 95 % CI: (1.045-1.156); p = 0.000)

PREDICTIVE FACTORS OF INTENSE STEATOSIS AND ADVANCED FIBROSIS

When comparing the results of non-intense (S1-S2) and intense steatosis (S3) groups we found that in the S3 group patients had a higher BMI (38.63 vs 32.67 kg/m^2; p = 0.003), higher

Table I. Baseline characteristics

Variable	Results
Obesity degree	
Normal weight	6 (5.8 %)
Overweight	14 (13.5 %)
Obesity grade I	34 (32.7 %)
Obesity grade II	17 (16.3 %)
Obesity grade III	33 (31.7 %)
BMI (kg/m^2)	34.57 (30.82-42.57)
Arterial hypertension	87 (83.7 %)
Dyslipidemia	72 (73.1 %)
Cardiovascular disease	33 (31.7 %)
Total cholesterol (mg/dL)	164 (138-200)
Triglycerides(mg/dL)	172 (119-221)
GOT/AST (U/L)	18 (15-26)
GPT/ALT (U/L)	22 (16-32)
GGT (U/L)	23 (17-35)
Total bilirrubin (mg/dL)	0.39 (0.28-0.54)
Platelets (× 10^9/L)	267 (228-326)
Albumin (g/dL)	4.4 (4.1-4.6)

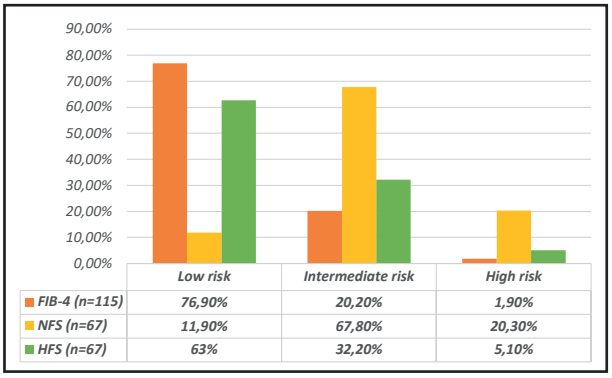

Figure 1.

Comparison of fibrosis risk according to the FIB-4, NFS and HFS indices.

levels of total cholesterol (170 vs 152.5 mg/dL; p = 0.036) and lower total bilirubin (0.35 vs 0.45 mg/dL; p = 0.045). None of the variables related to diabetes (time of evolution, HbA1c, microvascular complications or type of treatment) showed significant differences between both groups.

When performing a logistic regression analysis of factors related to S3 steatosis we found statistical significance in the univariate analysis for BMI, total cholesterol, total bilirrubin, and HSI score, but only lower total bilirubin (OR: 0.028; 95 % CI: [0.002-0.337]; p = 0.005) was found to be an independent factor for S3 steatosis in the multivariate analysis.

Table II shows the only variables that obtained statistical significance in the univariate analysis concerning the presence of advanced liver fibrosis (F3-F4). The following variables obtained statistical significance: sex (male), BMI, age, GOT/AST, GGT, and a high result obtained when calculating the HSI index. All of them except age were shown to be risk factors. When performing the multivariate analysis with these variables, only BMI (OR: 1.497; 95 % CI: (1.102-2.034); p = 0.01) maintained its statistical significance.

None of the other indices (FIB-4, NFS, HFS) obtained statistical significance in the univariate analysis when evaluating the risk of advanced liver fibrosis. We did not found statistical significance in the univariate or multivariate analysis of liver fibrosis and steatosis regarding control-of-diabetes parameters such as HbA1c and time of disease evolution (Table III).

DISCUSSION

The results obtained are comparable to similar relevant studies carried out in Asian countries where the presence of NAFLD has been evaluated in patients with type 2 diabetes. The most important are those carried out by Kwok et al. (20) (Hong Kong), Lee Lai et al. (21) (Malaysia) and Tuong et al. (22) (Vietnam). Although these studies were carried out in an Asian population, the mean BMIs obtained were 28.2 kg/m^2, 26.6 kg/m^2 and 24.9 kg/m^2, respectively, showing a trend towards westernization of these countries over the last years, which allows comparison with our study. Despite this, in these studies the prevalence of steatosis was 72.8 %, 72.4 % and 73.3 %, respectively, while it was 100 % in our study. This could be explained by the BMI of our sample where the median value was 34.45 kg/m^2. In the study carried out by Kwok et al. (20), the prevalence of liver steatosis measured by FibroScan® increased to 94.6 % if only the patients with a BMI > 30 kg/m^2 are taken into account. On the other hand, in the study carried out by Lai et al. (21), the prevalence of steatosis also increased if only obese patients were taken into account (89.1 %). Finally, in the study carried out by Tuong et al. in Vietnam, 100 % of obese patients had steatosis. Regarding the prevalence of advanced fibrosis (grades F3-F4, ≥ 9.5 kPa), in these studies this prevalence was 17.1 %, 21 % and 9.5 %, respectively, similar to ours (20.2 %).

Another interesting point of our work is the use of the HSI, HFS, NFS and FIB-4 scores and their comparison with the results obtained in the liver study using FibroScan®. The interpretation of the results obtained regarding the NFS and HFS scores is limited by the low percentage of patients for whom the calculation could be performed. This happened because albumin is not routinely determined in our center. The importance of this datum lies in the fact that the use of these scores in daily clinical practice may be limited for the same reason. As in the study by Singh et al. (23), There was great variability in the percentage of patients who were estimated to be at high risk for advanced fibrosis with the NFS and FIB-4 scores.

Table II. Association between presence of advanced liver fibrosis (F3-F4) in FibroScan® and the characteristics of patients with type 2 diabetes by univariate and multivariate logistic regression analysis

Variable	Univariate analysis			Multivariate		
	OR	IC (95 %)	p	OR	IC (95 %)	p
Male	3.814	(1.176-12.36)	0.026	4.415	(0.984-19.817)	0.053
BMI	1.141	(1.065-1.222)	< 0.001	1.497	(1.102-2.034)	0.01
Age	0.932	(0.889-0.976)	0.003	0.976	(0.910-1.048)	0.508
GOT/AST	1.035	(1.004-1.066)	0.026	1.02	(0.981-1.062)	0.32
GGT	1.016	(1.002-1.031)	0.024	1.017	(1-1.035)	0.051
HSI	1.086	(1.028-1.148)	0.003	0.795	(0.618-1.023)	0.075

Table III. Association between control and time of evolution of type 2 diabetes and intense hepatic steatosis and advanced hepatic fibrosis in the univariate analysis

Variable	Univariate analysis-Intense steatosis			Univariate analysis- Advanced fibrosis		
	OR	IC (95 %)	p	OR	IC (95 %)	p
HbA1c (%)	1.052	(0.851-1.302)	0.638	0.834	(0.609-1.143)	0.258
Time of evolution (years)	0.956	(0.905-1.01)	0.106	0.958	(0.892-1.028)	0.234

The HSI index is a predictor of steatosis. While the proportion of high-risk results according to the HSI index was 93.86 %, the proportion of S3 steatosis was 58.59 %. We do consider that it was more effective in ruling out steatosis since 2.63 % of patients obtained a low-risk result according to the HSI index compared to 0 % of patients who did not present any degree of steatosis in the study with FibroScan®. The HSI high-risk results can be explained by the formula itself since it takes into account the BMI (whose median in our study was 34.45 kg/m^2) and the presence of diabetes *mellitus* (which increases the result by 2 points). For this reason, in other studies, it has been considered that in presence of diabetes the HSI index makes poor discrimination on the risk of hepatic steatosis and overestimates it. Furthermore, it was not considered as a valid index in a study where liver steatosis in patients with type 2 diabetes measured by H-MR spectroscopy was compared with the results of the HSI (24).

On the other hand, the NFS and FIB-4 scores are predictors of fibrosis. Studies carried out to evaluate the role of these two scores have yielded results in favor of a good capability to diagnose advanced fibrosis by FIB-4 and in favor of ruling out advanced fibrosis in the case of a value < 1.455 in NFS (25). In our study, the NFS score overestimated the prevalence of fibrosis, since only 10.45 % obtained a value < -1.455, while the proportion of patients who obtained a F0-F1 degree of fibrosis with FibroScan® was 64.65 %. The results in terms of advanced fibrosis were more consistent since 24 % of patients obtained a high-risk result and 20.2 % of patients had advanced fibrosis with FibroScan®. However, FibroScan® could be performed only in 99 patients and not in the entire sample, so there could be a limitation in its interpretation. Regarding the FIB-4 score, the results were more similar to those obtained by FibroScan® to rule out liver fibrosis (low-risk estimated of 76.32 % by FIB-4 similar to 79.8 % of F0-F2). This is consistent with a similar study carried out in Italy (26) in which different scores for estimating the risk of liver fibrosis were compared. In it, FIB-4 was considered the best marker to avoid unnecessary referral to hepatologists. In our study, FIB-4 also underestimated the proportion of patients with advanced fibrosis (high-risk estimated of 1,75 %).

Predictive factors for intense steatosis in multivariate analysis were total cholesterol and a lower level of total bilirubin. Several studies have shown that bilirubin has an inverse association with cardiovascular disease, arterial hypertension and type 2 diabetes (27-29), probably due to its antioxidant, anti-inflammatory and antiatherogenic role (28). An inverse association between an elevated bilirubin level and the risk of this NAFLD in the general healthy Caucasian population has also been reported, although this association was observed in observational studies with low statistical power (30).

Bilirubin is produced as a consequence of red cells degradation by the enzyme heme-oxygenase in the spleen. This enzyme has two forms, one of them inducible (HO-1). The increase in this enzyme and therefore in bilirubin levels increases the expression

of PPARα, a transcription factor that promotes the utilization and catabolism of fatty acids. When this decreases, there is an increase in hepatic steatosis. In obese mice it has been shown that the increase in bilirubin decreases the expression of PPARα and thus the adiposity of the animals. Furthermore, a lower level of PPARα (31) has also been found in animal models with fatty liver. Another hormone that raises HO-1 through increased bilirubin levels is FGF21, which improves insulin sensitivity and reduces liver steatoasis. This is why mice with fatty liver secondary to obesity have been treated with bilirubin nanoparticles, thereby reducing steatosis and improving liver function. Other treatment routes include an HO-1-inducing diet with epoxyeicosatriene acid and physical exercise, with which bilirubin levels are used (32).

Cholesterol, especially for that coming from the diet, has shown an increased risk of liver disease because it produces a state of inflammation and hypoxia when it is accumulated in liver tissue (33). Furthermore, hypercholesterolemia produces a state of insulin resistance, related to NAFLD (33). Regarding advanced fibrosis, in the multivariate analysis, the predictive factors were BMI and a lower HSI index result. Regarding the HSI, it should be noted that this index was created as a predictor of steatosis, not fibrosis, and it can also overestimate the risk in patients with type 2 diabetes due to the formula itself.

GPT / ALT level was not a statistically significant predictor for either steatosis or fibrosis. It was statistically significant in the three studies similar to ours as mentioned previously (21-23), but it has been shown that transaminase levels should not be used to perform NAFLD screening since they can be normal, especially with a cut-off value of 30 U/L (34). Its usefulness lies in the fact that its elevation can serve to prompt clinical suspicion of this disease (35,36). Although the levels of GOP/AST and GGT were not statistically significant in the multivariate analysis, they were statistically significant for an increased risk of advanced fibrosis, which concur with the current evidence. In fact, in a study carried out in 2012 in the United Kingdom (37) it was found that patients with diabetes and NAFLD presented higher levels of GOT/AST and GGT, the latter being the most altered parameter in patients with diabetes in various studies (38). Platelets were not a statistically significant predictor either for intense steatosis ($p = 0.062$) or for advanced fibrosis ($p = 0.5$) since hypersplenism with sequestration and destruction of platelets occurs in cases of advanced cirrhosis with portal hypertension (39).

Likewise, it is worth highlighting the importance of the results in terms of the control and time of evolution of diabetes, since these two variables have not been demonstrated to be a risk factor for intense hepatic steatosis or advanced hepatic fibrosis. This means that any patient with type 2 diabetes has a high risk of suffering from fatty liver disease regardless control or time of evolution. This data is highly relevant when planning screening programs for these patients.

The limitations of our work lie in: 1) the patients were recruited in clinics where the prevalence of obesity is higher than in the general population, especially in Nutrition consultations; 2) a liver biopsy was not performed to verify the real prevalence of NAFLD, although the FibroScan® has shown to be accurate for measuring both steatosis and liver fibrosis in patients with NAFLD when compared with the histological evaluation (90 % sensitivity and specificity) (40). The sample size was smaller than that calculated, despite which the results did reach statistical significance.

CONCLUSIONS

In our study, up to 35.5 % of asymptomatic patients had liver fibrosis, this being severe to very severe in 20.2 % of cases. On the other hand, 100 % presented with some degree of steatosis and about 59 % exhibited S3 degree. The HSI score appears to overestimate the risk of intense steatosis. The NFS score appears to overestimate the risk of liver fibrosis while FIB-4 seems to underestimate the risk of advanced liver fibrosis. In the multivariate analysis, total cholesterol and a lower total bilirubin level were predictors of intense S3 hepatic steatosis. BMI and HSI were predictive for advanced fibrosis. Neither control of diabetes nor time of evolution were predictors for either intense steatosis or advanced fibrosis, which is relevant for planning screening programs. NAFLD is a common and potentially serious entity that may need to be included in the screening for complications in patients with type 2 diabetes and obesity. Larger population studies in non-obese type 2 diabetes patients are needed to confirm our findings.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Capacidad diagnóstica de la circunferencia de cuello para evaluar la obesidad en la población adulta joven. Análisis de datos de la segunda Encuesta Nacional de Salud 2009-2010. Chile

Diagnostic capacity of neck circumference to evaluate obesity in a young adult population. Data analysis from the second national health survey in Chile, 2009-2010

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Resumen

Introducción: Chile está dentro de los países con mayor tasa de malnutrición por exceso, lo que obliga a disponer de herramientas eficaces para evaluar el estado nutricional; así surge nuestro interés por explorar la posibilidad de utilizar la medición de la circunferencia del cuello (CCUE) como herramienta potencial de diagnóstico de fácil obtención y acceso, y bajo costo.

Objetivo: evaluar la capacidad diagnóstica de la circunferencia del cuello como predictor de obesidad en la población de 15-26 años de edad.

Materiales y métodos: dado que se encuentran disponibles, y son adecuados para nuestra investigación, se utilizarán datos extraídos de la Tercera Encuesta Nacional de Salud 2009-2010. Nuestro estudio se realizó aplicando el Método de Validación Diagnóstica por Criterio Concurrente. La muestra estuvo compuesta por 536 personas cuyas edades fluctuaban entre los 15 y 26 años, de quienes se tomaron los datos de IMC, para clasificarlas en las categorías de obesidad o normalidad (patrón oro), y la CCUE (en centímetros). Se excluyeron las personas con hipertiroidismo. Se obtuvieron indicadores de exactitud diagnóstica y valores predictivos. Se aplicó el SPSS, versión 25.

Resultados: según los rangos de edad y el sexo, los puntos de corte de la CCUE para clasificar la obesidad general presentaron sensibilidades y especificidades superiores a 0,85 con una área bajo la curva superior a 0,90, todos con $p < 0,001$.

Conclusión: existe evidencia a favor de que los puntos de corte de la CCUE presentan una adecuada capacidad de diagnosticar la obesidad en este grupo etario.

Palabras clave:

Antropometría. Obesidad. Circunferencia del cuello. Nutrición.

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Abstract

Introduction: Chile is among the countries with the highest rate of excess malnutrition, for that reason it is important to have effective tools to evaluate the nutritional status; interest in neck circumference (NC) measurement as a potential prognostic tool that is easy to access and low-cost has increased.

Objective: to evaluate the diagnostic capacity of neck circumference to predict obesity in the population aged 15-16 years, using data from the third National Health Survey 2009-2010.

Materials and methods: Concurrent Criteria of Diagnostic Validation were used for the study. The sample consisted of 536 people of ages from 15 to 26 years, where BMI data where taken in order to classify obesity versus normality (gold standard), as was NC (measured in centimeters). People with hyperthyroidism were excluded. Indicators of diagnostic accuracy were obtained; the SPSS, version 25 was used for calculations.

Results: according to age and gender ranks, the NC cut-off points to classify general obesity showed sensitivities and specificities above 0.85, with an area under the curve over 0.90, all with $p < 0.001$.

Conclusion: there is evidence that supports that NC cutoff points are a suitable tool for diagnosing obesity in this age group.

Keywords:

Anthropomretry. Obesity. Neck circumference. Nutrition.

INTRODUCCIÓN

En Chile, así como en muchos otros países del mundo, la obesidad y el exceso de peso presentan una prevalencia creciente desde los primeros años de vida. La obesidad es un problema de salud global y la malnutrición por exceso del adulto joven en Chile es consecuencia de una dieta caracterizada por un elevado aporte calórico proveniente de grasas saturadas, colesterol, azúcares y sodio (1), así como el déficit de actividad física que este grupo etario presenta. Así también se incluyen los factores genéticos, metabólicos, conductuales y hormonales.

El número de escolares y adolescentes con obesidad entre 5 y 19 años se han multiplicado por 10 en los últimos 4 decenios a nivel mundial (2) y Chile se encuentra dentro de los primeros países de la Organización para la Cooperación y Desarrollo Económico (OCDE), estando considerado como el país con la mayor tasa de población en estado nutricional de obesidad.

El mapa nutricional de la Junta Nacional de Auxilio Escolar y Becas (JUNAEB) del año 2019 señala que, entre los estudiantes de quinto básico, cuyas edades fluctúan entre los 9 y 10 años, existe un 23 % de alumnos que tienen obesidad y un 5 % que tienen obesidad severa, mientras que en primero medio, con edades entre los 14 y 15 años, existen un 14 % de obesidad y un 2 % de obesidad severa (3). Según la Tercera Encuesta Nacional de Salud 2016-2017, el 12,3 % de la población comprendida entre las edades de 15 a 19 años presenta obesidad, y un 1 % presentan obesidad mórbida (4).

Los pacientes con obesidad tienen mayor riesgo de desarrollar una variedad de afecciones comórbidas que incluyen enfermedades cardiovasculares (ECV), trastornos gastrointestinales, diabetes de tipo 2 (DM2), trastornos articulares y musculares, problemas respiratorios y problemas psicológicos (5). La obesidad se asocia con un aumento significativo de la mortalidad y con una disminución de la esperanza de vida de entre 5 y 10 años (6). Hay evidencia que indica que la mortalidad por causas como la ECV y el cáncer aumenta significativamente en las personas con obesidad en etapas 2 y 3. Los procesos metabólicos y cardiovasculares que son afectados por la obesidad están estrechamente (7) asociados a un estado inflamatorio crónico que se establece como un importante factor contribuyente a la resistencia a la insulina, la que a su vez es un factor desencadenante clave de la DM2. Además, la obesidad central, definida por la circunferencia de la cintura, es el componente esencial del síndrome metabólico (9). También hay un fuerte respaldo en la literatura sobre las relaciones entre la obesidad infantil y el asma, la mala salud dental (caries), la enfermedad del hígado graso no alcohólico (NAFLD) y la enfermedad por reflujo gastroesofágico (10). Esta patología también puede afectar el crecimiento y el desarrollo sexual, retrasando la pubertad en los niños y adelantando la pubertad en algunas niñas, relacionándose también con hiperandrogenismo y síndrome de ovario poliquístico (SOP) en las niñas (11).

Se ha propuesto la medición de la circunferencia del cuello (CCUE) como otra medida antropométrica de interés basándose en estudios que han demostrado que esta medida entrega información importante sobre patologías específicas como el síndrome metabólico (12). Por otra parte, recientes estudios han demostrado una correlación entre el índice de masa corporal (IMC) (10) y la medida de la circunferencia de cuello (13).

Dentro de las ventajas que tiene la medición de la circunferencia del cuello sobre otras mediciones antropométricas se puede destacar el breve tiempo que se requiere para obtenerla de los pacientes, el que no es invasiva, que no cambia durante el transcurso del día, que es de muy bajo costo dada la disponibilidad de instrumental, que es de fácil entrenamiento y que es factible aplicarla en personas con movilidad reducida o cuando razones culturales, psicológicas o religiosas impiden la aplicación de herramientas tradicionales para evaluar el estado nutricional, que requieren que el paciente se desvista para su evaluación (14).

Hasta el momento no existen estudios que permitan evaluar la capacidad diagnóstica de los puntos de corte de la CCUE respecto de la obesidad en base a la información obtenida de registros nacionales (15).

En consecuencia, el objetivo de este estudio es determinar la capacidad diagnóstica de la circunferencia de la CCUE en la detección de la obesidad en adolescentes y adultos jóvenes entre 15 y 26 años, registrados en la ENS 2009-10 (15).

MATERIALES Y MÉTODOS

El presente estudio de validación diagnóstica por criterio concurrente está basado en datos de la segunda Encuesta Nacional de Salud (ENS) 2009-2010, cuya información es representativa de la realidad poblacional de Chile (15).

De acuerdo con el censo nacional de 2002, la población del país ese año correspondía a 15.116.435 habitantes (16), mientras que la muestra de la ENS tiene representatividad nacional y regional con un diseño muestral estratificado multietápico por región administrativa y área geográfica (urbana/rural), resultando 29 estratos. La revisión del protocolo de la ENS 2009-10 fue encomendada y autorizada (con acuerdo de la Subsecretaría de Salud Pública del Ministerio de Salud) al Comité de Ética de Investigación de la Escuela de Medicina de la Facultad de Medicina de la Pontificia Universidad Católica de Chile (15).

Los sujetos elegibles para nuestro estudio fueron adolescentes entre 15 y 19 años, y adultos jóvenes entre los 20 y 26 años, de los cuales se contaba con datos disponibles para las variables "CCUE" y "estado nutricional", sin registro de enfermedades asociadas al tiroides para evitar alteraciones en la medida de la circunferencia del cuello. No obstante el carácter representativo de la ENS 2009-10, el análisis de esta submuestra puede disminuir el poder del estudio; sin embargo, permite utilizar una muestra homogénea.

El estado nutricional se obtuvo aplicando los rangos del índice de masa corporal (IMC). Para ello se calculó el IMC como peso/talla^2 y se clasificó de acuerdo con los indicadores básicos y puntos de corte de la Organización Mundial de la Salud (OMS), es decir: "Obeso" (IMC $\geq$ 30 kg/m^2) y "Obeso mórbido" (IMC > 40) (15). Según lo señalado por la ENS 2009-2010 (17), la CCUE se midió desde el punto medio entre la base del cuello y la parte superior del esternón en las mujeres y bajo la prominencia laríngea en los hombres; los participantes tenían que estar de pie, con la cabeza posicionada en el plano horizontal de Francfort. Las mediciones antropométricas de peso, talla y perímetro de cintura fueron realizadas por personal de enfermería capacitado; se consideraron las condiciones básicas de medición y eran conocidas las principales variables que influyen en la ocurrencia de errores en las mediciones, bajo protocolos descritos en la ENS 2009-2010 (17).

Las variables de tipo cuantitativo se describen con media aritmética y desviación típica, mientras que las de tipo cualitativo fueron la frecuencia absoluta y sus respectivos porcentajes. Luego, con el objetivo de estudiar la capacidad diagnóstica de la CCUE como predictor de obesidad, se levantaron curvas ROC para obtener sus áreas bajo la curva con un 95 % de confianza, según la edad y la zona rural/urbana. Con las curvas ROC se obtuvieron valores de sensibilidad y especificidad. Con esta información, el punto de corte de la CCUE con mayor exactitud diagnóstica es el que presenta el índice de Youden más alto (18). Con el punto de corte conseguido se calcularon los índices de exactitud diagnóstica: falsos positivos y negativos, y razón de verosimilitud positiva y negativa, con sus conversiones a probabilidades respectivas; indicadores predictivos de corte: valor predictivo positivo y negativo; más el porcentaje de eficacia (19). El análisis estadístico se procesó con el paquete V.25 (Fig. 1).

RESULTADOS

De la muestra de 536 sujetos entre 15 y 26 años, de los cuales el 58 % eran mujeres, el 31,2 % declararon una edad de entre los 18 y los 20 años; el 29,6 % provenían de zonas urbanas; el 75 % informaron de estudios medios (entre 9 y 12 años de escolaridad), mientras que el 19,8 %, 9,1 % y 8,2 % de la muestra se obtuvo de las regiones metropolitanas, de Coquimbo y Los Ríos, respectivamente (Tabla I).

En relación a los indicadores de capacidad diagnóstica de la circunferencia del cuello respecto de la obesidad, desagregada por sexo (Tabla II), se observa que en el caso de las mujeres con 34,5 cm presentó valores de sensibilidad y especificidad de 0,85 y 0,93, respectivamente, y valores predictivos por sobre el 75 %, más una eficacia del 90,5 %. Las razones de verosimilitud positiva y negativa fueron superiores a 10 e inferiores a 0,2; en el caso de los hombres, con un punto de corte en 38,75 cm se obtuvieron indicadores similares.

Respecto a los indicadores de capacidad diagnóstica de la circunferencia del cuello con relación a la obesidad, dividida entre un rango de edad (Tabla III), se observa que, en los hombres con 37,95 cm de CCUE, presentó valores de sensibilidad y especificidad de 0,88 y 0,93, respectivamente, con valores predictivos superiores al 50 %, más una eficacia superior al 90 % en ambos sexos. La razón de verosimilitud positiva fue mayor en los hombres (12,1 *versus* 8,26), mientras que la negativa fue mejor en las mujeres, con un punto de corte en 33,5 cm.

La tabla IV indica que las mujeres y los hombres de 18 a 20 años presentaron el mismo valor de sensibilidad, con 34,5 y 38,5 cm de CCUE, respectivamente. Tanto los falsos positivos y negativos como los valores predictivos positivos y negativos fueron similares en ambos grupos y, en el caso de las razones de verosimilitud positiva y negativa, presentaron valores mayores de 10 y menores de 0,2, respectivamente. La eficacia en ambos grupos fue superior al 90 %, al igual que sus áreas bajo la curva.

En el caso del grupo entre 21 y 23 años de edad (Tabla V) se encontró que los hombres con 40,5 cm de CCUE presentaron valores de sensibilidad y especificidad de 0,92 y 0,95, respectivamente, a diferencia de las mujeres, las cuales con 34,5 cm de CCUE obtuvieron una sensibilidad de 0,65. En el caso del resto de los indicadores, la circunferencia del cuello en los hombres presentó mejores valores que en las mujeres.

Respecto de los indicadores de capacidad diagnóstica de la CCUE en obesos de 24 a 26 años, según el sexo (Tabla VI), las mujeres con 33,6 cm de CCUE presentaron una sensibilidad de 1, mientras que los hombres con CCUE de 40,5 cm presentaron una especificidad de 0,96.

Los falsos positivos en mujeres fueron del 17,3 % y los falsos negativos en hombres alcanzaron un 22,2 %.

En relación a los valores predictivos positivo y negativo, en el caso de las mujeres, estos fueron del 67,9 % y 100 %, respectivamente, mientras que en el caso de los hombres, ambos valores fueron superiores al 85 %.

La razón de verosimilitud positiva en las mujeres fue de 5,78 y de 14,4 en los hombres; en el caso de la razón de verosimilitud negativa, en ambos fue igual a 0.

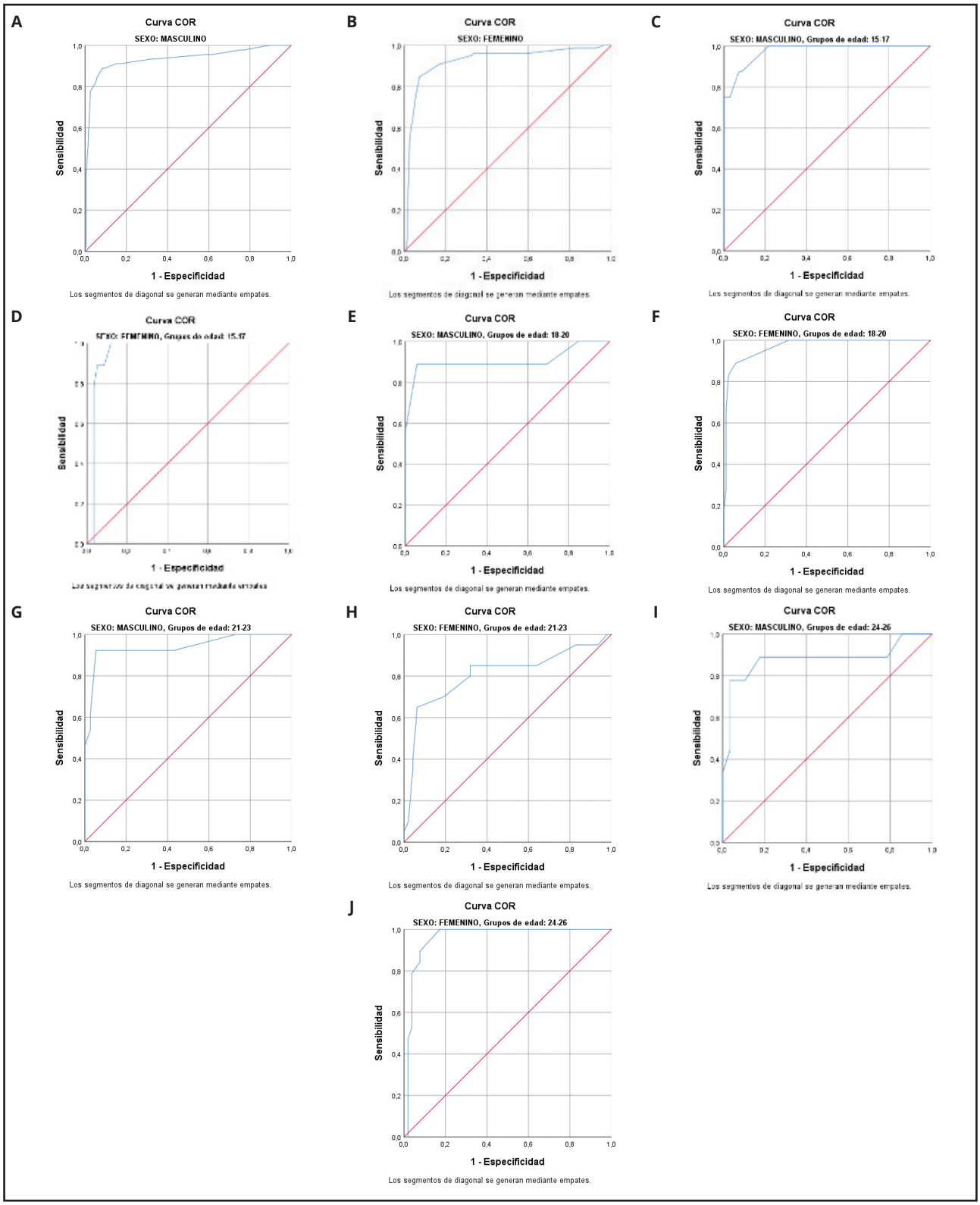

Figura 1.

Presenta las curvas ROC de los distintos escenarios evaluados en este trabajo. A. Curva ROC para masculino. B. Curva ROC para femenino. C. Curva ROC para masculino en el rango de edad de 15 a 17 años. D. Curva COR para femenino en el rango de edad de 15 a 17 años. E. Curva ROC para masculino en el rango de edad de 18 a 20 años. F. Curva ROC para femenino en el rango de edad de 18 a 20 años. G. Curva ROC para masculino en el rango de edad de 21 a 23 años. H. Curva ROC para femenino en el rango de edad de 21 a 23 años. I. Curva ROC para masculino en el rango de edad de 24 a 26 años. J. Curva ROC para femenino en el rango de edad de 24 a 26 años.

Tabla I. Distribución de los participantes del estudio según sus características sociodemográficas

Características sociodemográficas	n = 536	%
Sexo		
Mujer	311	58,0
Hombre	225	42,0
Edad (años)		
15-17	144	26,9
18-20	167	31,2
21-23	117	21,8
24-26	208	20,1
Área geográfica		
Urbano	480	89,6
Rural	56	10,4
Escolaridad (años)		
< 8	17	3,2
9-12	402	75,0
> 12	117	21,8
Región (15 regiones)		
I. Tarapacá	22	4,1
II. Antofagasta	37	6,9
III. Atacama	24	4,5
IV. Coquimbo	49	9,1
V. Valparaíso	23	4,3
VII. L Bdo O´Higgins	26	4,9
VII. Maule	36	6,7
VIII. Bio-Bío	32	6,0
IX. La Araucanía	27	5,0
X. Los Lagos	29	5,4
XI. Aysén	26	4,9
XII. Magallanes y Antártica	18	3,4
XIII. Metropolitana	106	19,8
XIV. Los Ríos	44	8,2
XV. Arica y Parinacota	37	6,9
Estado nutricional		
Normal	430	80,2
Obesidad tipo 1	73	13,6
Obesidad tipo 2	17	3,2
Obesidad tipo 3	16	3,0

Tabla II. Capacidad diagnóstica de la circunferencia de cuello para evaluar la obesidad (≥ 30 kg/m²), según cada sexo

Indicadores	Sexo	
	Femenino (339)	Masculino (236)
Mejor punto de corte	34,5 cm	38,75 cm
Sensibilidad	0,85	0,89

(Continúa en columna siguiente)

Tabla II (Cont.). Capacidad diagnóstica de la circunferencia de cuello para evaluar la obesidad (≥ 30 kg/m²), según cada sexo

Indicadores	Sexo	
	Femenino (339)	Masculino (236)
Especificidad	0,93	0,92
Índice de Youden	0,77	0,80
Falsos positivos	0,77	0,84
Falsos negativos	0,15	0,11
Valor predictivo positivo	0,77	0,71
Valor predictivo negativo	0,95	0,97
Razón verosimilitud positiva	11,58	10,58
Razón verosimilitud negativa	0,17	0,12
Eficacia	90,5 %	91,1 %
Área bajo la curva	0,92	0,92
Intervalo de confianza al 95 %	(0,88-0,96)	(0,88-0,99)
Valor p	< 0,001	< 0,001

Tabla III. Capacidad diagnóstica de la circunferencia de cuello por sexo para evaluar obesidad (≥ 30 kg/m²), en sujetos de 15 a 17 años

Indicadores	Edad 15 a 17 años	
	Femenino (n = 67)	Masculino (n = 77)
Mejor punto de corte	33,5	37.95
Sensibilidad	1,00	0.88
Especificidad	0,88	0,93
Índice de Youden	0,88	0,80
Falsos positivos	0,12	0,07
Falsos negativos	0	0,12
Valor predictivo positivo	0,56	0,58
Valor predictivo negativo	1,00	0,98
Razón verosimilitud positiva	8,26	12,1
Razón verosimilitud negativa	0	0,13
Eficacia	89,5 %	92,2 %
Área bajo la curva	0,96	0,98
Intervalo de confianza al 95 %	(0,91-1,00)	(0,93-1,00)
Valor p	< 0,001	< 0,001

Tabla V. Capacidad diagnóstica de la circunferencia de cuello por sexo para evaluar obesidad (≥ 30 kg/m²), en sujetos de 21 a 23 años

Indicadores	Edad 21 a 23 años	
	Femenino (n = 67)	Masculino (n = 50)
Mejor punto de corte	*34,50*	*40,50*
Sensibilidad	0,65	0,92
Especificidad Índice de youden	0,94 0,59	0,95 0,87
Falsos positivos	0,06	0,05
Falsos negativos	0,35	0,77
Valor predictivo positivo	0,81	0,85
Valor predictivo negativo	0,86	0,97
Razón verosimilitud positiva	10,1	17,0
Razón verosimilitud negativa	0,37	0,08
Eficacia	63,4 %	94 %
Área bajo la curva	0,81	0,94
Intervalo de confianza al 95 %	(0,68-0,94)	(0,85-1,00)
Valor p	< 0,001	0,001

Tabla VI. Capacidad diagnóstica de la circunferencia de cuello por sexo para evaluar obesidad (≥ 30 kg/m²), en sujetos de 24 a 26 años

Indicadores	Edad 24 a 26 años	
	Femenino (n = 71)	Masculino (n = 37)
Mejor punto de corte	33,6	40,5
Sensibilidad	1,00	0,78
Especificidad	0,83	0,96
Indice de Youden	0,83	0,74
Falsos positivos	0,17	0,36
Falsos negativos	0	0,22
Valor predictivo positivo	0,68	0,87
Valor predictivo negativo	1,00	0,93
Razón verosimilitud positiva	5,78	14,4
Razón verosimilitud negativa	0	0,23
Eficacia	87,3 %	91,8 %
Área bajo la curva	0,96	0,88
Intervalo de confianza al 95 %	(0,91-1,00)	(0,71-1,00)
Valor p	< 0,001	< 0,001

DISCUSIÓN

El objetivo de nuestro estudio es evaluar la capacidad diagnóstica de la CCUE como predictor de obesidad en la población de entre 15 y 26 años de edad.

En Chile existen pocos estudios de la medición de la CCUE en hombres y mujeres en relación con el estado nutricional de las personas. Esta medida podría convertirse en un importante indicador dado que, a diferencia de otras herramientas utilizadas habitualmente, es una medida fácil y rápida de obtener, pues constituye un método poco invasivo y fácil de aplicar, especialmente en las personas con movilidad reducida por su avanzada edad o en aquellas que están hospitalizadas.

Anatómicamente, podemos decir que el cuello está conformado por la parte superior de la columna vertebral en la espalda y los cartílagos que rodean la parte superior del sistema respiratorio. En torno a estos se encuentran tejidos blandos, donde se incluye la grasa. Al término de la edad adolescente se terminan de desarrollar estos tejidos, lo que produce un cambio en la circunferencia del cuello al que se asocia el aumento de masa grasa en el espacio de los tejidos blandos en los individuos sanos (20).

En nuestro estudio se determinó que el punto de corte de la CCUE para hombres y mujeres de entre 15 y 26 años es de 38,75 cm y 34,5 cm, respectivamente; esto es similar a lo reportado por un estudio peruano (21) que evaluó la CCUE como predictor de obesidad central en adultos jóvenes, hallando 39,47 cm en los hombres (sensibilidad = 0,93) y 34,4 cm en las mujeres (sensibilidad = 0,77). Por otra parte, un estudio mexicano (22) que evaluó a adultos jóvenes universitarios mostró una CCUE de 31,8 cm para las mujeres (sensibilidad = 0,72) y de 37,3 cm para los hombres (sensibilidad = 0,80). Los valores de sensibilidad en hombres y mujeres se pueden explicar por los diferentes porcentajes de depósitos de grasa visceral, que en el caso de los hombres representan el 20 % de la grasa corporal frente al 6 % en el caso de las mujeres (22), pudiendo la CCUE caracterizar de forma más adecuada esta medición. También la medición de la CCUE puede resultar diferente en hombres y mujeres ya que existen diferencias anatómicas, por lo que esta discrepancia no necesariamente es atribuible a la obesidad (13). En el desarrollo de este estudio se intentó excluir a los sujetos con hipertiroidismo para evitar distorsiones en los resultados, pero el carácter secundario de los datos no permitió asegurar este hecho.

Para los grupos etarios de 15 a 17 y 18 a 20 años, los puntos de corte de la CCUE en hombres y mujeres difieren en 4 cm, mientras que para el grupo de 21 a 23 la diferencia es de 5 cm y para el grupo entre 24 y 26 años esta es de 6 cm. Estos valores dan cuenta de dos aspectos: el primero tiene relación con un punto de corte en común, con buenos indicadores de capacidad diagnóstica que permiten establecer un tamizaje adecuado de la obesidad cuando el patrón oro corresponde al punto de corte del IMC, y que permitirá mayor facilidad y rapidez de esta medición.

Por otro lado, y de forma secundaria, una CCUE aumentada podría relacionarse con la presencia de síndrome metabólico (23) y riesgo cardiovascular (24). Esto se puede explicar con el estudio de Dixon y O'Brian (25), quienes concluyeron que la

CCUE es un buen predictor de índice elevado de insulina y de andrógenos libres en las mujeres premenopáusicas obesas, además de ser un buen predictor clínico de irregularidad menstrual, hirsutismo, infertilidad, resistencia a la insulina y síndrome de ovario poliquístico. Además, la CCUE se asocia a marcadores doblemente indirectos de masa grasa total y central en niños y adolescentes. En los adultos no hay duda de que el perímetro del cuello es un marcador válido para medir la adiposidad total y central (14). En efecto, un estudio realizado en la población chilena encontró adecuados indicadores de exactitud diagnóstica de la CCUE en relación al riesgo cardiovascular, con 37 cm en los hombres y 32 cm en las mujeres (23).

En un estudio realizado en India (19), en el que se obtuvieron valores de 37 cm en los hombres y 34 cm en las mujeres, se constataron valores de sensibilidad de 0,63 en los hombres y 0,66 en las mujeres, así como valores de especificidad de 0,84 en los hombres y 0,86 en las mujeres, concluyendo que la CCUE es un marcador válido para identificar individuos obesos, con una correlación positiva para la mayoría de las variables antropométricas.

Este nuevo método de medición antropométrica se puede convertir en una alternativa viable para los programas de prevención de la atención primaria en salud, allí donde el acceso a equipos de evaluación de mayor costo o la cultura no permitan realizar otra toma de mediciones (20).

Existe una relación significativa entre la CCUE y la glicemia elevada o la resistencia a la insulina (manifestada a través de la acantosis nigricans), de gran utilidad en los usuarios con edema, amputaciones o cifosis, entre otros, ya que se considera que el IMC y la circunferencia abdominal no son indicadores confiables en estos casos (26).

La CCUE y el perímetro abdominal tienen una asociación positiva con el IMC; en un estudio realizado en Brasil se demostró que la CCUE es un parámetro adicional e innovador para determinar la distribución de la masa corporal, que va asociada a la grasa visceral, aspectos que forman parte de los componentes del síndrome metabólico. También se demostró que esta medición antropométrica determina el tejido adiposo subcutáneo y tiene relación con el riesgo cardiometabólico (28). En efecto, los pacientes que presentan obesidad cervical presentan un IMC mayor que va de la mano con un mayor perímetro abdominal y a su vez una glucosa elevada, a diferencia de quienes presentan un CCUE dentro de los rangos de normalidad (26).

En consideración, esta medición refleja procesos bioquímicos complejos a nivel celular, como es el caso de los lípidos que, una vez ingeridos en la dieta o sintetizados a partir de carbohidratos, son transportados al tejido adiposo como quilomicrones o lipoproteínas de muy baja densidad. A medida que se acumulan lípidos en los adipocitos, estos se hipertrofian y, en el momento en que la célula alcanza su máximo tamaño, se forman nuevos adipocitos a partir de preadipocitos o células adiposas precursoras, estableciéndose una hiperplasia (29). Por tanto, la medición de la CCUE puede aproximarse a detectar esta condición hasta, eventualmente, en un mediano plazo desplazar a la circunferencia de la cintura, dada sus desventajas mencionadas anteriormente.

Cabe señalar que, nuestro estudio considera solamente una parte de la población chilena, por lo que sería interesante seguir investigando en otros grupos etarios para obtener un panorama más global de esta medida a fin de que pueda aplicarse de forma masiva para evaluar el estado nutricional. Aumentar el tamaño de la muestra para desarrollar el análisis por sub-grupos también será parte de los siguientes desafíos para encontrar puntos de cortes válidos a nivel nacional.

En conclusión, la medición de la CCUE es un indicador válido para identificar la obesidad en el rango etario descrito en nuestro estudio, indicando que tiene un 91 % de eficacia como patrón de referencia. Además, cabe destacar que es un método poco invasivo, fácil y rápido de aplicar.

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ARÁN

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Trabajo Original

Obesidad y síndrome metabólico

Sensitivity and specificity of body mass index and main risk factors for cardiovascular disease in middle-income urban participants in Guanajuato, Mexico

Sensibilidad y especificidad del índice de masa corporal y principales factores de riesgo de enfermedad cardiovascular en participantes de zona urbana de ingresos medios en Guanajuato, México

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Abstract

Introduction: several studies have questioned body mass index (BMI) as an accurate diagnostic tool for obesity and therefore a predictor of cardiovascular risk. But BMI is widely used currently.

Objective: we analyzed the sensitivity and specificity of BMI and compared cardiovascular risk factors in middle-income urban participants in Guanajuato, Mexico, at different ages.

Design: an analytical and cross-sectional study was carried out in 385 apparently healthy subjects, stratified by age ranges (20 to 59 years old). A high global CVD risk was obtained with the Framingham risk score (Framingham Risk Score > 20 %). The odds ratio was used to assess the association between high global CVD risk and the dietetic and anthropometric variables. Sensitivity, specificity, and correlation statistical analyses were carried out between BMI and other anthropometric variables with high cardiovascular risk, and this was integrated to derive recommendations to improve risk factor detection ($p < 0.05$ and power of 80 %).

Results: a high global CVD risk was found in 4 % of the sample. BMI ≥ 30 kg/m^2 had a sensitivity of 77 % for the detection of high cardiovascular risk; waist circumference ≥ 90 cm (men) or ≥ 80 cm (women) and body fat percentage ≥ 25% (men) or ≥ 35 % (women) had a sensitivity of 100 %. BMI showed a significant association with high global CVD risk (OR = 6.1; 95 % CI, 1.6-22.6, $p < 0.01$), but was not able to predict high global CVD risk in at least 30 % of the cases. There was not significative difference by age group for waist circumference, body fat percentage, total cholesterol, and low-density lipoprotein. Regarding the comparison of dietary intake of the stratified population by age group, intake of cholesterol, added sugars, fiber, sodium were highest in the 20 years group.

Conclusions: a higher intake of cholesterol, simple sugars, and sodium was observed in the 20-year-old age group. The use of BMI with waist circumference and percentage of body fat used together allow a better assessment of cardiovascular risk. We need to integrate this new recommendation to increase early detection of main risk factors for cardiovascular disease.

Keywords:

Cardiovascular risk. Obesity. Body fat percentage. Body mass index.

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Resumen

Introducción: diversos estudios han cuestionado el índice de masa corporal (IMC) como herramienta diagnóstica certera de la obesidad y por tanto predictor de riesgo cardiovascular. Pero el IMC es ampliamente utilizado actualmente.

Objetivo: se analizó la sensibilidad y especificidad del IMC y se compararon factores de riesgo cardiovascular en participantes de diferentes edades de zonas urbanas de ingresos medios en Guanajuato, México.

Diseño: se realizó un estudio analítico y transversal en 385 participantes, aparentemente sanos, estratificados por rangos de edad (20 a 59 años). El alto riesgo global de ECV se obtuvo con la puntuación de riesgo de Framingham (puntuación de riesgo de Framingham > 20 %). Se calculó la odds ratio para evaluar la asociación entre el alto riesgo global de ECV y las variables dietéticas y antropométricas. Se realizó un análisis estadístico de sensibilidad, especificidad y correlación entre el IMC y otras variables antropométricas con el alto riesgo cardiovascular, y se integró para derivar recomendaciones para mejorar la detección de factores de riesgo ($p < 0,05$ y potencia del 80 %).

Resultados: se encontró un alto riesgo global de ECV en el 4 % de la muestra. El IMC ≥ 30 kg/m^2 tuvo una sensibilidad del 77 % para la detección del alto riesgo cardiovascular; la circunferencia de la cintura ≥ 90 cm (hombre) o ≥ 80 cm (mujer) y el porcentaje de grasa corporal ≥ 25 % (hombre) o ≥ 35 % (mujer) tuvo una sensibilidad del 100 %. El IMC mostró una asociación significativa con un alto riesgo global de ECV (OR = 6,1; IC 95 % 1,6-22,6; $p < 0,01$) pero no fue capaz de predecir un alto riesgo global de ECV en al menos el 30 % de los casos. No hubo diferencia significativa por grupo de edad para circunferencia de cintura, porcentaje de grasa corporal, colesterol total y lipoproteínas de baja densidad. Con respecto a la comparación de la ingesta dietética de la población estratificada por grupos de edad, la ingesta de colesterol, azúcares añadidos y sodio fue mayor en el grupo de 20 años.

Conclusiones: se observó una mayor ingesta de colesterol, azúcares simples y sodio en el grupo de edad de 20 años. El uso del IMC con la circunferencia de la cintura y el porcentaje de grasa corporal utilizados conjuntamente permiten lograr una mejor evaluación del riesgo cardiovascular. Necesitamos contar con herramientas para aumentar la detección temprana de los principales factores de riesgo de enfermedad cardiovascular.

Palabras clave:

Riesgo cardiovascular. Obesidad. Porcentaje de grasa corporal. Índice de masa corporal.

INTRODUCTION

Cardiovascular disease (CVD) is the main cause of premature death and disability. In 2012, 17.5 million people died, and it is expected that in 2030 the number of deaths will be 23.6 million (1). Obesity is associated with a 20 to 40 % higher risk of death (2). Obesity is related to the development of CVD, including atherosclerosis and symptomatic coronary disease, heart failure, and atrial fibrillation (3). Obesity increases the risk of CVD comorbidities such as hypertension, dyslipidemia, glucose intolerance and diabetes (4). One of the first subclinical stages in the atherosclerotic process is a deterioration of endothelial-dependent vasodilation. A mediator of endothelial dysfunction is the level of oxidative stress, which correlates with the accumulation of adipose tissue (5). When production of reactive oxygen species is high, the process of cellular damage occurs and can facilitate the development of CVD (6).

Currently, body mass index (BMI) is considered the main estimator of obesity, which is very practical to obtain. BMI is related to fat mass as estimated by bioimpedance ($r = 0.75$, $p < 0.01$ and $r = 0.82$, $p < 0.01$, for men and women, respectively) (7). Yet, the correlation of BMI and fat mass varies in childhood and adolescence, in older adults, and in people with different catabolic processes. A BMI > 30 kg/m^2 has a specificity of 95 % in men and 99 % in women for the diagnosis of obesity, and a sensitivity of 36 % and 49 %, with a higher number of false negatives (8).

Several studies have questioned the usefulness of BMI as a predictor of cardiovascular risk. Asthon determined that cardiovascular risk increases from a BMI of 22 kg/m^2 in women aged 30 to 64 years (OR: 1.58; 95 % CI, 1.2-2.0) (9). In Asia, given the increase in the prevalence of diabetes, cardiovascular risk factors and the high body fat percentage in the population, the WHO modified the cut points to 23 kg/m^2 for overweight and 25 kg/m^2 for the diagnosis of obesity. Flegal reported a lower mortality from any cause with a BMI of 24 to 30.9, it being lowest between 27 and 27.9 kg/m^2 (10). Other studies found a lower mortality from all causes between BMI 23.7 (95 % CI, 23.4-24.3) to 27 kg/m^2 (95 % IC: 26.5-27.6), and the risk of mortality caused by excess weight is observed with a BMI ≥ 30 kg/m^2 (11,12).

Among causes associated with lifestyle, nutrition plays an important role in the etiology of CVD. Poor quality diets are rich in refined grains and added sugars, salt, unhealthy fats, and foods of animal origin; and low in whole grains, fruits, vegetables, legumes, fish and nuts (12). In Mexico, according to the National Health and Nutrition Survey (ENSANUT) of 2016, the prevalence of overweight and obesity was 72.5 %, this being higher for the group of 40 to 49 years in men and 50 to 59 years in women, but for the population aged 20 years and over, women presented an increase in the figures for overweight plus obesity from 73.0 % (2012) to 76.8 % (2018); for men, the figures for overweight and obesity also showed an increase from 2012 to 2018, with 69.4 % to 73.0 % (13).

The estimation of cardiovascular risk has been the cornerstone in clinical guidelines for the evaluation of obesity, and there is growing interest in the development of a more sensitive risk prediction for risk cardiovascular factors, which implies going beyond traditional risk factors using only or always BMI. We need to integrate a recommendation to increase early detection of the main risk factors for cardiovascular disease with different parameters in addition to BMI, and derivate these to analyze the sensitivity and specificity of BMI and other main cardiovascular risk factors (anthropometric, dietetic, biochemical and sociodemographic variables) in middle income urban participants in Guanajuato, Mexico, at different age ranges, as well as cardiovascular risk.

MATERIALS AND METHODS

We carried out a cross-sectional, comparative study in 385 adults (33 %, $n = 125$, males) of 20 to 59 years of age. The sample size required was 82 participants for each group; we used the r test considering a correlation of 0.70 between CVD and the presence of obesity as measured by BMI; a bilateral alpha of 0.05 and a beta of 20. The selection criteria were adults of both sexes without a history of CVD (coronary heart disease, cerebrovascular disease or congenital heart disease), middle-income urban participants from health clinics, educational centers and local businesses of the city of Leon, Guanajuato, Mexico. We obtained an informed consent for each participant. The population was stratified for every 10 years (20 to 29, 30 to 39, 40 to 49 and 50 to 59). The independent variable was BMI and the response was the percentage of high global CVD risk (Framingham Risk Score > 20 %). The biochemical variables (LDL, HDL, triglycerides and glucose), anthropometric (body fat percentage, waist circumference and hip circumference), clinical (blood pressure) and dietary (consumption of lipids, carbohydrates, proteins, sugar and fiber) were measured. Physical activity and gender were considered confounding factors.

ANTHROPOMETRIC

Anthropometric measurements were taken following the International Society of Advancement of Kinanthropometry (ISAK) protocol. The weight, body fat percentage and fat mass were measured with the Tanita SC-240 bioimpedance (BIA) scale. A calculation of BMI was obtained, and was considered obesity at a value ≥ 30 kg/m^2. The measure of impedance is obesity and body fat percentage > 25 % in men and 35 % in women (14). The cut-off point for waist and hip circumference was considered at 80 cm in women and 90 cm in men (15).

BIOCHEMICAL

A blood sample of 10 ml was taken in the morning after a period of ten to twelve hours fasting for the determination of glucose levels, triglycerides, cholesterol, low density lipoprotein (LDL), and high density lipoprotein (HDL), performed by dry chemistry with the KODAK EKTACHEM DT60 II® (16).

CLINICAL

Blood pressure was taken according to the indications in the Draft of the Official Mexican Standard PROY-NOM-030-SSA2-2017 for the prevention, detection, diagnosis, treatment, and control of systemic arterial hypertension (17). The high global CVD risk at ten years was calculated using the Framingham risk score, which considers the variables sex, age, systolic pressure, presence of treatment for hypertension, presence of smoking, diabetes, total cholesterol, and HDL cholesterol. The individuals were classified as a high global CVD risk (10-year risk of a CVD event, 20 %) when it was greater than 20 % (18,19).

DIETARY

A food consumption questionnaire designed by the authors and a 24-hour food recall were applied (20). Nutrient content was calculated for proteins, carbohydrates and fats in the diet, grams of sugar, and fiber. All analyses were performed with the Nutrikcal® software, version 4.0. Food intakes were adjusted for 1,000 calories to determine the percentages of consumption. For the calculation of the OR, the percentage of dietary lipids (35 %) (21), the percentage of saturated fatty acids (7 %) (22), the consumption of cholesterol (300 mg) (19), sugar (25 g) (23), sodium (2000 mg) (24), dietary fiber (25 g) per day (25), and the consumption of industrialized juice were considered binary variables. A percentage of adequate adequacy was considered with a range of 90 to 100 % (26).

STATISTICAL ANALYSIS

The BMI percentiles of the total sample were calculated. Normality tests were performed with the Kolmogorov-Smirnov test. The differences between the groups were determined by one-way ANOVA for the variables with normal distribution, and the Kruskal-Wallis test for non-parametric variables. The association between cardiovascular risk and the rest of variables was tested using Spearman's correlation. The odds ratio was calculated for the dietary and anthropometric variables in relation to the high global CVD risk. The tests were performed with a significance lower than 0.05 and a power of 80 %. Receiver operating characteristic (ROC) curve analyses were performed to calculate the sensitivity and specificity of BMI for the diagnosis of obesity. All tests were performed with the SPSS program, version 18.0.

ETHICS ASPECTS

This study was carried out considering the Declaration of Helsinki in its 2013 version, according to the Regulations of the General Law on Health in Research on Human Beings, and following ethical principles. Each participant signed an informed consent form. The project was approved by the Institutional Committee on Bioethics in Research of the University of Guanajuato (CIBI-UG-P037-2015).

RESULTS

The study included a sample of 885 participants, the prevalence of high global CVD risk was 4 % ($n = 13$), 2 % in the forty-year group and 11 % for the fifty-year group (Table I). For the

Table I. Sample characteristics by age group, gender, and high global CVD risk (n = 385)

Age group (years)	Total *n* (%)	Obesity *n* (%)	Overweight *n* (%)	Women *n* (%)	Men *n* (%)	10-Year CVD risk > 20 %* *n* (%)	Women 10-Year CVD risk > 20 % *n* (%)	Men 10-Year CVD risk > 20 % *n* (%)
20-29	82 (21)	20 (24)	24 (29)	48 (58)	34 (42)	0 (0)	0 (0)	0 (0)
30-39	88 (23)	33 (38)	32 (36)	62 (70)	26 (30)	0 (0)	0 (0)	0 (0)
40-49	112 (29)	51 (46)	47 (42)	80 (71)	32 (29)	2 (2)	0 (0)	2 (6)
50-59	103 (27)	37 (36)	44 (43)	70 (68)	33 (32)	11 (11)	2 (3)	9 (27)
Total	385 (100)	141 (37)	147 (38)	260 (67)	125 (33)	13 (4)	2 (1)	11 (9)

**10-Year CVD risk > 20 %: high global CVD risk (10-year risk of a CVD event > 20 %) according to the Framingham CVD risk assessment tool.*

construction of percentiles with the results of BMI with the values for both genders, a BMI of 25 kg/m^2 was in the 50th percentile for the twenty-year group, 27 for the thirty-year group, 29 for the forty-year group, and 28 for the fifty-year group (Fig. 1).

Significant differences for multiple CVD risk factors were found including systolic blood pressure ($p < 0.01$) and total cholesterol levels ($p < 0.01$). The fifty-year group showed a lower BMI ($p < 0.01$), waist circumference ($p < 0.01$) and percentage of body fat ($p < 0.01$) compared to the forty -year group (Table II). Total cholesterol levels were greater for the fifty-year group when comparing groups, it was the same for the low-density lipoproteins ($p < 0.01$) (Table II).

In the evaluation of dietary variables, significant differences were observed with a greater consumption for the twenty-year group in energy consumption ($p < 0.01$), lipids ($p < 0.01$), monounsaturated fatty acids ($p = 0.04$), polyunsaturated fatty acids ($p = 0.04$) and sodium intake ($p < 0.01$) (Table III). For the consumption of beverages with added sugars, 70 % ($n = 280$) of the sample reported consuming soft drinks, and 26 % ($n = 98$) industrialized juices.

The twenty-year group showed an early exhibition for the consumption of sugary drinks ($p < 0.01$), a higher frequency of industrialized juice consumption at present ($p < 0.01$), a greater amount of industrialized juice ingested per day ($p < 0.01$), and an increased consumption of industrialized food per day ($p < 0.01$).

A significant correlation was obtained between the BMI and the body fat percentage ($r = 0.8$, $p < 0.01$), fat mass ($r = 0.9$, $p < 0.01$), waist circumference ($r = 0.9$, $p < 0.01$), and hip circumference ($r = 0.9$, $p < 0.01$), for the total sample (Table IV).

The high global CVD risk showed a significant correlation with waist circumference ($r = 0.4$, $p < 0.01$), BMI ($r = 0.3$, $p < 0.01$), fat mass ($r = 0.3$, $p < 0.01$) and body fat percentage ($r = 0.2$, $p < 0.01$) in all age groups (Table IV). Regarding the anthropometric risk factors for the high global CVD risk, the odds ratio of obesity diagnosed by a BMI > 30 kg/m^2 was 6.1 (95 % CI, 1.6-22.6, $p < 0.01$).

For the dietary variables, an odds ratio of 3.2 (95 % CI, 1.0-9.9, $p = 0.03$) was obtained for higher consumption of 300 mg/dl of cholesterol per day (Table V).

For the sensitivity and specificity of the BMI for the total sample and the anthropometric parameters for high global CVD risk, the waist circumference and the percentage of body fat percentage had a sensitivity of 100 %, BMI of 77 % (Table VI).

The sensitivity and specificity of BMI for the current diagnosis of obesity according to WHO (BMI > 30 kg/m^2) had a specificity of 93 % in men and 100 % in women, while sensitivity had values of 51 % and 57 %, respectively (Table VI). Regarding the calculation of BMI cutoffs to detect obesity according to body fat percentage, for men, the area under the curve was 0.93 for a BMI of 26.65 kg/m^2, with a sensitivity of 90 % and a specificity of 85 %. For women, the area under the curve was 0.95 with a BMI of 25.5 kg/m^2, with a sensitivity of 90 % and a specificity of 83 %.

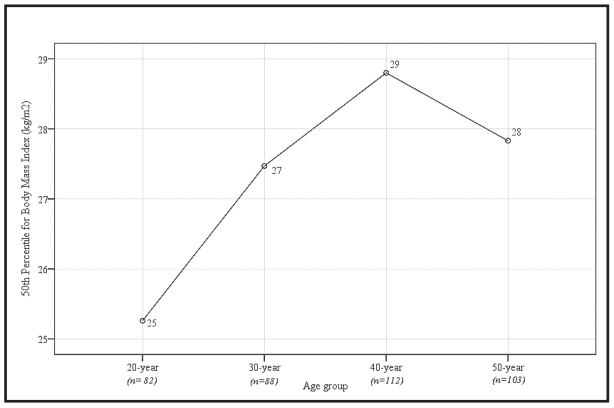

Figure 1.

BMI percentiles by age group ($n = 385$).

Table II. Comparison of the clinical, biochemical and anthropometric variables by age group

Variable	Total Median (ranges)	Age group Median (ranges)				p*	p
		20-year group	30-year group	40-year group	50-year group		
n (%)	385 (100)	82 (21.3)	88 (22.9)	112 (29.1)	103 (26.8)		
Systolic blood pressure (mmHg)	120 (90-190)	110 (90-150)	110 (90-170)	120 (90-160)*†	120 (90-190)*	0.00	0.00
Diastolic blood pressure (mmHg)	80 (60-130)	80 (60-100)	80 (60-110)	80 (60-112)*†	80 (60-130)*	0.00	0.00
Waist circumference (cm)	89 (61-128)	82 (61-113)	88 (66-128)*	91 (65-127)*	84 (64-128)*	0.37	0.00
Body mass index (kg/m^2)	27.3 (16-52)	25 (16-45)	27 (17-52)*	29 (20-46)*	28 (20-46)*	0.01	0.00
Body fat percentage (%)	35 (11-49)	26 (11-49)	34 (13-54)*	38 (18-51)*	36 (17-49)*	0.19	0.00
Glucose (mg/dL)	98 (70-248)	93 (70-201)	93 (72-126)	97 (77-202)*	97 (72-248)*†	0.00	0.00
Total cholesterol (mg/dL)	179 (104-257)	160 (104-257)	171 (113-246)	180 (107-273)*	204 (117-263)*†‡	0.14	0.00
High-density lipoprotein (mg/dL)	43 (10-81)	43 (12-72)	41 (17-68)	41 (10-81)	43 (13-77)	0.00	0.12
Low-density lipoprotein (mg/dL)	104 (23-189)	92 (37-176)	103 (23-156)	104 (48-181)*	130 (51-189)*†‡	0.22	0.00
Triglycerides (mg/dL)	137 (53-357)	116 (53-355)	128 (64-350)	161 (56-355)*†	156 (58-357)*	0.00	0.00

The data are expressed as medians and ranges. p: normality test with the Kolmogorov Smirnov test. p: mean difference test using one-way ANOVA and Kruskal-Wallis for variables with non-parametric distribution. *Tukey-Kramer post-hoc test for multiple comparisons significant at p < 0.05 with respect to the 20-year group. †Tukey-Kramer post-hoc test for multiple comparisons significant at p < 0.05 with respect to the 30-year group. ‡Tukey-Kramer post-hoc test for multiple comparisons significant at p < 0.05 with respect to the 40-year group.*

Table III. Comparison of dietary intake of the stratified population by age group

Variable	Total Median (ranges)	Age group Median (ranges)				p*	P
		20-year group	30-year group	40-year group	50-year group		
n (%)	385 (100)	82 (21.3)	88 (22.9)	112 (29.1)	103 (26.8)		
Energy (kcal)	1718 (731-5573)	1927 (794-5573)	1596 (756-3556)*	1722 (867-3630)*	1678 (731-4996)*	0.00	0.00
Lipids (%) Lipids (g)	29 (6-59) 55 (9-502)	29 (8-55) 66 (21-221)	28 (8-56) 50 (12-145)	30 (7-52) 53 (9-502)	26 (6-59) 50 (10-196)*	0.98 0.00	0.18 0.00

(Continues on next page)

Table III (Cont.). Comparison of dietary intake of the stratified population by age group

Variable	Total Median (ranges)	Age group Median (ranges)				p*	P
		20-year group	30-year group	40-year group	50-year group		
SFA[a] (%) SFA (g)	7 (1-23) 13 (1-190)	6 (1-18) 14 (2-62)	7 (1-21) 13 (2-53)	8 (1-17) 14 (1-190)	6 (1-23) 12 (1-71)	0.01 0.00	0.20 0.21
MFA[b] (%) MFA (g)	9 (1-27) 16 (1-215)	9 (1-25) 19 (3-67)	8 (2-23) 15 (4-61)	9 (1-21) 17 (1-215)	8 (1-27) 15 (1-67)*	0.08 0.00	0.35 0.04
PFA[c] (%) PFA (g)	4 (1-12) 7 (1-50)	4 (1-9) 9 (2-32)	4 (1-11) 7 (2-31)	4 (1-11) 7 (1-50)	4 (1-12) 7 (2-19)*	0.00 0.00	0.58 0.04
Cholesterol (mg)	177 (2-2173)	212 (17-1186)	174 (41-785)	174 (6-2173)	168 (2-804)	0.00	0.07
Added sugars (g)	33 (0-183)	35 (0-175)	33 (4-142)	32 (0-183)	32 (0-120)	0.00	0.76
Fiber (g)	16 (1-74)	15 (3-74)	17 (3-48)	16 (1-53)	16 (1-63)	0.00	0.75
Sodium (mg)	1538 (92-12566)	2024 (323-9918)	1433 (278-4897)*	1412 (92-12566)	1445 (93-4970)*	0.00	0.00

[a]Saturated fatty acids. [b]Monounsaturated fatty acids. [c]Polyunsaturated fatty acids. Data are expressed as medians and ranges. p: normality test with the Kolmogorov Smirnov test. p: mean difference test using one-way ANOVA and Kruskal-Wallis for variables with non-parametric distribution. *Tukey-Kramer post-hoc test for multiple comparisons significant at p <0.05 respect to the 20-year group.*

Table IV. Correlation coefficients between body mass index (BMI), 10-year CVD risk, and anthropometric variables

Body mass index						
		Total	20 years	30 years	40 years	50 years
n (100 %)	*p**	82 (21.3)	88 (22.9)	112 (29.1)	103 (26.8)	82 (21.3)
Waist circumference (cm)	0.19	0.9†	0.9†	0.9†	0.9†	0.8†
Hip circumference (cm)	0.04	0.9†	0.9†	0.9†	0.9†	0.8†
Body fat percentage (%)	0.37	0.8†	0.7†	0.8†	0.7†	0.7†
Fat mass (kg)	0.02	0.9†	0.9†	0.9†	0.9†	0.9†
10-year CVD risk[a]						
BMI	0.01	0.3†	0.3†	0.5†	0.2*	0.2†
Waist circumference (cm)	0.19	0.4†	0.4†	0.3†	0.4†	0.5†
Hip circumference (cm)	0.04	0.1†	0.2*	0.5†	0	0
Body fat percentage (%)	0.37	0.2†	0	0.5†	0	0
Fat mass (kg)	0.02	0.3†	0.2*	0.5†	0.1	0

[a]10-Year CVD risk: 10-year risk of a CVD event according to the Framingham CVD risk assessment tool. p: normality test with the Kolmogorov Smirnov test for the total sample (n = 385). Spearman's correlation test was used. *The correlation was significant at a level of 0.05, unilateral. †The correlation was significant at a level of 0.01, unilateral.*

Table V. Odds ratios (OR) for the anthropometric and dietary variables with 10-year CVD risk

Variable	OR (95 % IC)	*p*
Anthropometric variables		
Body mass index > 30 (kg/m^2)	6.1 (1.6-22.6)	0.00
Dietetic variables		
> 35 % lipids[a]	0.9 (0.2-3.4)	0.90
> 7 % saturated fatty acids[b]	1.1 (0.3-3.5)	0.77
> 10 % saturated fatty acids[c]	2.8 (0.9-8.9)	0.07
> 300 mg cholesterol[d]	3.2 (1.0-9.9)	0.03
> 25 g added sugar[e]	2.2 (0.6-8.2)	0.22
> 25 g fiber[f]	1.3 (0.3-5.0)	0.66
> 30 fiber[g]	0.8 (0.1-6.3)	0.83
> 2000 mg sodium[h]	2.1 (0.7-6.4)	0.18
Consumption of industrialized juice[i]	0.8 (0.2-3.2)	0.84
Sausage consumption[j]	1 (0.2-3.7)	0.99

[a]> 35 % lipids; consumption > 35 % of calories from lipids per day. [b]> 7 % saturated fatty acids; consumption > 7 % of calories from saturated fatty acids per day. [c]> 10 % saturated fatty acids; consumption > 10 % of calories from saturated fatty acids per day. [d]> 300 mg cholesterol; consumption > 300 mg of cholesterol per day. [e]> 25 g sugar; consumption > 25 g of added sugar per day. [f]> 25 g fiber; consumption > 25 g of fiber per day. [g]> 30 g fiber; consumption > 30 g of fiber per day. [h]> 2000 mg sodium; consumption > 2000 mg of sodium per day. p: the level of statistical significance was established at p < 0.05.

Table VI. Sensitivity and specificity of body mass index (BMI) for the total sample and anthropometric parameters for the determination of 10-year CVD risk

Variable	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
IMC (kg/m^2)				
Female	51	100	100	53
Male	57	93	94	52
10-year CVD risk[a]				
BMI (kg/m^2)	77	65	7	99
Waist circumference (cm)	100	35	5	100
Body fat percentage (%)	100	30	5	100

[a]10-year CVD risk > 20 %: high global CVD risk (10-year risk of a CVD event > 20 %) according to the Framingham CVD risk assessment tool.

DISCUSSION

The indicators of cardiovascular disease have been widely described and adapted to other formats such as the Pan American Health Organization, but given the lifestyle changes, it is necessary to reevaluate these instruments and diagnostic indicators such as BMI, the most widely used tool for diagnosing obesity and an independent predictor of CVD risk.

According to the list of WHO/ISH risk prediction charts by epidemiological sub-regions, Spain is in classification A for "very low child mortality and very low adult mortality", Mexico is in classification B for "low child mortality and low adult mortality", and the Democratic People's Republic of Korea in D for "high child mortality and high adult mortality". However, in our study, the proportion of participants with a cardiovascular risk greater than 20 %, according to the Framingham risk score, was only 4 %

compared to studies reporting 30.4 % in Spain (men and women of 55-74 years, $n = 5966$) and 12 % in South Korea (men aged 25-65 years, $n = 180$) (27-29).

Although the frequency of high global CVD risk was lower than expected for the total sample, the fifty-year group ($n = 103$), with the highest frequency of cases with high global CVD risk ($n = 11$), showed differences with respect to the twenty-year group with greater waist circumference, systolic blood pressure, BMI, body fat percentage, fasting glucose levels and triglycerides ($p < 0.05$). Only LDL cholesterol represented a significant difference for the fifty-year group compared to the rest of the groups ($p < 0.01$).

On the other hand, in the forty-year group the prevalence of high global CVD risk was two percent ($n = 2$) and presented values of diastolic blood pressure, BMI, and body fat percentage even higher than the fifty-year group ($p < 0.05$). It should be considered that according to studies, up to 49.7 % of people without cardiovascular risk factors (blood pressure < 140/90 mmHg, fasting glucose < 126 mg/dl, total cholesterol < 240 mg/dl and LDL cholesterol < 160 mg/dl) can present subclinical atherosclerosis, and among the variables that are associated independently with their presence are LDL cholesterol levels (OR, 1.14; 95 % CI, 1.08-1.19, $p < 0.01$), so that their evaluation should be considered for primary prevention even in individuals conventionally considered without risk factors (30).

No cases with high global CVD risk were found in the younger groups (20 and 30 years). However, it should be noted that the Framingham score was designed based on a population over 30 years old, and the strength of the association between the factors of individual risk and mortality differs by ethnicity; as such, it may not identify individuals with predisposing lifestyles to develop long-term cardiovascular disease (28).

HIGH CARDIOVASCULAR RISK AND ANTHROPOMETRIC VARIABLES

According to our study, BMI ($r = 0.3$, $p < 0.01$) and waist circumference ($r = 0.4$, $p < 0.01$) are the anthropometric variables with the greatest association with global CVD risk in all age groups, and BMI is a risk factor for high global CVD risk (OR, 6.1; 95 % CI, 1.6-22.6).

The fifty-year group showed a mean BMI and waist circumference less than the forty-year group ($p < 0.05$); however, it had a greater number of participants with high global CVD risk; these variations could be associated with body composition, low subcutaneous fat and the presence of visceral fat. Visceral fat increases with age and suggests a phenotype with less capacity to capture free fatty acids in adipose tissue (31). In a study of adults with type 2 diabetes with a mean age of 65 ± 12 years, the area of visceral and subcutaneous fat was measured by computed axial tomography and showed an association with the thickness of the carotid intima-media; according to their results, having high visceral fat and decreased subcutaneous fat is significantly associated with carotid intima-media thickness ($\beta = 0.42$, $p < 0.001$), which provides evidence that high visceral fat with low-fat subcutaneous accumulation is an important determinant for carotid atherosclerosis, and subcutaneous fat may protect against atherosclerosis. However, there are no cutoffs to classify the relationship between subcutaneous and visceral fat with cardiovascular risk (32).

SENSITIVITY AND SPECIFICITY OF BMI FOR THE DIAGNOSIS OF OBESITY

Despite the significant association between BMI and body fat percentage ($r = 0.8$, $p < 0.01$), the current cut-off points for the detection of obesity showed excellent specificity (93 % for men and 100 % for women) but poor sensitivity with values of 53 % and 50.89 % for men and women. A higher body fat percentage is associated with greater resistance to hepatic and muscular insulin; thus, the low sensitivity of BMI leaves about half of the people with obesity, defined by body fat percentage, without a diagnosis of risk (33). It is worth mentioning that there is no strong basis for choosing any single measure of obesity as a gold standard (34); but, it is known that a low BMI and high body fat percentage are independently associated with increased mortality (35). Although there are high-tech imaging options such as computed tomography and magnetic resonance with excellent accuracy, their cost, technical complexity and lack of portability exclude their routine use. On the other hand, the use of BIA finds that 61.25 % of women classified as nonobese by BMI are false negatives (34); however, more longitudinal evidence is needed to strengthen this relationship.

According to our results, the cut-off value recommended by the WHO for the detection of obesity does not reflect the actual excess of adipose tissue (8,10). Our data agree with the results by Romero-Corral and collaborators, who determined that BMI has a sensitivity of 49 % and, according to the literature, it can decrease to 25.6 % when it comes to postmenopausal caucasian women (8).

According to Gómez Ambrosi and his research in the American population, the cutting points that diagnose obesity with greater precision are 29 kg/m^2 in men and 27 kg/m^2 in women. We propose cutoffs for the diagnosis of obesity by BMI, based on body fat percentage, at 25.5 kg/m^2 for women and 26.6 kg/m^2 for men. We agree with the recommendation issued by Gómez Ambrosi to include the evaluation of body composition in routine practice for the diagnosis of obesity. Although there is no recommended universal method to measure body fat percentage, bioelectrical impedance analysis (BIA) is considered a portable, non-invasive and low-cost method; however, its reliability and precision can be influenced by the type of instrument, hydration, and the prediction equation used (36). The clinical evaluation of excess fat in individuals with normal BMI should begin at an early age, and obesity should be evaluated by fat mass and fat-free mass (33).

RISK FACTORS FOR THE INCREASE IN CARDIOVASCULAR RISK: DIETARY INTAKE

Although we did not show participants with high global CVD risk, the group with the highest dietary risk behaviors was the twenty-year group, with a higher energy and sodium consumption than the rest of the groups ($p < 0.01$). Although it also had a higher consumption of lipids, total cholesterol, and sugar grams, differences were not statistically significant.

The dietary guidelines for Americans, in its 2010 version, recommend keeping daily cholesterol intake below 300 mg (37); and describe that reduction of dietary cholesterol to 300 mg per day is not included in the 2015 edition since this parameter is no longer considered necessary when constructing healthy eating patterns. However, the OR of consumption of more than 300 mg of cholesterol per day in our population for high global CVD risk was 3.2 (95 % CI, 1.0-9.9, $p = 0.03$). Only cholesterol levels were shown to be a factor of high global CVD risk, although the results may be limited by the size of our sample. Significant differences were observed in age of onset of consumption of beverages with added sugars ($p < 0.01$), which is worrisome because, while in the twenty-year group there were no cases with high global CVD risk, and the high-risk population was concentrated in the fifty-year group, the exposure to these risk products started earlier in the younger groups ($p < 0.01$).

In the present study, the consumption of industrial juice was higher in the twenty-year group, with significant differences when compared with the rest of groups ($p < 0.01$). According to studies, regular consumption of sugary drinks (two soft drinks per day compared to one soft drink per month) has been associated with a 35 % increase in the risk of coronary heart disease in women, even after taking into account other factors like diet and lifestyle (19).

In our sample, 100 % of patients with high global CVD risk reported a positive soda consumption of at least one cup of soda twice a week, and average sugar consumption of 40 ± 32 grams per day. The WHO recommends that the maximum sugar energy consumption be less than 5 %, about 25 grams of sugar per day (30); and according to the Collin, drinking 24 ounces of sweetened drinks or more per day represents a double risk of death from heart disease compared to those who drink less than one ounce per day (HR, 2.5; 95 % CI, 1.3-4.8) (38).

On the other hand, a high sodium intake increases blood pressure and mortality from CVD (31); prospective studies suggest a J-shaped association between sodium intake and CVD risk. In our sample, sodium intake was higher in the younger group as compared to the fifty-year group ($p < 0.01$).

In a review of 23 epidemiological studies ($n = 274,683$) the lowest risk of cardiovascular events and deaths occurred with an intake between 2.7 and 5 g of sodium per day (39); however, according to the expert consensus of the Institute of Medicine (IOM) and the AHA, the average sodium intake in the US population is currently 3,440 mg per day and should be reduced. According to the 2015-2020 American Dietary Guidelines, it is recommended to maintain sodium intake below 2300 mg per day for adults and children over 14 years of age (37).

Regarding the relationship between the intake of processed meats and cardiovascular risk, the OR for consumption of sausages was 1 (95 % CI, 0.2-3.7, $p = 0.99$). Processed red meats are associated with an increase in cardiovascular diseases and strokes (39). However, for our population, the relationship between these variables was not conclusive.

Regarding the limitations of the study, we found a low frequency of high global CVD risk according to the Framingham Risk Score, which could have limited the positive and negative predictive values as well as the association with cardiovascular risk. It should be considered, when studying cigarette smoking as a risk factor for stroke, that in the Framingham cohort 55.6 % of men and 36.1 % of women smoked; and although smokers showed a lower weight compared to non-smokers ($p < 005$), they presented an increased risk of hypertension, heart attack, and stroke. However, in the present study, the prevalence of smoking was lower than 10 % for the total sample. Integrating the population from the twenty-year group can make a difference by how old you are and that, to some extent, risk expression could be contained in this age, so the sample should be higher for this age group.

Another limitation is the quantification of sodium intake and antioxidants, which was carried out by means of a 24-hour recall, a retrospective dietary evaluation method, however, the gold standard is 24-hour urinary sodium excretion, which was not feasible. Finally, a recent study that derives from the analysis of the 2018 health and nutrition survey, reflects figures similar to those studied in our population, which reflects an urgent call to action in the face of overweight and obesity figures, mainly in the age group of 20 years, which was the group with the highest metabolic and cardiovascular risks, mainly reflected in the dietary analysis (40).

CONCLUSIONS

BMI presented a significant association with cardiovascular risk according to the Framingham risk score for all age groups; however, it did not significantly predict high global CVD risk in 30 % of cases. Although biochemical values were mostly adequate for the twenty-year group, dietary consumption did not reflect the same behavior, where this group had higher intakes than the other age groups for cholesterol, sugar additives, energy, and saturated fats. Among the different age groups, BMI was found to be a specific diagnostic test in men and women (93 % and 100 %, respectively), as well as positive predictive values. However, when considering high global CVD risk, the results suggest that BMI should be integrated with waist measurement and body fat percentage to obtain a higher sensitivity. Waist circumference and percentage of body fat as determined by bioimpedance showed an adequate sensitivity; however, several factors must be taken into account, such as the type of instrument or equipment, as well as the prediction equation used. A surveillance strategy for these variables should be integrated for the population in their twenties.

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Trabajo Original

Valoración nutricional

Hydration status according to impedance vectors and its association with clinical and biochemical outcomes and mortality in patients with chronic kidney disease

Estado de hidratación por vectores de impedancia y su asociación con desenlaces clínicos, bioquímicos y mortalidad en pacientes con enfermedad renal crónica

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Abstract

Background: the evaluation of hydration status and body composition in patients with kidney disease is vital for proper management, since overhydration is associated with cardiovascular complications. Patients with chronic kidney disease (CKD) begin to show perceptible alterations in hydration during the intermediate stages of the disease; however, there is little information regarding the evaluation of blood volume status through bioelectrical impedance vector analysis (BIVA) in this population.

Objective: to determine the association between hydration status measured with BIVA and biochemical and clinical parameters and mortality in patients with stage G3a, G3b and G4 CKD.

Material and methods: a cross-sectional study was conducted with patients with stage G3a, G3b and G4 CKD who underwent bioelectrical impedance analysis (BIA). The following biochemical and clinical parameters were determined: serum and urinary albumin, hematocrit, serum electrolytes and creatinine, estimated glomerular filtration rate (eGFR, using the CKD-EPI formula), 24-hour urine output and blood pressure. The clinical and biochemical variables were associated with the components of the BIA. According to the resistance/height (R/H) and reactance/height (Xc/H) values, the BIVA results were individually plotted on reference ellipses to identify patients with abnormal hydration states. The patients were classified by group according to hydration status and CKD stage z-scores, and differences in clinical, biochemical and BIA parameters were identified. Mortality was determined by hydration status.

Results: a total of 138 subjects, 69 men and 69 women, were studied. An association was found between the BIVA components (R/H, Xc/H and phase angle (PA) and serum albumin (albumin and R/H, $r = -0.38$, $p = 0.001$; Xc, $r = 0.59$, $p = 0.000$; PA, $r = 0.58$, $p \leq 0.0010$). When the biochemical and clinical parameters were compared by hydration status, significant differences were found in eGFR ($p = 0.01$), serum calcium ($p \leq 0.001$), serum albumin ($p \leq 0.001$), hemoglobin ($p = 0.04$), hematocrit, ($p = 0.04$) and mean arterial pressure ($p = 0.03$). The patients were followed for a median of 65.5 months (IQR: 53.0 to 207.0), and 12 (8.6 %) patients with CKD died. The Kaplan-Meier curves showed that patients with overhydration had a significantly higher risk of death than patients with normal hydration.

Conclusions: there is an association between the hydration status evaluated by BIVA and clinical and biochemical variables. Patients with overhydration are significantly more likely to die than patients with normal hydration.

Keywords:

Bioelectrical impedance.
Impedance vector analysis.
Chronic kidney disease.
Body composition.
Mortality.

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Resumen

Antecedentes: la evaluación del estado de hidratación y la composición corporal es imprescindible para los pacientes con enfermedad renal crónica (ERC) en estadios intermedios, ya que en esta etapa inician con alteraciones hídricas perceptibles; sin embargo, existe poca información en dicha población sobre la evaluación del estado de volemia mediante el análisis de vectores de bioimpedancia eléctrica (BIVA).

Objetivo: asociar el estado de hidratación medido por BIVA con parámetros bioquímicos, clínicos y mortalidad en pacientes con ERC G3a G3b y G4

Material y métodos: estudio transversal en el cual se incluyó a pacientes con ERC en estadios G3a G3b y G4 a los que se les realizó un análisis de impedancia bioeléctrica (IBE) y en los que se determinaron parámetros bioquímicos y clínicos: albúmina sérica y urinaria, hematocrito, electrólitos y creatinina séricos, tasa de filtrado glomerular estimada (TFGe) (fórmula CKD-EPI), diuresis de 24 horas y presión arterial. Las variables clínicas y bioquímicas se asociaron con los componentes de la IBE. Los valores de resistencia/estatura (R/H) y reactancia/estatura (Xc/H) se graficaron individualmente sobre las elipses de referencia para identificar a pacientes con estados de hidratación anormales. Se ubicaron grupos según el estado de hidratación y estadio de ERC en z-score y se identificaron las diferencias de parámetros clínicos, bioquímicos y de IBE. Se determinó la mortalidad según el estado de hidratación.

Resultados: se estudiaron 138 sujetos 69 hombres y 69 mujeres. Se encontró una asociación entre los componentes de los BIVA y albúmina sérica (albúmina y R/H, r = -0,38, p = 0,001; Xc, r = 0,59, p = 0,000; ángulo de fase, r = 0,58, p ≤ 0,00110). Al comparar los parámetros bioquímicos y clínicos por estado de hidratación se encontraron diferencias significativas en TFGe (p = 0,01), calcio sérico (p ≤ 0,001), albúmina sérica (p ≤ 0.001), hemoglobina (p = 0,04), hematocrito (p = 0.04) y presión arterial media (p = 0.03). Se identificó el fallecimiento de 12 (8,6 %) pacientes con ERC, con una mediana de seguimiento de 65,5 meses (RIC: 53,0 a 207,0). Las curvas de Kaplan-Meier mostraron que los pacientes con sobrehidratación tenían significativamente mayor riesgo de morir que los pacientes con normohidratación.

Conclusiones: existe asociación entre el estado de hidratación evaluado por BIVA y variables clínicas y bioquímicas. Los pacientes con sobre hidratación son significativamente más propensos a morir que los pacientes con normohidratación.

Palabras clave:

Bioimpedancia eléctrica.
Vectores de impedancia.
Enfermedad renal crónica.
Composición corporal.
Mortalidad.

INTRODUCTION

Chronic kidney disease (CKD) is characterized by a total or partial and irreversible loss of renal function and is accompanied by endocrine, gastrointestinal, neurological, electrolytic and water alterations (1,2).

Fluid overload is important to evaluate due to its close relationship with cardiovascular complications, which are the main cause of death in renal patients regardless of age, dialysis modality, cause of end-stage renal disease (ESRD), race or geographic region (3–5).

In CKD, water overload is relevant in terms of its association not only with mortality but with nutritional alterations and systemic inflammation accompanied by an increase in catabolism, which further increases morbidity and mortality. This entity is known as protein-energy wasting (PEW) and has a prevalence of between 28 and 54 % in patients receiving replacement therapy (6,7); it is somewhat less common (11 to 54 %) in patients with stages 3 and 4 CKD (8,9).

PEW is also associated with an increase in the number of hospitalizations, longer hospital stays and higher morbidity and mortality (10,11). Therefore, an adequate evaluation of the nutritional status that includes body composition measurements is of vital importance (12).

At present, bioelectrical impedance analysis (BIA) is one of the most widely used methods for determining body composition because of its accuracy and ease use. BIA offers a non-invasive evaluation of the composition of the human body that allows estimation of total body water (TBW); furthermore, based on the physiological principle of constant tissue hydration, which assumes that 73 % of the fat-free mass (FFM) is water, BIA can obtain the FFM and consequently, the fat mass (FM), using a simple equation based on two compartments (FFM kg = total weight kg - FM kg). BIA analysis is based on the relationship between the electrical properties of the human body, the body composition of different tissues, and the total water content of the body (13). Like all indirect methods for estimating body composition, BIA depends on some assumptions related to body's electrical properties, composition, state of maturation, hydration, age, sex, race and physical condition (13).

Given that in the vast majority of patients with kidney disease, the assumption of normality of hydration is not met, bioelectrical impedance vector analysis (BIVA) has been used to avoid biasing the diagnosis of body composition. BIVA is based on the components of bioimpedance (Z), resistance (R) and reactance (Xc), standardized by height and phase angle (PA), and not on estimates from prediction equations (14,15). This method has been well studied in patients in advanced stages of CKD who are receiving renal replacement therapy; however, its use has been less studied in patients in intermediate stages of CKD, which limits the possibility of testing its usefulness for detecting early changes in body composition that indicate fluid alterations and could help reduce the number of complications and mortality in this population. Therefore, our objective was to determine the association between the hydration status measured by BIVA and biochemical and clinical parameters and mortality in patients with stage G3a, G3b and G4 CKD.

MATERIALS AND METHODS

This is a subanalysis of data collected in two studies; the first one was a cross-sectional study of 81 patients recruited from the Salvador Zubirán National Institute of Medical Sciences and Nutrition (INCMNSZ) in 2004. The objective of this previous study was to evaluate hydration status using BIVA and to identify its association with anthropometric, clinical, and biochemical variables. The second study was a blinded randomized controlled trial of 57 participants recruited from the INCMNSZ in 2015, who underwent different clinical and nutritional assessments, including BIA.

For both studies, the inclusion criteria were as follows: patients from the nephrology outpatient clinic of the INCMNSZ with an estimated glomerular filtration rate (eGFR) of 15 to 59 ml/min/1.73 m^2 (KDIGO stages G3a, G3b and G4) (16), and were males or females between 18 and 65 years of age. Exclusion criteria included patients who were receiving some type of replacement therapy; those who had amputations, pacemakers or a metal prosthesis; and those who had an erroneous BIA measurement.

Both studies were approved by the Ethics Committee and the Human Biomedical Research Committee of the INCMNSZ. All patients provided written informed consent to participate in the study.

CLINICAL AND BIOCHEMICAL ANTHROPOMETRIC DATA

A fasting blood sample was taken and was processed in the laboratory of the nephrology department to determine the following parameters: urea nitrogen, creatinine, glucose, sodium, potassium, calcium, phosphorus, albumin, cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, hemoglobin, hematocrit and albumin in urine. Systolic and diastolic blood pressure was measured by a lead nurse.

Body weight was measured in all patients with a Tanita BWB 800 scale (Tanita Corp., Tokyo, Japan), and height was measured with a Harpenden wall stadiometer (Holtain, Ltd., UK); these data were used to obtain the body mass index (BMI). The glomerular filtration rate was estimated with the CKD-EPI formula. All of this information, as well as the results of the BIA studies, was recorded on the data collection sheet for each participant.

BIOELECTRICAL IMPEDANCE ANALYSIS (BIA) DATA

For the BIA, the patients were asked to fast for a minimum of 4 hours prior to the study, not to perform strenuous exercise in the 24 hours before the study, not to consume alcoholic beverages in the 48 hours prior to the study, not to wear any metallic objects (e.g., jewelry) and, in the case of women, not to be menstruating. All patients were evaluated using a Quadscan 4000 multi-frequency device (Bodystat LDT®, Isle of Man, UK), which performed measurements at 5, 50, 100 and 200 kHz. For the BIA measurements, the patients were instructed to remove heavy clothing, glasses and shoes; to stay still; and not to speak during the measurement. BIA measurements were performed according to the criteria established by the National Institutes of Health Technology Assessment Conference Statement (17). The participants were placed in a supine position with their arms and legs away from the body and the palms of the hands facing down. Electrodes were placed in pairs on the right extremities, on the back of the hand and foot near the phalanx-metacarpal and phalanx-metatarsal joints, on the styloid process of the wrist and between the medial and lateral malleolus of the ankle for introducing the BIA current. After the measurement, the impedance value at a frequency of 50 kHz was collected from the equipment. This impedance value was used to determine the R, Xc and PA using the Bodystat Phase Software provided by the BIA analyzer manufacturer (Bodystat LDT®, Isle of Man, UK).

BIOELECTRICAL IMPEDANCE VECTOR ANALYSIS (BIVA)

BIVA does not depend on models, estimates or equations, since it is only affected by z-scores or individual variability. It is based on a graph called the RXc chart, which was created by Piccoli et al. (14) and in which the R standardized by height (R/H) is located on the abscissa and the Xc standardized by height (Xc/H) is located on the ordinate axis. Each individual vector can be compared with the reference population of ellipses that represent 50, 75 and 95 % by sex. The impedance vector can vary or can migrate to different areas; long vectors are interpreted as states of dehydration, short vectors are interpreted as overhydration, and migration to the left or right is considered indicative of changes in the body tissues (18,19). Different alterations in body composition can be detected by analyzing impedance vectors.

The R and Xc data standardized by height were plotted using the BIVA tolerance software and the reference values for Mexican population (20) to obtain the impedance vectors on the RXc graph. In order to conduct a group analysis according to the CKD stage and hydration status, the BIVA Confidence software was employed (21) following the methodology proposed by Piccoli et al. (22) , in which the values of R and Xc were transformed into z-scores (z [R] and z [Xc]) considering the reference intervals, which allows a set of tolerance ellipses independent of sex to be defined. Group vectors are represented as the mean and 95 % confidence intervals of the z-score.

MORTALITY

The electronic clinical record of each of the participants was reviewed to determine deaths from all causes as of March 2020. Only the date of mortality was recorded and not the cause.

STATISTICAL ANALYSIS

The general characteristics of the participants are presented as measures of central tendency and dispersion according to their distribution and the type of variable. Continuous variables are presented as mean and standard deviation or median and interquartile range. Categorical variables are presented as frequencies and percentages. To determine the distribution of the variables, the Kolmogorov-Smirnov normality test was used.

A Pearson (parametric variables) or Spearman (non-parametric variables) correlation analysis was performed to evaluate the relationship of the BIVA components (R, Xc, PA, R/H and Xc/H)

and other clinical and biochemical indicators. The coefficients were interpreted as follows: 0-0.29 = weak correlation; 0.30-0.69 = moderate correlation; and 0.70-1.0 = strong correlation (23). The individual hydration status was assessed using the BIVA tolerance program (21). For group analysis, the differences between the group vector patterns were analyzed with the Hotelling t^2 test. To compare the anthropometric, biochemical and clinical parameters according to hydration status and CKD stage, an independent samples t^2 test was used for variables with parametric distribution, and the Mann-Whitney U analysis was used for variables with a nonparametric distribution. To compare the variables according to the CKD stage, one-way ANOVA was used for parametric variables, and the Kruskall Wallis test was used for nonparametric variables. Survival analysis was performed using the Kaplan-Meier method and weight adjusted Kaplan-Meier method (24) to make unbiased comparisons between time-varying groups and control for confounding (sex, age, and body mass index), and the log-rank test was used to identify differences between the curves according to hydration status.

We assessed the multivariate effects of covariates with the Cox proportional hazard analysis to estimate the relative hazards of the mortality crude and adjusted by the following base-line variables: model 1, age group, sex, body mass index, and model 2, age group, sex, body mass index and eGFR. Hazard ratios (HR) and corresponding 95 % confidence interval (CI) were estimated.

The SPSS 26 program was used to perform the statistical analyzes, and the MedCalc program was used to obtain the survival curves. A p-value < 0.05 was considered statistically significant.

RESULTS

Table I shows the general characteristics of the population, as well as the clinical and biochemical parameters and the impedance components. Most parameters were in normal ranges, with the exception of calcium concentrations 8.9 (8.4-9.4), triglycerides 187.9 ± 71.7, hematocrit 34.9 (31.7-40.8) and uremic toxins, such as urea nitrogen 44.6 (34.1-63.6) and creatinine 2.23 ± 0.8.

Positive associations were found between the three BIA components and albumin (albumin and R/H, $r = -0.38$, $p = 0.001$; Xc, $r = 0.59$, $p \leq 0.0010$; PA, $r = 0.58$, $p \leq 0.0010$). Other biochemical parameters that showed positive correlations were hemoglobin concentration and hematocrit, although they were correlated with only two of the BIA components, Xc/H and PA (hemoglobin and Xc/H, $r = 0.31$, $p = 0.01$; hemoglobin and PA, $r = 0.44$ $p = 0.000$); hematocrit and Xc/H, $r = 0.30$, $p = 0.010$; hematocrit and PA, $r = 0.44$, $p \leq 0.0010$). In contrast, a negative correlation was observed between blood glucose concentrations and Xc/H and PA (glucose and Xc/H, $r = -0.41$, $p = 0.025$; glucose and PA, $r = -0.44$, $p = 0.015$).

Subsequently, the R/H and Xc/H values were plotted on the impedance vectors of the reference population. Patients with overhydration and normal hydration were identified and were plotted as groups on the z-score graphs (Fig. 1).

Table I. General characteristics, clinical and biochemical parameters, and bioelectrical impedance analysis components in the study population

	General n = 138
	$\bar{x}$ ± *SD* Median (IQR)
Age (years)	53 (37.5-65.25)
Sex (M/F)	69/69
Height (cm)	162 (152-169)
Weight (kg)	66.6 (60.7-73.1)
BMI (kg/m^2)	24.17 (22.9-28.2)
eGFR (ml/min)	31.87 (21.2-42.5)
Etiology of CKD	n (%)
Diabetes *mellitus*	61 (44 %)
Arterial hypertension	33 (24 %)
Lupus	14 (10 %)
Polycystic kidney disease	14 (10 %)
Glomerulonephritis	8 (6 %)
Unknown	8 (6 %)
Resistance (ohms)	513.73 ± 108.68
Reactance (ohms)	51.85 (39.8-61.5)
R/H (ohms/m)	318.88 ± 72.15
Xc/H (ohms/m)	32.85 (24.5-38.77)
Phase angle	5.7 (4.7-6.2)
Urea nitrogen (mg/dL)	44.6 (34.1-63.6)
Creatinine (mg/dL)	2.6 (1.8-4.1)
Glucose (mg/dL)	87.0 (79.5-95)
Sodium (mmol/L)	139.0 (136.9-140.8)
Potassium (mmol/L)	4.7 ± 16.6
Calcium (mg/dL)	8.9 (8.4-9.4)
Phosphorus (mg/dL)	4.3 (3.3-4.9)
Albumin (g/dL)	3.5 ± 0.7
Cholesterol (mg/dL)	193.5 ± 46.0
Triglycerides (mg/dL)	187.8 ± 71.7
HDL cholesterol (mg/dL)	49.3 ± 16.1
LDL cholesterol (mg/dL)	103.7 ± 43.0
Hemoglobin (mg/dL)	12.1 (10.7-13.7)
Hematocrit (%)	34.9 (31.7-40.8)
Albumin (g/d)	1.4 (0.60-4.4)
Diuresis (mL)	2012.0 ± 716.9
Mean arterial pressure (mmHg)	95.8 ± 13.3

BMI: body mass index; eGFR: estimated glomerular filtration rate; R/H: resistance/height; Xc/H: reactance/height.

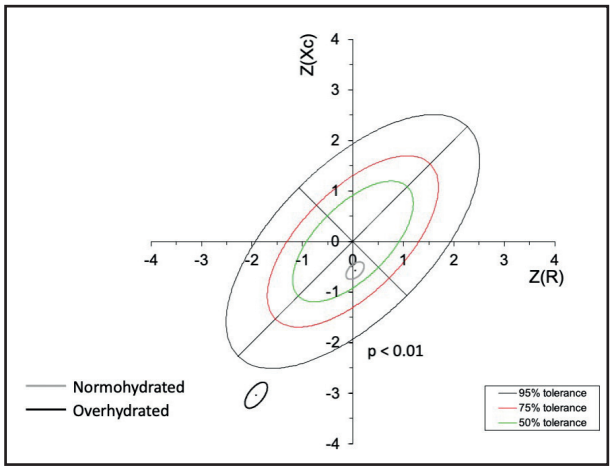

Figure 1.

Z-score graph by hydration status.

Table II shows the differences in the evaluated parameters between the normally hydrated and overhydrated patients according to the BIVA. There was higher proportion of women (61 %) among the patients with volume overload; additionally, the patients in this group were older and heavier and showed lower values of R, Xc and PA values than the patients with normal hydration. The patients with volume overload also had lower concentrations of albumin, calcium, hemoglobin and hematocrit, greater albuminuria and a higher mean arterial pressure.

Table III shows the differences in the evaluated parameters by CKD stage. Statistically significant differences in the proportions of patients with overhydration were found, with a greater prevalence among patients in stage G3b (53 %). PA also showed significant differences between the stages of CKD; it was smaller in the patients in more advanced stages. Regarding the biochemical parameters, differences were observed in the uremic toxins BUN and creatinine,in addition to phosphorus concentrations, hemoglobin, hematocrit (and in urinary volume).

Subsequently, the means of the vectors were plotted by group according to the z-scores for CKD stage. Three groups were located in the lower right quadrant, which indicated a pattern of both overhydration and cachexia. However, for the patients in stages G3a and G3b a portion of the sample fell within the normal quadrants, while the majority of the patients in stage G4 were located below the tolerance ellipse of 75 %; in other words, migration of the mean of the vector towards the lower part of the ellipses is noted as the CKD advances (Fig. 2).

The mean duration of follow-up was 119.6 months (median, 65.5 months). Of the 138 patients included in the mortality prediction analysis, 12 (8.7 %) died, with a median of 52.2 months (IQR: 38.5-77.7 months) of follow-up until death was recorded. Nine (75 %) patients who died were in the overhydrated group. Patients in the overhydration group were significantly more likely to die, as demonstrated by the Kaplan-Meier curves (Fig. 3).

Table II. Anthropometric, bioelectrical impedance, clinical and biochemical parameters of the overhydrated population compared to normohydrated patients

	Normohydrated n = 79	Overhydrated n = 59	p
	$\bar{x}$ ± SD *Median (IQR)*	$\bar{x}$ ± SD *Median (IQR)*	
Age (years)	45.0 (33.0-64.0)	60.0 (47.0-66.0)	< 0.001*
Sex (M/F), n (%)	46.0 (58.0) / 33.0(42.0)	23.0 (39.0) / 36.0 (61.0)	0.02*
Height (cm)	160 (152.0-170.0)	164 (157.0-169.0)	0.21
Weight (kg)	65.7 (56.5-70.4)	68.4 (61.9-75.7)	0.02*
BMI (kg/m^2)	23.1 (22.9-27.6)	26.7 (23.0-29.0)	0.06
EGFR (ml/min)	34.2 (24.5-45.9)	26.9 (20.1-41.5)	0.01*
Resistance (ohms)	575.8 ± 75.6	430.5 ± 88.9	< 0.001*
Reactance (ohms)	60.2 (55.4-66.5)	38.54 (26-43.1)	< 0.001*
Resistance/height (ohms/m)	358.5 ± 54.02	265.7 ± 57.8	< 0.001*
Reactance/height (ohms/m)	36.7 (34.0-41.2)	23.7 (13.4-26.3)	< 0.001*
Phase angle (°)	5.9 (5.6-6.3)	4.7 (4-5.4)	< 0.001*
Urea nitrogen (mg/dL)	34.5 (23.7-43.2)	41.35 (34.4-52.7)	0.26
Creatinine (mg/dL)	1.99 (1.61-2.3)	2.39 (1.7- 3.1)	0.16
Glucose (mg/dL)	87.05 ± 9.7	106.33 ± 41.6	0.05
Serum sodium (mmol/L)	134.8 ± 21.6	138.01 ± 4.04	0.42
Potassium (mmol/L)	4.6 ± 0.4	4.8 ± 0.6	0.18
Calcium (mg/dL)	9.30 (8.80-9.6)	8.5 (7.9-9.0)	< 0.001*
Phosphorus (mg/dL)	4.14 ± 1.2	4.56 ± 1.2	0.18
Albumin (g/dL)	3.87 ± 0.60	3.07 ± .67	< 0.001*
Cholesterol (mg/dL)	192.6 ± 40.4	195.0 ± 56.6	0.88
Triglycerides (mg/dL)	184.9 ± 79.8	193.1 ± 56.7	0.75
HDL (mg/dL)	49.4 ± 15.8	48.9 ± 17.3	0.92
Hemoglobin (g/dL)	12.6 ± 2.2	11.6 ± 1.8	0.04*
Hematocrit (%)	37.2 ± 6.5	34.2 ± 5.3	0.04*
Albumin in urine (g/d)	1.1 (0.40-3.8)	2.6 (.95-6.0)	0.09
Mean pressure (mm/Hg)	92.8 ± 12.67	100.0 ± 13.4	0.03*
Urinary volume (ml)	2102.1 ± 593.5	1896.8 ± 848.3	0.28

*eGFR: estimated glomerular filtration rate. Differences between normohydrated and overhydrated patients: *p < 0.05. Non-parametric analyses were used in variables reported by median and interquartile range (IQR). Parametric analyses were used in variables reported by mean and standard deviation.*

Table III. Anthropometric, electrical bioimpedance, clinical and biochemical parameters of the study population according to stage of chronic kidney disease

	Stage G3a n = 24	Stage G3b n = 36	Stage G4 n = 78	p
	$\bar{x} \pm SD$ *Median (IQR)*	$\bar{x} \pm SD$ *Median (IQR)*	$\bar{x} \pm SD$ *Median (IQR)*	
Overhydration/normohydration, n (%)	*2/22 (8/92)*	*19/17 (53/47)*	38/40 (49/51)	0.03*
Age (years)	40 (26.5-67.5)	59 (41.2-67.0)	61 (44.0-72.0)	0.93
Sex, M/F	10/14	19/17	40/38	0.02*
Height (cm)	170 (162.0-175.0)	161 (150.0-171.0)	160.0 (153.0-165.0)	0.16
Weight (kg)	62.2 (55.1-78.7)	71.9 (66.6-87.8)	68.4 (61.2-75.9)	0.24
BMI (kg/m^2)	22.7 (18.7-26.4)	28.3 (24.5-33.0)	27.0 (24.5-29.7)	0.17
eGFR (ml/min)	54.5 (46.5-57.7)	38.1 (33.7-41.5)	20.6 (18.1-24.7)	< 0.001*
Resistance (ohms)	555.5 ± 96.7	512.2 ± 70.9	509.3 ± 107.9	0.30
Reactance (ohms)	58.5 (48.0-62.8)	52.55 (43.1-61.4)	47.4 (63.6-58.6)	0.04*
Resistance/height (ohms/m)	332.8 ± 64.8	318.4 ± 54.5	323.9 ± 73.6	0.90
Reactance/height (ohms/m)	34.55 (27.8-37.7)	33.1 (27.2-38.4)	29.5 (21.9-37.4)	0.27
Phase angle (°)	5.9 (4.9-6.5)	5.8 (5.1-6.3)	5.09 (4.1-5.8)	< 0.001*
Urea nitrogen (mg/dL)	19.7 (17.9-25.0)	34.1 (28.1-40.0)	48.6 (39.4-63.4)	< 0.001*
Creatinine (mg/dL)	1.55 (1.4-1.6)	1.81 (1.6-2.1)	2.86 (2.3-3.3)	< 0.001*
Glucose (mg/dL)	86.4 ± 7.5	92.27 ± 31.4	99.44 ± 28.3	0.69
Serum sodium (mmol/L)	139.3 ± 1.8	140.0 ± 2.7	139.5 ± 9.2	0.76
Potassium (mmol/L)	4.4 ± 0 .5	4.76 ± 0.4	4.63 ± 0.6	0.48
Calcium (mg/dL)	9.6 (9.2-9.8)	9.3 (8.5-9.7)	9.1 (8.5-9.5)	0.12
Phosphorus (mg/dL)	2.9 ± 0 .4	3.8 ± 0.8	3.9 ± 0.7	0.04*
Albumin (g/dL)	4.2 ± 0.3	3.9 ± 0.8	3.4 ± 0.8	0.11
Cholesterol (mg/dL)	187.5 ± 40.5	193.8 ± 50.5	184.1 ± 50.3	0.90
Triglycerides (mg/dL)	186.3 ± 115.8	196.3 ± 77.4	192.6 ± 48.7	0.97
HDL (mg/dL)	46.8 ± 12.1	52.0 ± 18.7	52.3 ± 18.6	0.80
Hemoglobin (g/dL)	15.1 ± 0.6	14.1 ± 1.3	12.4 ± 1.6	< 0.001*
Hematocrit (%)	44.7 ± 2.2	41.6 ± 4.1	36.4 ± 4.7	< 0.001*
Albumin in urine (g/d)	2.24 ± 2.9	3.6 ± 2.3	3.6 ± 4.6	0.76
Mean pressure (mm/Hg)	90.83 ± 11.3	90 ± 11.1	95.2 ± 13.9	0.62
Urinary volume (ml)	2773 ± 562.2	802.4 ± 401.2	658.2 ± 304.1	0.01*

*Differences between patients by stage of chronic kidney disease, *p < 0.05. Non-parametric analyses were used in variables reported by median and interquartile range (IQR). Parametric analyses were used in variables reported by mean and standard deviation.*

In table IV, multivariate Cox proportional hazards regression showed that increased mortality risk was associated ($p < 0.05$) with hydration status and urine volume except for adjusted hydration status by age, sex, BMI, and eGFR. Patients with overhydration status had a 4-fold greater risk than normohydrated patients for mortality (HR, 4.39; 95 % CI, 1.11-17.2). Higher urinary volume was associated with a lower risk of mortality (all $p < 0.05$). The rest of the variables did not show a statistically significant association with mortality.

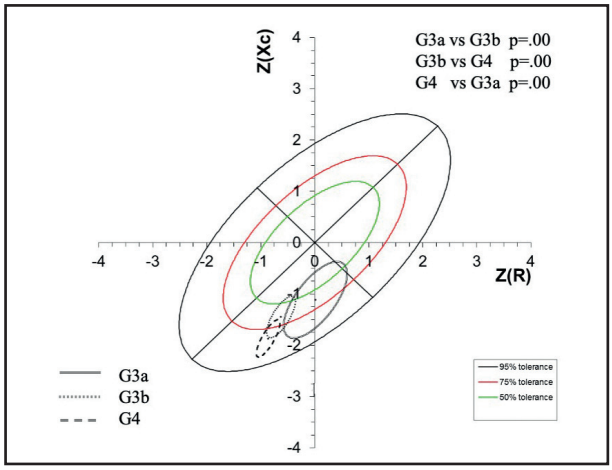

Figure 2.

Z-score graph by CKD stage.

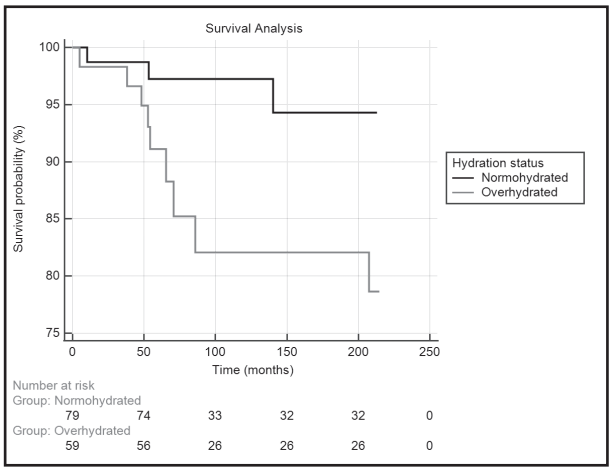

Figure 3.

Survival of normally hydrated and overhydrated patients according to impedance vectors adjusted by aged sex and body mass index.

Table IV. Multivariate Cox regression models for survival analysis

Variable	Crude		Model 1		Model 2	
	Hazard ratio (95 % CI)	p	Hazard ratio (95 % CI)	p	Hazard ratio (95 % CI)	p
Age (years)						
18-39	1		1		1	
40-60	1.2 (0.28-5.0)	0.79	1.09 (0.24-4.8)	0.78	1.2 (0.12-12.7)	0.84
> 60	1.04 (0.23-4.6)	0.95	0.94 (0.20-4.3)	0.51	1.4 (0.14-13.9)	0.77
Hydration status						
Normohydrated	1	0.04	1	0.034	1	0.28
Overhydrated	3.93 (1.06-14.5)		4.39 (1.11-17.2)		2.32 (0.49-10.9)	
Phase angle						
> 4.5°	1	0.67	1	0.63	1	0.23
< 4.5°	0.72 (0.15-3.3)		0.68 (0.14-3.2)		0.25 (0.028-2.3)	
Glucose (mg/dL)	1.01 (0.98-1.04)	0.44	1.0 (0.97-1.05)	0.62	1.0 (0.95-1.05)	0.90
Albumin (g/dL)	0.95 (0.26-3.4)	0.94	0.78 (0.22-2.7)	0.71	0.98 (0.26-3.6)	0.99
Hemoglobin (g/dL)	1.16 (0.77-1.7)	0.47	1.0 (0.57-1.8)	0.95	1.3 (0.63-2.9)	0.43
Hematocrit (%)	1.07 (0.94-1.22)	0.30	1.0 (0.84-1.18)	0.99	1.05 (0.86-1.2)	0.59
Albumin in urine (g/d)	1.05 (0.84-1.2)	0.65	0.99 (0.76-1.2)	0.71	0.96 (0.74-1.2)	0.79
Mean pressure (mm/Hg)	1.01 (0.96-1.0)	0.51	1.0 (0.94-1.0)	0.97	1.02 (0.94-1.0)	0.94
Urinary volume (ml)	0.99 (0.99-1.0)	0.04	0.98 (0.99-1.0)	0.02	0.99 (0.99-1.0)	0.02

Model 1 adjusted for sex, age; BMI: body mass index. Model 2 adjusted for sex, age; BMI: body mass index; eGFR: estimated glomerular filtration rate.

DISCUSSION

The present study included patients in the intermediate stages of CKD who were not receiving replacement treatment, because at this stage, some patients show the onset of complications, including alterations in body composition. The purpose of the study was to analyze body composition through the BIVA method, with the objective of demonstrating the clinical utility of this tool for improving medical and nutritional treatment, even before any type of dialysis begins.

Regarding the BIA components, low average PA, R/H and Xc/H values were observed for the entire population. This allowed the estimation of short vectors that indicate water retention (14,25), a clinical sign that is present primarily in the advanced stages of CKD but is not necessarily absent in the intermediate stages, as could be observed in the BIVA graphs. This highlights the relevance of BIVA at any stage of CKD; using the results of conventional BIA can lead to bias because these values use prediction equations that are based on healthy populations without alterations in body components.

Regarding biochemical parameters, the general population showed normal concentrations, with the exceptions of serum concentrations of urea nitrogen and creatinine, which is to be expected in cases of renal disease progression (26). An increase in triglycerides and decreases in calcium, hemoglobin and hematocrit were also expected to be observed.

The patients showed normal diuresis and mean arterial pressure, while their median glomerular filtration rate was 31.87 (21.2-42.5) ml/min, which can identify the general stage G3b population, according to the KDIGO classification (27). This represents a decrease in the glomerular filtration rate from moderate to severe, a situation associated with the following conditions, which are listed from the most to the least prevalent according to the Spanish Society of Nephrology (27): hypertension, hyperparathyroidism, anemia, acidosis, vitamin D deficiency, hyperphosphatemia and hypoalbuminemia. The study population presented a decrease in calcium concentrations, most likely associated with vitamin D deficiency, as well as anemia; however, participants did not present a lack of blood pressure control, even though this is the second most common cause of CKD, nor were alterations in blood concentrations of phosphorus and albumin observed. It is worth mentioning that the presence of acidosis was not evaluated.

When groups of patients were graphed onto the z-score ellipses (15), it was observed that a significant percentage of the population had alterations in water status (43 %), and these patients showed a higher glomerular filtration rate (Table II). Some studies (28,29) have described that as a patient progresses to CKD, alterations in body composition occur. It has been shown that FM and lean mass decrease significantly as the effects of anorexia and low nutritional intake begin to emerge, generating a common catabolic state called PEW syndrome. These alterations in body composition can be partially stabilized with effective treatments to control uremia and with an increased dietary intake. However, a complete normalization of FM and lean mass rarely occurs (28).

Patients who were identified as overhydrated were older, heavier and, as expected, had lower R, Xc and PA values than patients without volume overload. This finding has been mentioned in other studies (25), since it has been established that with BIVA, an individual's hydration level is determined by vector length in such a way that short vectors indicate greater body fluid volumes and less resistance, while a lower PA is associated with deterioration of nutritional status and an increased risk of mortality (20,25,30). Xc, on the other hand, determines the capacity of cell membranes to store energy, since they act as electrical capacitors; when an electric current passes through them, they act as conductors, and the cellular content acts as a dielectric material, storing the charge when the current passes between the intracellular and extracellular compartments. In this way, when there is alteration in the cell membranes, as in the case of fluid retention, the Xc decreases.

Regarding the biochemical parameters of the overhydrated patients (Table III), lower blood concentrations of albumin, hemoglobin and hematocrit and higher albuminuria and mean arterial pressure were observed. These results could have occurred for two reasons: first, and with a focus on albumin concentrations, hypoalbuminemia is an important risk factor that increases both mortality and morbidity in patients with CKD; however, it must be considered that although hypoalbuminemia is normally attributable to malnutrition or wasting or a chronic inflammatory state, it can also be the result of hemodilution caused by volume expansion with respect to the low concentrations of hemoglobin and hematocrit, and it can be explained by the secondary presence of anemia in renal disease. It is worth mentioning that both groups of patients showed very low values for these two variables and therefore, we cannot refer to hemodilution alone as the main cause of these low concentrations. Albuminuria was more common in patients with overhydration, as expected; this finding is related to hypoalbuminemia and decreased oncotic pressure. The presence of volume overload can also have repercussions for blood pressure; in the patients with overhydration, the mean arterial pressure was significantly higher in the group with fluid retention, although it is worth mentioning that within normal ranges.

Regarding the correlations between the BIA components (R/H, Xc/H and PA) and the biochemical and clinical parameters, a significant association was found between the BIA components and albumin. This association can corroborate the diagnosis of overhydration by BIVA, since albumin, hematocrit and hemoglobin are closely related to extracellular fluid content. The correlations found in the present study are similar to those identified by Picolli et al. (31) in 1998, in which albumin and hemoglobin were correlated in a group of hemodialysis patients; this study found the albumin concentrations were negatively correlated with R/H and positively correlated with Xc/H, while hemoglobin was positively correlated with both BIA components. It is worth mentioning that the correlation coefficient obtained for most of the evaluated variables was lower than $r = 0.6$, indicating moderate correlations.

The negative correlation between blood glucose concentrations and Xc/H is noteworthy because there are no studies that have directly observed this relationship. The only related study is

one by Amaral et al. conducted in 2007 (32), which investigated alterations in glucose concentrations in aqueous solutions and blood samples using spectroscopic impedance and found that R and PA were the most informative parameters. These parameters reflect changes in the capacity of the cell membrane and therefore show that the number of hematocytes or the volume increase proportionally with glucose levels.

In the analysis by CKD stage, as expected, significant differences were found in eGFR, BUN, creatinine, phosphorus, hemoglobin, hematocrit and urinary volume, due to the progression of the disease itself and as it progresses, changes in composition. body and biochemical parameters are more present (33).

The most frequent cause of mortality in advanced CKD is cardiovascular disease (CV). Some known CV factors (traditional and new), such as male sex, age and diabetes, are associated with overhydration and have an increased prevalence in overhydrated patients (34-36). Although this study did not found in the multivariate Cox regression analysis other causes that influence the mortality of patients with CKD in intermediate stages (probably due to small sample size), one of its findings was that overhydration itself is a long-term risk factor for mortality. In fact, our results coincide with those of studies by Vega et al. (37) and Bansal et al. (38) in which a higher mortality rate was found in patients with short vector lengths, which denote greater overhydration in patients in the intermediate and advanced stages of CKD. Therefore, BIVA is an easy and useful tool that can be used to help detect high-risk patients (39). Although our study lacks longitudinal measurements, it is likely that the frequently use of BIVA, for example, at each clinical visit, could improve patient survival (40), since patients with overhydration could receive closer follow-up, adjustments of diuretics use if necessary, and more frequent visits to the nephrologist.

Body composition influences mortality in the intermediate stages of CKD, as previously described (41,42). Therefore, it is important to monitor body composition before the final stages of kidney disease. BIVA is a useful tool that can be correlates with clinical and biochemical parameters to evaluate alterations in the hydration status of patients in stages 3 and 4 of CKD.

We recognize two main limitations of our study. One is the failure to study the association between mortality and other factors (such as cause of mortality, comorbidities, inflammation, medication, etc) in addition to overhydration. The other is the probable underreporting of deaths in the clinical record; if the death did not occur in the hospital, it is not registered, and therefore, the mortality rate could be lower and comparable to that reported in other studies (37).

CONCLUSIONS

Patients who are diagnosed with fluid overload by BIVA have lower concentrations of calcium, albumin and hematocrit; lower PA values; and higher mean arterial blood pressure values than patients with normal hydration, indicating an association between these variables and hydration status. Patients with overhydration according to BIVA have a higher mortality compared to those who do not present overhydration. BIVA is a useful tool for the evaluation of body composition and hydration status in patients with stage G3 and G4 CKD who are not undergoing dialysis.

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Trabajo Original

Valoración nutricional

Agreement between vector analysis and body composition measurements by four types of bioelectrical impedance technology in hemodialysis patients

Concordancia del análisis vectorial y medidas de composición corporal de cuatro tipos de tecnología de impedancia bioeléctrica en pacientes en hemodiálisis

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Abstract

Background: the differences in bioelectrical impedance vector analysis (BIVA) results from different analyzers that use different bioelectrical impedance analysis (BIA) measurement technologies are not known. This study aimed to identify the degree of agreement between the BIVA results of four different BIA measurement techniques and to evaluate the degree of agreement between their estimates of fat-free mass (FFM) and fat mass (FM) and those determined by the gold-standard method of dual-energy X-ray absorptiometry (DEXA) in a subgroup of patients without overhydration.

Methods: a cross-sectional study was conducted with hemodialysis (HD) patients with end-stage renal disease (ESRD) aged 18 to 65 years. BIA was measured with four different techniques: spectroscopic (BIA-BIS), multifrequency (BIA-MF), single-frequency (BIA-SF), and segmental multifrequency (BIA-MS) techniques. The differences and concordance between the components of the BIA (resistance, reactance, and phase angle) of the four devices were analyzed. Patients with a normal hydration status were identified, and concordance between FM and FFM measurements with each impedance device and DEXA was observed only in these patients.

Results: thirty patients were included. The concordance between the components of BIA ranged from good to excellent (phase angle: intraclass correlation coefficient (ICC) = 0.82, 95 % confidence interval (CI): 0.77-0.93; resistance: ICC = 0.98, 95 % CI: 0.92-0.99). The overall concordance for BIVA diagnosis between the analyzers was substantial for hydration (k = 0.71, 95 % CI: 0.71-0.72) and for body tissues (k = 0.68, 95 % CI: 0.67-0.68). Bland–Altman plots showed the lowest bias between BIA-BIS and DEXA for both FM and FFM.

Conclusions: the agreement among the four devices was good for diagnosis by BIVA. The BIA-BIS analyzer and DEXA had the lowest bias for both FFM and FM, although with higher limits of agreement. The lowest limits of agreement were found with the BIA-MS analyzer

Keywords:

Bioimpedance vector analysis. Bioimpedance analysis. Body composition. Agreement. Hemodialysis.

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Resumen

Antecedentes: se desconoce si existen diferencias en el diagnóstico dado por el análisis de vectores de impedancia bioeléctrica (BIVA por sus siglas en inglés) entre los analizadores que utilizan distintas tecnologías de medición de impedancia bioeléctrica (IBE). Este estudio tuvo como objetivo identificar el grado de concordancia entre el diagnóstico por BIVA de cuatro técnicas diferentes de medición de IBE, así como evaluar el grado de concordancia entre sus estimaciones de masa magra (MM) y masa grasa (MG) en comparación con el método de absorciometría de rayos X de energía dual (DEXA) en un subgrupo de pacientes sin sobrecarga de volumen.

Métodos: se realizó un estudio transversal en pacientes con enfermedad renal crónica avanzada (ERCA) en hemodiálisis (HD) con edades entre los 18 a 65 años. La IBE se midió con cuatro diferentes tecnologías: espectroscópica (IBE-BIS), multifrecuencia (IBE-MF), una sola frecuencia (IBE-SF) y multifrecuencia segmental (IBE-MS). Se analizaron las diferencias y concordancias entre los componentes de la IBE (resistencia, reactancia y ángulo de fase) de los cuatro analizadores. Se identificaron pacientes con estado de hidratación normal, y solo en ellos se evaluó la concordancia de FFM y FM entre cada analizador de impedancia y DEXA.

Resultados: se incluyeron 30 pacientes. La concordancia entre los componentes del IBE varió de buena a excelente (ángulo de fase: coeficiente de correlación intraclase (ICC) = 0,82, IC del 95 %: 0,77-0,93; resistencia: ICC = 0,98, IC del 95 %: 0,92-0,99). La concordancia general en el diagnóstico de BIVA entre los analizadores fue substancial para la hidratación (k = 0,71, IC del 95 %: 0,71-0,72) y los tejidos corporales (k = 0,68, IC del 95 %: 0,67-0,68). Los gráficos de Bland-Altman mostraron un sesgo más bajo entre BIA-BIS y DEXA tanto para FM como para FFM.

Conclusiones: la concordancia entre el diagnóstico por BIVA, entre los cuatro dispositivos, fue sunstancial. El analizador BIA-BIS y DEXA mostraron los sesgos más bajos, tanto para FFM como para FM, aunque con límites de concordancia más altos. Los límites más bajos de concordancia se encontraron con el analizador BIA-MS.

Palabras clave:

Análisis de vectores de bioimpedancia. Bioimpedancia eléctrica. Hemodiálisis. Composición corporal. Concordancia.

INTRODUCTION

End-stage renal disease (ESRD) is characterized by a definitive, total or almost total, irreversible loss of renal function, which is accompanied by endocrine, gastrointestinal, neurological, electrolytic, and water alterations (1). Overhydration becomes important due to its role in the development of cardiovascular complications, which are the main cause of death in kidney disease patients regardless of age, type of dialysis modality, cause of ESRD, race, or geographic region (2). In ESRD, overhydration is relevant for its association with mortality, in addition, nutritional alterations and systemic inflammation, accompanied by an increase in catabolism, are also evident and further increase morbidity and mortality. This entity is known as protein-energy wasting (PEW), which has a prevalence of 28-54% in patients on renal replacement therapy (3) and to a lesser extent (11-54 %) in patients in stages 3 and 4 of chronic kidney disease (CKD) (4-6). PEW is also associated with more hospitalizations, longer hospital stays, and higher morbidity and mortality. Therefore, adequate evaluation of nutritional status including measurements of body composition is vital (7).

One of the most commonly used methods of measuring body composition owing to its accuracy and ease of application is bioelectrical impedance analysis (BIA), which offers a noninvasive evaluation of human body composition to estimate total body water (TBW) based on the physiological principle of constant tissue hydration, which assumes that 73 % of lean body mass (LBM) is water, and the LBM from fat mass (FM) is determined using a simple equation based on two compartments (LBM = total weight – FM). BIA studies are based on the relationship between the electrical properties of the human body, the body composition of different tissues, and the total water content in the body (8). Similar to all indirect methods of estimating body composition, BIA depends on some assumptions related to the electrical properties of the body, its composition, its state of maturation, its level of hydration, age, sex, race, and health/physical condition (8).

Given that in most patients with kidney disease, the assumption of normal hydration is not met, one of the tools that has been used to unbias the diagnosis of body composition is bioelectrical impedance vector analysis (BIVA). This method is based on the components of bioimpedance (Z), resistance (R), and reactance (Xc) standardized by height and phase angle (PA) and not by estimates from prediction equations (9,10). Different body composition analyzers currently on the market use different measurement techniques, such as monofrequency (a single frequency), multifrequency (more than one frequency), spectroscopy (frequencies from 0 to infinity), and segments (measurement of the trunk and extremities at multiple frequencies) (11,12). These analyzers can vary in size and cost, among other characteristics. Results and diagnoses regarding body composition obtained through the different measurement techniques may differ, but no evidence of such disparities is available.

Our main objective was to identify the degree of agreement between the components of BIA analysis and BIVA results obtained through four different measurement technologies (monofrequency, multifrequency, spectroscopy, and segmental techniques). Additionally, we evaluated the degree of agreement between the estimates of FFM and FM by BIA and by the gold-standard method of dual X-ray absorptiometry (DEXA).

MATERIALS AND METHODS

STUDY DESIGN AND PARTICIPANTS

A cross-sectional study was conducted in a group of patients with ESRD. Convenience sampling was used. Patients who were seen at the outpatient replacement therapy consultation of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ) were invited to participate in the study. Those who accepted the invitation were scheduled for an appointment to undergo BIA and DEXA measurements. They were asked to

fast for 4 hours, not to drink alcohol 48 hours before, and not to perform strenuous exercise on the day of the measurement. Male and female patients aged 18 to 65 years and diagnosed with ESRD who were on HD were included. Patients who did not meet the requirements of fasting, alcohol consumption, or exercise, women who were menstruating, and those with amputation of extremities, metal implants, pacemakers, or extensive tattoos were excluded.

ANTHROPOMETRIC AND CLINICAL EVALUATION

On the day of the visit, after the HD session, body weight was measured with a Tanita BC-533 scale (Tanita Corp., Tokyo, Japan) and height with a Harpenden wall stadiometer (Holtain Ltd., UK). From these, the body mass index (BMI) was calculated. Blood pressure was measured by the nurse in charge at the end of the HD session. Biochemical data were collected from the clinical record of the patient within the week after the measurement. The glomerular filtration rate (GFR) was estimated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. All the information, as well as the results of the BIA and DEXA studies, were collected on the data collection sheet for each participant.

DEXA

To perform the whole-body DEXA study, the research team ensured that 1 day before the appointment, the patient had not received oral contrast administration in the previous 5 days or undergone an isotopic study in the previous 2 days (13) The DEXA scan was performed after the HD session in a standardized manner as recommended by the manufacturer. The patient was placed in the supine position, centered on the table with the arms stretched to the sides of the body, the hands facing the legs without touching them, and thumbs up. The patient was asked to hold still until the examination arm finished the evaluation (13). The measurement was carried out with a Discovery QDR series machine (Hologic, Bedford, Massachusetts United States). After the scan, the results sheet was printed, which showed the values for FM (g), fat percentage (%), and FFM (g) = lean mass + bone mineral content.

EVALUATION OF BODY COMPOSITION BY CONVENTIONAL BIA AND BIVA

Conventional BIA analysis

Body composition was evaluated by BIA 10 minutes after the DEXA scan, as well as after the HD session, using four BIA analyzers: Spectroscopic BIA (BIA-BIS): Body composition monitor (Fresenius Medical Care®, Germany), which is a spectroscopic impedance analyzer (bioimpedance spectroscopy) based on 50 different frequencies ranging between 5 and 1000 kHz. Multifrequency BIA (BIA-MF): Quadscan 4000 (Bodystat LTD®, Isle of Man, UK), which performs measurements at 5, 50, 100, and 200 kHz. Single-frequency BIA (BIA-SF): Quantum IV (RJL systems®, Michigan, United States), which performs measurements at 50 kHz. Segmental multifrequency BIA (BIA-MS): InBody S10 (InBody®, Seoul, Korea), which performs measurements at 1, 5, 50, 250, 500, and 1000 kHz.

BIA measurements were performed according to the criteria established by the National Institutes of Health Technology Assessment Conference Statement (14). The electrodes were placed in pairs on the right extremities, located on the back of the hand and foot near the phalanx-metacarpal and phalanx-metatarsal joints, in the styloid process of the wrist, and between the medial and lateral malleolus of the ankle, through which the current of each BIA analyzer was introduced. For scanning by the BIA-MS analyzer, eight electrodes were placed: two on both feet and two on both hands. The measurements were performed one time with each analyzer consecutively at an interval of 2 to 3 minutes, which was only the time required to connect the electrodes of each analyzer between measurements.

Information on body components was recorded. FFM (kg and %), FM (kg and %), TBW (l and %)., intracellular water (ICW) (l and %), and extracellular water (ECW) (l and %) were estimated according to the prediction equations included with each analyzer. The BIA-SF analyzer software provided the option to choose the equation, so the formula for the Mexican-American population was chosen.

BIVA

Body composition was analyzed using the bioimpedance vector analysis method of Piccolli et al. (15,16), and different alterations in body composition were qualitatively detected. The values of the BIA components (R, Xc, and PA of each body composition analyzer at 50 kHz) were recorded to draw the BIVA graph (17) and to standardize the measurements of the analyzers by taking them at the same frequency (50 kHz). For each analyzer, the data were obtained as follows: BIA-BIS: The Fluid Management Tool (Cole-Cole section) provided by the manufacturer was used. BIA-MF: data were derived using Bodystat Phase Software provided by the manufacturer. BIA-SF: the data were recorded directly from the analyzer screen. BIA-MS: the data were obtained from the screen directly. However, in this case, given that the Xc values were recorded by segment, the values of the whole body were calculated by adding the values of the trunk and the extremities of the right side according to the manufacturer's instructions. The R value was calculated using the formula:

$$R = \sqrt{Z^2 - Xc^2}$$

Once the data for each patient were obtained with the different analyzers, the impedance vectors were plotted individually on the RXc graph after standardizing the R and Xc by height and considering the reference values (18) to identify both the state of hydration and body tissues. Subsequently, the data were plotted as a group in BIVA confidence software (19) to identify the differences between the analyzers. The individual or group vectors located within the ellipses of 50 and 75 % indicate a normal body composition, both in body tissues and hydration status, whereas those located outside the 75 % ellipses represent alterations in body composition.

HYDRATION DEFINITION

Vector displacements parallel to the major axis indicated changes in hydration. Vectors within the 50 % tolerance ellipse were considered to indicate normal hydration, whereas lengthening of vectors > 75 % percentile of the upper range of percentiles indicated dehydration. Conversely, shortening of vectors > 75 % percentile reference ellipses in the lower range indicated overhydration. Vectors positioned to the left of the major axis reflected increasing cell mass, and vectors to the right indicated decreasing cell mass. Thus, > 75 % tolerance ellipses of the upper right quadrant indicated lean patients and > 75 % tolerance ellipses of the lower quadrant indicated cachectic patients, whereas > 75 % tolerance ellipses of the upper left quadrant indicated athletic patients and > 75 % tolerance ellipses of the lower left quadrant indicated obese patients (9). The cut-off points for the hydration status was the same for the ellipses plotted by the 4 different devices.

ETHICS STATEMENTS

This study was approved by the Ethics Committee and Human Biomedical Research Committee of the INCMNSZ, with approval number 1771. All patients who participated signed informed consent forms.

STATISTICAL ANALYSIS

The general characteristics of the participants are presented in measures of central tendency and dispersion according to their distribution and type of variable. Continuous variables are presented as the mean and standard deviation or the median and interquartile range. Categorical variables are presented as frequencies and percentages. To identify the distribution of the variables, the Shapiro-Wilk normality test was used.

To determine the differences in the components of BIA (R, Xc, R/H, Xc/H, and PA) between the four analyzers, as well as differences in the body compartments (FFM, FM) given by the analyzers and DEXA, we used one-way repeated-measures analysis of variance for parametric variables and the Friedman test for nonparametric variables, followed by the Bonferroni and Dunn post hoc tests, respectively. For the MS measurements, Dunnett's post hoc test was used. To compare the measurements by the analyzers within the RXc graph of the BIVA, Hotelling's T^2 test was applied to both the female and male graphs. To evaluate the agreement between the measurements of the BIA components (R, Xc, R/H, Xc/H, and PA) by the four analyzers, as well as the agreement between the measurements of body compartments (FFM and FM) by the BIA devices and DEXA, the intraclass correlation coefficient (ICC) was calculated, and the value for absolute agreement with its confidence intervals (95 % CI) was calculated. To interpret the ICC, the scale according to Koo and Li was used (20), where ICC < 0.5 is considered poor agreement, ICC = 0.50 to 0.75 moderate agreement, ICC = 0.75 to 0.9 good agreement, and ICC > 0.9 excellent agreement.

To analyze the concordance of the diagnoses given when plotting the average of the R/H and Xc/H of each machine on the RXc graph, the Fleiss kappa test was used (κ). The results were interpreted according to those recommended by Landis and Koch (21): $\kappa < 0.0$ was considered poor agreement, $\kappa = 0.0$ to 0.20 slight agreement, $\kappa = 0.21$ to 0.4 fair agreement, $\kappa = 0.41$ to 0.6 moderate agreement, $\kappa = 0.61$ to 0.80 substantial agreement, $\kappa >$ 0.81 almost perfect agreement, and $\kappa = 1$ perfect agreement.

Bland-Altman plots were drawn to visually evaluate the agreement between the measurements made with DEXA and the different BIA analyzers, and the 95 % limits of agreement were estimated for the differences in the means between DEXA and each BIA analyzer.

In all tests, $p < 0.05$ was considered statistically significant. All statistical analyses were performed with IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp, except for the Bland-Altman plots, which were drawn with MedCalc Statistical Software, version 18.5, Ostend, Belgium. Hotelling's T^2 test was performed on the BIVA confidence spreadsheet (19).

RESULTS

CHARACTERISTICS OF THE PARTICIPANTS

A total of 32 patients were evaluated, two of whom were excluded from the analysis for having erroneous measurements by one of the BIA devices. Table I shows the general characteristics of the population enrolled.

BIA RESULTS

The comparison of the BIA data, both raw and standardized by height, is shown in table II. Statistically significant differences were found between the data.

The agreement between the BIA components is shown in table II. High ICCs were observed for both raw and standardized strength by height. The ICC for PA was low, although the value obtained indicated good concordance (0.82, 95 % CI: 0.67-0.90).

IMPEDANCE VECTORS

With the data obtained from the components of the BIA by each analyzer standardized by height (R/H and Xc/H), the BIVA results were plotted by sex. When placing the male population in a group on the RXc graph, the measurements by the four analyzers were located in the lower-right quadrant, following a clear pattern of overhydration and malnutrition, which is characteristic of the HD population (Fig. 1.A). No significant differences were found when performing the pairwise comparison. Notably, however, the measurement performed by the BIA-MF analyzer indicated that part of the group evaluated by this analyzer was located in the normality ellipses, that is, in the 50th-75th percentiles of the tolerance ellipses. In the females, the measurements of the four analyzers were also located in the lower-right quadrant, but the ellipses of the women did not show an altered hydration status but rather a clear pattern of malnutrition. As in the males, no significant differences were identified in the pairwise comparisons between

Table I. General characteristics of the population

	Mean ± SD Median (IQR) n = 30
Age (years)	30.01 (26.23-46.05)
Height (m)	1.61 ± 0.15
Weight (kg)	55.53 (47.42-74.12)
BMI (kg/m^2)	21.82 (19.91-27.76)
Sex (F/M) (n [%])	17 (56 %)/13 (44 %)
SBP (mmHg)	141.82 ± 26.55
DBP (mmHg)	85.18 ± 16.75
MAP (mmHg)	104.03 ± 19.21
eGFR (ml/min)	7.72 (4.93-10.42)
Albumin (mg/dl)	3.98 ± 0.51
Serum Cr (mg/dl)	7.12 (4.92-11.31)
Glucose (mg/dl)	84.51 (73.54-117.51)
Urea (mg/dl)	112.82 ± 54.93
Comorbidities (n/%)	
Hypertension	8/27
Diabetes *mellitus*	6/20
Systemic lupus erythematosus	9/30
Hepatic cirrhosis	2/7
Glomerulopathies	7/23
Cardiovascular disease*	8/27

*SD: standard deviation; IQR: interquartile range; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; eGFR: estimated glomerular filtration rate; Serum Cr: serum creatinine. *Myocardial infarction, coronary thrombosis, ischemic heart disease, heart failure.*

Table II. Comparison and intraclass correlation coefficients between raw and height-standardized electrical impedance components of the BIA-BIS, BIA-MF, BIA-SF and BIA-MS analyzers

	BIA-BIS Mean ± SD or Median (IQR) n = 30	BIA-MF Mean ± SD or Median (IQR) n = 30	BIA-SF Mean ± SD or Median (IQR) n = 30	BIA-MS Mean ± SD or Median (IQR) n = 30	p	Bonferroni/Dunn post hoc test p					ICC n = 30	95 % CI
						BIS-MF	BIS-SF	BIS-MS	MF-SF	MF-MS	SF-MS	
R (ohms)	588.91 (480.02-684.41)	564.32 (441.11-668.05)	593.82 (483.72-674.55)	641.91 (531.14-762.52)	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.98	0.92-0.99
Xc (ohms)	48.81 ± 15.81	51.65 ± 15.70	44.37 ± 14.42	52.29 ± 15.92	0.00	0.03	0.89	0.12	0.10	1.00	0.11	0.87	0.77-0.93
PA (°)	4.71 (4.21-6.34)	5.23 (4.11-6.42)	4.43 (3.63-5.21)	5.14 (4.23-6.32)	0.00	0.00	1.0	0.12	0.00	1.00	0.00	0.82	0.67-0.90
R/H (ohms/meters)	371.40 ± 106.61	356.41 ± 110.43	374.37 ± 108.21	404.91 ± 116.87	0.00	0.01	1.0	0.00	0.00	0.00	0.00	0.98	0.94-0.99
Xc/H (ohms/meters)	30.75 ± 10.72	32.52 ± 10.72	28.01 ± 9.51	32.92 ± 11.22	0.00	0.01	0.89	0.06	0.09	1.0	0.10	0.90	0.83-0.95

SD: standard deviation; IQR: interquartile range; BIA: bioelectrical impedance analysis; BIS: bioimpedance spectroscopy; MF: multifrequency; SF: single frequency; MS: multifrequency segmental; ICC: intraclass correlation coefficients; CI: confidence interval; R: resistance; Xc: reactance; PA: phase angle; R/H: resistance/height; Xc/H: reactance/height.

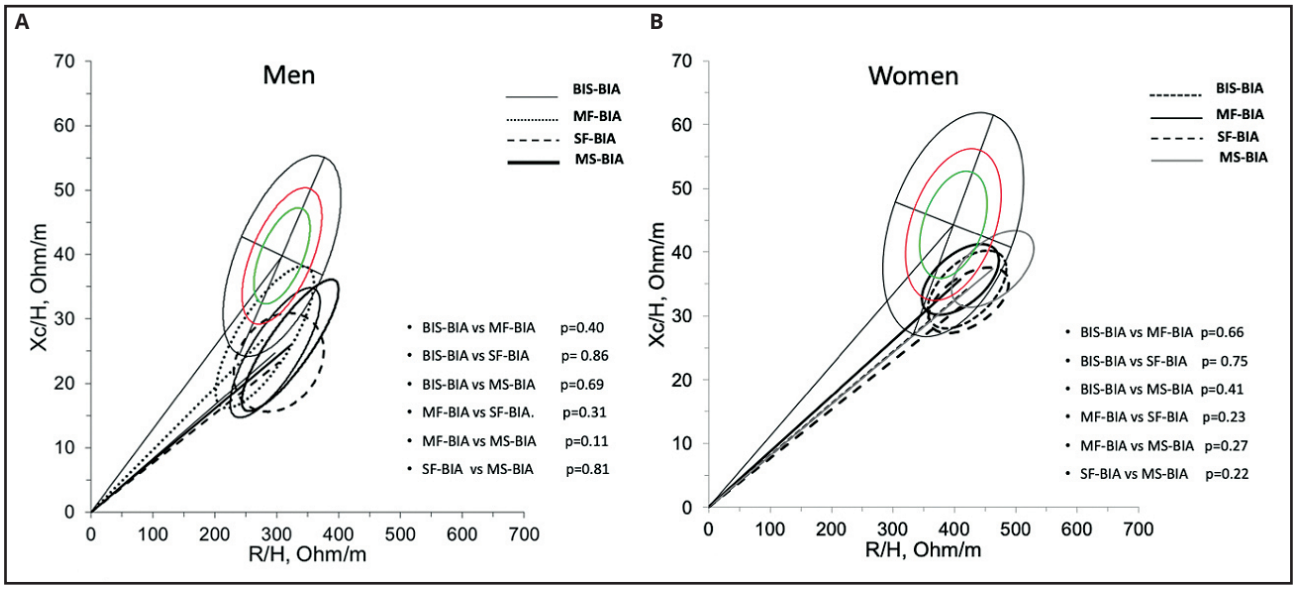

Figure 1.

A and B. Graph of impedance vectors in men and women on HD as evaluated by the BIA-BIS, BIA-SF, BIA-MF, and BIA-MS analyzers (BIA-BIS: spectroscopic; BIA-MF: multifrequency; BIA-SF: single-frequency; BIA-MS: segmental multifrequency; Xc/h: reactance/height; R/H: resistance/height).

the analyzers, although the vector of the BIA-MS analyzer was longer, which located some of the female population evaluated in the quadrant of lean body compositions (Fig. 1B).

After plotting both men and women by groups, the concordance between the diagnoses obtained was analyzed according to the quadrant where the R/H and Xc/H measurements were located in the RXc graph of each analyzer. These are presented both by hydration status and by the state of body tissues in table III. The overall agreement and the agreement by hydration status according to the κ index indicated substantial concordance in the diagnoses by the analyzers. The concordance of the diagnoses by body tissues was moderate for the lean category but substantial for the rest of the categories, with the exception of obesity (Table III).

FAT AND FAT FREE MASS, BIA ANALYSIS, AND DEXA

After the evaluation using the impedance vectors, the FFM and FM, measurements were compared between each analyzer and DEXA. TBW, ICW and ECW measurements were also compared only between the four impedance devices. The patients who underwent scans with any of the four analyzers while having edema or dehydration were identified to exclude them from the analysis to ensure that only measurements of patients were included where the prediction equations of FFM, FM, TBW, ICW and ECW could be applied without bias, complying with the assumptions of normal hydration with which the formulas were derived.

When evaluating the body composition of the 14 normohydrated patients, statistically significant differences were found in the FFM and FM compartments between the five methods. Total body water, intracellular and extracellular data were also reported, however these results were compared only between the four impedance analyzers finding statistically significant differences between body water compartments. Table IV shows these results in both percentages, kilograms and liters. The measurements of FFM (kg) by the BIA-BIS analyzer were the lowest, while those obtained by the BIA-MF analyzer were the highest. Consequently, the values of the FM measurements by BIA-BIS were the highest and by BIA-MF the lowest. In the case of TBW measurements, a similar pattern of the FFM measurements was observed, the highest were recorded by the BIA-MF, but not for ICW and ECW, where the device with the highest measurements was the MS-BIS. In contrast, the lowest measurements were recorded by BIA-BIS device for TBW, ICW and ECW (Table IV).

To evaluate the agreement between the FM and FFM values estimated by DEXA and the four body composition analyzers, the absolute agreement ICC was calculated for each body compartment (Figs. 2 and 3). All the ICC scores showed a concordance between good and excellent. The BIA-MF analyzer had the lowest ICC in the FFM compartment, while the BIA-MS analyzer had the highest ICC in the FFM compartment. In the FM compartment, the lowest ICC values were also given by the BIA-MF analyzer, and the highest ICC values were given by the BIA-BIS analyzer.

The Bland-Altman plot in figure 2 indicates the degree of agreement between measurements by each of the analyzers and by DEXA. In the case of FFM, the lowest average bias of -2.5 kg was found for the measurements performed with the BIA-BIS analyzer.

Table III. Concordance between the diagnoses for hydration status and body tissues according to the quadrant where the data were located in the RXc graph

Hydration	BIA-BIS n (%) n = 30	BIA- MF n (%) n = 30	BIA-SF n (%) n = 30	BIA-MS n (%) n = 30	Total	κ (95 % CI)
Normohydration Expected value	16.00 17.50	19.00 17.50	16.00 17.50	19.00 17.50	70.00	0.71 (0.69-0.78)
Overhydration Expected value	13.00 11.80	10.00 11.80	14.00 11.80	10.00 11.80	47.00	0.73 (0.72-0.73)
Dehydration Expected value	1.00 0.8	1.00 0.8	0.00 0.8	1.00 0.8	3.00	0.65 (0.65-0.66)
Total	30.00	30.00	30.00	30.00	120.00	0.71* (0.71-0.72)
Body tissues						
Normal Expected value	17.00 16.80	18.00 16.80	16.00 16.80	16.00 16.80	67.00	0.78 (0.78-0.79)
Lean Expected value	2.00 10.00	4.00 10.00	1.00 10.00	5.00 10.00	12.00	0.56 (0.56-0.57)
Cachectic Expected value	11.00 3.00	7.00 3.00	13.00 3.00	9.00 3.00	40.00	0.62 (0.62-0.63)
Obese Expected value	0.00 0.30	1.00 0.30	0.00 0.30	0.00 0.30	1.00	-0.00 (-0.01-0.00)
Total	30.00	30.00	30.00	30.00	120.0	0.68* (0.67-0.68)

*BIA: bioelectrical impedance analysis; BIS: bioimpedance spectroscopy; MF: multifrequency; SF: single frequency; MS: multifrequency segmental; κ: kappa; CI: confidence interval. *Fleiss's global κ index.*

Table IV. Body composition of patients evaluated with the four BIA devices and DEXA

	DEXA Mean ± SD or Median (IQR) n = 14	BIA-BIS Mean ± SD or Median (IQR) n = 14	BIA-MF Mean ± SD or Median (IQR) n = 14	BIA-SF Mean ± SD or Median (IQR) n = 14	BIA-MS Mean ± SD or Median (IQR) n = 14	p
FFM kg	27.79 (23.75-34.56)	23.85 (17.4-31.91)	35.05 (29.31-40.04)[a]	32.15 (26.92-38.12)[a]	32.3 (27.11-38.14)[a]	0.000
FFM %	56.58 ± 8.37	49.96 ± 15.76	69.92 ± 8.17[a]	65.66 ± 9.90[a]	64.04 ± 10.42[a]	0.000
FM kg	18.86 (15.89-25.4)	17.21 (12.22-22.42)	13.12 (11.92-17.63)[a]	16.60 (13.47-22.93)[a]	13.23 (10.3-22.54)[a]	0.000
FM %	40.42 ± 8.51	34.72 ± 11.176	30.06 ± 8.17[a]	34.33 ± 9.96	31.74 ± 11.13	0.000
TBW lt		23.20 (18.97-28.68)	28.35(24.0-31.98)	24.10 (19.1-28.38)	25.25 (21.2-29.8)	0.000[b]
TBW %		45.79 ± 7.36	54.13 ± 6.05	46.78 ± 7.24	48.79 ± 7.39	0.000[b]
ICW lt		12.10 (9.9-14.98)	14.4 (11.5-18.28)	12.6 (9.5-14.7)	15.55 (12.83-18.27)	0.000[b]
ICW %		29.86 ± 4.64	24.99 ± 5.42	24.29 ± 5.07	28.21 ± 3.14	0.000[b]
ECW lt		9.70 (8.38-11.53)	10.60 (9.2-12.70)	11.50 (9.6-13.4)	12.85 (11.40- 14.38)	0.000[b]
ECW %		20.14 (16.60-21.47)	22.09 (19.07-22.55)	22.80 (20.53-23.73)	25.75 (22.85-27.3)	0.000[b]

SD: standard deviation; IQR: interquartile range; BIA: bioelectrical impedance analysis; BIS: bioimpedance spectroscopy; MF: multifrequency; SF: single frequency; MS: multifrequency segmental; FFM: fat-free mass; FM: fat mass; TBW: total body water; ICW: intracellular water; ECW: extracellular water. [a]p < 0.05 FFM and FM comparison between DEXA and the designated analyzer, Dunnett post-hoc test TBW. [b]p < 0.05 TBW, ICW, ECW comparison between devices, ANOVA (mean ± SD) or Friedman test (median [IQR]).

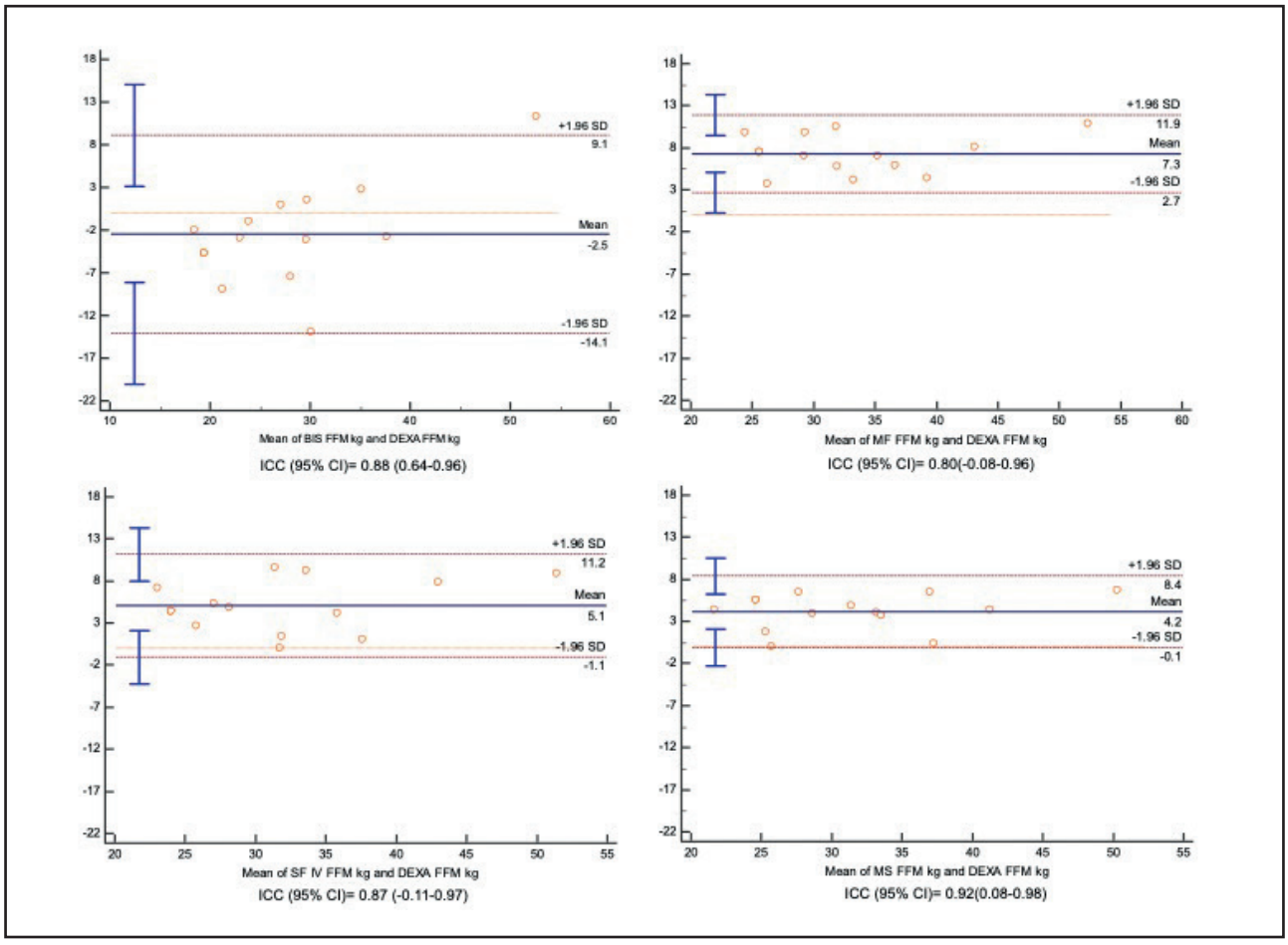

Figure 2.

Bland-Altman plots of FFM measurements to visually evaluate the agreement between the DEXA measurements and those of the different electrical impedance devices. The solid blue lines in the middle represent the mean bias. The dotted lines represent the upper and lower limits of agreement (± 1.96 standard deviation [SD]). The error bars in blue represent the 95 % confidence interval for the upper and lower limits of agreement (BIS: bioimpedance spectroscopy; MF: multifrequency; SF: single-frequency; MS: segmental multifrequency; FFM: fat-free mass).

The limits of agreement were wide (95 % CI: 14.1-9.1 kg), followed (in order from lowest to highest bias) by the measurements performed with the BIA-MS (4.2 kg [95 % CI: -0.1 to 8.4 kg]), BIA-SF (5.1 kg [95 % CI: -1.1 to 11.2 kg]), and BIA-MF (7.3 kg [95 % CI: 2.7-11.9 kg]) analyzers.

The Bland-Altman plot in figure 3 indicates the degree of agreement between measurements by each of the analyzers and by DEXA for FM. A lower average bias of -2.4 kg was identified for the measurements performed with the BIA-BIS analyzer, but it had wide limits of agreement (-8.3 to 3.6 kg). The same was true for the BIA-SF analyzer, which also had wide limits, although the bias was small (-2.8 kg). Despite showing a greater average bias than the two aforementioned analyzers, BIA-MS (-4.0 kg) and BIA-MF (-5.0) showed narrower limits of agreement (-8.5 to 0.5 kg and -9.7 to -0.2 kg, respectively).

DISCUSSION

The present study shows the performance of vector diagnosis when body composition measurements are performed with different types of impedance emitted according to the technology of four body composition analyzers. In Mexico, different body composition analyzers are available on the market. In this study, those available in the area of nutrition at the Department of Nephrology of the National Institute of Medical Sciences and Nutrition Salvador Zubirán were compared. The impedance vector method was used because this tool qualitatively evaluates the state of hydration and body composition, in addition to being one of the most commonly used methods in patients with renal diseases (22-28). The present study scanned all the patients with a single-frequency device (BIA-SF), two multifrequency devices (BIA-MF, BIA-MS; one of them segmental), and a spectroscopic device (BIA-BIS). Single-frequency analyzers normally operate

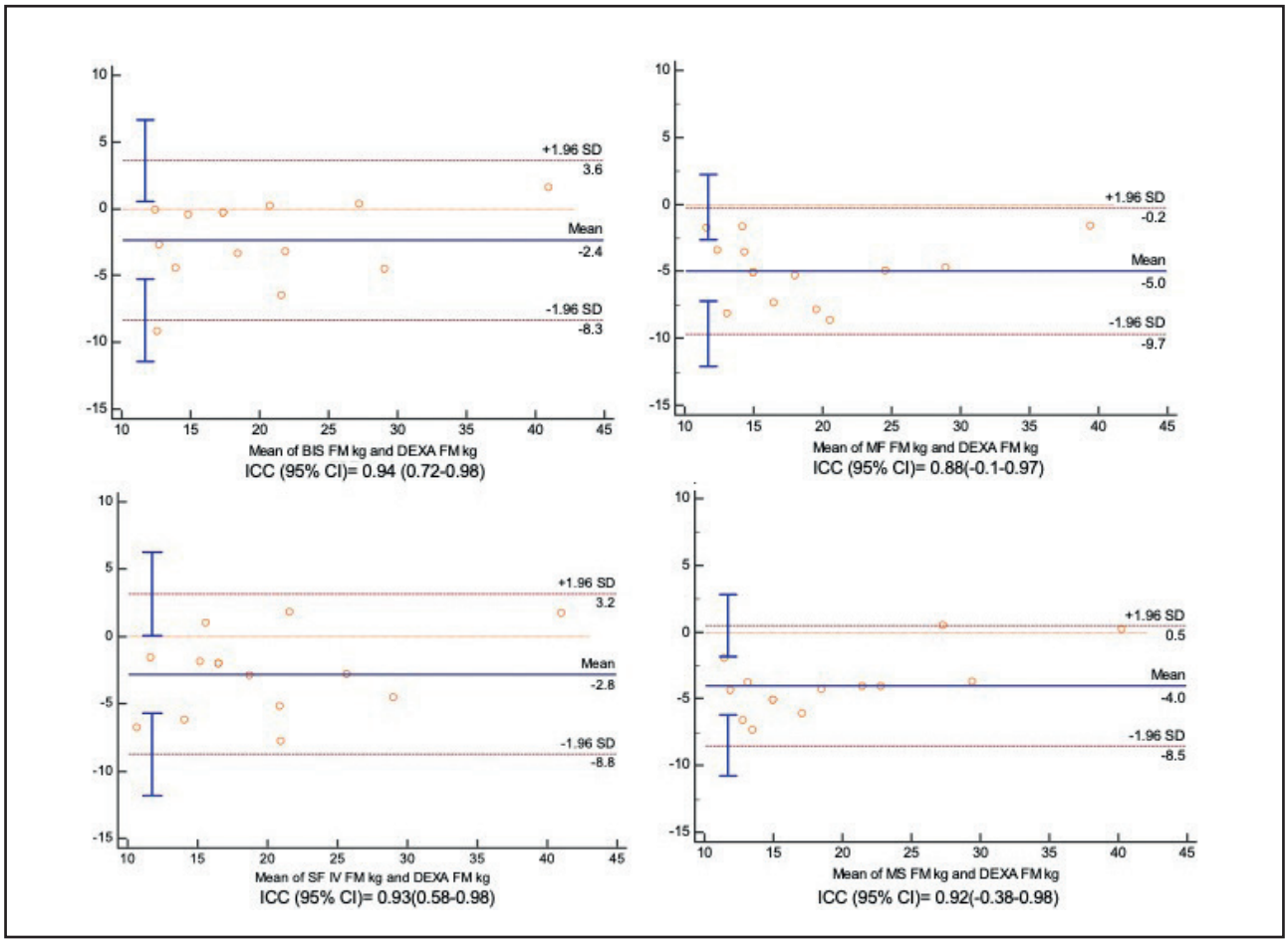

Figure 3.

Bland-Altman plots of the FM measurements to visually evaluate the agreement between the DEXA measurements and those of the different electrical impedance devices. The solid blue lines in the middle represent the mean bias. The dotted lines represent the upper and lower limits of agreement (± 1.96 SD). The error bars in blue represent the 95 % confidence interval for the upper and lower limits of agreement (BIS: bioimpedance spectroscopy; MF: multifrequency; SF: single-frequency; MS: segmental multifrequency; FFM: fat-free mass).

at 50 kHz, which allows them to calculate body resistivity and estimate TBW and FFM (8,29,30). TBW quantification with single-frequency devices is sufficiently precise, but monofrequency radiation passes only through extracellular water, not intracellular water (31,32). Multifrequency analyzers use empirical linear regression models for different frequencies, such as 1, 5, 50, 100, 200, 500, and 1000 kHz, to estimate TBW, extracellular water, and intracellular water to calculate FFM. They can precisely distinguish variations in hydration levels. At frequencies below 5 kHz and above 200 kHz, multifrequency devices have less bias and greater precision than single-frequency devices when estimating extracellular water (32). Unlike multifrequency devices, BIS devices use mathematical models and equations (Hanai equations) to adjust a polynomial curve called a Cole-Cole plot to quantify the relationships between R and the different fluid compartments for values of R from 0 to infinity and thereby derive empirical prediction equations.

In our study, the R and Xc values were taken at a frequency of 50 kHz in all the analyzers to standardize them and be able to plot them by the BIVA method (17). However, the differences in the measurements of the devices have an impact on the gross bioelectrical estimation and therefore on the analysis of the components of BIA (R, Xc, R/H, Xc/H, and PA), as reflected in our study and that of Tinsley (28). These authors compared a BIA multifrequency device (mBCA 515/514, Seca®, GmbH & Co, Hamburg, Germany) with a BIS bioelectric spectroscopy device (SFB7, ImpediMed®, Carlsbad, CA, USA) in adult women and found significant differences in R, Xc, and PA ($p < 0.0001$) (28).

Despite the differences between the measurement methods for R, Xc, and PA, the agreement observed between the measurements of these components was good to very good, which is in line with the findings of Bernal (29) when comparing a BIA-SF analyzer (RJL Quantum X, RJL systems®, Michigan, United Sta-

tes) with a BIA-MF analyzer (Bodystat Quadscan 4000, Bodystat LTD®, Isle of Man, UK) in a population with stable chronic heart failure. Similar results were found in the article by Silva, where multifrequency bioelectrical impedance spectroscopy (BIS, Xitron 4200) was compared with a single-frequency device (SF-BIA, BIA-101, RJL/Akern Systems) in two populations, active adults and elite athletes, and excellent concordance correlation coefficients and excellent concordance correlation coefficients were obtained (33). These results are consistent with the lack of significant differences in the ellipses generated with the R/H and Xc/H measurements in men or in women. However, when the diagnoses by location were analyzed in the RXc graph, the κ index showed substantial concordance for hydration status and body tissues ($\kappa = 0.71$, $\kappa = 0.68$, respectively). This result was probably influenced by the sample size and the number of categories, which increases in the classification of body composition, since more categories usually correspond to a lower κ, which is in line with the findings of Bernal (29), who calculated κ to be greater for both the states of hydration ($\kappa = 0.91$) and body tissues ($\kappa = 0.92$), although the sample included 406 patients. Although the sample number influences the concordance of the diagnosis, great care must be taken when interpreting the impedance vectors, especially in patients on HD, since an inaccurate diagnosis of hydration status can have repercussions for the treatment chosen and therefore lead to serious complications in patients.

Although DEXA has been considered the gold standard to evaluate body composition (31,32,34), this method is accurate for measuring certain body compartments, such as FM and FFM, but not TBW; thus, we could not compare measurements of this parameter by the different devices, so only the measurements are recorded in an informative way but not comparative with any gold standard.

The body compositions (FFM, FM) of the HD patients evaluated in this study differed between the analyzers, which was expected since each analyzer can have different prediction equations. When determining the ICC, the values of the four analyzers for the different body components reveal that the agreement with DEXA according to the Koo and Li scale (20) was good to excellent. In this analysis, the ICC considers any difference between measurements as discordance regardless of whether they are constant or proportional; when more sources of discrepancy exist, the ICC will be lower because the analyzers measure the same value (35,36). The highest concordance values of FFM were obtained by the BIA-MS analyzer. These data are consistent with those found by Buckinx (37), who evaluated the same BIA-MS analyzer as we did, with DEXA as the gold standard, in healthy subjects and obtained high ICCs for all the individual body segments (ICC = 0.82 (0.77-0.86) in the trunk, ICC = 0.87 (0.83-0.90) in the right arm, ICC = 0.92 (0.90-0.94) in the left arm, and ICC = 0.18 (0.49-0.30) in the left leg). Unfortunately, they did not estimate the ICC of the whole body. In the body compartment of FM, the MF analyzer obtained the lowest ICC values, and although the agreement was good, these results coincided with those found by Revindranath (38) (ICC = 0.82 [0.68-0.89]). The ICC of the BIA-BIS analyzer was the highest for FM, showing excellent concordance; however, this finding differs somewhat from the results of the Ellegård study (39). These authors obtained good agreement (0.76) using BIA-BIS equipment (Xitron Hydra 4200, Xitron Technologies, San Diego, CA, USA) in postpartum women with obesity or overweight; therefore, the discrepancies may be related to the populations studied.

The concordance found in the Bland-Altman plot between DEXA and the BIA analyzers revealed a lower bias in the measurement of FFM with the BIS equipment than with the other equipment. These results are similar to those found by Eyre (40). In a population with ESRD on peritoneal dialysis and HD, both studies found that BIA underestimated FFM, although the underestimation was greater in our study (-2.5 kg) than in Eyre's study (-0.38 [2.76 to -3.52] kg).

As shown by our Bland-Altman plot, the analyzer with the least bias in the measurement of FM was again the BIA-BIS, with an underestimation of -2.8 kg, which is in line with Bellafronte (41), who also found an underestimation, although the value was lower, in a population in HD in both men -0.19 (-8.26 to 8.64) kg and women -0.20 (-6.58 to 6.17) kg. Importantly, despite the small difference between the BIA-BIS analyzer and DEXA in our study, the limits of agreement were wide; in contrast, the BIA-MS analyzer showed a greater bias but much narrower limits of agreement for both the FFM and FM evaluations.

The greatest limitation of the present study is the sample size. The study must be replicated in clinically healthy patients without comorbidities that can affect hydration status, since although we verified our findings in a subsample without overhydration, this subsample was very small given that it was a population with ESRD. Another recommendation is that the manufacturers of the analyzers should publish the prediction equations with which the body components are determined to analyze the variables that can cause differences in the measurements. One of the strengths of the study is that the assumptions of normohydration were met to compare FM and FFM estimates between each analyzer and DEXA, reducing the biases that can arise when using the prediction equations in patients who are dehydrated. Another strength is that this is one of the few studies to show agreement in both the vector analysis and the body components with more than two BIA analyzers.

CONCLUSIONS

The present study showed that the BIA BIS, MF, SF, and MF demonstrate substantial agreement with respect to BIVA diagnosis of hydration and body tissue status. The agreement between the components of BIA evaluated by four technologies is good. The four BIA measurement techniques showed very good agreement with DEXA, all with high ICCs. The concordance of the Bland-Altman-Altman plot showed the lowest bias for the BIA-BIS analyzer for both FFM and FM, although the limits of agreement were wide. The narrowest limits of agreement were found with the BIA-MS analyzer.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Is Ramadan fasting associated with low scores of Healthy Eating Index?

¿Está asociado el ayuno de Ramadán con puntuaciones bajas en el Índice de Alimentación Saludable?

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Abstract

Background: intermittent fasting diets that reduce or completely restrict food intake for specific periods have become more popular in recent years. Fasting in Ramadan is also an example of these intermittent fasting practices. In fasting practices focusing on the duration of nutrition, less emphasis was placed on the information on the dietary pattern.

Objective: this study aims to evaluate the Healthy Eating Index (HEI) and diet quality in fasting individuals in Ramadan.

Material and methods: this study was a cross-sectional study, conducted with adults aged 18-65 years. Food consumption record was taken with a 24-h-record with food consumption form. Diet quality and adequacy were assessed with the HEI, Nutrient Adequacy Ratio (NAR), and Average Adequacy Ratio (MAR) from food consumption records.

Results: according to study results, HEI and NAR Ca scores were statistically significantly lower in the fasting group than in the non-fasting group ($p < 0.05$). In the non-fasting group, HEI scores showed a negative correlation with body mass index (BMI) (kg/m^2) and waist-hip ratio ($r = -0.023$, $r = -0.148$, $p < 0.05$).

Conclusion: this study claimed that fasting might be associated with low scores of HEI. These results suggest that specific nutritional recommendations should be developed for fasting individuals.

Keywords:

Diet quality. Fasting. Ramadan.

Resumen

Introducción: las dietas de ayuno intermitente que reducen o restringen por completo la ingesta de alimentos durante periodos específicos se han vuelto más populares en los últimos años. El ayuno en Ramadán también es un ejemplo de estas prácticas de ayuno intermitente. En las prácticas de ayuno centradas en la duración de la nutrición, se ha puesto menos énfasis en la información sobre el patrón dietético.

Objetivo: este estudio tiene como objetivo evaluar el índice de alimentación saludable (IAS) y la calidad de la dieta en personas en ayunas en Ramadán.

Material y métodos: se trata de un estudio transversal, realizado con adultos de 18 a 65 años. El registro de consumo de alimentos se tomó con un registro de 24 horas con formulario de consumo de alimentos. La calidad y la adecuación de la dieta se evaluaron con el IAS, el índice de adecuación de nutrientes (NAR) y la ratio de adecuación promedio (MAR) de los registros de consumo de alimentos.

Resultados: de acuerdo con los resultados del estudio, las puntuaciones de HEI y NAR Ca fueron estadísticamente significativamente más bajas en el grupo que hace ayuno que en el grupo sin ayuno ($p < 0,05$). En el grupo sin ayuno, las puntuaciones HEI mostraron una correlación negativa con el índice de masa corporal (IMC) (kg/m^2) y la relación cintura-cadera ($r = -0,023$, $r = -0,148$, $p < 0,05$).

Conclusión: este estudio afirmó que el ayuno podría estar asociado con puntuaciones bajas de IAS. Dichos resultados sugieren que se deben desarrollar recomendaciones nutricionales específicas para las personas que hacen ayuno.

Palabras clave:

Calidad de la dieta. Ayuno. Ramadán.

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INTRODUCTION

Intermittent fasting diets reduce or completely restrict food intake for specific periods (16-48 hours) and are associated with various health benefits (1,2). These benefits are decrease in levels of glucose, insulin, total cholesterol, tumor necrosis factor alpha (TNFα), interleukin 6 (IL-6) levels, increase in insulin sensitivity and adiponectin levels, improvement in synaptic plasticity, neurogenesis, and cognitive function, and decrease in inflammation (2). Interest has undoubtedly increased significantly on fasting and its consequences on health in general recently (3).

Fasting in Ramadan is also an example of these intermittent fasting practices, which include a fasting period that lasts for an average of 12 hours. Although Ramadan fasting is applied within the scope of religious beliefs to fulfill the requirements of faith, it can also positively affect health status. Usually, this seasonal shift impacts the amount of daily fasting time that occurs in any given location with two meals and (sunrise [Sahur] to sunset [Iftar]) (4,5). Ramadan is the ninth month of the Islamic lunar calendar and fasting during Ramadan is the religious duty of all healthy adult Muslims (6).

Intermittent fasting focuses on when one can consume meals within a day or a week (7). However, the type and pattern of foods consumed in fasting practices are critical in interpreting their health effects. For this reason, it is essential to evaluate the compatibility of the foods consumed with healthy nutrition recommendations. Religious rituals are considered among the principal factors that impact dietary behaviors and food choices (8). Some studies in high and upper-middle income countries claimed that Muslims eat unhealthier foods high in carbohydrates and fat during Ramadan (9,10). However, studies evaluating the dietary habits of fasting individuals in different Muslim countries reveal different results, some of them reporting an increase in saturated fat and trans-fatty acid intake during this period, and others showing that sodium and fiber intake were decreased, whereas micronutrient intake was increased or remained unchanged (11-13). In studies evaluating body weight, it is seen that there are also different results in different Muslim societies. Abizari and Ali (2018) reported an increase in diet variety and a decrease in body weight after fasting (5), while another study reported an increase in body weight (10). These results suggest that the nutritional habits of individuals change during Ramadan and may vary between societies.

The Healthy Eating Index (HEI) and dietary quality indices are defined as measurement tools that summarize the general nutritional quality, comply with the nutritional guidelines and help to monitor the changes in the general diet in a simple and fast way, as well as allowing a quick assessment of the nutritional adequacy of the individuals (14-16). The HEI is an assessment that measures the quality of an individual's diet based on recommendations in the American National Dietary Guidelines. This index evaluates 12 food groups including total fruit (total of fruit and fruit juices), whole fruits, green leafy vegetables and citrus fruits and other vegetables, total grains, whole grains, milk and its products, meat and products, vegetable oils, saturated fats, sodium, fats, alcohol and energy from added sugar (15). The consumption of an appropriate combination of various foods helps to ensure nutrient adequacy (16). At this point, dietary adequacy indices appear to provide a general assessment. However, there are few studies investigating the diet quality during fasting. In the light of this information, this study aims to evaluate the HEI and diet adequacy in fasting individuals.

METHODS

This study was a cross-sectional study, conducted with adults aged 18-65 years during Ramadan in Samsun (Turkey). The sample number of the study was calculated with the Minitab Power Analysis Program, and it was aimed to reach 423 people with 0.05 sampling error and 95 % reliability in the survey (17). Ethical approval of the study was obtained from the Ondokuz Mayis University Clinical Research Ethics Committee (No. 2021/162).

Data collection was carried out following the principles of the Declaration of Helsinki, after obtaining consent from the participants. The survey was announced on-line and administered to the participants who agreed to participate in the study using the Google Docs form. Participants began the survey by providing electronic informed consent. The survey included questions eliciting demographic information, fasting status and food consumption records. Individuals who could not complete the questionnaire form and were outside the specified age range were excluded from the study.

Food consumption was taken with a 24-h-record with food consumption form. In recording food consumption amounts, information was given about the net quantities known by household measurements (water glass, tea glass, coffee cup, mug, tablespoon [wiping, heaping], ladle, dessert spoon, small, medium, large size, etc.). The amount of energy and nutrients it provides was calculated using the Nutrition Data Base Software (8.1), and the daily amount of food types and nutrients was found (18).

Diet quality and adequacy were assessed with the HEI, Nutrient Adequacy Ratio (NAR), and Average Adequacy Ratio (MAR) (2). These indices were calculated from the food consumption records.

HEI scoring is calculated with the amounts per 1,000 kcal (g) and the percentages of energy contribution, especially for saturated fat and added sugar. In HEI-2005, diet is scored out of 100 points, and a score above 80 indicates good nutrition, 51-80 indicates adequate nutrition, and a score below 50 indicates malnutrition (15,19).

Diet quality was obtained by evaluating the NAR and MAR calculations. NAR scores were calculated by dividing the intake of 12 nutrients, including energy, protein, vitamin C, vitamin D, thiamine, riboflavin, and iron, by daily requirements. Each nutrient adequacy ratio is taken as 100 % of the recommended dietary intake values to compensate for low intakes of nutrients and to prevent high intakes of certain nutrients. The MAR value was obtained by dividing the NAR value by the total nutrients (16).

Anthropometric measurements are based on self-declaration. BMI was calculated by dividing body weight (kg) by height squared (BMI = weight [kg]/length [m^2]). The World Health Organization (WHO) classification was used to evaluate BMI. Accordingly, individuals with a BMI of < 18.5 kg/m^2 are underweight, with 18.5-24.9 kg/m^2 are normal weight, with 25.0-29.9 kg/m^2 are overweight, and with > 30.0 kg/m^2 are obese (20).

Statistical analyses were performed using the SPSS 22.0 program. Descriptive variables are given as mean ± standard deviation (X ± SD), and nominal variables as frequency and percentage. Normality test was performed to determine whether the parametric test assumptions were met. According to the results of this test, the difference between the means was calculated using the t-test or the Mann-Whitney U-test. The differences between the groups were evaluated with the Chi-squared test and the Kruskal-Wallis test, respectively. Differences were considered as significant at $p < 0.05$.

RESULTS

The general characteristics of the participants are given in table I. Accordingly, 66.9 % of all participants are female, and 33.1 % are male.

The participants' HEI, NAR and MAR scores according to fasting status are given in table II. Accordingly, HEI and NAR calcium scores were statistically significantly lower in the fasting group than in the non-fasting group. There was no difference between the groups in other NAR components and MAR scores.

Anthropometric measurements of participants according to fasting status and HEI groups are given in table III. While there was no difference between the groups in anthropometric measurements according to fasting status, body weight (kg), waist circumference (cm), neck circumference (cm), waist-hip ratio and BMI (kg/m^2) were statistically different in the poor diet group compared to the other group and significantly higher ($p < 0.05$).

The correlations between HEI scores and anthropometric measurements are given in table IV. Accordingly, in the non-fasting group, HEI scores showed a negative correlation with BMI (kg/m^2) and waist-hip ratio ($r = -0.023$, $r = -0.148$, $p < 0.05$).

Table I. Participants characteristics

Characteristics	Summary values (n = 405) n (%)
Gender	
Male	134 (33.1)
Female	271 (66.9)
Age (years)	33.0 ± 13.4
Marital status	
Married	170 (41.9)
Single	235 (58.1)

(Continues on next column)

Table I (Cont.). Participants characteristics

Characteristics	Summary values (n = 405) n (%)
Educational status	
Literate	7 (1.7)
Primary-secondary school	76 (18.7)
High school	134 (33.1)
Associate-Bachelor's	180 (44.7)
Graduate	7 (1.7)
Employment status	
Employee	252 (62.3)
Unemployed	153 (37.7)
Smoking	
Yes	93 (23.0)
No	312 (77.0)
Alcohol	
Yes	44 (10.9)
No	361 (89.1)
Chronic disease	
Yes	78 (19.3)
No	327 (80.7)
Fasting status	
Yes	130 (32.1)
No	275 (67.9)

Table II. HEI, NAR and MAR scores according to fasting status

HEI, NAR and MAR scores	Fasting status		
	Yes (n = 130) Mean ± SD	No (n = 275) Mean ± SD	p
HEI	47.23 ± 12.4	50.09 ± 13.0	*0.038**
NAR calcium	0.69 ± 0.3	0.78 ± 0.3	*0.003**
NAR protein	1.34 ± 0.5	1.39 ± 0.5	0.275
NAR iron	1.03 ± 0.6	0.99 ± 0.7	0.280
NAR vitamin A	1.68 ± 2.4	1.90 ± 3.5	0.171
NAR vitamin C	1.54 ± 1.1	1.56 ± 1.1	0.849
NAR folate	0.41 ± 0.2	0.43 ± 0.2	0.562
NAR niacin	1.57 ± 0.7	1.64 ± 0.7	0.268
NAR thiamin	0.81 ± 0.4	0.83 ± 0.4	0.789
NAR riboflavin	1.18 ± 0.4	1.28 ± 0.6	0.161
NAR vitamin B12	1.82 ± 1.6	1.90 ± 3.2	0.657
NAR vitamin D	0.10 ± 0.3	0.10 ± 0.2	0.791
NAR energy	0.81 ± 0.4	0.79 ± 0.3	0.902
MAR	1.08 ± 0.4	1.13 ± 0.7	0.621

*HEI: Healthy Eating Index; NAR: Nutrient Adequacy Ratio; MAR: Average Adequacy Ratio. Mann-Whitney U Test. *Significant at the 0.05 level.*

Table III. Anthropometric measurements of participants according to fasting status and HEI groups

	Fasting status				HEI groups			
Anthropometric measurements	**Yes (n = 130)**	**No (n = 275)**	**Total (n = 405)**	***p***	**Needs improvement (n = 177)**	**Poor diet (n = 227)**	**Total (n = 404)**	***p***
	Mean ± SD				**Mean ± SD**			
Body weight (kg)	71.30 ± 16.7	69.85 ± 15.4	70.32 ± 15.8	0.484	68.53 ± 16.0	71.69 ± 15.6	70.30 ± 15.8	*0.021**
Height (cm)	166.25 ± 9.6	166.72 ± 8.9	166.57 ± 9.1	0.534	166.37 ± 9.1	166.70 ± 9.2	166.60 ± 9.1	0.870
Waist circumference (cm)	85.63 ± 15.5	84.47 ± 16.2	84.84 ± 16.0	0.308	82.55 ± 15.2	86.60 ± 16.4	84.80 ± 15.9	*0.007**
Hip circumference (cm)	102.03 ± 13.8	100.22 ± 12.6	100.80 ± 13.0	0.276	99.8 ± 12.0	101.60 ± 13.7	100.80 ± 13.0	0.242
Neck circumference (cm)	34.99 ± 4.8	34.94 ± 7.01	34.95 ± 6.4	0.498	34.73 ± 8.0	35.11 ± 4.8	34.94 ± 6.4	*0.033**
Waist/hip ratio	0.839 ± 0.1	0.843 ± 0.12	0.84 ± 0.1	0.951	0.83 ± 0.1	0.85 ± 0.1	0.84 ± 0.1	*0.006**
BMI (kg/m^2)	25.77 ± 5.6	25.10 ± 5.0	25.31 ± 5.2	0.290	24.73 ± 5.4	25.80 ± 5.1	25.31 ± 5.2	*0.011**

*HEI: Healthy Eating Index; BMI: body mass index. Mann-Whitney U test; Chi-squared test. *Significant at the 0.05 level.*

Table IV. Correlation between HEI scores and anthropometric measurements

HEI scores according to fasting status		**Height (cm)**	**Body weight (kg)**	**Waist circumference (cm)**	**Hip circumference (cm)**	**Neck circumference (cm)**	**BMI (kg/m^2)**	**Waist to hip ratio**
Fasting status		**r**	**r**	**r**	**r**	**r**	**r**	**r**
Yes	HEI scores	0.000	-0.150	-0.350	-0.280	-0.600	-0.070	-0.410
No	HEI scores	-0.040	-0.107	-0.970	0.016	-0.035	*-0.123**	*-0.148**

*HEI: Healthy Eating Index; BMI: body mass index; r: Spearman correlation coefficient. *Correlation is significant at the 0.05 level.*

DISCUSSION

Intermittent fasting diets are associated with positive health benefits. However, these diets' dietary adequacy present controversial results (11-13). The common dietary practice of Ramadan fasting is to consume one large meal at Iftar and one lighter meal at Sahur; some Muslims also consume an additional meal before sleeping (4). Hence, changes in eating behavior during Ramadan are expected and dietary diversity might be affected positively or negatively. This study was aimed to evaluate dietary patterns with the HEI and diet adequacy in fasting individuals.

The main findings were that HEI and NAR Ca scores of the non-fasting (n = 275, 67.9 %) individuals were found to be statistically significantly higher than in the fasting group (130, 32.1 %) ($p < 0.05$). There was no difference between the other NAR components and MAR scores groups. There are not many studies in the literature evaluating the HEI scores of individuals who fast during Ramadan. However, one study reported that there is no difference between two intervention groups: intermittent energy restriction (IER) intervention group and continuous energy restriction (CER) control group in terms of HEI scores (21). When the studies evaluating the diet diversity of individuals were examined, one study showed that mean dietary diversity scores (DDS) increased significantly during Ramadan while mean daily meal frequency decreased (5). Another study reported strong evidence that Muslim women have more diverse diets during Ramadan (9). However, in another study, researchers reported the dietary intake of fasting individuals (n = 120, 20-45 years) had not enough diversity (17). Shatila et al. (2021) reported decreased Ca intake during Ramadan (806.5 ± 233.0 mg/d and 672.0 ± 264.9 mg/d, respectively), similar to our results. Although our study was conducted with a cross-sectional design, a different design with a control group with NAR scores presents similar results. The mentioned study also reported a decrease in vitamin C, vitamin A, and folate intake. However, no differences were found for these nutrients between fasting and non-fasting group ($p > 0.05$). Having dietary intakes of macronutrients within the acceptable reference range for protein, carbohydrate, and

fat, with higher intakes of many of the micronutrients (vitamin A, β-carotene, vitamin C, folate, and magnesium) and fiber, suggests that an intermittent fasting regimen, such as the one followed in Ramadan, may be a more practical dietary modification than caloric restriction (8).

Religion and religious rituals and fests have been considered among the fundamental factors that impact human dietary behaviors and food selections. Ramadan fasting represents one of the clearest examples of how religious beliefs influence human dietary behavior for three main reasons: first, the significant shift in food patterns from diurnal and nocturnal eating time to nocturnal eating for 29-30 consecutive days; second, dietary choices during this month are closely tied to traditions and customs, with certain dishes consumed solely during Ramadan; and lastly, particular eating habits during Ramadan, whereby during the month meals are generally consumed together with family members (8). Ramadan as increasing dishes at mealtimes could mean reduced portion sizes for both dishes (5).

When the anthropometric measurements of the individuals were examined according to their fasting status, no statistically significant difference was found between the groups. The response of anthropometric measurements to dietary changes takes a long time. For this reason, no difference was expected in these parameters according to fasting status. When anthropometric measurements are evaluated according to HEI groups, body weight (kg), waist circumference (cm), neck circumference (cm), waist-hip ratio and BMI (kg/m^2) are significantly higher in the poor diet group than in the need's improvement group. There is no group with a "good nutrition" score. This suggests that although HEI scores are higher than those in fasting, individuals who do not fast also need general nutritional recommendations. Saraf-Bank et al. (2017) evaluated BMI and waist-hip ratio according to the Quartiles of Healthy Eating Index-2010, concluding that BMI and waist-hip ratio values were highest in the group with the lowest HEI quartile in their study (22). Tande et al. (2008) reported that dietary consumption that follows the HEI is associated with a lower risk for abdominal obesity (23). These results are essential to evaluate the effects of dietary patterns on anthropometric measurements. When the correlation of HEI scores and anthropometric measurements according to fasting status is evaluated, HEI scores and waist-hip ratio are negatively correlated in the non-fasting group. Researchers have reported that there may be changes in body weight during Ramadan (5). High HEI scores of the non-fasting group may have shown positive effects on BMI and waist-hip circumference. However, at this point, the initial body weight of the individuals is also important.

CONCLUSION

Studies on the interaction of intermittent fasting and health have focused on diabetes, obesity, and metabolic changes. However, the dietary pattern has several effects on human health. Diet, energy, macronutrients and micronutrients intake during Ramadan have been reported to increase, decrease, or not change in different populations. The number of studies investigating the effect of fasting on diet quality is insufficient. Hence our study results make a good contribution on this topic. These results present that fasting might be associated with low scores of HEI and indicates the need for population-based studies about fasting in Ramadan. However, the fact that there is no one in the "good nutrition" group of HEI shows that there is a need for general nutrition recommendations in society and for future studies investigating the reasons for this issue. Another point is that food choice during Ramadan also depends on local habits and traditions, and our study reveals essential data for our country. Although Ramadan fasting is safe for all healthy individuals, those with various diseases such as diabetes should consult their physicians and dietitians for a specific recommendation.

STRENGTHS

Results related to fasting in the literature focus on body weight and metabolic changes. However, the number of studies on meal content, diet pattern and food selection is limited. Therefore, this study makes a significant contribution to the literature on this subject, providing HEI, NAR and MAR values in fasting and non-fasting individuals.

LIMITATIONS

The absence of anthropometric findings before and after Ramadan makes it challenging to compare the results. For this reason, an evaluation was made on the correlation between diet quality indices and anthropometric measurements.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Epidemiología y dietética

Influencia del perfil de las donantes en la bacteriología pre- y pospasteurización de la leche humana donada

Influence of donor profile on pre and post-pasteurization bacteriology of donated human milk

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Resumen

Introducción: la leche humana es el patrón oro en la nutrición de los neonatos. Por ello, los bancos de leche se convierten en elementos esenciales para garantizar su disponibilidad y seguridad cuando la leche materna no está disponible. La manipulación que se realiza de la leche es un punto crítico para asegurar la seguridad microbiológica de las muestras. Por ello, analizar la flora de la leche donada es fundamental para tomar medidas de mejora de los bancos de leche.

Objetivos: analizar los resultados microbiológicos positivos en un banco de leche humana entre las muestras de leche cruda donadas y tras su pasteurización y evaluar si existe relación entre los aislamientos, el perfil de la donante y los circuitos de leche donada.

Métodos: estudio observacional descriptivo que analiza las características de la leche donada y los resultados microbiológicos positivos de muestras de leche donadas en nuestro banco desde junio de 2016 hasta diciembre de 2020. Todas las donantes firmaron un consentimiento informado.

Resultados: durante el período de estudio fueron donados 1587 litros de leche cruda por 266 mujeres destacando que, a pesar de la pandemia, 2020 ha sido el año en el que más volumen se ha dispensado (280 L). Se obtuvieron 221 lotes de leche con al menos un aislamiento microbiológico positivo (14,2 % total), de ellos 149 previos y 46 posteriores a la pasteurización. La tasa de descarte pre y pospasteurización es variable a lo largo de los años con descenso en 2020 prepasteurización (3,9%) e incremento pospasteurización (5,3%). Los gérmenes más frecuentemente aislados fueron cocos grampositivos, seguidos por Enterobacterias prepasteurización detectándose un descenso en la positividad a *S. aureus* tras establecerse un protocolo de erradicación. En las muestras pospasteurización predomina el género *Bacillus.* Se ha encontrado una relación aunque no estadísticamente significativa ($p > 0,05$)

entre mujeres con mayor volumen de donación y/o ingreso de su hijo/a en Neonatología y una mayor frecuencia cultivos positivos.

Conclusiones: el análisis bacteriológico de las muestras es parte fundamental del control de calidad. Nuestros resultados traducen una buena sistemática de extracción y transporte, así como un buen entrenamiento de los profesionales del banco. No obstante, es necesario mejorar los procesos para reducir la tasa de contaminación y la cantidad de leche desechada.

Palabras clave:

Banco de leche. Donantes. Perfil microbiológico.

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Abstract

Introduction: breastfeeding is the gold standard for infant's nutrition. Human milk bank is an essential tool to guarantee availability and safety in those situations when breastfeeding is not an option. The manipulation during the extraction of the human milk by the donors is a critical point to ensure an adequate microbiological safety. Therefore, knowing the bacterial flora that prevails in donated milk is essential to draw conclusions that can lead to taking measures in the management of the bank.

Objectives: to analyze the prevalence of microorganisms in milk samples donated to the milk bank and how the bacterial flora behaves according to the profile of the donors and the donor milk circuits.

Methods: the present work is a retrospective descriptive observational study that analyzes characteristics and the positive microbiological results within our milk bank samples from June 1, 2016 to December 31, 2020. All milk bank donors voluntarily signed an informed consent that authorizes the use of data to investigation.

Results: during the study period, a total of 1,587 liters of raw milk were donated by 266 women, highlighting that, despite the SARS-CoV-2 virus pandemic, 2020 has been the year in which more volume of milk has been dispensed. The results show that 221 batches had at least one positive microbiological isolation (149 of them were before and 46 after pasteurization). Pre and post-pasteurization rate varies over the years with a decrease in the pre-pasteurization discard rate (3,9%) and increase in the post-pasteurization rate (5,3%). The most frequently isolated germs found in pre-pasteurization cultures were gram positive cocci and Enterobacter and a decrease in the positivity to *S. aureus* after establishing an eradication protocol. In post-pasteurization cultures, the most commonly found germs are *Bacillus.* Regarding the donor's profile, it was found a non statistically significant that those women with the highest donation volume and/or admission of their offspring in Neonatology were associated with higher frequency of positive cultures.

Conclusions: bacteriological analysis of milk samples is an essential part of quality control for a milk bank. Our results reflect a good extraction system and transportation, as well as good training from the bank's professionals. Nevertheless, improvement of processes is necessary to reduce the rate of contamination and the amount of discarded milk.

Keywords:

Milk bank. Donors. Microbiological profile.

INTRODUCCIÓN

La lactancia materna (LM) es el método *gold standard* para la nutrición del recién nacido. Así, tanto la Organización Mundial de la Salud (OMS) como la Academia Americana de Pediatría (AAP) se reafirman en su recomendación del uso de la LM como método de alimentación exclusivo durante los seis primeros meses de vida, iniciando entonces la alimentación complementaria, manteniendo la LM como una fuente nutricional fundamental y poniéndole fin siempre que el lactante y la madre así lo deseen (1). Por ello, los bancos de leche se convierten en elementos esenciales para garantizar su disponibilidad y seguridad cuando la leche de la propia madre no está disponible. Esta afirmación cobra especial relevancia en aquellos neonatos con riesgo de enterocolitis necrotizante (2), fundamentalmente, pacientes prematuros menores de 32 semanas y/o de peso menor de 1.500 g y aquellos intervenidos de cirugía abdominal o cardiopatías congénitas de manera precoz.

Además, la OMS establece desde 2005 que, "cuando no se disponga de la leche de la propia madre, la siguiente opción para la alimentación del niño es la leche pasteurizada de madres donantes seleccionadas, sobre todo si se trata de niños enfermos o prematuros" (3).

En España, en 2001 aparece el primer banco de leche, establecido en Palma de Mallorca, y en el año 2008 se crea la Asociación Española de Bancos de Leche Humana (AEBLH) con la finalidad de promover la LM y la colaboración entre los distintos bancos de leche humana.

En el Hospital Álvaro Cunqueiro, la actividad del banco de leche se inicia en junio de 2016, convirtiéndose así en el noveno a nivel nacional y siendo, además, la referencia para las provincias de Pontevedra y Ourense.

Si bien en el momento actual todavía no existe legislación en Europa que regule la donación de leche humana (4), existen diversos grupos de expertos que se reúnen para desarrollar una serie de recomendaciones con el objetivo de ser el órgano de referencia para la creación y el funcionamiento de los bancos de leche materna en Europa a través de la European Milk Bank Association (EMBA) (5,6).

No obstante, cada banco de leche ha de elaborar sus propios protocolos de trabajo en base a estos consensos internacionales y a la evidencia científica disponible, buscando como objetivos principales garantizar la disponibilidad de una cantidad de leche suficiente para sus potenciales receptores y asegurar un óptimo control de calidad que garantice un perfil microbiológico seguro y una alta calidad de la leche desde el punto de vista nutricional.

El proceso de selección de las donantes se lleva a cabo mediante una entrevista de idoneidad, así como un cuestionario de salud general. Además, se deben realizar estudios serológicos de las donantes de forma sistemática. Es necesario explicar a las nuevas donantes los procedimientos de lavado de manos e higiene local del pecho, así como las técnicas de extracción de leche manual o mediante extractor eléctrico (siendo en este caso válidos los extractores propios de la donante y los prestados por el banco), así como los procesos de almacenamiento (refrigeración y congelación), etiquetado y transporte de la LM.

La leche congelada es custodiada en el banco de leche y procesada en un tiempo que, idealmente, es inferior a tres semanas. Además, se debe realizar una descongelación controlada al baño maría evitando que la leche supere los 8 °C.

Los controles de calidad del banco de leche son llevados a cabo por personal experto de una manera sistemática y meticulosa. Así, tras la descongelación, se realiza una prueba de acidez Dornic (7,8) previa obtención de 4 ml de cada lote, llevando a cabo posteriormente una serie de controles microbiológicos prepasteurización fundamentales, sobre todo en aquellas muestras de madres donantes en las que exista algún cultivo positivo para *Staphylococcus aureus (S. aureus).* En este caso, se lleva a cabo

una búsqueda del estado de portador nasal para lograr la erradicación de dicho germen. Una vez demostrada la seguridad microbiológica inicial, se lleva a cabo la pasteurización de la leche donada mediante el método Holder (9). Se analizará, además, el contenido de proteínas y, si es posible, de otros micronutrientes y macronutrientes. Finalmente, es necesario realizar un nuevo análisis microbiológico de cada lote de leche tras la pasteurización y se deben desechar aquellos lotes con un contenido microbiológico que no garantice su seguridad.

Los objetivos del presente trabajo son: a) analizar los resultados microbiológicos positivos en un banco de leche humana entre las muestras de leche cruda donadas y tras su pasteurización; y b) evaluar si existe relación entre los aislamientos identificados con el perfil de la donante y los circuitos de leche donada.

POBLACIÓN Y MÉTODOS

Este es un estudio observacional descriptivo retrospectivo que analiza las características de la leche donada y los resultados microbiológicos positivos de muestras de leche donadas en nuestro banco desde el 1 de junio de 2016 hasta el 31 de diciembre de 2020. Todas las donantes firmaron un consentimiento informado que autoriza el uso de muestras para investigación.

Para la elaboración de este trabajo se analizaron todos los lotes elaborados en el Banco de Leche de Vigo (BLV) en el periodo de estudio y se recogieron los datos microbiológicos de todas las muestras que habían obtenido un resultado positivo en cultivos prepasteurización o pospasteurización a partir del análisis de los lotes.

Además, se utilizó el programa estadístico SPSS 22 para realizar los análisis de estadística descriptiva y los test de Chi-cuadrado y t de Student para analizar la diferencia de frecuencias en tabla de contingencia y de medias, respectivamente, entre las mujeres con mayor número de muestras contaminadas frente al resto, en cuanto a las variables "hijo/a ingresado en Neonatología" y "volumen total de leche donada".

RESULTADOS

En el periodo de estudio, donaron leche materna 266 mujeres, que entregaron un total de 1.587 litros de leche cruda. Así, se procesaron 1.487 lotes de leche cruda donada y se dividieron los litros de leche cruda donada que fue aceptada tras ser recogida en el BLV (descartando en un primer momento las muestras en las que se percibían malas condiciones del envase, características organolépticas inadecuadas, etc.).

La distribución anual de los lotes se muestra en la tabla I. Así, cabe destacar que, a pesar de la pandemia SARS-CoV-2, en 2020 se objetiva un incremento de leche donada, así como de leche procesada en nuestro banco de leche (30 litros más, un 11,9 % más respecto al año previo). Además, 2020 es el año en que se ha repartido un mayor volumen de leche.

Se han obtenido 221 lotes de leche donada con al menos un aislamiento microbiológico positivo (14,2 %); de ellos, 149 eran previos y 46 eran posteriores a la pasteurización. En cuanto a la tasa de descarte prepasteurización y pospasteurización en función de los litros descartados por aislamiento microbiológico, es variable a lo largo de los años, con un descenso entre 2019 y 2020 del descarte prepasteurización (3,7 %) tras la modificación del protocolo y un incremento pospasteurización (5,3 %).

En el análisis microbiológico prepasteurización, se obtuvieron 254 aislamientos bacterianos entre los 149 lotes en los que se obtuvo un cultivo con resultado positivo, puesto que en algunos de los cultivos se halló un recuento polimicrobiano. Los grampositivos suponen el 59,4 % del total de aislamientos obtenidos. Los gérmenes coagulasa-negativo suponen el 34,2 % del total y representan el germen más frecuentemente aislado en los cultivos prepasteurización. El *S. aureus* supuso un 12,5 % del total de aislamientos.

En el análisis microbiológico pospasteurización, se obtuvieron 46 aislamientos bacterianos positivos de los 1.528 lotes en los que se realizó cultivo pospasteurización. El género *Bacillus* supone el 73,9 % del total de aislamientos obtenidos y es el *Bacillus cereus* la especie más frecuentemente aislada.

Tabla I. Distribución anual de leche donada

Indicador/año	2016	2017	2018	2019	2020
Volumen donado	120	370	415	379	403
Volumen pasteurizado	115	318	376	313	365
Volumen dispensado	111	227	267	252	280
Volumen descartado Prepasteurización (%)	4,8 (4 %)	37 (10 %)	93 (23 %)	29,4 (7,7 %)	20,1 (4,9 %)
Volumen descartado Pospasteurización (%)	3,7 (3,3 %)	13,8 (4,3 %)	9,5 (2,3 %)	14 (4,4 %)	26,7 (7,3 %)

De un total de 266 mujeres donantes en el periodo de estudio, menos de un 25 % tuvo algún cultivo positivo durante su periodo de donación (n = 65). No obstante, la lectura destacada es que un 75,5 % de las mujeres donantes (n = 201) no tuvieron ningún cultivo positivo durante el periodo de estudio.

De nuestras donantes, 38 tuvieron a su hijo/a ingresado en la Unidad Neonatal. Además, dentro del grupo de donantes con al menos un cultivo positivo, el 23 % (n = 15) tenía a su hijo/a ingresado en la Unidad Neonatal durante el periodo de donación. El motivo del ingreso mayoritario en los neonatos hijos de estas donantes era la prematuridad. Un 26,6 % de estos neonatos ingresados fueron, además, receptores de leche de banco (n = 4). Todas estas madres han mantenido su donación al banco de leche por un periodo de tiempo superior al ingreso de sus hijos.

Si establecemos grupos comparativos, un 7,6 % (n = 15) de mujeres con al menos un cultivo positivo tuvieron a su hijo/a ingresado frente a un 11,4 % (n = 23) sin ningún cultivo positivo, sin que se evidencien diferencias entre la bacteriología aislada. Aplicando la tabla de contingencia y el estadístico de Chi-cuadrado, se objetiva una diferencia no estadísticamente significativa ($p > 0,05$) en cuanto a un mayor porcentaje de madres con hijos ingresados en la Unidad de Neonatología en donantes con lotes con aislamiento microbiológico positivo frente a aquellas sin dichos aislamientos.

DISCUSIÓN

La manipulación que realizan tanto las donantes como el personal de los bancos de la leche donada es un punto crítico para asegurar su seguridad microbiológica. Por tanto, conocer la flora que predomina en la leche donada es fundamental para tomar medidas que puedan mejorar la educación de las donantes en este proceso, así como los procedimientos técnicos que se lleven a cabo en el banco de leche.

El control de calidad y los procesos técnicos en los bancos de leche son así puntos fundamentales para garantizar la seguridad de los receptores, jugando el análisis microbiológico un papel esencial.

El BLV utiliza un sistema mixto donde se combina la medición de acidez en grados Dornic y el empleo de cultivos prepasteurización según criterios determinados junto con cultivos pospasteurización.

Además, se ha detectado una tasa de cultivos positivos pospasteurización del 5,3 %, es decir, inferior a la tasa general descrita en otros estudios (10), siendo la gran mayoría de microorganismos aislados *Bacillus cereus.* Esto demuestra la eficacia de la pasteurización mediante el método Holder, ya que las toxinas de este microorganismo son termorresistentes.

Casi el 80 % de las donantes no ha tenido nunca un resultado de cultivo positivo, lo cual implica, en general, una buena sistemática de extracción y transporte por parte de las donantes y un buen entrenamiento en los procesos de asepsia por parte de los profesionales del banco de leche.

Aunque el ingreso o no del hijo/a de la donante en la Unidad de Neonatología no implique un cambio en el tipo de flora bacteriana detectada en la leche, sí podría implicar un mayor descuido de las medidas de higiene en probable relación al estrés, la falta de tiempo y los continuos desplazamientos al hospital, convirtiéndose de esta forma en una posible diana de refuerzo del proceso educativo en medidas de asepsia para reducir el número de pérdidas de leche.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Epidemiología y dietética

Cambios en el comportamiento alimentario de personas adultas con elevado nivel académico durante las diferentes etapas del confinamiento domiciliario por COVID-19 en Iberoamérica

Changes in the eating behavior of highly educated adults during the different stages of home confinement by COVID-19 in Iberoamerica

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Resumen

Introducción: la pandemia por COVID-19 ha obligado a los gobiernos de los países afectados a aplicar medidas preventivas que incluyen la cuarentena o el confinamiento domiciliario. Se ha visto que, en general, esta situación ha afectado los patrones alimentarios de la población.

Objetivo: evaluar los cambios en los hábitos alimentarios y en la adquisición de los alimentos durante las diferentes etapas del confinamiento domiciliario ocasionado por COVID-19 en la población adulta de alto nivel educativo en diferentes países de Iberoamérica.

Métodos: se realizó un estudio observacional y transversal en el que participaron 9.572 personas de 58 países diferentes con estudios universitarios. El instrumento utilizado para la recolección de datos fue una encuesta diseñada por la Universidad Internacional Iberoamericana de México (UNINI-México) para estudiar los hábitos alimentarios durante el confinamiento domiciliario por COVID-19 como parte del estudio HALCON-COVID-19.

Resultados: la mayoría de los encuestados indicaron haber mantenido su peso durante la cuarentena (57,3 %), aunque reportaron haber reducido su actividad física (23,9 %) y repecto al consumo de alimentos, reportaron haber disminuido el consumo de alimentos ultraprocesados (53,4 %), de bebidas alcohólicas (43,3 %) y de chocolates y golosinas (41,1 %), mientras que aumentaron en su dieta el consumo de vegetales (37,7 %), frutas (37 %) y huevos (30,6 %).

Conclusiones: las personas que no comían de forma saludable previamente, han empeorado la calidad de su dieta durante el periodo de confinamiento además de haber reducido su actividad física, sin embargo, aquellos que tenían un estilo de vida más sano lo han mantenido durante este el periodo.

Palabras clave:

Hábitos alimentarios. Confinamiento. Pandemia. COVID-19. Peso corporal. Consumo de alimentos.

Abstract

Introduction: the COVID-19 pandemic has forced governments of affected countries to implement preventive measures including quarantine or house confinement. This situation has generally been seen to have affected the dietary patterns of the population.

Objective: to evaluate changes in dietary habits and food acquisition during the different stages of home confinement caused by COVID-19 in the highly educated adult population in different Latin American countries.

Methods: an observational and cross-sectional study was carried out in which 9,572 people from 58 different countries and with university studies participated. The instrument used for data collection was a survey designed by the International Ibero-American University of Mexico (UNINI-México) to study food habits during home confinement due to COVID-19 as part of the HALCON-COVID-19 study.

Results: most of the respondents indicated having maintained their weight during quarantine (57.3 %), although they reported having reduced their physical activity (23.9 %) and eliminated the consumption of ultra-processed foods (53.4 %), alcoholic beverages (43.3 %), chocolates and sweets (41.1 %), while including vegetables (37.7 %), fruits (37 %) and eggs (30.6 %) in their diet.

Conclusions: people who usually do not eat healthily have been even more affected in the way they eat during confinement, reducing their physical activity and increasing their body weight, while those with healthier lifestyles have not changed their habits or even maintained their healthy lifestyles during the pandemic.

Keywords:

Dietary habits. Confinement. Pandemic. COVID-19. Body weight. Food consumption.

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INTRODUCCIÓN

En diciembre de 2019, el nuevo coronavirus SARS-CoV-2 fue identificado como el agente causante de una serie de enfermedades respiratorias atípicas (1). Desde entonces, los casos de COVID-19 han aumentado rápidamente, afectando a más de 197 países alrededor el mundo (2). En consecuencia, la Organización Mundial de la Salud (OMS) declaró la COVID-19 una pandemia el 11 de marzo de 2020 (3).

La COVID-19 ha obligado a los gobiernos y las autoridades de los países afectados a aplicar medidas preventivas que incluyeron cierres forzosos, distanciamiento social, autoaislamiento y cuarentena para frenar la propagación del COVID-19 (4). Como resultado de tales medidas, se estima que cuatro mil millones de personas a nivel mundial se vieron obligadas a ponerse en cuarentena en sus hogares durante semanas o meses, dependiendo del país, entre marzo y junio de 2020 (5). Un confinamiento domiciliario puede desencadenar una alta prevalencia de angustia psicológica, que se manifiesta de forma más frecuente con bajo estado de ánimo e irritabilidad, disturbios emocionales y agotamiento, ira, insomnio, estrés postraumático y síntomas depresivos (6).

Un confinamiento domiciliario relacionado con una pandemia puede calificarse como un evento estresante que afecta a los patrones de alimentación (7). Diversas investigaciones han evidenciado cómo muchos individuos han manifestado efectos psicológicos y problemas para adaptarse al nuevo estilo de vida de la cuarentena derivados del hastío y la recepción continua de información sobre la COVID-19 a través de los medios de comunicación.

Estas investigaciones sugieren que hay dos influencias principales en la modificación de los hábitos dietéticos durante el confinamiento domiciliario. La primera de ellas se manifiesta en aquellos que han conservado su rutina laboral (adaptada al teletrabajo), entre quienes se ha observado una mayor tendencia al almacenamiento de alimentos, y aquellos que han interrumpido su rutina laboral, entre los que han prevalecido una mayor sensación de aburrimiento y un mayor consumo de alimentos de mayor contenido calórico.

El estrés lleva a los sujetos a comer en exceso, especialmente, alimentos ricos en azúcar (8), cuyo consumo se asocia a una reducción del estrés ya que estimulan la producción de serotonina, con un efecto positivo sobre el estado de ánimo (9). Esto se asocia con un incremento del riesgo de desarrollar obesidad y enfermedades cardiovasculares, más allá de un estado crónico de inflamación, que se ha demostrado que aumenta el riesgo de las complicaciones más graves de la COVID-19 (10).

La mayoría de las encuestas sobre las fuentes dietéticas de energía, la composición de la dieta y los patrones alimentarios durante la pandemia de la COVID-19 se han realizado en países norteamericanos o europeos, lo que implica que hay relativamente poca información disponible sobre la ingesta dietética durante la pandemia en Latinoamérica. Por todo ello, el objetivo principal del estudio es identificar y analizar las modificaciones en los patrones de consumo alimentarios, sus determinantes y el impacto sobre el estado de salud durante las diferentes etapas del confinamiento de la población de elevado nivel académico en diferentes países iberoamericanos, a fin de desarrollar estrategias en materia de alimentación, nutrición y estilos de vida saludable para mejorar y/o mantener el estado de salud y nutricional de la población confinada de cara a la presente y posibles futuras pandemias. De forma secundaria, con este estudio también se pretende conocer las modificaciones en el peso corporal.

MATERIALES Y MÉTODOS

Para comprobar la hipótesis, se evaluaron los cambios en los hábitos alimentarios y en la adquisición de los alimentos durante las diferentes etapas del confinamiento domiciliario ocasionado por la COVID-19 en la población adulta de alto nivel académico en diferentes países de Iberoamérica. Para ello, se han analizado las alteraciones en la elección de alimentos, los cambios en la frecuencia de ingestas, la modificación de hábitos en la cesta de la compra y cómo ha influido el confinamiento en la percepción del cambio de peso corporal, así como las variaciones en las rutinas de actividad física, la utilización de servicios de entrenamiento físico y el asesoramiento nutricional por parte de un profesional de la salud.

Se realizó un estudio observacional y transversal. La población objeto de estudio está representada por alumnos de posgrado, profesores y resto del personal académico, además de contactos personales relacionados con la comunidad educativa de la Universidad Internacional Iberoamericana. La muestra fue seleccionada mediante muestreo no probabilístico por conveniencia. En total, participaron 9.572 personas de 58 países diferentes de Iberoamérica.

El instrumento utilizado para la recolección de datos fue una encuesta validada por el método Delphi y diseñada por un grupo de investigadores de la Universidad Internacional Iberoamericana de México (UNINI-México), para estudiar los hábitos alimentarios durante el confinamiento domiciliario por COVID-19 en un estudio llamado HALCON-COVID-19 (11) (Fig. 1).

Para distribuir la encuesta se compartió el enlace a través de diferentes redes sociales, como Facebook, Instagram y WhatsApp, así como mediante correos electrónicos difundidos por profesores, personal académico y sus contactos. Se pidió, asimismo, a los destinatarios que compartieran el enlace para aumentar el número de personas que recibiesen la invitación y poder aumentar el número de participantes y las conclusiones obtenidas.

En el estudio participaron adultos mayores de 18 años, de ambos sexos, que se encontrasen confinados durante el periodo del mismo y que estuviesen interesados en participar. Se excluyeron menores de 18 años, personas con falta de acceso a internet y personas con limitación para rellenar la encuesta,

Se consideraron los hábitos alimentarios y la adquisición de alimentos. Se evaluaron variables sociodemográficas como país de residencia, edad, sexo, estado civil, miembros del hogar, número de hijos y trabajo actual. Las variables relacionadas con el confinamiento fueron: si hubo o no confinamiento domiciliario;

Figura 1.
Encuesta estudio HALCON-COVID-19.

días de duración del mismo; porcentaje dedicado al gasto de alimentos; realización de compras a domicilio; criterios para elegir alimento; alimentos cuyo consumo ha disminuido, aumentado, eliminado o incluido; número de compras al mes; frecuencia de comidas al día y actividad física; enfermedades crónicas; y peso y talla.

En relación a la organización del cuestionario, la primera sección corresponde a los datos sociodemográficos y de estilo de vida y consta de 25 ítems. Incluye datos como país de residencia, sexo, edad, niveles de estudio, profesión y entorno laboral, lugar de confinamiento, días de confinamiento, tipo de vivienda, estado civil, edades, miembros de la familia que conviven en el hogar, ingresos familiares, frecuencia de compras de alimentos al mes y compras a domicilio, entre otras.

La segunda sección se refiere a los datos antropométricos y de salud y consta de siete ítems. En ella se incluyen preguntas relacionadas con el peso corporal y la talla, además de cambios en el peso ocurridos en el confinamiento domiciliario, así como expectativas de peso. En relación a la salud, se incluye la presencia de enfermedades crónicas y sentimientos percibidos durante el confinamiento.

La tercera sección se centra en la actividad física y consta de tres ítems. Se hacen preguntas sobre la realización de actividad física, el nivel de práctica de la misma y si se utiliza algún tipo de servicio de entrenamiento profesional en línea.

La cuarta sección versa sobre alimentos y hábitos alimentarios y cuenta con once ítems. Incluye preguntas sobre asesoramiento nutricional, modificación en frecuencia de consumo de alimentos, así como la eliminación o inclusión, disminución o aumento del consumo, el número de comidas y cuáles son los criterios a la hora de elegir los alimentos.

El instrumento de recolección de datos está representado por un cuestionario autoadministrado con preguntas cerradas y abiertas, divido en dos partes: la primera, con cuestiones que recogen aspectos sociodemográficos y de estilo de vida; y la segunda, relacionada con la antropometría y la salud. Ambas partes contienen preguntas similares, pero en la segunda se incluyen cuestiones sobre el periodo de desconfinamiento domiciliario.

De acuerdo a la Ley Federal de Protección de Datos Personales en Posesión de Particulares (LFPDPPP) de México, la información personal y los datos de los participantes fueron anónimos. La encuesta se realizó de acuerdo con las regulaciones nacionales e internacionales de Helsinki del año 2013. No se requirió la aprobación del Comité de Ética debido a la naturaleza anónima de la encuesta en línea y la imposibilidad de rastrear datos personales sensibles.

Los datos fueron analizados utilizando el *software* estadístico IBM® SPSS® versión 25. Las variables fueron analizadas cualitativamente y expresadas como porcentaje (%) y números (n). Se realizaron comparaciones entre las variables continuas (peso, talla e índice de masa corporal [IMC]) con las variables sociodemográficas (variables nominales) de relevancia. Esta comparación se realizó con los estadísticos: estudios t de Student y ANOVA, según la cantidad de categorías y opciones de respuesta de la variable. Se consideró significativo el valor de $p \leq 0,05$.

RESULTADOS

Se recolectaron datos de 9.572 personas, 3.241 hombres (33,9 %) y 6.631 mujeres (66,1 %), que viven en un entorno urbano (91 %), principalmente, de 25-34 años (32,8 %) y 35-44 (29,8 %).

La muestra se caracteriza por tener mayoritariamente de uno a tres miembros convivientes en la familia (53,7 %), estar tanto casados/as (42,4 %) como soltero/as (37,3 %), sin hijos/as a cargo (50,6 %) y con hijos/as a cargo (49,4 %) (un hijo/a el 21,2 % y dos hijos/as el 19,9 %). La edad de los niños/as es muy variable, aunque se sitúa principalmente en el rango de 0-5 años (17 %) (Tabla I).

El 72,7 % se encontraba en confinamiento total y el 22,6 %, en confinamiento parcial. Procedían, en su mayoría, del continente americano (48,7 % de América del Sur, 25,2 % de América del Norte y 19,8 % de América Central) y, concretamente, de México (24,2 %), Colombia (13 %) y Ecuador (10,7 %) (Fig. 2).

Respecto al nivel de estudios, el 95,2 % de la muestra posee al menos una licenciatura, seguidos de maestría y, en tercer lugar, doctorado, por lo que se trata de una muestra poblacional de alto nivel académico.

Respecto al porcentaje de los ingresos familiares destinados a la alimentación, casi la mitad (44,6 %) de la muestra dedica el 20-40 % de los ingresos familiares a la misma, un 27,9 % dedica el 41-60 % de los ingresos y un 7,1 %, el 61-80 %. Destaca que un 17,6 % de la muestra dedica menos del 20 % de los ingresos familiares a la alimentación (Fig. 3).

En cuanto a los cambios en la frecuencia de ir a la compra, hay un incremento en la cantidad de veces al mes en que se hace la compra de alimentos después del confinamiento (Tabla II).

Tabla I. Datos sociodemográficos de la población de estudio

Datos demográficos	Frecuencia	Porcentaje
Estado civil		
Soltero/a	3.568	37,3 %
Casado/a	4.058	42,4 %
Unión libre	1.179	12,3 %
Divorciado/a	664	6,9 %
Viudo/a	88	0,9 %
No hay datos	15	0,2 %
Miembros de la familia convivientes		
1 a 3	5.136	53,7 %
4 a 6	4.044	42,2 %
7 a 9	343	3,6 %
Más de 10	49	0,5 %
Nivel de estudios		
Primaria	4	0,05 %
Secundaria	56	0,6 %
Bachillerato	381	4 %
Licenciatura	4.623	48,3 %
Maestría	3.974	41,5 %
Doctorado	513	5,4 %
No hay datos	21	0,15 %
Género		
Femenino	3.241	33,9 %
Masculino	6.331	66,1 %
Edad		
15-24 años	680	7,1 %
25-34 años	3.141	32,8 %
34-44 años	2.851	29,8 %
45-54 años	1.879	19,6 %
55 o más	1.021	10,7 %

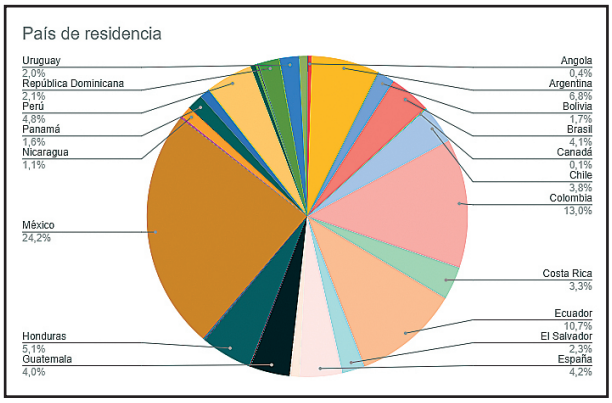

Figura 2.

Países de residencia de la población participante.

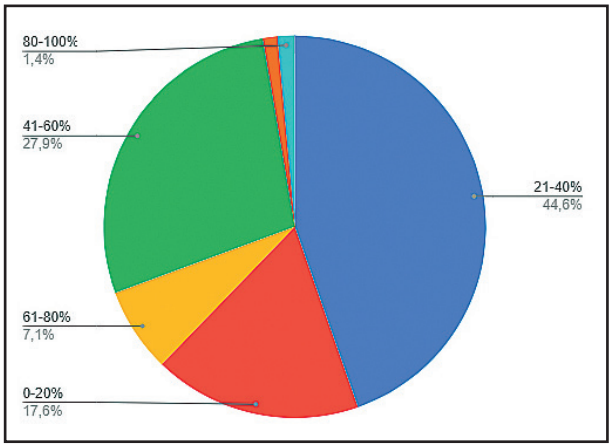

Figura 3.

Porcentaje de los ingresos familiares totales dedicados a la alimentación.

Tabla II. Resultados descriptivos de las variables: cantidad de veces de compra mensual antes y después del confinamiento y realizar compras de alimentos a domicilio

	Antes de la cuarentena		Durante la cuarentena	
Compra mensual	**Frecuencia**	**Porcentaje**	**Frecuencia**	**Porcentaje**
1-3	4.047	42,3 %	6.501	67,9 %
4-6	3.815	39,9 %	2.481	25,9 %
7-9	896	9,4 %	391	4,1 %
Más de 10	814	8,5 %	199	2,1 %
Compras a domicilio			**Frecuencia**	**Porcentaje**
No			3.686	38,5 %
Antes no, pero ahora sí compro a domicilio			1.870	16,5 %
Antes no y ahora tampoco			1.499	15,7 %
Antes sí, pero ahora compro más frecuentemente			611	6,4 %
Antes sí pero ahora no compro a domicilio			933	9,7 %

El análisis de datos respecto a las modificaciones en los hábitos de compra a domicilio determina que, durante el tiempo del confinamiento, el 16,5 % compra comida a domicilio, mientras que antes de la cuarentena no lo hacía. Un 6,4 %, además, indica que compra más frecuentemente.

Son de especial relevancia las modificaciones y nuevas prácticas alimentarias, con varios alimentos que se vieron eliminados, reducidos, incluidos o incrementados en el consumo. Los alimentos que un mayor porcentaje de los individuos encuestados redujo o eliminó de su dieta durante el tiempo de confinamiento fueron: ultraprocesados (53,4 %), seguido de bebidas alcohólicas (43,3 %), chocolates y golosinas (41,4 %). Los alimentos más reducidos también son los ultraprocesados (33,7 %), chocolates y golosinas (35,1 %) y bebidas alcohólicas (28,7 %). Solo un 22,3 % refiere que no eliminó ningún alimento, siendo un 14,9 % los que no redujeron el consumo de ningún alimento en especial.

Por otra parte, los alimentos cuyo consumo aumentó fueron: vegetales (37,7 %), huevos (30,6 %) y alimentos frescos en general (27,8 %). Asimismo, la población incrementó el consumo de frutas (34,5 %), pan o tortillas de cereal (24,1 %).

El 16,8 % no aumentó el consumo de ningún alimento en especial, mientras que el 25,8 % no añadió nuevos alimentos a su dieta mientras estaba confinado.

En el confinamiento, el 14,5 % redujo el número de comidas, el 20,7 % incrementó el número de las mismas y el 64,8 % mantuvo el mismo número de comidas, la mayor parte de ellos (72,1 %) con tres o cuatro ingestas diarias. Tuvo en cuenta, principalmente, la elección de alimentos más saludables como principal criterio para hacer las compras el 73,3 %, seguido de la accesibilidad para la adquisición de los mismos (43,1 %). Según la percepción de los encuestados, el 29,1 % considera que ha mejorado su alimentación, un 21,8 % cree que ha empeorado y el 49,2 % piensa que se ha mantenido igual. Aquellos que redujeron o eliminaron el consumo de alimentos ultraprocesados, alcohol, chocolate y golosinas e incrementaron el consumo de vegetales, frutas y alimentos frescos consideran que su alimentación ha mejorado (Tabla III).

En el análisis de los datos relativos al IMC, la muestra posee un rango de entre 12,02 y 92,95, con una media de 26,10, la cual se puede incluir, según la clasificación de la OMS, dentro de la categoría de "sobrepeso" (18). Aunque la mayoría (57,3 %) mantuvo su peso durante la cuarentena, el 28,2 % indicó estar aumentando o haber aumentado de peso debido a un mayor consumo de alimentos procesados, alcohol, golosinas y chocolates. Solo el 14,5 % de la población indica haber bajado de peso en su confinamiento.

Al realizar la comparación mediante la prueba de t de Student, los resultados reflejan que el IMC presenta diferencias significativas entre las medias de los hombres y las mujeres, entendiendo que en esta muestra los hombres tienen más peso, son más altos y están dentro de la categoría de sobrepeso. Respecto a la relación del IMC con la edad, las personas de la muestra mayores de 35 años poseen un mayor peso, son más altas y están dentro de la categoría de sobrepeso (Tabla IV).

Tabla III. Resumen de los alimentos reducidos, incluidos, eliminados y aumentados durante el confinamiento

	Eliminados		Reducidos		Incluidos		Aumentados	
	F	%	F	%	F	%	F	%
Ninguno	2.134	22,3 %	1.428	14,9 %	2.472	25,8 %	1.604	16,8 %
Alimentos frescos	461	4,8 %	829	8,7 %	2.670	27,8 %	1.657	17,4 %
Alimentos ultraprocesados	5.100	53,4 %	3.218	33,7 %	491	5,2 %	433	4,6 %
Bebidas alcohólicas	4.131	43,3 %	2.755	28,7 %	405	4 %	407	4,2 %
Carnes	764	8 %	1.442	15,1 %	2.297	24 %	1.660	17,4 %
Cereales o tubérculos	535	5,6 %	1.115	11,6 %	2.452	25,7 %	1.748	18,2 %
Chocolates y golosinas	3.966	41,4 %	3.360	35,1 %	845	9,4 %	885	9,4 %
Frutas	507	5,3 %	1.322	14,1 %	3.546	37 %	3.306	34,5 %
Huevos	262	3 %	521	5,3 %	2.925	30,6 %	2.825	29,5 %
Ingredientes congelados para cocinar	2.282	24 %	1.733	18,2 %	1.444	15,2 %	737	7,6 %
Lácteos	750	7,8 %	1.137	11,9 %	2.098	22,1 %	1.584	16,5 %
Latas y conservas	2.198	22,9 %	2.076	21,7 %	1.897	19,9 %	1.013	10,6 %

(Continúa en página siguiente)

Tabla III (Cont.). Resumen de los alimentos reducidos, incluidos, eliminados y aumentados durante el confinamiento

	Eliminados		Reducidos		Incluidos		Aumentados	
	F	%	F	%	F	%	F	%
Leche y derivados	46	0,5 %	65	0,7 %	86	0,9 %	137	1,6 %
Leguminosas	511	5,3 %	754	7,9 %	2.577	27 %	1.664	17,4 %
Pan o tortillas de cereal	1.225	12,8 %	2.507	26,2 %	2.217	23,2 %	2.303	24,1 %
Pescado	1.388	14,5 %	1.524	15,8 %	2.027	21,1 %	1.154	12 %
Vegetales	403	4,2 %	1.067	11,2 %	3.605	37,7 %	3.009	31,5 %

Tabla IV. Comparación de variables talla, peso e IMC según sexo

			n	Media	Desviación típica	Sig.
Peso (kg)	Sexo	Masculino	3.241	81,53	18,09	0,000
		Femenino	6.331	66	16,18	
	Rango de edad	15-24 años	680	63,13	15,43	0,000
		25-34 años	3.141	68,73	18,04	
		35-44 años	2.851	72,89	19,12	
		45-54 años	1.879	74,19	18,02	
		55 o más	1.021	74,50	17,16	
Talla (cm)	Sexo	Masculino	3.241	172,81	7,75	0,000
		Femenino	6.331	160,92	7,11	
	Rango de edad	15-24 años	680	162,49	8,83	0,000
		25-34 años	3.141	164,32	9,31	
		35-44 años	2.851	165,38	9,09	
		45-54 años	1.879	165,48	9,22	
		55 o más	1.021	166,30	9,36	
IMC	Sexo	Masculino	3.241	27,30	5,95	0,000
		Femenino	6.331	25,49	6,13	
	Rango de edad	15-24 años	680	23,77	4,57	0,000
		25-34 años	3.141	25,38	6,05	
		35-44 años	2.851	26,58	6,54	
		45-54 años	1.879	27,02	6,01	
		55 o más	1.021	26,87	5,65	

IMC: índice de masa corporal.

DISCUSIÓN

En el presente estudio se evaluaron los cambios en los hábitos alimentarios de la población adulta de alto nivel educativo, en diferentes países de Iberoamérica, y cómo ha influido el confinamiento en la percepción del cambio del peso corporal y la actividad física durante las diferentes etapas del confinamiento domiciliario ocasionado por la COVID-19.

Según Sidor and Rzymski (12), la cuarentena relacionada con una pandemia puede clasificarse como un evento estresante y, en general, se sabe que estos eventos afectan los patrones de alimentación. Dependiendo de si el estrés es agudo o crónico, se puede inducir hipofagia o hiperfagia y atracones, lo que eventualmente resulta en un cambio de peso significativo. En general, el 43,5 % de las personas encuestadas por Sidor and Rzymski (12) informaron haber comido más durante la cuarentena, lo que demuestra claramente que el confinamiento puede representar un riesgo dietético significativo.

Esto puede relacionarse con las consecuencias psicológicas y emocionales asociadas al brote de COVID-19, que pueden aumentar el riesgo de desarrollar conductas alimentarias disfuncionales (13). Se conoce que las emociones negativas pueden llevar a comer en exceso; es lo que se conoce como "comer emocional".

En un metaanálisis realizado por Evers y cols. (14), se evaluó cómo las emociones afectan a los patrones dietéticos. Los resultados de dicho metaanálisis evidencian que los consumidores mostraron un aumento de la ingesta en respuesta a las emociones. Para contrastar y responder a la experiencia negativa del autoaislamiento, las personas podrían ser más propensas a buscar recompensas y gratificaciones fisiológicamente asociadas con el consumo de alimentos, incluso anulando otras señales de saciedad y hambre (15). Además, los sentimientos de aburrimiento, que pueden surgir de quedarse en casa durante un periodo prolongado, a menudo se relacionan con comer en exceso. Según Havermans y cols. (16), comer cuando se está aburrido no está impulsado por un mayor deseo de satisfacer los estímulos de incentivos, sino principalmente por el impulso de escapar de la monotonía.

En la encuesta EHLC-COVID-19, casi la mitad de los encuestados (44,0 %) seguían una "dieta" antes del estallido de la pandemia. Sin embargo, el encierro parece haber influido en la capacidad de controlar la relación con la comida. El aislamiento, la falta de estímulos, el aburrimiento y los cambios en las rutinas alimentarias tuvieron efectos en el 86,0 % de los encuestados, que manifestaron no poder controlar suficientemente su dieta. En particular, podría existir una correlación entre el consumo de alimentos muy apetecibles, como los ultraprocesados, y un deterioro de la coordinación temporal de la inmunidad innata y adaptativa. Se ha demostrado que tal deterioro aumenta la probabilidad de infección por COVID-19, así como de un curso clínico más grave (17).

En un estudio similar, denominado "Hábitos alimenticios y cambios en el estilo de vida en el confinamiento de COVID-19" (EHLC-COVID-19) y llevado a cabo por Di Renzo y cols. (18), la percepción de aumento de peso se observó en el 48,6 % de la población, lo que concuerda con los hallazgos de este estudio, donde la mayoría de los encuestados mantuvieron su peso durante la cuarentena (57,3 %), mientras que un 38,8 % indicó que les gustaría adelgazar unos kilos.

La mayoría de los sujetos de la muestra eliminaron en mayor medida alimentos ultraprocesados (53,4 %), bebidas alcohólicas (43,3 %) y chocolates y golosinas (41,1 %), mientras que decidieron incluir en su dieta vegetales (37,7 %), frutas (37 %) y huevos (30,6 %). Esto concuerda con los resultados de Di Renzo y cols. (18), quienes hallaron que la población italiana incrementó el consumo de postres caseros, pan y pizza. Por otro lado, ha disminuido el consumo de *snacks,* carnes procesadas y bebidas carbonatadas y azucaradas y se han consumido más alimentos incluidos dentro de la dieta mediterránea, manteniendo alta la calidad nutricional (18). Janssen y cols. (19) también encontraron que, en Dinamarca, Alemania y Eslovenia, las personas compraron con menos frecuencia comida ultraprocesada durante el confinamiento. Además, hubo una reducción general en el consumo de alimentos frescos y un aumento en aquellos productos alimentarios con una vida útil más larga.

Según la percepción de la muestra, su alimentación se mantiene igual comparándola antes y después del confinamiento (49,2 %). Hacen entre tres y cuatro comidas al día (64,8 %) y dicha frecuencia se mantiene en el confinamiento (64,8 %). Además, reportan que han reducido la cantidad de comida que han consumido durante la cuarentena (75,1 %). El 73,3 % procura elegir alimentos más naturales y más saludables para lograr mejorar la respuesta inmune en caso de una posible contaminación. Esto contrasta con los resultados de Di Renzo y cols. (18), en los cuales el 17,8 % de los que respondieron a la encuesta tenían menos apetito, mientras que el 34,4 % de los que respondieron dijo que aumentó su apetito.

Al igual que en el estudio EHLC-COVID-19, López-Moreno y cols. (20) demostraron que el 38,8 % de los encuestados en su estudio experimentaron un aumento de peso, mientras que el 31,1 % perdió peso durante el confinamiento. En este caso, el incremento de peso corporal se correlacionó positivamente con la edad ($Rs = 0,14$, $p < 0,05$) y el IMC ($Rs = 0,20$, $p < 0,05$). También se encontró que el 44,7 % de los participantes no había realizado ejercicio físico durante el confinamiento y, en este sentido, se encontraron diferencias por sexo ($p < 0,05$), edad ($p < 0,05$) e IMC ($p < 0,05$) (20). Esto concuerda con los resultados obtenidos en el presente estudio, en el cual las variables de IMC presentan diferencias significativas. Los hombres de la muestran tienen más peso, son más altos y están dentro de la categoría de sobrepeso ($p = 0,000$), y las personas de la muestra mayores de 35 años poseen un mayor peso, son más altas y están dentro de la categoría de sobrepeso ($p = 0,000$). Respecto a la percepción del peso corporal, aquellas personas que piensan que han mantenido o están manteniendo el peso durante el confinamiento son las que tiene un menor peso y un IMC normal ($p = 0,000$). En cuanto a las expectativas en el peso corporal, aquellos que no se preocupan del mismo son los que tienen menor peso, son más altos y tienen un IMC normal ($p = 0,000$).

En el estudio llevado a cabo por Di Renzo y cols. (21), la percepción de aumento de peso resultó estar presente en las personas que iniciaron teletrabajo.

En el presente trabajo se ha visto cómo los hábitos alimentarios de la mayoría de los sujetos de alto nivel educativo de los países evaluados han cambiado como consecuencia de la situación de pandemia. El impacto de la crisis de la COVID-19 en los comportamientos relacionados con el peso corporal, incluidos los hábitos alimentarios y la actividad física, parece ser variable, ya que las personas que usualmente no comen de forma saludable han reducido aún más su actividad física e incrementado su peso, mientras que las personas con estilos de vida más sanos no han cambiado sus hábitos durante la pandemia o incluso los han mejorado.

Para concluir, sería interesante estudiar en mayor profundidad las modificaciones en los estilos de vida y su impacto para la salud, con el fin de desarrollar estrategias en materia de alimentación, nutrición y seguridad alimentaria que sirvan para el afrontamiento de nuevas realidades y de los riesgos pandémicos y ambientales futuros. Conocer las modificaciones y nuevas prácticas alimentarias resultado del estado de confinamiento permitirá el desarrollo de directrices de alimentación y nutrición que permitan mitigar los efectos negativos de una mala alimentación durante el confinamiento y potenciar los recursos con los que cuenten las comunidades. Dado que la población de estudio se refiere a personas de alto nivel educativo, sería necesario seguir investigando para ver la forma en que afecta la pandemia por COVID-19 a los hábitos alimentarios de otros grupos poblacionales.

Dentro de las fortalezas del estudio, se tuvo libre acceso a la hoja de recogida de los datos del cuestionario. También se tuvo total apoyo por parte de la Universidad Internacional de México (UNINI), que facilitó todo el material relativo a la propuesta del estudio. Como limitaciones, cabe destacar la dificultad para analizar los datos debido a las múltiples respuestas a determinadas preguntas y a las diferencias de unidades de medida utilizadas en diferentes países. Además, los datos son subjetivos y solamente tienen validez las respuestas de los encuestados a las preguntas planteadas.

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ARÁN

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Trabajo Original

Epidemiología y dietética

Overweight and obesity in the Mexican school-age population from 2015 to 2019

Sobrepeso y obesidad en la población mexicana en edad escolar entre 2015 y 2019

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Abstract

Introduction: between 2006 and 2020, obesity in Mexico increased across all age groups and displayed a homogenizing evolutionary trend throughout, prevalence overweigth and obesity (Ow+Ob) has 38.2% in school age children.

Objectives: to analyze the changes of Ow+Ob in a cohort with four years of evolution of students from Mexico elementary schools and to evaluate its association with socio-demographic factors.

Methods: information comes from a nutritional surveillance system of 52,545 elementary schools, with weight and height measurements from 2,008,474 children from six to eleven years old. A follow-on panel longitudinal analysis was performed from 2015 to 2019 in a dynamic cohort with three measurements. Ow+Ob prevalences were obtained; through a logistic regression with random effects, odds ratios (OR) were calculated, adjusting by sociodemographic characteristics ($p < 0.05$).

Results: between 2015 and 2019, positive OR were observed for Ow+Ob development in 2017-2018 (OR = 1.02) and 2018-2019 (OR = 1.06). Students from the northern and southern regions of the country showed a greater probability of suffering Ow+Ob (OR = 1.58 and 1.64) when compared with the center. Attending to community or indigenous schools was a protective factor (OR = 0.54) whereas attending to a private school increased the risk (OR = 1.75). Adjusted Ow+Ob prevalences showed an accelerated increasing trend in males through all the periods.

Conclusions: in Mexico, obesity in school children is a growing problem related to sociodemographic factors, therefore, urgent actions are needed for its restraining.

Keywords:

Childhood obesity. Nutrition surveillance. Schoolchildren. Obesity. Epidemiology. Overweight.

Resumen

Introducción: México se sitúa dentro de los primeros lugares a nivel mundial en cuanto a sobrepeso y obesidad en escolares, con una prevalencia del 38,2 %.

Objetivo: analizar los cambios de sobrepeso y obesidad (Sob+Ob) durante cuatro años en una cohorte de alumnos de escuelas primarias en México y evaluar su asociación con factores sociodemográficos.

Métodos: la información proviene de un sistema de vigilancia nutricional en escolares. Se realizó un análisis longitudinal de panel con seguimiento a través de una corte dinámica de tres mediciones realizadas entre 2015 y 2019. Se obtuvieron las prevalencias de Sob+Ob a través de una regresión logística con efectos aleatorios y se calcularon razones de momios (OR), ajustando por características sociodemográficas.

Resultados: entre 2015 y 2019 se observaron OR positivos para el desarrollo de Sob+Ob, 2017-2018 (OR = 1,02) y 2018-2019 (OR = 1,06). Los estudiantes de las regiones norte y sur del país mostraron una mayor probabilidad de sufrir Sob+Ob (OR = 1,58 y 1,64) en comparación con el centro. La asistencia a escuelas comunitarias o indígenas fue un factor protector (OR = 0,54), mientras que la asistencia a una escuela privada aumentó el riesgo (OR = 1,75). Las prevalencias ajustadas de Sob+Ob demostraron una tendencia creciente acelerada en los hombres a lo largo de todos los periodos.

Conclusiones: en México, la obesidad en escolares es un problema creciente relacionado con factores sociodemográficos, por lo que se requieren acciones urgentes para su contención.

Palabras clave:

Obesidad infantil. Vigilancia nutricional. Población escolar. Epidemiología. Obesidad. Sobrepeso.

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INTRODUCTION

Obesity epidemics has become a public health challenge worldwide due to its growing prevalence and its role as a chronic diseases risk factor, mainly type-2 diabetes, cardiovascular diseases (1,2), respiratory disorders, muscle-skeletal conditions, depression and some types of cancer (3-5). This disease presence, at early stages of life, is associated with cardiometabolic alterations (1,2,6,7), abnormal levels of serum lipids (8), high blood pressure and the presence of insulin-resistance markers like HOMA index (1,9,10). COVID-19 pandemics showed how obesity and the set of alterations that comes along with it represent an adverse results risk factor for infectious diseases (11,12).

The Word Health Organization (WHO) has informed that Ow+Ob affects 41 million of children under five years old, 340 million of children and teenagers from five to 19 years old and 1.9 billion of adults of 20+ years old (3). Among the countries members of the Organisation for Economic Co-Operation and Development (OECD), Mexico is the second place in obesity in all its population and it is among the first ones in childhood obesity (6,7).

According to the 2020 National Health and Nutrition Survey (ENSANUT 2020), Ow+Ob prevalence in Mexico has reached 8.4 % in children under five, 38.2 % in school-age children (5-11 years old), 43.8 % in adolescents (12-19 years old) and 74.1 % in adults (13). Between 2006 and 2020, obesity increased across all age groups and displayed a homogenizing evolutionary trend throughout the Mexican population notwithstanding its diverse geographic and sociodemographic characteristics (14).

Previously described ciphers reveal an overwhelming problem: the fast increase and the general damage triggered by the obesity epidemic indicates that, whereas in the country actions like sweetened beverages taxation, new food nutritional labeling, and school guidelines for food selling and distribution have been applied, this has not been enough to address the problem through an efficient public policy (15,16).

A particular example is one state-level program carried out in schools of the Mexican Morelos state aimed to promote the development of healthy life styles. However, prevalences of 15.5 in children under five years old and 26.3 in school-age population were reported; in other words; a difference greater than 10 % in groups between three and 12 years old (17).

Beginning in 2015, the National Registry of Weight and Height (RNPT, by its initials in Spanish) was implemented in Mexico, coordinated by the Division of Nutrition of the National Institute of Medical Sciences and Nutrition "Salvador Zubirán" (INCMNSZ) and the National System for Integral Family Development (SNDIF). It integrated efforts from various sectors, including health and education, at the federal, state and municipal (county like entities) levels. Its objective was to assess the nutritional status of the Mexican population on the basis of anthropometric measurements, specifically, weight and height of Primary School children (18).

Previous publications have described the methodology used by the RNPT, as well as the results it obtained with regard to the pattern of nutritional status (19), particularly obesity, and its relationship to specific geographic and socioeconomic factors. Regarding methodology, it should be noted that anthropometric measurements were registered in a periodical manner through an on-line surveillance system (SIVNE) for children attending elementary-school first to sixth grade. Such publications described in their results sections the nutritional status behavior, focusing mainly in obesity and its association with geographical and socioeconomic factors, emphasizing the transversal results from the 2015-2018 period (20).

The objective of the present study is to describe the trend of overweight and obesity during four years (2015-2019) in a dynamic cohort of children enrolled in Mexican elementary schools. Likewise, it aims to quantify the influence of some sociodemographic factors like sex, geographical factors like the country regions, and the school-related like modality (private, public or indigenous) over overweight and obesity in the children.

METHODS

STUDY DESIGN

A longitudinal analysis was performed in a dynamic cohort of children that attended to public schools and were followed from 2015 to 2019. Having three measurements (one by year) during the cited period of analysis was a requisite for the children to be included in such cohort.

We obtained the data from the RNPT open-access files. This project was approved by the INCMNSZ research and ethics committees. The information pertained to the entire country and was collected through the online platform of the Nutritional Surveillance System for School Children (SIVNE®, by its Spanish initials).

Individuals with previously diagnosed, non-visible health problems or with evident ones were excluded from the study. Inclusion criteria were: children between six and eleven years, evaluated yearly at least in three out of four school years of the study (2015-2019).

TECHNICAL INFORMATION

Ávila et al. described in an RNPT publication (18) the mechanisms used to collect and record the anthropometric measurements of the children. Data on the studied Ow+Ob children included: type of institution, geographic location and socioeconomic level. Concisely, personnel from the Division of Nutrition of INCMNSZ was in charge of advisory, training and anthropometric standardization and equipment usage, as stated by internationally accepted protocols. This schema was replicated in cascade, finally reaching SNDIF community promoters and school teachers who made the measurements. The gathered information was verified by supervisors who were also responsible for keeping contact with the promoters and teachers, in order to provide feedback about the process of obtaining the information.

Weight and height measurements were performed at the schools, and measurements were made on light clothes. A digital SECA 803 (SECA®, Hamburg, Germany) with a total capacity of 150 kg and 100 g of precision was used for weight measurements. Height was obtained in standing position, in contact with the wall, avoiding objects over the head and without shoes. A SECA stadiometer model 206 (SECA®, Hamburg, Germany) was used with a reach of 200 cm and 1 mm precision.

DEFINITION OF OVERWEIGHT AND OBESITY

Based on the child growth standards of the WHO, five variables (date of birth, sex, weight, height and date of measurement) were used to calculate the exact ages and z-scores for the indicator body mass index (BMI) for age (BAZ) (21).

To determine the prevalence of Ow+Ob, the BAZ scores were categorized in accordance with the WHO standards. Overweight was defined as any value between +1 and +1.99 standard deviations (SD) above the median, obesity is greater than 2 standard deviations above the median (21,22). Ow+Ob included both categories grouped.

We cleaned the RNPT data for the anthropometric measurements taken each school year. The inclusion criterion centered on students with weight and height measurements that allowed for estimating the BAZ within a plausibility interval of ± 5 SD and a height for age z-score (HAZ) between -6 and +6.

COVARIATES OF INTEREST

The time variable was defined as school years, in accordance with the academic calendars published by the Ministry of Public Education (SEP, by its Spanish initials). With annual intervals between August 2015 and June 2019, this variable covered the four most recent school years: 2015-2016, 2016-2017, 2017-2018 and 2018-2019.

Sociodemographic characteristics like age or sex were studied using yearly groups of age (six to eleven) for both genres (female or male).

As geographic characteristic, three great country regions were studied (1: north; 2: center; 3: south) based on the ENSANUT classification. Such regions were assigned according to the state in which each school was located.

School modality (1 = public; 2 = private; 3 = community or indigenous) was assigned according to the SEP criteria and the provisions framed in the General Education Law (LGE). Articles 36, 37 and 146 of the LGE establish a code for the classification of schools named CCT (Spanish initials for Work Center Code); this code reflects social, regional and sociocultural groups all over the country. Accordingly, officially sustained schools are divided in: a) public; b) private; and c) community (CONAFE) or indigenous. Due to the fact that community and indigenous schools share the enrollment of similar population (rural, indigenous or immigrant), they were all grouped into a single category.

STATISTICAL ANALYSES

For statistical analyses, STATA version 14 software and version 24 of the Statistical Package for Social Sciences developed by the Social Protection System in Health (SPSS) were used, both under the INCMNSZ, MX institutional license. All analyses used static panel data (xtset) to assess the students and their measurements across the four previously mentioned school years.

For the continuous variables (age, BAZ, HAZ, weight and height), intra- and inter-group statistical distribution were calculated, as well as minimum, maximums, means and standard deviations. For categorical variables (school year, type of school and region), the relative frequencies (xttab) and transition probabilities in the prevalence of Ow+Ob between the first and last year analyzed (xttrans) were estimated. For the latter, we estimated and adjusted the change percentage by dividing it into the initial Ow+Ob percentage.

To estimate de Odds Ratio (OR) of Ow+Ob with 95 % confidence interval (95 % CI), a random effects (RE) panel data analysis and a logistic regression model (re xtlogit model) were constructed adjusting the OR by the previously mentioned sociodemographic characteristics. The Haussman test was applied to differentiate between fixed and random effects (23,24). As the differences in the estimators of the models were not systematic, it was decided to use the random effect method, which allowed for using fixed variables over time, assuming that the individual effects did not correlate with the explanatory variables in the model.

The OR of Ow+Ob and their respective 95 % CI were adjusted for sex, age group, type of school and geographic region. To illustrate the results, predictive margin plots (marginsplot) were generated.

RESULTS

A total of 2,008,474 students from 52,545 schools were analyzed during the four most recent school years, consolidating the data from 6,025,422 anthropometric measurements (Table I, section Ia).

The greatest number of measurements were recorded during the 2017-2018 school year, representing 30.9 % of the total evaluated from 2015 to 2019 (Table I, section Ib). Participation pattern distribution is shown in section II from table I.

The 50.7 % of evaluated population were male (1,018,296) and 49.3 % (990,178) were female. This is a distribution similar to the one reported by the SEP (Table I, section IIIa). The distribution of the 6,025,422 anthropometric measurements was concentrated in more than 45 % in the third and fourth school grades (Table I, section IIIb).

The northern region of the country included 42.8 % of the evaluated population, 26.8 % inhabited the central region and 30.4 % the south, being this last one the only one that shows a similar distribution and without statistically significant differences with the reported by the Education System (Table I, section IIIc).

Table I. Description of patterns and frequency of evaluations by sociodemographic characteristics, descriptive statistics of the characteristics of the students, period 2015-2019

I. General panel information					
a) General panel information				**b) Measurements per school year**	
				School year	**n**	**%**
Students evaluated = 2,008,474				2015-2016	1,144,471	19.0
Total anthropometric measurements = 6,025,422				2016-2017	1,399,768	23.2
				2017-2018	1,860,752	30.9
Schools evaluated = 52,545				2018-2019	1,620,431	26.9
II. Participation patterns by school year, anthropometric measurements registered					
School year				**n**	**%**
2015-2016	**2016-2017**	**2017-2018**	**2018-2019**		
	x	x	x	864,003	43.0
x		x	x	608,706	30.3
x	x	x		388,043	19.3
x	x		x	147,722	7.4
III. Distribution of anthropometric measurements by sociodemographic characteristic and national comparative					
a) Sex		**n = 2,008,474**		**SEP n = 14,137,862**	
		n	**%**	**n**	**%**
Male		1,018,296	50.7	7,199,504	50.9
Female		990,178	49.3	6,938,358	49.1
b) Anthropometric measurements by school grade		**n = 6,025,422**		**SEP n = 14,137,862**	
		n	**%**	**n**	**%**
First	(1st)	617,294	10.2	2,338,484	16.5
Second	(2nd)	831,098	13.8	2,376,958	16.8
Third	(3rd)	1,357,319	22.5	2,368,142	16.8
Fourth	(4th)	1,419,737	23.6	2,360,907	16.7
Fifth	(5th)	1,056,705	17.5	2,347,305	16.6
Sixth	(6th)	743,269	12.3	2,346,066	16.6
c) Geographic region		**n = 2,008,474**		**SEP n = 14,137,862**	
		n	**%**	**n**	**%**
Center		538,548	26.8	6,321,032	44.7
North		860,087	42.8	3,568,857	25.2
South		609,838	30.4	4,247,973	30.0

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Table I (Cont.). Description of patterns and frequency of evaluations by sociodemographic characteristics, descriptive statistics of the characteristics of the students, period 2015-2019

d) Type of school	n = 2,008,474		SEP n = 14,137,862	
	n	%	n	%
Public	1,762,969	87.8	11,885,628	84.1
Private	150,205	7.5	1,350,710	9.6
Indigenous and community	95,298	4.7	901,524	6.4

IV. Descriptive characteristics of the study population, intra and inter groups					
Variable	Mean	sd (overall)	sd (between)	sd (within)	Min-max
z-score (BMI/age)	0.49	1.40	1.23	0.67	(-5.0, 5.0)
Weight (kg)	31.7	10.2	8.9	4.9	(12.6, 106.3)
Height (cm)	131.7	11.2	9.4	6.1	(99.6, 181.3)
Age (years)	8.7	1.5	1.2	0.9	(6.0, 11.6)

SEP: Ministry of Public Education; BMI: body mass index; sd: standard deviation.

In addition, 87.8 % of the population attended public schools, 7.5 % privates and 4.7 % community or indigenous schools, which is representative of the National System of Public Education in Mexico.

The average age was 8.7 ± 1.5 years, with a variation of 1.2 years among individuals and 0.99 years for each student across the four school years. Weight varied between 12 and 106 kg, with a mean of 31.3 kg and variations between 8.9 y 4.9 kg among individuals and school years, respectively. The overall mean and SD observed in height measurements were 131.7 cm and 11.28 cm, respectively. The SD was 9.4 cm among school years and 6.1 cm among individuals (Table I, section IV). The z-scores for the BAZ indicator had a SD of ± 5; the overall mean was 0.49, with a SD of 1.4 and variations of 1.23 and 0.67 among individuals and school years, respectively (Table I, section IV).

TRANSITION PROBABILITIES OF OVERWEIGHT AND OBESITY

Table II shows Ow+Ob prevalences and its change estimation between the initial and final periods. Initial prevalence (ip) of overweight in the study group was 34.1 % and the final (fp) was 37.2 % (Table II, section Ia).

According to the study characteristics, the greater Ow+Ob prevalence was found in males when compared with females (Table II, section Ib) of 36.4 % in ip and 40 % in fp. The raise in the change percentage and change adjusted by sex showed the same order: 3.6 % in males and 2.5 % in females in change percentage and 10.0 % and 7.9 % in the adjusted percentage by gender.

By geographic region, the northern region presented the greater prevalence, with 35.8 % and 38.8 % for ip and fp, respectively (Table II, section Ic). The increases found in adjusted percentage of overweight and obesity were as follows in descendent order: south 11.9 %, center 10.2 %, and north 8.7 % (Table II, section IIc).

Regarding school modality, the greater prevalence was identified in private schools, being 40.6 % in ip and 43.9 % in fp (Table II, section Id).

ODDS RATIO (OR)

All estimates obtained from the model were statistically significant at the 99.99 % confidence level ($p < 0.001$) (Table III).

For students who underwent nutritional monitoring from 2015 to 2019, a positive OR of 2 % for developing Ow+Ob in 2017-2018 and of 6 % in 2018-2019 was observed. The progressive OR increase across the last two school years was estimated compared to the first year analyzed (2015-2016) (Table III, section a).

Students from the northern and southern regions had a higher OR for developing Ow+Ob than those in the central region, with scores of 58 % and 64 %, respectively (Table III, section b).

The evaluated populations in community and indigenous schools showed an OR that suggests a protective effect to develop Ow+Ob (OR = 0.54) for those that attend public schools, while the OR for private schools was 1.75 (Table III, section c).

About sex-age interaction, a directly proportional relation was identified between age and the OR increase to develop Ow+Ob; in females, the OR oscillated between 1.44 and 2.87 whereas in

Table II. Transition probabilities of overweight or obesity and percentage of change from 2015 to 2019, according to sociodemographic characteristics

Characteristics	I. Estimated prevalence of overweight and obesity				II. Percentage of change (%)	
	Initial (ip)		Final (fp)		General change	Change adjusted
	n	%	n	%		
a) Global	685,333	34.1	747,232	37.2	*3.1*	*9.0*
b) Sex						*1*
Male	370,188	36.4	407,093	40.0	*3.6*	*0.0*
Female	315,151	31.8	340,140	34.4	*2.5*	*7.9*
c) Geographic region						
Center	167,655	31.1	185,301	34.4	*3.3*	*10.5*
North	307,877	35.8	333,346	38.8	*3.0*	*8.3*
South	209,992	34.4	228,586	37.5	*3.0*	*8.9*
d) Type of school						
Public	603,565	34.2	225,611	37.4	*3.1*	*9.2*
Private	61,017	40.6	26,813	43.9	*3.3*	*8.2*
Indigenous and community	20,845	21.9	4,802	23.0	*1.2*	*5.3*

Table III. Logistic model with panel data and random effects, to estimate the relative risk of overweight or obesity

n = 6,025,422 Students = 2,008,474		
Category	Overweight and obesity	
	OR	95 % CI
a) School year (ref. 2015-2016)		
2016-2017	0.98*	(0.97, 0.99)
2017-2018	1.02*	(1.01, 1.03)
2018-2019	1.06*	(1.05, 1.08)
b) Region (ref. center)		
North	1.58*	(1.56, 1.61)
South	1.64*	(1.61, 1.66)
c) Type of school (ref. public)		
Private	1.75*	(1.68, 1.83)
Indigenous and community	0.54*	(0.51, 0.57)
d) Sex and age (ref. female, 6 years)		
6 years male	1.45*	(1.42, 1.48)
7 years female	1.44*	(1.41, 1.47)
7 years male	2.05*	(2.01, 2.09)
8 years female	2.08*	(2.04, 2.11)
8 years male	3.11*	(3.05, 3.18)
9 years female	2.62*	(2.57, 2.68)
9 years male	4.48*	(4.39, 4.58)
10 years female	2.89*	(2.83, 2.96)
10 years male	5.71*	(5.58, 5.85)
11 years female	2.87*	(2.80, 2.95)
11 years male	5.86*	(5.70, 6.02)

(Continues on next column)

Table III (Cont.). Logistic model with panel data and random effects, to estimate the relative risk of overweight or obesity

n = 6,025,422 Students = 2,008,474		
Category	Overweight and obesity	
	OR	95 % CI
e) Region and type of school (ref. public-center)		
North-private	0.86*	(0.82, 0.9)
North-indigenous and community	0.55*	(0.51, 0.6)
South-private	1.28*	(1.2, 1.36)
South-Indigenous and community	0.39*	(0.36, 0.42)
Cons.	0.065*	(0.065, 0.066)

**p < 0.001.*

boys it was between 1.45 and 5.86. In women, the OR fluctuated between 1.44 and 2.87, whereas in men such interval was between 1.45 and 5, suggesting that in men the OR increases more rapidly, related with the age mainly from the nine years onwards (Table III, section d). Section e) of table III shows the interaction between geographical region and school type. Students in private schools in the southern region were unique in showing a greater OR for developing Ow+Ob than those in public schools in the central region (OR = 1.28). In the schools of community and indigenous type from the southern region the OR is 2.56 times lower than in the public schools of the central region.

ADJUSTED RISK OF OVERWEIGHT AND OBESITY BY LOGISTIC REGRESSION

In boys as in girls, the adjusted Ow+Ob probability displayed a general increasing trend between 2015 and 2018 for all time periods and age groups, being greater and remarkably accelerated in 9-11 years old male population (Fig. 1). With the exception of the 2016-2017 school year (Fig. 1B) in which 9-year-old males had the lowest overall adjusted prevalences, the minimum adjusted prevalences were in the 2015-2016 school year for age and sex. Older age represented a major risk factor for developing Ow+Ob. We identified the period between nine and eleven years as the critical stage among school years, with this age span witnessing a marked and accelerated increase in Ow+Ob OR (Fig. 1). Lower figures and a slower increase rate for female than male students at all ages was observed.

Modality and geographic region analyses allow us to distinguish an ascending trend in the overweight and obesity development (Fig. 2), except for private schools from the southern region, which shown a greater OR in the 2015-2016 school year than in the following years.

DISCUSSION

Age and degree of obesity at the diagnose time are basic parameters to evaluate and predict this problem development and their associated comorbidities during childhood, adolescence and adulthood. An analysis of data from the four most recent school years has exposed that the obesity epidemic continues growing in Mexico. This is occurring even though it has been recognized as the principal health problem facing the country and that it was

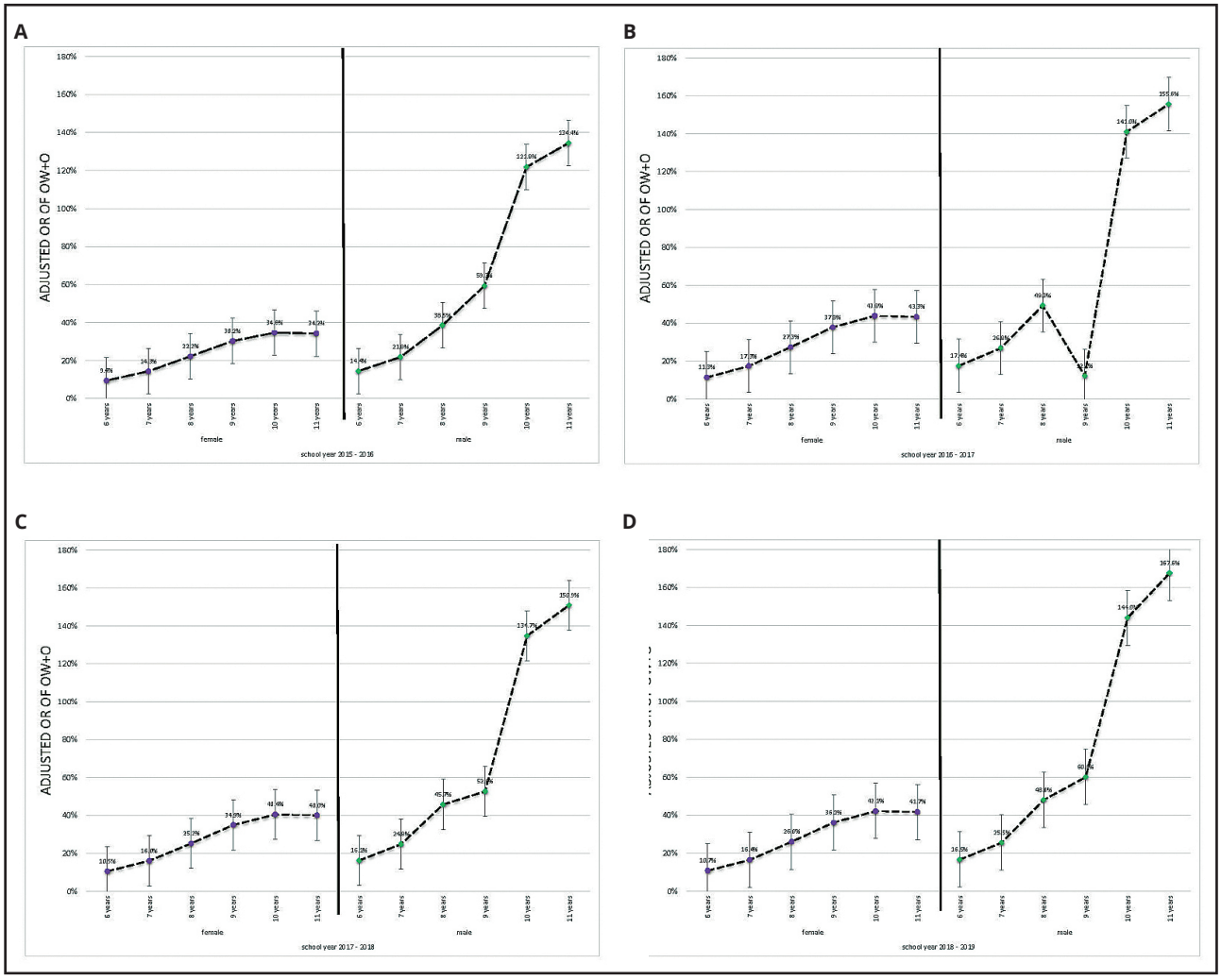

Figure 1.

A. Adjusted OR and CI of overweight or obesity by age and sex, school year 2015-2016. B. Adjusted OR and CI of overweight or obesity by age and sex, school year 2016-2017. C. Adjusted OR and CI of overweight or obesity by age and sex, school year 2017-2018. D. Adjusted OR and CI of overweight or obesity by age and sex, school year 2018-2019.

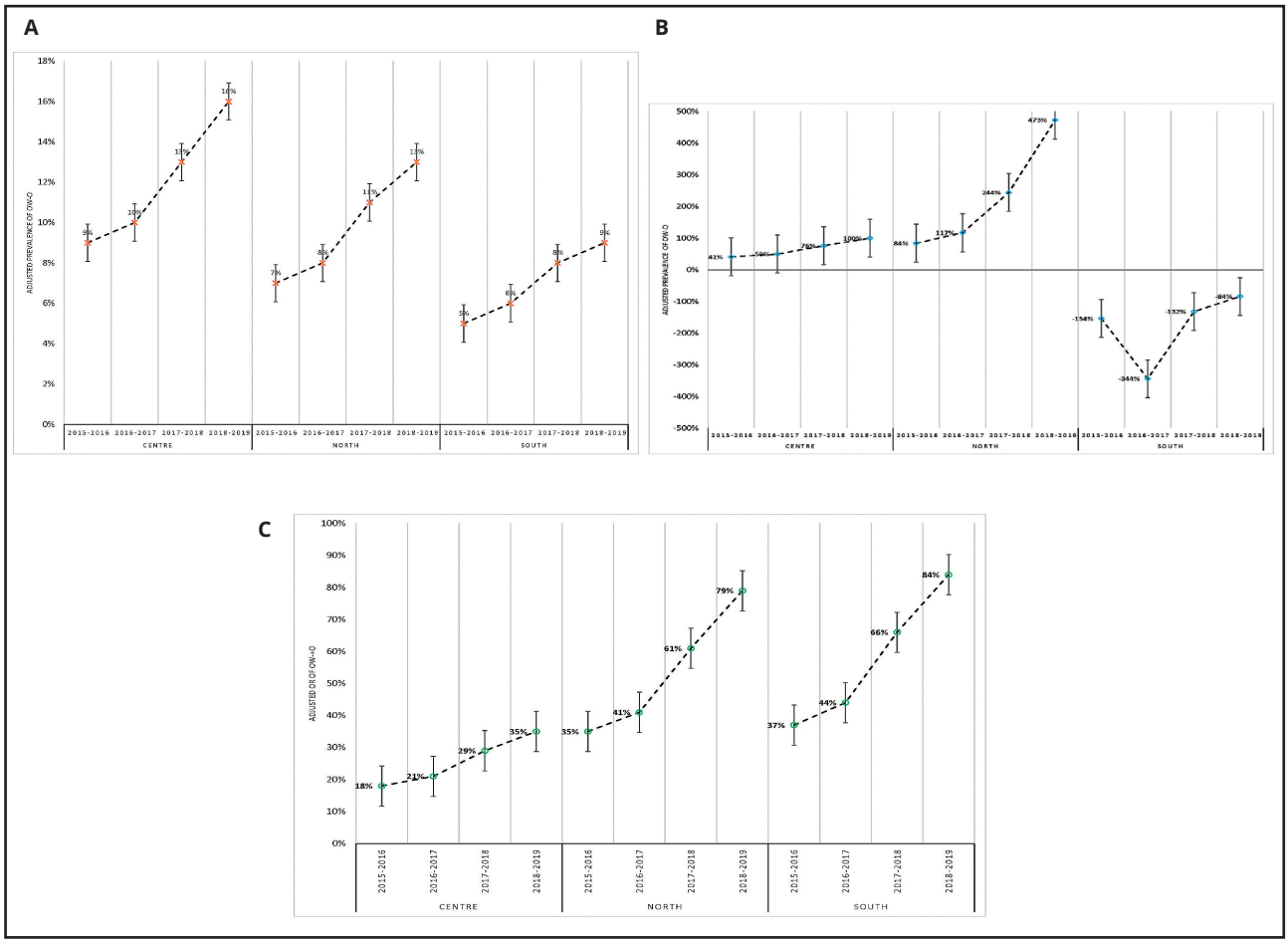

Figure 2.

A. Adjusted OR and CI of overweight or obesity by geographic region and school year, indigenous and community schools. B. Adjusted OR and CI of overweight or obesity by geographic region and school year, public schools. C. Adjusted OR and CI of overweight or obesity by geographic region and school year, private schools.

the subject of a national epidemiological emergency declaration in November 2016, and reaffirmed in February 2018 (25).

By age, the risk for developing Ow+Ob increases rapidly until age ten in females, when a slight decrease takes place, most likely associated with the arrival of puberty. Over the period studied, both male and female students increased their Ow+Ob prevalence at a national level; however, males did so starting from a higher initial level (36.4 *vs* 31.8) and increased at a more rapid rate (10.8 *vs* 7.9 %). These results are in line with those reported by researchers in longitudinal studies conducted in other countries such as the United States (2015) (26), China (2018) (27) and Brazil (2013) (28). Studies with follow-up panel in Europe involving 3,876 students from 18 schools between 2007 and 2010 found similar patterns (29). In Italy, a longitudinal study of 632 students of both sexes reported a constant increase in Ow+Ob, which was greater among males of all ages in the primary school years (30).

The results of the present study are in agreement with trend analyses and reviews that have been conducted about childhood obesity in Latin America and Mexico, and also with other studies in Mexican children about such problem and its relation with the main causes and factors (social, cultural, and intake of energetically dense food) involved in obesity development (14,31,32).

According to our analysis by geographical location, schools in the more economically developed northern region showed the highest prevalence of Ow+Ob and the greatest adjusted OR increase among the periods studied. The association between socioeconomic level and the prevalence of obesity among students has been widely documented over the past decades (33,34). However, this has begun to change in developing countries. Ow+Ob in the student population is now rising most markedly among the disadvantaged population and minority groups suffering high levels of social vulnerability (35,36). Likewise, in Mexico, the greatest increase in the prevalence of Ow+Ob has recently been documented among these groups (14,19).

Ow+Ob prevalences in the center and south of Mexico were lower than in the north; particularly for public and private schools, but all regions showed a similar tendency to increase. Students evaluated in private schools showed greater probability of suffering OW when compared with those of public schools.

Although a great heterogeneity is observed, it is not possible to establish a clear trend in adjusted relative probability of Ow+Ob during the study period. While the students from the northern region had an OR of 0.89, in the south this risk was 1.62. In contrast, this could indicate that in families and in the school environment with better socioeconomic conditions of the most developed regions, modifications that tend to control the Ow+Ob have been produced.

The substantial differences among different social groups in our longitudinal study, as well as those observed in other countries, highlight the existence of diverging patterns contributing to the obesity epidemic among the student population. These differences are rooted in the socioeconomic conditions of the groups. While greater economic capacity may initially result in a higher rate of students with obesity in wealthier families, a diversity of patterns was found, all of them beginning at an early age.

Given the generalized and progressive increase of Ow+Ob in the analyzed panel, the school environment represents a major contributor to this serious public health problem.

Based on evidence from our work and other studies on the subject (16,37,38), we can recommend school years as an appropriate time span for implementing effective interventions to reduce the risk of Ow+Ob. The ineffectiveness of current strategies in addressing or at least containing the obesity epidemic in Mexico and its serious consequences calls for reconsidering the current approach.

An understanding of the dynamics and different patterns generating this epidemic during the school years constitutes the technical basis for deciding what actions needs to be taken, how to gear them towards the appropriate population in a timely manner, and how to evaluate their effectiveness.

To account with epidemiologic intelligence systems, based on nutritional surveillance through the gathering of transversal and longitudinal data, allows the identification of changes in the growth. Particularly SIVNE and RNPT, with the evaluation of the population from the schools and a follow-up during a six-year-period, would be cost-effective in order to implement a public policy that could build a link between health and education sectors participations. Longitudinal follow-up of more than two million students across Mexico represents the principal strength of our study. This was achieved through the participation of 52 thousand schools and the recording of more than six million weight and height measurements. We based our estimates on a panel analysis, which allowed us to incorporate unobservable individual effects and offers a picture of the dynamics of change in Ow+Ob over time.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Epidemiología y dietética

Beliefs concerning non-nutritive sweeteners consumption in consumers, non-consumers, and health professionals: a comparative cross-sectional study

Creencias sobre el consumo de edulcorantes no nutritivos en consumidores, no consumidores y profesionales de la salud: estudio transversal comparativo

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Abstract

Introduction: the consumption of non-nutritive sweeteners (NNS) has increased. Recent studies have reported possible metabolic effects of NNS, and this may influence the perception regarding their consumption in the general population and health professionals.

Objective: to describe and compare the beliefs about NNS in consumers, non-consumers, and health professionals; and to explore the reasons and opinions of health professionals for recommending or not their consumption.

Methods: surveys were applied to 100 consumers, 100 non-consumers and 100 health professionals (dietitians and physicians) to evaluate a positive, negative, or neutral attitude towards certain beliefs regarding NNS, including the information they have, safety, price, side effects and taste. In addition, the opinion of health professionals for recommending or not the consumption of NNS and the related reasons was evaluated.

Results: statistically significant differences regarding the safety, side effects and taste of NNS were found between the three groups ($p < 0.01$). The most frequent opinion of health professionals (48 %) is that NNS should be limited, used as a transition and in certain patients. Consumers tend to have a more positive opinion about NNS except for the price, non-consumers have a more neutral position except for taste, and health professionals have a more negative perception of NNS in all aspects.

Conclusions: the beliefs regarding NNS differed among the studied groups, which might influence their consumption or recommendation of its use.

Keywords:

Non-nutritive sweeteners. Public opinion. Health personnel. Sweetening agents. Diabetes *mellitus*.

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Resumen

Introducción: el consumo de edulcorantes no nutritivos (ENN) se ha incrementado. Estudios recientes han reportado posibles efectos metabólicos de los ENN, por lo que la percepción de su consumo podría haber cambiado en población general y profesionales de la salud.

Objetivo: describir y comparar las creencias sobre los ENN en consumidores, no consumidores y profesionales de la salud, así como conocer las principales opiniones de los profesionales de la salud para recomendar o no el consumo de ENN.

Métodos: se aplicaron encuestas a 100 consumidores, 100 no consumidores y 100 profesionales de la salud (nutriólogos y médicos) para evaluar actitudes positivas, negativas o neutras en torno a ciertas creencias de los ENN, la información que creen tener, seguridad, precio, efectos secundarios y sabor. Además, se evaluó la opinión de los profesionales de la salud para recomendar o no su consumo y las razones asociadas.

Resultados: se encontraron diferencias entre los tres grupos en torno a la seguridad, los efectos secundarios y el sabor de los ENN ($p < 0.01$). La postura más frecuente de los profesionales de la salud (48 %) es que los ENN deben limitarse, utilizarse transitoriamente y en ciertos pacientes. Se observó una postura más positiva con respecto a los ENN en los consumidores excepto por su precio, más neutral en los no consumidores excepto por su sabor y más negativa en los profesionales de la salud en todos los aspectos.

Conclusiones: las creencias sobre los ENN difieren entre los grupos estudiados, lo cual puede influir en su consumo o en la recomendación de su uso.

Palabras clave:

Edulcorantes no nutritivos. Opinión pública. Personal de salud. Agentes endulzantes. Diabetes *mellitus.*

INTRODUCTION

The non-nutritive sweeteners (NNS) are a class of food additives that are used to sweeten foods and beverages without providing energy, including saccharin, aspartame, acesulfame potassium, sucralose, stevia, neotame, advantame, and monk fruit (1). The consumption of NNS has increased over time since today they are present in many products to reduce their calories and sugar content due to the global pandemic of obesity and diabetes (2,3). However, the use of these substances has been controversial because they have been linked to different effects on health, including an increase in insulin resistance and changes in gut microbiota and in appetite regulating hormones (4,5). The consumption of NNS has been evaluated around the world in different populations, including children, teenagers, adults, pregnant women and people living with diabetes (6-14). Nevertheless, little is known regarding the perception and beliefs that the population has regarding the NNS. In recent years, new scientific evidence has emerged reporting that some NNS such as sucralose and saccharin could promote insulin resistance by different pathways, suggesting that they are not metabolically inert (15-19). Thus, the perception of the population about the NNS may have changed recently and it is relevant to evaluate the opinion towards different aspects of NNS such as safety, taste, side effects, information, and price, discerning between consumers and non-consumers. Also, the perception of health professionals about the NNS could influence their patients' preference for using these substances. A qualitative study made in 75 dietitians of five different European countries described their perception and concerns about the use of NNS, concluding that there are four main approaches regarding the advice given about NNS: a) they should not be used; b) they are permissible only as a transitional product; c) client's informed preferences should determine its use; and d) they should be allowed or recommended (20). Therefore, the aim of this study is to describe and compare the beliefs concerning NNS consumption in consumers, non-consumers, and health professionals. In addition, a secondary objective was to identify the most common opinions of health professionals (dietitians and physicians) to recommend or not the use of NNS and the associated reasons.

MATERIAL AND METHODS

DESCRIPTION OF PARTICIPANTS AND ETHICS

The study was evaluated and approved by the ethics and research committees of the National Institute of Medical Sciences and Nutrition "Salvador Zubirán" in Mexico City (registration number 3282), and followed the principles established in the Declaration of Helsinki. All the participants received a full explanation of the study procedures and informed consent was obtained before enrollment. The selection criteria for each group were: a) consumers: people living with any type of diabetes, over 18 years old, who attended the nutrition consultation for the first time, and that reported a consumption of ≥ 3 products containing NNS in the last month; b) non-consumers: people without any diagnosed disease, over 18 years old, excluding health professionals, and that reported consumption of < 3 products containing NNS in the last month; and c) health professionals: registered dietitians or physicians who had no relationship with the researchers of this study. Exclusion criteria for all groups was inability to answer the questionnaire (e.g., illiteracy, mental health diseases, etc.) and elimination criteria was incomplete questionaries. The recruitment for the group of consumers was performed in the Diabetes Clinic of our institute; for the group of non-consumers, an invitation to participate in the study was made through social media, and relatives of patients and administrative personnel of our institute were also invited. Finally, for the group of health professionals, the participants were recruited through social media ads and in universities where registered dietitians and physicians were studying a postgraduate degree.

STUDY DESIGN

This is a comparative cross-sectional study. The participation of the volunteers included in the study consisted in one visit to collect general data (sex, age, education level, presence of diseases, profession, working information, etc.), to apply a questionnaire regarding the beliefs concerning NNS consumption, and a food frequency questionnaire (FFQ) of products containing NNS.

To evaluate the beliefs regarding NNS consumption, five questions were asked:

1. Do you think you have enough information about NNS?
2. Do you believe that the consumption of NNS is safe for your health?
3. Do you think that NNS are expensive?
4. Do you believe that the consumption of NNS causes discomfort such as headache, nausea, abdominal bloating and/or other?
5. Do you think that NNS have a pleasant taste?

Participants answered these items according to a Likert rating scale, which is used to evaluate a positive, negative, or neutral attitude to an idea, considering the following options: a) agree; b) neither agree nor disagree; and c) disagree. The FFQ to evaluate NNS consumption consisted in asking the regularity of consumption (daily, weekly, or monthly) of eight different categories of products (sugar substitute sachets, beverages, dairy, gelatins, gums and mints, water flavoring enhancers powders, cereals, and desserts) according to a questionnaire previously elaborated by our group including products in the Mexican market. This instrument has face validity and a good reliability, with an intraclass correlation coefficient (ICC) of 0.94 (95 % CI: 0.88-0.97, $p < 0.001$) for the inter-subject concordance and with an ICC of 0.82 (95 % CI: 0.56-0.93, $p < 0.001$) for the intra-subject test-retest reliability (8). In addition, health professionals were questioned about their opinion for recommending the use of NNS in four different approaches according to the study described in the introduction. Also, the main reasons for recommending or not recommending NNS consumption were asked in the health professional's group and if their perception of NNS has changed in recent years.

STATISTICAL ANALYSIS

Variables distribution was evaluated with the Kolmogorov-Smirnov normality test for each group and they are presented as means ± standard deviations or as medians (interquartile range), as appropriate. Qualitative variables are described as frequencies and percentages. Differences in the proportions of the answers in the questions of the beliefs between groups were evaluated with the Chi-squared test for trend. Data were collected and analyzed using IBM SPSS Statistics version 25.0 software and a p value < 0.05 was considered as significant.

RESULTS

The general characteristics of the participants in the three groups are shown in table I. The proportion of women was higher in the three groups, being 52 %, 63 % and 72 % in the groups of consumers, non-consumers and health professionals, respectively. The consumers group showed higher age, with a mean of 52.1 ± 14.2; and the group of non-consumers was the youngest, with a mean age of 25.5 ± 5.6. Half of the health professionals were dietitians and half physicians. In addition, type 2 diabetes *mellitus* was the most common type (71 %) in the consumers' group.

Table I. General characteristics of the participants by group (consumers, non-consumers and health professionals)

	Consumers (n = 100)	Non-consumers (n = 100)	Health professionals (n = 100)
Female sex, n (%)	52 (52)	63 (63)	72 (72)
Age (y)	52.1 ± 14.2	25.5 ± 5.6	29.9 ± 6.1
Products containing NNS consumed in the last month	5 (4-6)	1 (0-2)	3.5 (1-6)
Type of diabetes, n (%)			
T1DM	23 (23)	---	---
T2DM	71 (71)	---	---
Other	6 (6)	---	---
Profession, n (%)			
Dietitian	---	---	50 (50)
Physician	---	---	50 (50)
Education level, n (%)			
None	2 (2)	---	---
Elementary school	11 (11)	---	---
Middle school	15 (15)	4 (4)	---
High school	19 (19)	21 (21)	---
Bachelor's degree	50 (50)	61 (61)	78 (78)
Postgraduate degree	3 (3)	14 (14)	22 (22)

NNS: non-nutritive sweeteners; T1DM: type 1 diabetes mellitus; *T2DM: type 2 diabetes* mellitus. *Values are means ± standard deviations, medians (interquartile ranges) or frequencies (percentages).*

Among the main characteristics of the group of health professionals described in table II, most of the participants did not have postgraduate studies (78 %). Sixty-five health professionals had only one job and 14 % were unemployed. A significant proportion of the health professionals worked in private practice (49 %) or in a public health institution (39 %), and the most common work field was clinical (77 %).

The frequency of consumption of the different categories of products containing NNS is described in table III, finding that the most common categories consumed in the consumers group were beverages (80 %), sugar substitute sachets (77 %) and gelatins (61 %). In the non-consumers group, 24 % of the participants did not consume any product and the most common category of products consumed was gums and mints (41 %). The prevalence of NNS consumption in the health professionals group was 76 % and the most common categories consumed were beverages (53 %), sugar substitute sachets (53 %), gums and mints (51 %) and desserts (50 %).

In the evaluation of the beliefs concerning NNS consumption, showed in table IV, no significant difference was found between groups regarding the information they think they have about NNS ($p = 0.53$). However, a higher proportion of consumers (46 %) believed having enough information in contrast with the proportion of health professionals (36 %). The questions related to safety, side effects and taste showed significant differences between groups ($p < 0.01$), observing that most consumers (54 %) agreed that NNS are safe for health compared to health professionals, where the majority (48 %) disagreed with this idea. Seventy-three consumers disagreed that NNS cause side effects such as headache, nausea, abdominal bloating and/or others, while 51 % of health professionals agreed and 40 % of the non-consumers neither agreed nor disagreed regarding this belief. Most of the consumers agreed that NNS have a pleasant taste (62 %), in comparison with 52 % of the non-consumers and 42 % of the health professionals, who disagreed with this idea. Finally, no differences were found between groups regarding the idea that NNS are expensive ($p = 0.93$), observing that 61 % of the consumers and 55 % of the health professionals agreed, while 43 % of the non-consumers neither agreed nor agreed.

Table V shows the different opinions concerning the use and recommendation of NNS in the health professionals group. Forty-eight health professionals agreed that NNS should be limited, used only as a transition and in certain patients, while the least common opinion (7 %) was that NNS can be recommended or at least allowed. The main reasons for recommending the use of NNS were replacement of carbohydrates or sugars (46 %), glyce-

Table II. Description of the working characteristics in the group of health professionals

	n = 100
Postgraduate degree, n (%)	
None	78 (78)
Specialist degree	11 (11)
Master's degree	10 (10)
Doctor's degree	1 (1)
Professional experience (y)	4 (2-7)
Number of jobs, n (%)	
Not currently working	14 (14)
One	65 (65)
Two	20 (20)
Three	1 (1)
Workplace, n (%)	
Public health institution	39 (39)
Private health institution	9 (9)
Private practice	49 (49)
Academic institution	7 (7)
Other	5 (5)
Work field, n (%)	
Clinical	77 (77)
Research	3 (3)
Education	10 (10)
Industry	2 (2)
Administrative	8 (8)
Other	3 (3)

Values are medians (interquartile ranges) or frequencies (percentages).

Table III. Frequency of consumption of the different categories of products with NNS by group (consumers, non-consumers and health professionals)

Category	Consumers (n = 100)	Non-consumers (n = 100)	Health professionals (n = 100)
Sugar substitute sachets	77 (77)	17 (17)	53 (53)
Beverages	80 (80)	24 (24)	53 (53)
Dairy	50 (50)	15 (15)	47 (47)
Gelatins	61 (61)	1 (1)	43 (43)
Gums and mints	54 (54)	41 (41)	51 (51)
Water flavoring enhancers powder	23 (23)	5 (5)	24 (24)
Cereals	39 (39)	4 (4)	43 (43)
Desserts	41 (41)	3 (3)	50 (50)

NNS: non-nutritive sweeteners. Data are presented as frequencies and percentages.

Table IV. Description and comparison of the beliefs concerning NNS consumption by group (consumers, non-consumers and health professionals)

Belief	Consumers (n = 100)	Non-consumers (n = 100)	Health professionals (n = 100)	p*
Information†, n (%)				
Agree	46 (46)	42 (42)	36 (36)	
Neither agree nor disagree	6 (6)	16 (16)	34 (34)	0.53
Disagree	48 (48)	42 (42)	30 (30)	
Safety‡, n (%)				
Agree	54 (54)	20 (20)	21 (21)	
Neither agree nor disagree	24 (24)	48 (48)	31 (31)	< 0.01
Disagree	22 (22)	32 (32)	48 (48)	
Price§, n (%)				
Agree	61 (61)	37 (37)	55 (55)	
Neither agree nor disagree	13 (13)	43 (43)	26 (26)	0.93
Disagree	26 (26)	20 (20)	19 (19)	
Side effects¶, n (%)				
Agree	13 (13)	24 (24)	51 (51)	
Neither agree nor disagree	14 (14)	40 (40)	24 (24)	< 0.01
Disagree	73 (73)	36 (36)	25 (25)	
Taste‖, n (%)				
Agree	62 (62)	27 (27)	31 (31)	
Neither agree nor disagree	25 (25)	21 (21)	27 (27)	< 0.01
Disagree	13 (13)	52 (52)	42 (42)	

*NNS: non-nutritive sweeteners. Data are presented as frequencies and percentages. *Differences were evaluated with Chi-squared test for trend. †Question 1: Do you think you have enough information about the NNS? ‡Question 2: Do you believe that the consumption of NNS is safe for your health? §Question 3: Do you think that the NNS are expensive? ¶Question 4: Do you believe that the consumption of NNS causes discomforts such as headache, nausea, abdominal bloating and/or others? ‖Question 5: Do you think that the NNS have a pleasant taste?*

mic and/or lipid control (31 %) and weight loss (27 %), while the main reasons for not recommending the use of NNS were that they are not a healthy habit (36 %), encourage the preference for sweet taste (30 %) and are harmful to health (22 %). Seventy-seven health professionals agreed that their perception regarding the use and recommendation of NNS changed in recent years, while only 8 % disagreed and 15 % neither agreed nor disagreed. No significant differences were found in the opinion about the use of NNS and the reasons for recommending or not the use of NNS between dieticians and physicians or between consumers and non-consumers of the group of health professionals.

Table V. Opinions concerning the use and recommendation of NNS in the group of health professionals

	n = 100
Opinion about the use of NNS	
They should not be used; the natural flavor of food is preferable	16 (16)
They should be limited, used only as a transition and in certain patients	48 (48)
The decision of consumption must be made by the patient in an informed way	29 (29)
They can be recommended or at least allowed	7 (7)
Reasons for recommending NNS	
Replacement of carbohydrates or sugars	46 (46)
Reduction of caloric intake	13 (13)
Weight loss	27 (27)
Glycemic and/or lipid control	31 (31)
Cavities prevention	3 (3)
Reasons for not recommending NNS	
They are harmful to health	22 (22)
They encourage the preference for sweet taste	30 (30)
It is not a healthy habit	36 (36)
They can stimulate appetite	16 (16)

NNS: non-nutritive sweeteners. Data are presented as frequencies and percentages.

DISCUSSION

The consumption of NNS has increased worldwide, especially in adults, but still the knowledge about NNS among the population is low (3,21). A study conducted in 741 Irish adults showed that 73.5 % of the participants knew NNS, however, they were able to identify on average only two of all the NNS approved for use in Europe and 89.2 % reported being unaware of the acceptable daily intake (ADI) of NNS (22). Interestingly, in our study, health professionals had the lowest proportion that answered

having enough information about NSS. It is important that both dietitians and physicians are well informed about NNS, since their recommendation regarding these products will influence the consumption of the population. A study in Mexican patients with diabetes reported that 53.3 % of the participants consumed NNS based on the recommendation of a relative, friend or by their own decision, which means that the opinion of a health professional is not always taken into consideration (8).

Both consumers and health professionals showed a high prevalence of consumption of different categories of products with NNS (at least four categories in each group were consumed in ≥ 50 % of the participants); however, it has been mentioned in the literature that Mexico has a higher percentage of packaged products with NNS compared to other countries like the United States, New Zealand and Australia (23).

Regarding the safety of NNS, most of the consumers (54 %) agreed that the consumption of NNS was safe in comparison to the health professionals group, where 48 % disagreed with this idea. A study conducted in Italian adolescents showed that 24.5 % of the participants stated that a frequent consumption of tabletop sweeteners could be very dangerous for health, similarly to white sugar (25.5 %). Only 9.1 % considered that the consumption of tabletop sweeteners does not cause health damage at all, in comparison to other sweeteners like honey (34.5 %) and brown sugar (22.7 %). In the same study, 14.5 % of the participants though that sugar-free drinks can cause a lot of damage to health and 17.3 % that these beverages are not harmful at all (24). A recent study in Canadian adults reported that most of the participants perceived the high-fructose corn syrup and aspartame as less healthy than table sugar (63.9 % and 52.4 %, respectively), while raw sugar was considered to be healthier than table sugar by 47.8 % of the population (25).

In reference to the other beliefs, the consumers were more prone to consider that NNS do not cause side effects and have a pleasant taste; however, the majority considered that they are expensive. The non-consumers were more neutral in their answers, except that this group disagreed that NNS taste pleasant, which may be one of the main reasons why they avoid these products. The health professionals revealed a tendency to have a more negative attitude towards NNS, since most agreed that NNS cause side effects and are expensive, while disagreed that they are tasty. A recently published study conducted in UK adult population showed that the main reasons for consuming NNS were that they are healthier than sugars, are low in calories, satisfy sweet cravings or simply are ingredients in foods and products that the population consumed; nevertheless, 44.9 % of the participants neither agreed nor disagreed that NNS are tasty (26).

The previously mentioned study in Mexican patients with diabetes reported that the consumption of NNS correlated with the belief that they are safe for health, do not cause discomfort and have a pleasant taste ($p < 0.01$) (8). The study conducted in Italian adolescents concluded that most of participants strongly disagreed that eating sugar-free products caused them to spend more, to have stomachache or to eat worse tasting products (24). We can conclude that consumers have a more positive opinion about NNS, although there are differences in the perception of the products price that could depend mainly on the socioeconomic level.

Finally, the main approach (48 %) for the use and recommendation of NNS in the health professionals was that NNS should be limited, used only as a transition and in certain patients. Lowest proportions of health professionals recommended (7 %) or not recommended (16 %) NNS. This is in agreement with the current position of the American Diabetes Association (ADA) guidelines, where it is established that beverages sweetened with NNS may serve as a short-term replacement strategy but health professionals should promote a lower consumption of both caloric and non-caloric sweeteners, preferring the natural flavor of food (27). The main reasons for recommending the use of NNS observed in our study were replacement of carbohydrates or sugars, glycemic and/or lipid control and weight loss; while the main reasons for not recommending the use of NNS were that they are not a healthy habit, encourage the preference for sweet taste and are harmful to health. The study carried out in an Irish population mentioned that 34.3 % of the participants opined that NNS should not be used, 20.9 % considered that NNS should be used and 44.8 % declared no opinion regarding this (22). Also, the qualitative study in European dietitians noted that there is a lack of reliable and consistent information sources regarding NNS, that there is uncertainty surrounding sweeteners and how to use them in dietetic practice, and that health professionals worry about their safety (20).

The limitations of the study include the sample size and that other beliefs and perceptions regarding the use of NNS could also be explored, such as which are considered to be the safest or the most harmful, in which life stages is safer to consume them or to analyze the association of NNS consumption with diet quality and other sociodemographic variables. However, this is a motivation to make a bigger study in general population with a higher number of participants and including other interesting outcomes to evaluate the current perceptions of the NNS at different ages, socioeconomic levels, schooling, health status, etc. This topic is relevant due to the fact that apparently the population perceive the healthiest sweeteners based on a natural origin rather than on energy content or associated metabolic effects (25). Nowadays, it has been reported that some NNS like sucralose may not be inert and potentially could cause certain negative health effects (28).

The strength of the study is that this information has not been reported in the Mexican population and that the approaches of health professionals towards the use and recommendation of NNS have been barely explored. Also, it is important to recognize the differences between the beliefs of consumers, non-consumers, and health professionals to understand the main reasons for consuming/recommending them and to identify the principal needs to empower consumers to make informed decisions, as well as that health professionals have sufficient and reliable information to correctly guide the population.

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Trabajo Original

Otros

Efectos de la ingesta de una bebida energética rica en miel sobre glucosa, insulina, triglicéridos y proteínas totales en jóvenes sanos

Effects of honey-rich energy drink intake on glucose, insulin, triglycerides and total protein in healthy young people

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Resumen

Introducción: las bebidas energéticas han ganado protagonismo en diferentes grupos poblacionales.

Objetivo: el objetivo de esta investigación fue estudiar el efecto de la ingesta de una bebida energética rica en miel (BeeBad EnegyDrink®, Parodi Group, Italia) y una bebida energética popular con azúcares libres sobre la insulina, la glucemia, las proteínas totales y los triglicéridos.

Material y métodos: quince estudiantes varones participaron en el estudio (20,85 ± 2,67 años). Se realizaron dos evaluaciones separadas en tres días. Se obtuvieron muestras sanguíneas antes de ingerir la bebida energética en estado de ayuno, 30 minutos, 60 minutos y 120 minutos después de ingerir las bebidas energéticas. El primer día, los participantes ingirieron la bebida energética rica en miel (BeeBad EnegyDrink®, Parodi Group, Italia) mientras que el segundo día los participantes ingirieron la bebida energética con azucares libres.

Resultados: hubo diferencias significativas en glucosa e insulina a lo largo del tiempo ($p < 0,01$). Respecto a las diferencias entre bebidas energéticas, hubo diferencias en los valores de insulina, que fueron menores después de tomar la bebida energética rica en miel ($p < 0,05$). Además, el incremento de la glucosa e insulina a los 30 minutos fue menor tras ingerir la bebida energética rica en miel.

Conclusiones: la ingesta de bebidas energéticas rica en miel produce menores elevaciones de insulina y glucosa en comparación con una bebida energética popular con azúcar libre en sujetos sanos. Atendiendo a los resultados, las bebidas energéticas ricas en miel podrían ser una alternativa a las bebidas energéticas convencionales.

Palabras clave:

Miel. Fructosa. Bebida energética. Glucosa. Insulina.

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Abstract

Introduction: energy drinks have become more popular in different population groups.

Aims: the research aimed to study the effect of the intake of a honey-rich energy drink (BeeBad EnegyDrink®, Parodi Group, Italy) and a popular energy drink with free sugars on insulin, glycemia, total protein and triglycerides.

Material and methods: fifteen male students participated in the study (20.85 ± 2.67 years). Two separate evaluations were performed on three days. Blood samples were obtained before ingesting the energy drink in a fasting state, 30 minutes, 60 minutes and 120 minutes after ingesting the drinks. On the first day participants ingested the honey-rich energy drink (BeeBad EnegyDrink®, Parodi Group, Italy) while on the second day participants ingested the energy drink with free sugars.

Results: there were significant differences in glucose and insulin over time ($p < 0.01$). Regarding the differences between energy drinks, there were differences in insulin values, being lower after taking the honey-rich energy drink ($p < 0.05$). In addition, the increase in glucose and insulin at 30 minutes was lower after ingesting the honey-rich energy drink.

Conclusions: ingestion of honey-rich energy drink produces lower elevations of insulin and glucose compared to a popular energy drink with free sugar in healthy subjects. Based on the results, honey-rich energy drinks could be an alternative to conventional energy drinks.

Keywords:

Honey. Fructose. Energy drink. Glucose. Insulin.

INTRODUCCIÓN

Los carbohidratos (CHO) son esenciales para la práctica deportiva. La depleción del glucógeno puede conducir a hipoglucemia y, por ende, a una disminución del rendimiento (1). Las pruebas de numerosos estudios indican que la alimentación con CHO durante el ejercicio de unos 45 minutos o más puede mejorar la capacidad de resistencia y el rendimiento (2). Los mecanismos por los que la alimentación con CHO antes y durante el ejercicio mejora el rendimiento incluyen el mantenimiento de los niveles de glucosa en sangre, el mantenimiento de niveles elevados de oxidación de CHO y el ahorro de glucógeno hepático y, posiblemente, muscular esquelético (3). Por ello, es común realizar una ingesta previa y durante el ejercicio para evitar la depleción de glucógeno, especialmente en deportes intermitentes o de larga duración (4). No obstante, una carga previa y durante el ejercicio con comida rica en CHO puede resultar poco digestiva, causando malestar intestinal durante la actividad física. Los atletas suelen tomar bebidas con un 6-8 % de CHO, lo que favorece la digestión y el vaciado gástrico (5). Además, la ingesta en bebida de reposición ayuda a la rehidratación. En este aspecto, las bebidas energéticas (BE) suelen postularse como una de las opciones para los atletas (6).

Las BE aparecieron por primera vez en Europa y Asia en la década de los 60. Este tipo de bebida ha ganado especial protagonismo, como demuestra su consumo por parte de diversos grupos demográficos, como jóvenes, trabajadores, estudiantes, deportistas profesionales y deportistas aficionados (7). Las BE suelen contener cafeína y taurina, lo que potencia el rendimiento físico (8). Otro ingrediente común en la mayoría de las BE es algún tipo de fuente de CHO (glucosa, sacarosa o maltodextrina), importantes para la reposición de glucógeno. La prevalencia del consumo de BE entre los atletas es limitada y varía entre los estudios. Un análisis transversal de los datos de una encuesta en un estudio de cohorte de 2.287 adultos jóvenes demostró que los hombres que dedicaban más tiempo a la actividad física tenían un mayor consumo de BE (9). En atletas jóvenes, Petróczi y cols. (6) mostraron que el 41,7 % de la población examinada consumía BE, las cuales constituían el suplemento elegido con mayor frecuencia.

Un aspecto importante a tener en cuenta en las bebidas deportivas es su composición. Este tipo de bebidas suelen contener principalmente CHO simples, como glucosa y sacarosa. Los CHO simples presentan un índice glucémico (IG) elevado, lo que afecta al estado posprandial. Es conocido que los CHO con alto IG producen un llenado más rápido de los depósitos de glucógeno y un incremento brusco de los niveles de insulina, impidiendo la lipólisis (10). Este hecho podría conducir a una hipoglucemia y producir un efecto rebote (10). Estudios previos han relacionado la hiperinsulinemia con un mayor riesgo de eventos cardiovasculares (11). Se sabe que los niveles elevados crónicos de glucosa e insulina en sangre también pueden desencadenar la formación de productos finales de glicación avanzada, causando estrés oxidativo (12). Por otro lado, otros estudios han analizado la influencia de CHO con menor IG como la fructosa. Numerosos trabajos han reportado la mejora del rendimiento de larga duración tras la ingesta de CHO de bajo IG en comparación con CHO de alto IG (13-15). El consumo de CHO de bajo índice permitiría una mayor lipólisis y oxidación de grasas debido a un menor incremento de la insulina, preservando así el depósito de glucógeno (16). Sin embargo, la reposición del glucógeno es más lenta (10). Un estudio reciente observó que la ingesta de una barra de nutrición deportiva a base de lentejas de bajo IG proporcionaba un beneficio metabólico (menor tasa de oxidación de carbohidratos) y una modesta mejora en la carrera de agilidad y en la altura de salto al final de la prueba (17).

Las proteínas son combinaciones de aminoácidos que actúan como elementos estructurales o de transporte. En el plasma, las proteínas contribuyen principalmente a mantener el volumen del fluido circulante y al transporte. El estudio de las proteínas totales es importante para evaluar el estado nutricional (18). Un estudio previo mostró que, tras la ingesta de cuatro huevos, los valores de proteínas totales ascendieron durante las siguientes tres horas (19).

Se ha sugerido que la miel, debido a su alto contenido en CHO, puede ser una fuente de energía adecuada para atletas o aficionados (20). La miel puede desempeñar dicho papel debido a su composición (38,5 % de fructosa, 31,0 % de glucosa, 17,1 % de agua, 7,2 % de maltosa, 4,2 % de trisacáridos/otros hidratos de carbono, 1,5 % de sacarosa y 0,5 % de proteí-

nas) (21). Sin embargo, no existe demasiada evidencia científica sobre la cuestión. Un estudio reciente indicó la necesidad de investigar los posibles escenarios de los efectos de la miel (22). Debido a los componentes de la miel, la respuesta posprandial podría ser diferente en comparación con el azúcar libre característico de las bebidas deportivas o BE convencionales. Así, sería interesante investigar el comportamiento de la glucemia y la insulina tras su ingesta en un periodo de dos horas posteriores. Por ello, el objetivo de esta investigación fue estudiar el efecto de la ingesta de una BE rica en miel (fructosa y glucosa, principalmente; BeeBad EnegyDrink®, Parodi Group, Italia) y una BE popular con azúcares libres de alto IG (sacarosa y glucosa) sobre la insulina, la glucemia, las proteínas totales y los triglicéridos.

MATERIAL Y MÉTODOS

PARTICIPANTES

Quince sujetos varones participaron en el presente estudio (Tabla I). Todos los participantes eran estudiantes universitarios del Grado de Ciencias del Deporte y vivían en la ciudad de Cáceres (Extremadura). Los participantes fueron informados del propósito del estudio y firmaron un consentimiento informado. El protocolo fue revisado por el Comité de Bioética de la Universidad de Extremadura siguiendo las directrices de la declaración ética de Helsinki, actualizada en Fortaleza (2013), para la investigación en humanos (código: 31/2020). Un código fue asignado a cada participante para el tratamiento y la recolección de muestras con el objetivo de mantener el anonimato.

Para la participación en el estudio, los sujetos debían cumplir los siguientes requisitos: ser hombre, no tener trastornos metabólicos como diabetes y obesidad, no tomar medicaciones, permanecer en estado de ayuno al menos ocho horas el día de la extracción sanguínea y no tomar frecuentemente BE y cafeína.

Se indicó a todos los participantes que evitaran cualquier tipo de ejercicio extenuante y que se abstuvieran de consumir cafeína y alcohol durante los dos días previos a la extracción. No se permitió comida o bebida después de las 21:00 h del día anterior (Tabla I).

DISEÑO DEL ESTUDIO

En el presente estudio experimental se utilizaron dos tipos de BE de similar composición (Tabla II). En cada evaluación, separadas en tres días, todos los sujetos ingirieron un envase completo de cada bebida. Durante las evaluaciones se obtuvieron muestras sanguíneas antes de ingerir la bebida en estado de ayuno (inicial), 30 minutos, 60 minutos y 120 minutos después de ingerir las bebidas. El primer día, los participantes ingirieron una BE rica en miel (BEM) (BeeBad EnegyDrink®, Parodi Group, Italia) mientras que, el segundo día, los participantes ingirieron una BE popular con azúcares libres (BEA). Ambos envases tenían el mismo aspecto con el fin de evitar interpretaciones de los sujetos. La cantidad ingerida de cada bebida fue de 250 ml. Los ingredientes de la BEM eran: agua carbonatada, miel (13,8 %), acidificante, ácido cítrico, aromas naturales, jalea real (0,01 %), propóleos (0,01 %), extracto de *ginseng* (0,01 %), extracto de maca (0,01 %) y vitaminas (niacina, ácido pantoténico, vitamina B6, vitamina B12). Los ingredientes de la BEA eran: agua, sacarosa, glucosa, acidulante (ácido cítrico), dióxido de carbono, taurina (0,4 %), correctores de acidez (carbonatos de sodio, carbonatos de magnesio), vitaminas (niacina, ácido pantoténico, vitamina B6, vitamina B12), aromas y colorantes (caramelo natural, riboflavinas) (Tabla II).

Tabla I. Características de la muestra

	Día 1	Día 2
Edad (años)	20,85 ± 2,67	
Altura (m)	1,74 ± 0,06	
Peso (kg)	72,32 ± 7,90	73,10 ± 7,12
IMC	23,74 ± 2,28	23,96 ± 2,05
Grasa (kg)	11,51 ± 3,87	12,14 ± 3,32
Grasa (%)	15,88 ± 5,14	16,39 ± 3,17
Masa libre de grasa (%)	60,82 ± 7,20	59,45 ± 8,61
Masa libre de grasa (kg)	84,11 ± 5,16	83,18 ± 6,42

IMC: índice de masa corporal.

Tabla II. Composición de las BE por 100 ml

	BEA	BEM
Energía (kj)	45	45
Grasas (g)	0	0
Grasas saturadas (g)	0	0
Carbohidratos (g)	11	11
Azúcar (g)	11	11
Proteínas (g)	0	0
Sal (g)	0,04	0
Cafeína (mg)	32	32

BEM: bebida energética con miel; BEA: bebida energética con azúcar libre.

ANTROPOMETRÍA Y COMPOSICIÓN CORPORAL

Las medidas antropométricas y de composición corporal se realizaron por la mañana en ayunas con la menor ropa posible y siempre a la misma hora. Todas las valoraciones se realizaron antes de las extracciones sanguíneas. La altura corporal fue medida con un tallímetro (Seca 220). El peso corporal, la masa grasa y la masa libre de grasa fueron evaluadas mediante bioimpedancia eléctrica utilizando un analizador BF-350 (Tanita Corp., Japón).

EXTRACCIÓN SANGUÍNEA

Las extracciones sanguíneas se realizaron siempre a la misma hora para limitar el impacto de los ritmos circadianos. La primera muestra se extraía a las 8:30 h a.m. Se obtuvieron 10 ml de sangre venosa antecubital de cada participante en cada extracción utilizando una jeringa de plástico con una aguja de acero inoxidable. Se obtuvieron muestras de sangre venosa utilizando ácido etilendiaminotetraacético (EDTA) como anticoagulante. La sangre se centrifugó inmediatamente a 3.000 r.p.m. durante diez minutos (P-selecta®, Meditronic). La muestra de sangre se recogió en un tubo de polipropileno. Luego, la muestra de sangre se centrifugó a 3.000 r.p.m. durante 15 minutos a temperatura ambiente para obtener plasma. El plasma se colocó en tubos estériles y se almacenó a -80 °C hasta su uso.

DETERMINACIÓN DE GLUCOSA, INSULINA, TRIGLICÉRIDOS Y PROTEÍNAS TOTALES

La glucosa, los triglicéridos y las proteínas totales fueron determinados mediante espectrofotometría (Coulter Electronics LTD, Model CPA; Northwell Drive, Luton, Reino Unido). La insulina fue determinada mediante ensayo por inmunoabsorción ligado a enzimas (ELISA) con un ER-500 (Sinnowa, Alemania). Todas las mediciones fueron realizadas por el mismo técnico e instrumento.

ANÁLISIS ESTADÍSTICO

El análisis estadístico se realizó con el *software* IBM SPSS Statistics versión 21.0 (IBM Co., Armonk, NY, Estados Unidos). Los resultados se expresan como media y desviación estándar. Se estudió la normalidad de las variables a través del test de Shapiro-Wilk. Los datos se analizaron mediante el análisis de varianza (ANOVA) de dos factores (tiempo y bebida). Se utilizó eta cuadrado parcial (η^2) como medida del tamaño del efecto de ANOVA. Los rangos para evaluar las magnitudes fueron $\eta^2 \geq 0{,}01$, $\eta^2 \geq 0{,}06$ y $\eta^2 \geq 0{,}14$ para pequeñas, medianas y grandes, respectivamente. Se consideró estadísticamente significativa una $p \leq 0{,}05$. Se realizó la prueba post-hoc Bonferroni para conocer las diferencias en el tiempo.

RESULTADOS

A continuación, se representan los resultados obtenidos en el presente estudio. En la tabla III se muestran las diferencias entre BE en glucosa, insulina, proteínas totales y triglicéridos a lo largo de las extracciones. Se observaron diferencias significativas entre BE en insulina ($p < 0{,}05$). En cuanto al efecto del tiempo, se apreciaron diferencias significativas en glucosa e insulina ($p < 0{,}01$). Concretamente, hubo diferencias muy significativas entres los valores en 30 minutos y el resto de mediciones en cuanto a la glucosa ($p < 0{,}01$), así como entre inicial y 60 minutos en insulina ($p < 0{,}01$). No se observaron diferencias en la interacción grupo x tiempo.

En la figura 1 se muestra que los porcentajes de incrementos en los 30 minutos de glucosa e insulina son más elevados en BEA en comparación con BEM.

Tabla III. Diferencias entre bebidas en la evolución a lo largo del tiempo de glucosa, insulina, proteínas y triglicéridos

		Inicial (IC 95 %)	30 minutos (IC 95 %)	60 minutos (IC 95 %)	120 minutos (IC 95 %)	Efecto grupo	η^2	Efecto tiempo	η^2	Grupo x tiempo	η^2
Glucosa (mg/dl)	BEM	80,87 ± 6,35* (71,74-90,00)	109,60 ± 26,67 (100,48-118,73)	83,15 ± 13,15* (74,02-92,27)	82,35 ± 5,27* (73,22-91,48)	0,20	0,01	0,00	0,47	0,24	0,04
	BEA	83,74 ± 6,51* (74,62-92,87)	125,02 ± 25,17 (115,89-134,15)	83,58 ± 23,43* (74,46-92,71)	80,34 ± 4,54* (71,21-89,46)						
Insulina (mUI/ml)	BEM	5,50 ± 3,07* (1,93-9,08)	19,28 ± 9,52 (15,71-22,85)	10,53 ± 4,58*† (6,96-14,11)	5,87 ± 2,30* (2,30-9,45)	0,03	0,05	0,00	0,53	0,26	0,04
	BEA	6,65 ± 2,39* (3,08-10,22)	26,50 ± 12,69 (22,92-30,07)	12,10 ± 6,51*† (8,52-15,67)	6,38 ± 2,04* (2,81-9,95)						

(Continúa en página siguiente)

Tabla III (Cont.). Diferencias entre bebidas en la evolución a lo largo del tiempo de glucosa, insulina, proteínas y triglicéridos

		Inicial (IC 95 %)	30 minutos (IC 95 %)	60 minutos (IC 95 %)	120 minutos (IC 95 %)	Efecto grupo	η^2	Efecto tiempo	η^2	Grupo x tiempo	η^2
Proteínas totales (mg/dl)	BEM	66,83 ± 3,77 (62,57-71,10)	69,26 ± 2,86 (65,00-73,52)	71,27 ± 5,37 (67,01-75,40)	71,30 ± 5,16 (67,03-75,56)	0,12	0,02	0,59	0,02	0,42	0,03
	BEA	68,20 ± 4,33 (63,94-72,46)	66,43 ± 4,33 (62,17-70,69)	65,46 ± 13,61 (61,20-69,73)	69,15 ± 13,37 (64,89-73,41)						
Triglicéridos (mg/dl)	BEM	72,93 ± 46,83 (49,96-95,90)	61,46 ± 41,48 (38,49-84,43)	67,68 ± 38,38 (44,71-90,65)	46,53 ± 21,59 (23,56-69,49)	0,91	0,00	0,09	0,06	0,92	0,00
	BEA	76,01 ± 50,30 (53,04-98,97)	66,98 ± 47,73 (44,01-89,95)	58,80 ± 48,06 (35,83-81,76)	43,37 ± 30,79 (20,40-66,34)						

*BEM: bebida energética miel; BEA: bebida energética azúcar; IC: intervalo de confianza. *p < 0,01 30 minutos vs. resto de mediciones. †p < 0,01 inicial vs. 60 minutos.*

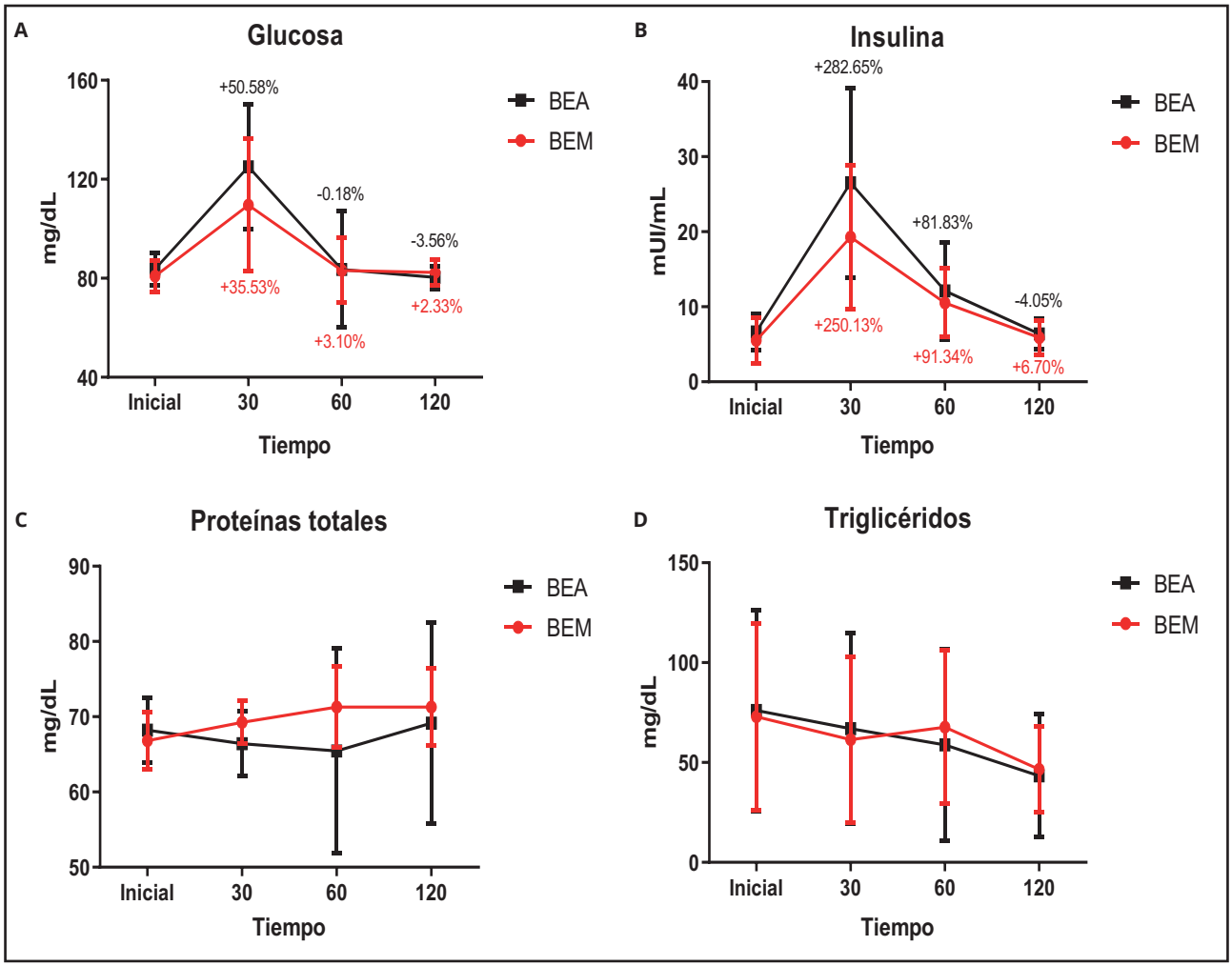

Figura 1.

Representación gráfica de la evolución de glucosa, insulina, proteínas totales y triglicéridos en las diferentes bebidas. Los porcentajes fueron establecidos en relación a los valores iniciales. A. Evolución de la glucosa según la BE. B. Evolución de la insulina según BE. C. Evolución de las proteínas según BE. D. Evolución de triglicéridos según BE. BEM: bebida energética miel; BEA: bebida energética azúcar.

DISCUSIÓN

El objetivo de la presente investigación fue estudiar el efecto de la ingesta de BEM (BeeBad EnegyDrink®, Parodi Group, Italia) y una BEA de alto IG sobre la glucosa sanguínea, las proteínas totales y los triglicéridos en condiciones basales. La miel es un alimento con IG glucémico bajo, lo que produce un lento incremento de la glucemia e impide el aumento repentino de glucosa en sangre y carga glucémica media (22). Los beneficios de la miel en la salud y en el rendimiento están siendo cada vez más investigados (22) y se están mostrando beneficios para la recuperación postesfuerzo (23). Es sabido que la miel tiene una amplia gama de beneficios para la salud, como la disminución de los radicales libres y de mediadores inflamatorios (22). Por ello, la miel está cada vez más presente en diversos productos (24).

Los valores basales de glucosa e insulina observados en la presente investigación son similares a los obtenidos en otros estudios (25,26). Aunque no se observaron diferencias significativas ente BEM y BEA en la glucosa sanguínea, se puede apreciar en la figura 1A una menor tendencia al incremento de la glucosa, especialmente a los 30 minutos, en BEM. Los estudios llevados a cabo con alimentos de alto IG *vs.* bajo IG mostraron diferencias entre la concentración de glucosa sanguínea a lo largo del tiempo (27,28), siendo menor la glucemia en aquellos alimentos/bebidas de bajo IG. Respecto a los niveles de insulina, en el presente estudio se observaron diferencias entre bebidas ($p < 0,05$) y fueron los 30 minutos el momento de mayor elevación. Estos resultados coinciden con los observados por Hollenbeck y cols. (29) y Alfenas y cols. (30), quienes compararon la respuesta de la insulina y la glucemia entre comidas de diferentes IG. Igualmente, Lee y cols. (31) observaron que la cinética de la insulina difería según el tipo de carbohidrato ingerido, siendo la glucosa el carbohidrato que mayores valores de insulina producía. Respecto a los estudios que analizan la respuesta posprandial de BE, Nowak y cols. (26) observaron incrementos en la glucemia tras la ingesta. Igualmente, González-Domínguez y cols. (32) observaron en refrescos con alto contenido en azúcar incrementos de la glucemia a diferencia de los refrescos bajos en azúcar.

La causa de que no sea significativa la diferencia en la glucosa sanguínea podría tener relación con el contenido similar de cafeína en las BE. Se ha reportado que la cafeína incrementa la glucosa sanguínea incluso cuando la ingesta de CHO es de bajo IG (33,34). El principal efecto fisiológico de la cafeína es el antagonismo del receptor de adenosina (35). La cafeína altera la tolerancia a la glucosa a través del antagonismo de los subtipos A1 y A2 del receptor de adenosina relacionados con la captación de glucosa en los músculos esqueléticos. Se ha observado que la administración de cafeína durante una pinza hiperinsulinémica-euglucémica (prueba utilizada para detectar resistencia a la insulina) da como resultado una disminución del 50 % en la captación de glucosa estimulada por insulina en el músculo esquelético, lo que se traduce en una reducción del 23-30 % en la captación de glucosa en todo el cuerpo (33). También se ha propuesto que la captación de glucosa mediada por insulina se ve afectada por la liberación de epinefrina estimulada por cafeína (36). La cafeína estimula la liberación de epinefrina, que ejerce acciones opuestas a las de la insulina a través de la estimulación β-adrenérgica (37).

La ingesta de BE se acompañó de un estado transitorio de hiperinsulinemia relacionado con el incremento de la glucemia. Es sabido que este estado favorece la captación de glucosa y promueve que el organismo pase del catabolismo al anabolismo. Además, cabe señalar que la coingesta de cafeína puede agudizar el estado de hiperinsulinemia provocado por los CHO mediante la elevación de los niveles de epinefrina en sangre (32,38). La diferencia en los valores de insulina entre BE podría deberse a la miel presente en BEM. El contenido de fructosa de la miel varía del 21 al 43 % y la relación fructosa/glucosa, de 0,4 a 1,6 (39). La fructosa tiene un índice glucémico de 19, en comparación con la glucosa, que tiene 100, o la sacarosa, con 60 (40). Diferentes estudios revelan el efecto hipoglucemiante de la miel. Sin embargo, el mecanismo de este efecto sigue sin estar claro. Se sugirió que la fructosa, los minerales (selenio, zinc, cobre y vanadio), los ácidos fenólicos y los flavonoides podrían tener un importante papel (39).

Existe evidencia de que la fructosa tiende a reducir la glucosa en sangre. Los mecanismos implicados en este proceso pueden incluir la reducción de la tasa de absorción intestinal y la prolongación del tiempo de vaciado gástrico (39). La fructosa estimula la glucoquinasa en los hepatocitos, la cual juega un papel importante en la captación y el almacenamiento de glucosa como glucógeno en el hígado. La glucosa, por otro lado, que está presente junto a la fructosa en la miel, mejora la absorción de la fructosa y promueve sus acciones hepáticas a través de su entrega mejorada al hígado (39,41). Por lo tanto, este menor incremento de la glucemia tras la ingesta de BEM derivaría igualmente en un menor incremento de los niveles de insulina, observado en el presente estudio. El consumo de un carbohidrato de IG bajo da como resultado una respuesta de glucosa plasmática lenta y gradual, mientras que un carbohidrato de IG alto da como resultado un rápido aumento de la concentración de glucosa en sangre, seguido de un rápido retorno a los valores iniciales o por debajo (hipoglucemia de rebote), como se observó en el presente estudio (10).

Por otro lado, se observa una disminución de los triglicéridos a lo largo del tiempo en ambas BE, sin ser significativo. Esta disminución podría deberse, en parte, al incremento de los valores de insulina. Los adipocitos son el lugar principal de almacenamiento de triacilglicerol en los individuos sanos (42). La insulina aumenta el almacenamiento de triglicéridos en los adipocitos. Además, la inhibición de la lipólisis por parte de la insulina no solo favorece el almacenamiento de lípidos, sino que también disminuye los niveles de ácidos grasos circulantes (43). Respecto a las proteínas totales, al igual que con los triglicéridos, no se observaron cambios significativos. Este hecho podría estar relacionado por la ínfima cantidad de proteínas presente en este tipo de bebidas.

Cabe destacar las posibles aplicaciones prácticas de este estudio, pudiendo ser la BEM una alterativa de BE para atletas. Esta bebida podría aplicarse antes y durante el ejercicio debido a que presenta una respuesta glucémica y de la insulina menor que otras bebidas con azúcares libres.

El presente estudio tiene algunas limitaciones: a) ausencia del control de la ingesta nutricional los días previos; b) ausencia del género femenino; c) no se valoró la sensibilidad a la insulina de los participantes, aunque todos eran jóvenes sanos; y d) no se evaluaron los niveles de condición física o de actividad física de los participantes.

CONCLUSIÓN

La ingesta de BEM produce menores elevaciones de insulina y glucosa en comparación con una BEA en sujetos sanos. Dada su composición, la adición de miel en las BE podría ofrecer una alternativa viable y natural a las formas tradicionales de provisión de CHO exógenos en jóvenes.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Otros

The impact of the introduction of a clinical nutrition unit in a hospital: a retrospective observational study

El impacto de la implantación de una unidad de nutrición clínica en un hospital: estudio observacional retrospectivo

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Abstract

Objectives: the study describes the evolution over the years of the use of artificial nutrition, in particular after the introduction of a dedicated Clinical Nutrition and Dietetic Service.

Methods: a single-center, retrospective observational study performed with data collected from 2014 to 2019 at the Regional Hospital of Locarno, Switzerland.

Results: from 2014 to 2019, there has been an increase in the number of patients identified as being at risk of malnutrition. We observed a reduction in the use of parenteral nutrition in all services, especially after the introduction of the dedicated Clinical Nutrition and Dietetic Service. There would seem to be a switch from enteral to oral nutrition with increased use of oral nutritional supplements.

Conclusions: the introduction of a dedicated Clinical Nutrition and Dietetic Service in the care of patients with nutritional issues would seem to reduce the use of artificial invasive nutrition, despite an increase in the number of patients identified as being at risk of malnutrition.

Keywords:

Malnutrition. Parenteral nutrition. Enteral nutrition. Oral nutritional supplement. Nutritional team.

Resumen

Objetivos: el estudio describe la evolución a lo largo de los años del uso de la nutrición artificial, en particular después de la introducción de un Servicio de Nutrición Clínica y Dietética dedicado.

Métodos: estudio observacional retrospectivo de un solo centro realizado con datos recopilados de 2014 a 2019 en el Hospital Regional de Locarno, Suiza.

Resultados: del 2014 al 2019 ha habido un aumento en el número de pacientes identificados en riesgo de desnutrición. Observamos una reducción en el uso de la nutrición parenteral en todos los servicios, especialmente después de la introducción del Servicio de Nutrición Clínica y Dietética dedicado. Parecería haber un cambio de nutrición enteral a oral con un mayor uso de suplementos nutricionales orales.

Conclusiones: la introducción de un Servicio de Nutrición Clínica y Dietética dedicado a la atención de pacientes con problemas nutricionales parecería reducir el uso de la nutrición artificial invasiva, a pesar del aumento en el número de pacientes identificados con riesgo de desnutrición.

Palabras clave:

Malnutrición. Nutrición parenteral. Nutrición enteral. Suplemento nutricional oral. Equipo nutricional.

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BACKGROUND

A balanced diet has been proved to improve people's current and future health (1,2). Correct dietary intakes become even more important during diseases and consequently during hospitalisations (3,4). The prevalence of patients at risk of malnutrition can reach up to 50 % in the hospital setting; these patients should be first identified and then treated (5,6).

When faced with a patient at risk of malnutrition, or malnourished, or who cannot adequately cover energy/protein needs, physicians should evaluate the best intake and, if necessary, introduce artificial nutrition (7,8).

Previous studies have found that invasive (enteral or parenteral) artificial nutritional therapies were not always indicated or correctly prescribed (5,9). This has a negative impact at the level of both increased iatrogenic complications and costs (10). Continued re-evaluation of the adequacy of invasive therapies is also supported by the global campaign Choose Wisely, even though there are no strong recommendations in this specific field (11).

In the literature, the few data available, with weak evidence, would seem to reveal a favourable impact of the introduction of a dedicated Clinical Nutrition and Dietetic Service on the use of artificial nutrition considering all services of a hospital (12).

In this study, we illustrate how nutritional therapy has changed within our hospital after the introduction of a dedicated Clinical Nutrition Team, as a point of reflection for new research in this regard.

METHODS

STUDY DESIGN AND PARTICIPANTS

The single-centre, retrospective, observational study took place at the Regional Hospital of Locarno, Switzerland. This public hospital is equipped with services for Intensive Care, Internal Medicine, General and Trauma Surgery, Gynaecology, Obstetrics, and Paediatrics.

The study descriptively describes the evolution of nutritional therapy from 2014 to 2019.

Since mid-2017, the hospital has been equipped with a Clinical Nutrition and Dietetic department supporting physicians in the management of patients with nutritional issues, including malnourished patients and patients forced to fast after surgery. This support is to be considered a non-binding consultation for clinicians, who remain in charge of patient care in full decision-making and therapeutic autonomy.

DATA SOURCE

The data reported, such as the total number of patients and the proportions of malnutrition diagnoses, were provided by the Finance and Controlling Service of the hospital. These data are regularly provided to the managers of the Clinical Nutrition and Dietetic Service to monitor their progress. The diagnosis of malnutrition is reported in the patient's exit letter, thus encoded at the end of the hospital stay, according to the SWISS-DRG rules (13). Data concerning the products used for artificial nutrition were provided by the hospital pharmacy. We report the volume of products used for enteral nutrition and the total number of bottles of oral nutritional supplements (ONS). Data on the amount of maltodextrin or protein powder used in the kitchen for the enrichment of the basic diet are not available.

NUTRITIONAL TEAM

In the years preceding the introduction of the Clinical Nutrition and Dietetic Service, the hospital had a dietary service composed of 2.7 units of dietitians, who were called in case of need by physicians.

From 01JUN2017 a real Clinical Nutrition and Dietetic Service was created, composed of a medical unit (a doctor) at the head of the team and dietitians. The aim was to improve the management of malnourished patients and improve nutritional counselling in general.

With the introduction of the Clinical Nutrition and Dietetic Service, the application of malnutrition screening tools improved by using the Nutritional Risk Screening (NRS-2002), a tool recognised by the European Society for Clinical Nutrition and Metabolism (ESPEN) (4,14). Before 2017 the NRS-2012 was carried out in paper format, while with the introduction of the Clinical Nutrition and Dietetic Service it was integrated into the computerised and semi-automated medical record. In contrast, the elaboration process remained unchanged: the first part is carried out by nurses, the second part by physicians.

In practice, the three questions and parameters (weight and height) measured and/or asked when not obtained by the screening tools were made mandatory and have become an integral part of the compulsory admission nursing history. With this device we were able to apply screening systematically in the first 24-48 hours to all patients who are hospitalized.

If any of the four items resulted pathological, a red *alert* would appear in the patient's diagnosis list. The patient's physician, by activating the alert message, could gain access to the second part of the screening procedure. If the score exceeded three points, the patient was deemed to be "at risk of malnutrition", directly starting a request of consultation by the Clinical Nutrition and Dietetic Service.

In addition, the Clinical Nutrition and Dietetic Service provided training sessions for physicians and nurses, in addition to the usual bedside teaching during consultations.

RESULTS

The number of patients who were treated by the hospital remained more or less constant from 2014 to 2019: on average 7,544 pts/year (CI, 7,364-7,735) (Table I). The percentage of patients with a malnutrition diagnosis reported in the exit letter increased over the years from 1.6 % (117 patients) in 2014 to 9.2 % (703 patients) in 2019 (+ 501 %). The greatest increase

occurred after 2017: + 2.35 % from 2015 to 2016, + 3.4 % in 2017, + 5.5 % in 2018, + 9.2 % in 2019, respectively. There was a net increase, in fact a doubling, in annual consultations starting from 2017, the year following the introduction of the Clinical Nutrition and Dietetic Service (from about 1,666/year in 2016 to 3,212/year in 2019) (Table I).

Table II shows the details about the artificial nutrition used. The amount of total parenteral and enteral artificial nutrition used decreased steadily from 3,660,250 ml in 2014 to 1,560,750 ml in 2019 (- 57 %) (Table II and Figs. 1 and 2).

The volume of parenteral nutrition used steadily decreased from a maximum of 1,981,250 ml in 2014 to a minimum of 488,750 ml in 2019 (- 75 %). The reduction started already in 2015, but since 2017 there was a net decrease in the prescription of parenteral nutrition in the Internal Medicine and Intensive Care departments. In Internal Medicine, the average annual utilisation dopped by 44 % after the introduction of the Clinical Nutrition and Dietetic Service. For Intensive Care, we observed a 75.5 % decline. The same trend was observed also in other departments (gynaecology, haemodialysis).

The Surgery Department had a steady reduction over the years. However, the largest drop started from the second half of 2017, where it changed from 456,250 ml to 93,750 ml (Table II and Fig. 3).

Enteral nutrition consumption tended to rise in the two-year period 2014-2016, then fluctuated and finally collapsed in 2019. Between 2014 and 2019, we observed a reduction in enteral nutrition by 36 % (from 1,679,000 ml to 1,072,000 ml). The use of ONS remained more or less constant until 2018, when there was a sudden increase (+ 80 %) (Table II).

Table I. Number of patients identified as malnourished and nutritional consultations

	2014	2015	2016	2017	2018	2019
Patients hospitalized per year (n)	7419	7735	7524	7611	7366	7611
Malnourished patients (n)	117	178	183	262	407	703
Malnourished patients (%)	1.6 %	2.3 %	2.4 %	3.4 %	5.5 %	9.2 %
Total nutritional consultations (n)	n.a.	n.a.	1666	1650	2617	3212

Table II. Consumption of artificial nutrition

	2014	2015	2016	2017	2018	2019
Parenteral Nutrition (ml/year)	1,981,250	1,694,375	1,184,375	776,875	605,625	488,750
Enteral Nutrition (ml/year)	1,679,000	1,739,500	1,925,500	1,618,000	1,714,000	1,072,000
ONS (bottles)	5,392	3,868	3,782	5,004	4,271	7,702
Parenteral nutrition by department						
Surgery (ml)	748,375	726,250	445,625	550,000	343,750	225,625
Internal medicine (ml)	460,000	333,125	449,375	106,875	140,625	168,750
ICU (ml)	561,250	458,750	261,875	90,000	131,250	78,125
Other departments (ml)	211,625	176,250	27,500	30,000	-10,000*	16,250
Paranteral nutrition by department and semester						
Surgery 1st semester (ml)	n.a	n.a	n.a	456,250	234,375	98,125
Surgery 2nd semester (ml)	n.a	n.a	n.a	93,750	109,375	127,500
Internal medicine 1st semester (ml)	n.a	n.a	n.a	44,375	58,125	131,250
Internal medicine 2nd semester (ml)	n.a	n.a	n.a	62,500	82,500	37,500
ICU 1st semester (ml)	n.a	n.a	n.a	78,750	37,500	26,250
ICU 2nd semester(ml)	n.a	n.a	n.a	11,250	93,750	51,875

ONS: oral nutritional supplement(s); n.a: not available; ICU: intensive care unit.

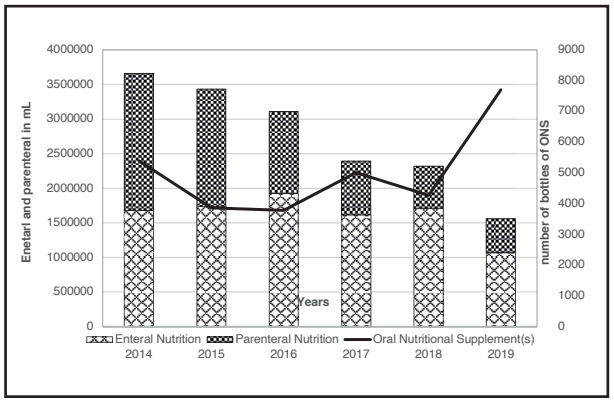

Figure 1.

Evolution of artificial nutrition over the years.

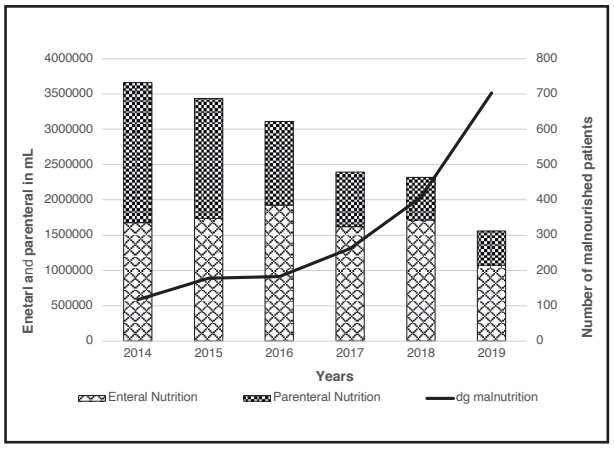

Figure 2.

Evolution of artificial nutrition (parenteral and enteral) over the years in relation to the number of malnourished patients.

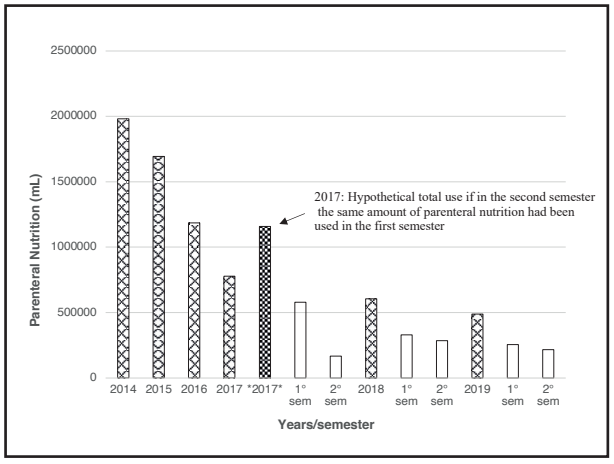

Figure 3.

Evolution of parenteral nutrition over the years, divided by semester after 2017 (introduction of the Clinical Nutrition and Dietetic Service mid-2017).

DISCUSSION

Over the years, we witnessed the introduction of a Clinical Nutrition and Dietetic Service in many hospitals, to help manage the problems related to nutrition. In certain countries, the creation of Clinical Nutrition and Dietetic Services is imposed by the legislation (15). This is because its efficacy and usefulness are increasingly supported by the literature, although data are often limited to specific departments and do not consider the whole hospital reality (16). As malnutrition is a very frequent problem in hospitalized patients and is associated with an increase in morbidity-mortality, its recognition and treatment are essential (7). The updated systematic review and meta-analysis of Gomes F et al. clearly demonstrates that the treatment of these patients improves their prognosis (17).

Our analysis demonstrates that with the introduction of the Clinical Nutrition and Dietetic Service the number of patients identified as being malnourished increased significantly. The integration of the nutritional risk screening in the computerised medical record certainly helped improve the process of screening. This certainly played a role, but it is not the only one, since we observed some differences between services, with the largest improved in the identification of malnourished patients in the Internal Medicine service. Since the screening tool was the same in all services, the hypothesis is that internists has first integrated the importance and usefulness of recognising and taking care of the patient at risk of malnutrition, after the various trainings in this regard, as compared to surgeons and physicians of other specialities. We must note that unfortunately there is still a "long and winding road" to go until malnutrition is identified in every inpatient. The increase in the number of patients recognised as having a nutritional problem led to a net increase in the consultations performed.

The impact of the Clinical Nutrition and Dietetic Service on the use of artificial nutrition is not well understood and described in the literature. Previous studies have focused on assessing the appropriateness of prescriptions for artificial nutrition, mainly parenteral nutrition, with prescription inadequacy up to a rate of 37 % of cases (5,18). Other studies have focused on the potential for economic savings achieved by both reducing the use of artificial nutrition and reducing the morbidity of patients at risk of malnutrition with an appropriate treatment (5,19,20).

In our retrospective analysis, we observed a decrease in parenteral nutrition over the years (Fig. 1), a decrease that occurred indistinctly in all services. The decline in Internal Medicine and Intensive Care Unit was clearly accentuated starting from 2017, the year of introduction of the Clinical Nutrition and Dietetic Service.

We can only speculate that the decline in parenteral use is the result of a more individualised patient care and optimisation in the use of less invasive nutritional strategies (enrichment of the basic diet, ONS, enteral nutrition). Indeed, in 2019, that is, after 1.5 years from the introduction of the Clinical Nutrition and Dietetic Service, we observed a net decrease in invasive nutrition in favour of ONS. These are pre-packaged industrial oral sup-

plements that the Nutritional Team often propose to accompany individualised diet regimens: supplementation of the regimen chosen for the patient's profile, adapted to the desired consistency and directly integrated in the kitchen with maltodextrin and/or proteins. The 2020 year analysis would have definitely been useful and would have allowed, 3 years after the introduction of the Clinical Nutrition Service, to confirm the trend detected. Unfortunately, with the arrival of the COVID-19 pandemic, the Hospital of Locarno has become a COVID centre and therefore the data are no longer comparable, as the patient case series has completely changed (21).

The net increase in consultations was achieved with an only modest increase in human resources (physician employed at 50 %). Therefore, even from a financial perspective, the Clinical Nutrition Service allows direct financial savings with less product purchase and indirect savings, as demonstrated in previous studies, reducing both iatrogenic complications related to invasive artificial nutrition and lowering the costs generated by the correct treatment of malnourished patients, who present fewer complications (5,17,18). Furthermore, the investment for the creation of the Clinical Nutrition Service is often relatively modest, as in most hospitals dietitians are already staff members and should only be re-inserted into a multidisciplinary clinical unit. Integration which, as our case teaches, can take place without conflicts.

Last but not least, indirectly, the improvement in the report in the outgoing letter of the malnutrition diagnosis can translate into increased hospital repayment for hospitalization.

We are aware of the weakness inherent to the retrospective study design: we cannot indeed not demonstrate that the observed changes traduce in improved patient care/prognosis.

We also recognise that other factors occurred in the long time lapse of six years may have influenced the reported results. In order to increase the authoritativeness of the results, we would need future study protocols with strong clinical endpoints, such as morbidity and mortality, endpoint with impact on DRG.

By supporting the Choose Wisely campaign, in light of the possibility of decreasing invasive nutrition without apparently negative repercussions, we hope that other physicians will join the campaign of continued revaluation of inappropriate or potentially harmful medical practices.

CONCLUSIONS

The introduction of a dedicated Clinical Nutrition and Dietetic Service helped increase the detection of patients at risk of malnutrition and led to a change in the use of artificial nutrition in favour of an oral, less invasive nutritional therapy.

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Trabajo Original

Otros

Awareness and usage of nutrition information and effect of sociodemographic characteristics on various aspects of food labels in Al-Ahsa, Saudi Arabia

Conocimiento y uso de la información nutricional y efecto de las características sociodemográficas sobre diversos aspectos del etiquetado de alimentos en Al-Ahsa, Arabia Saudí

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Abstract

Introduction: labels deliver basic product information, health safety and nutritional information.

Objectives: this study aims to assess consumers' knowledge, awareness, and practices in relation to food labels and the effect of sociodemographic characteristics on various aspects of food labels in Al-Ahsa.

Methods: a random sampling method was used to recruit participants (n = 403) and a validated electronic questionnaire was used to gather data.

Results: most of the participants (81.4 %) had moderate knowledge about general nutrition. The majority of them (58.8 %) placed high importance on reading food labels. Participants have positive opinions about the significance of reading food labels, and practice most of its aspects on a "frequent" basis. Lack of time was the main barrier for not utilizing food label information and obesity was the main concern if they did not read food labels. Results also demonstrate significant ($p \leq 0.01$) positive correlations between participants' nutrition knowledge and their rating of the significance and their opinion and practices of reading food labels. Participants' rating of the importance of reading food labels was positively correlated with participants' opinion and practices regarding food label. Results also indicate that participants' sex, age, body mass index, educational level and health status have significant ($p \leq 0.05$) effects on various aspects of food label under study. Finally, this study suggests some actions are required to enrich the knowledge, awareness, and practices regarding the food label among Saudi consumers in Al-Ahsa.

Conclusion: this study emphasizes the significance of education and awareness initiatives to empower consumers to understand and use nutrition facts labels in order to make healthy dietary choices.

Keywords:

Food labeling.
Nutrition knowledge.
Consumer awareness.
Sociodemographic.
Education.

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Resumen

Introducción: las etiquetas contienen la información básica del producto en términos de seguridad para la salud y composición nutricional.

Objetivos: este estudio pretende valorar el conocimiento, la concienciación y la práctica de los consumidores saudíes con respecto a las etiquetas de los productos, así como el efecto de las características sociodemográficas sobre varios aspectos de dichas etiquetas en la región de Al-Ahsa.

Métodos: se usó el método del muestreo aleatorio para reclutar a consumidores saudíes (n = 403) en Al-Ahsa y se empleó un cuestionario electrónico validado para recolectar los datos.

Resultados: la mayoría de los participantes (el 81,4 %) tenían conocimientos moderados acerca de la nutrición en general. La mayor parte de los participantes (58,8 %) daba mucha importancia a la lectura de la etiqueta alimentaria. Además, los participantes tienen opiniones positivas sobre la importancia de leer las etiquetas de los alimentos y practican la mayoría de los aspectos relacionados con las mismas de forma "frecuente". La falta de tiempo era el principal obstáculo para aprovechar la información nutricional de las etiquetas de los alimentos y la obesidad, la principal preocupación en caso de no leerlas. Los resultados muestran también correlaciones positivas significativas ($p \leq 0,01$) entre los conocimientos nutricionales de los participantes, su valoración de la importancia que tiene leer las etiquetas alimentarias y las prácticas derivadas de ellas. Además, la valoración que hacen los participantes de leer las etiquetas de los alimentos se correlacionó positivamente con su opinión sobre dichas etiquetas y las prácticas relacionadas con ellas. Los resultados también indican que el sexo, la edad, el índice de masa corporal, el nivel educativo y el estado de salud de los participantes tienen un efecto significativo ($p \leq 0,05$) sobre diversos aspectos de la etiqueta alimentaria sometida a estudio. Por último, este estudio sugiere que se precisan algunas acciones para enriquecer el conocimiento, la concienciación y las prácticas concernientes al etiquetado alimentario entre los consumidores saudíes de Al-Ahsa.

Conclusión: se resalta la importancia de las iniciativas de educación y concienciación para permitir a los consumidores comprender y usar las etiquetas de datos nutricionales a fin de que puedan elegir una dieta sana.

Palabras clave:

Etiquetado de productos.
Conocimiento nutricional.
Conciencia del consumidor.
Sociodemográfico.
Educación.

INTRODUCTION

A healthy and well balanced diet has a significant impact on body health and could control various nutrition-related diseases such as obesity, diabetes, and cardiovascular diseases. Particularly, around 73 % of deaths in Saudi Arabia are related to non-communicable diseases (1). A study on the prevalence of the chronic disease among elderly Saudi men showed a high percentage of obesity (77.8 %), followed by hypertension (71.3 %), diabetes (27.3 %), heart disease (16.4 %), asthma (9.7 %), ulcer (8.9 %), and cancer (2.0 %), respectively (2). On the other hand, iron-deficiency anemia was highly prevalent in females (94 %) (3). The Saudi Food and Drug Authority (SFDA) is an "institution that oversees all matters related to foods including food laws and regulations, information and education activities for the consumers" (1). Recently, the SFDA had issued a law that requires bakeries, restaurants, cafes, and ice cream parlors to provide their consumers with calorie information on written menus and monitors (4). It is an approach to promote a healthier lifestyle by reducing salt, sugar, and saturated and trans fats in products. Since 2007, the SFDA has been implementing mandatory prepackaged food labeling containing nutritional information such as calorie counts, carbohydrates, fats (saturated fat, trans fat), proteins, and other components, along with production and expiration dates (5).

Since nutrition has been recognized as an effective factor in order to control chronic diseases, nutritional awareness increased among the people which makes them learn how to choose healthy food. Labeling is defined as "any words, particulars, trademarks, brand names, pictorial matter or symbol relating to a food stuff and placed on any packaging, document, notice, ring or collar accompanying or referring to such food stuff" (6). It includes any statement provided about the food product, explanation or description, whether it is illustrated, written, printed, glued, engraved, or connected to the food package. The main purpose for this label is to provide basic information related to the product, health safety, and nutritional information, as well as to facilitate promotion. According to Anastasiou et al. (7), food companies should specify the quantities and types of fats, total fat, saturated fat, cholesterol, sodium, total carbohydrates, dietary fiber, sugar, protein, vitamin A and C, calcium and iron in one serving of the product.

Reading the food label has many benefits for consumers, such as identifying the food item, understanding the contents of the package, avoiding unwanted foods, choosing a taste they like, knowing the internal components of the food, identifying food additives and knowing the nutrition value. Because of its importance as one of the most powerful mediums to convey information from manufacturers to consumers, it should be detailed but simple, accurate and unbiased, and it should provide evidence-based health claims to assist consumers in their decision-making process by encouraging them to choose healthy foods (7). According to Kretser's (8) study, consumers are more likely to purchase healthy foods and beverages by utilizing information provided on food labels to achieve their health goals. Furthermore, choosing healthy food depends on other factors, including how information is perceived and understood. But this perception and understanding can be influenced by other factors such as nutrition knowledge (9), nutrition labeling content (10), and even socioeconomic factors (11). Regulatory measures on food labels alone would be insufficient if they were not accompanied by an assessment of consumers awareness regarding healthy choices and nutrition labels, and choosing a healthy diet depends on understanding and interpreting food labels (12). Drichoutis et al. (13) found that personality traits and behavioral and attitudinal factors influenced the use of food labels. A study carried out in India concluded that around 66 % of adolescents believe that nutrition details on food stuff labels are complex and are difficult to understand (14).

A previous study by Washi (15) revealed that most Saudi consumers were not familiar with the serving size, the nutritional content of the food product, and the health claims mentioned on the labels. Another study by Al-Barqi et al. (1) on students in health colleges reported that food label use was low among the

participants. Research shows that nutrition knowledge promotes food label use, while time constraints pose a serious obstruction. To our knowledge, no study has been found that assessed the knowledge and awareness of the Saudi consumers in the Al-Ahsa Governorate in Saudi Arabia about the use of food labels. Therefore, the objective of this study was to assess Saudi consumers' knowledge, awareness, and practices in relation to food labels. The results may provide valuable information for the SFDA in order to evaluate the impact of their efforts, policies and regulations associated with food labeling on Saudi consumer's behaviors through its frequent and effective use.

MATERIALS AND METHODS

STUDY DESIGN AND PARTICIPANTS

A cross-sectional study was carried out on 403 consumers (males and females ≥ 18 years) in Al-Ahsa, Saudi Arabia. Random sampling was used to recruit Saudi consumers in Al-Ahsa. All consumers participating in the study provided their informed consent, after their roles and responsibilities in the study were explained clearly. All participants signed their consent forms on a voluntary basis and were informed that they are free to withdraw at any time.

INSTITUTIONAL REVIEW BOARD STATEMENT

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of King Saud University (Ref. No. KSU-HE-20-407).

INSTRUMENTS

Empirical data on Saudi consumers' knowledge, awareness, and practices related to food label were collected through a self-reported instrument. An electronic questionnaire containing 43 items was created to collect data. It consisted of six sections. The questions were adapted from previous studies (1,16,17).

Section 1

Participants' sociodemographic and health characteristics included gender, age, height (cm), weight (kg), marital status, educational level, and health status.

Section 2

The aim of this section was to assess participants' nutritional knowledge. This section contains one question to assess the participants nutrition knowledge (self-assessment) on a 5-point Likert scale (5 = very high knowledge, 4 = high knowledge, 3 = moderate knowledge, 2 = little knowledge, 1 = very little knowledge). Based on the mean scored, participants were classified as follow: 1-2.33, 2.34-2.67 and 2.68-5 were indicative of low, moderate and high knowledge, respectively. The questions were adapted from previous studies (1,17). The other questions in this section were multiple-choice questions with only one correct answer to assess the nutrition knowledge of participants (Nutrition knowledge scoring). A 10-point score was used to assess their reply of multiple-choice questions. Based on the points scored, participants were grouped as follow: scores of 0-3, 4-7, and 8-10 were indicative of low, moderate and high, respectively.

Section 3

This section aimed to evaluate participants' awareness of the food label. The questions were related to participants' awareness of reading and understanding the food label. Frequency categories were yes and no for reading and understanding the food label, and the willingness to buy the product in case of having no food label. Then, on a 3-point Likert scale (1 = little important, 2 = moderately important, 3 = very important), participants were requested to answer questions related to their attitudes towards the importance of food label. In case of having difficulties in understanding the food label, participants were requested to identify the reasons for this difficulty on a yes/no scale. Four reasons were identified for such difficulty: language differences, the small print size and font, limitation in understanding and other difficulty.

Section 4

This section identifies participants' opinions about food labels. On a 5-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree and 5 = strongly agree), participants were asked to answer the questions associated with their opinions about the significance of the food label to consumers and their health, food label's accuracy and honesty, as well as their keenness to buy the unhealthy products.

Section 5

This section aimed to measure the practices regarding food label by participants. The participants were requested to answer the questions associated with their practices regarding food labels in terms of using these labels, reading the production and expiration date, checking calorie, fats and sugar contents, checking and monitoring warning information, checking the product's price before purchasing and manufacturer's name, and reading storage conditions. All answers were made on a 5-point Likert scale (1 = never, 2 = rarely, 3 = often, 4 = frequently and 5 = always).

Section 6

This last section focused on some general areas regarding food label use. It contained questions related to barriers that hinder the use of labels and health worries if the participant does not read the food label. Options were provided and the participants were supposed to choose the best option.

STATISTICAL ANALYSIS

Data was analyzed using IBM SPSS statistics software version 21. Results were presented as percentage or mean ± standard deviation (SD). Pearson's correlation test was performed to estimate the correlation between the participants' knowledge, awareness and practices in relation to food labels. One-sample t test was used to test whether the sample mean is statistically different from a known or hypothesized population mean (= 3). Independent-samples t test and one-way ANOVA were performed to determine the difference of participants' knowledge, awareness and practices regarding food labels according to certain variables: sex, body mass index (BMI), age, educational level, marital status and health status. Statistical significance level was set at p-value ≤ 0.05.

RESULTS

SOCIODEMOGRAPHIC AND HEALTH CHARACTERISTICS OF PARTICIPANTS AND NUTRITION KNOWLEDGE ASSESSMENT AND SCORING OF THE PARTICIPANTS

The data obtained on sociodemographic and health characteristics of the participants (n = 403) is summarized in table I. The majority of participants (74.2 %) were female and 51.1 % were between 19 and 30 years old. About 59 % of the participants were married and 72 % of them held a university degree. The BMI of almost 50 % of them was normal while almost 47 % were either overweight or obese. The majority of participants (82.9 %) did not have any chronic diseases. The most common chronic disease reported by the participants was blood pressure, followed by diabetes.

Participants' self-assessment of nutrition knowledge was at a moderate level (3.0 ± 0.807). The majority of participants (81.4 %) had moderate knowledge about general nutrition and the mean score (5.79 over 10) also indicated that participants' nutrition knowledge was at moderate level (Table I).

Table I. Sociodemographic, health characteristics, nutrition knowledge assessment and scoring of the participants characteristics

Variables	Frequency	Percent	Mean ± SD
Sociodemographic and health characteristics			
Sex			
Male	104	25.8	
Female	299	74.2	
Age (years)			
19-30	206	51.1	
31-40	94	23.3	
41-50	70	17.4	
51 or above	33	8.2	
Marital status			
Single	150	37.2	
Married	239	59.3	
Other	14	3.4	
Education level			
Uneducated	0	0	
School (middle and secondary)	75	18.6	
University (Bachelor)	289	71.7	
University (higher studies)	39	9.7	

(Continues on next page)

Table I (Cont.). Sociodemographic, health characteristics, nutrition knowledge assessment and scoring of the participants characteristics

Variables	Frequency	Percent	Mean ± SD
Sociodemographic and health characteristics			
Body mass index (BMI)			
Underweight	18	4.5	
Normal	195	48.4	
Overweight	109	27	
Obese	59	14.6	
Extremely obese	22	5.5	
Health status			
Not having chronic disease	334	82.9	
Having chronic disease	69	17.1	
*Chronic disease**			
Hypertension	30	43.5	
Diabetes	19	27.5	
High cholesterol	8	11.6	
Obesity	11	15.9	
Other	22	31.9	
Nutrition knowledge assessment and scoring of the participants			
Self-assessment of nutrition knowledge			3.0 ± 0.807
Nutrition knowledge scoring			
Low	31	7.7	
Moderate	328	81.4	5.79 ± 1.482
High	44	10.9	

**Some participants may have two or more chronic diseases at the same time. Data has been represented as frequency and percentage or mean + standard deviation.*

PARTICIPANTS' AWARENESS OF FOOD LABEL

According to our results, 57.6 % of participants read the products food label and 52.1 % confirmed that food label was easy to understand (Table II). On the other hand, some participants struggled in understanding these labels due to their small size and font of print (23.6 %). The majority of participants (62.3 %) do not like to buy products without food label. Around 58.8 % of participants indicate that it is very important to read the food label.

PARTICIPANTS' OPINION AND PRACTICES IN RELATION TO FOOD LABELS

Results showed that the opinions of participants about some aspects of food label were significantly high ($p \leq 0.01$) in the score (mean = 4.13, SD = 0.587) (Table III). Participants strongly ($p \leq 0.01$) believed that reading and understanding food labels is important and beneficial to the consumer (mean = 4.56, SD = 0.634) and it may prevent some diseases (mean = 4.5, SD = 0.67). In addition, participants believed that the nutritional warnings on food labels are honest (mean = 3.89, SD = 0.958), and the information mentioned on the food labels was accurate (mean = 3.57, SD = 0.996). All t values were significant ($p \leq 0.01$), indicating that the means of the sample were significantly ($p \leq 0.01$) different from the proposed value of three.

Results in table III revealed that participants practiced some of the food label uses on a "frequent" basis (mean = 3.73, SD = 0.849). Participants "always" read the production and expiration date (mean = 4.57, SD = 0.842) and checked the price of the product before purchasing (mean = 4.38, SD = 0.978). However, the results indicated some "frequently" practices regarding food labels such as checking the name of the manufacturer and warning information. Some practices fall into the category of "often", such as checking calorie, sugar and fat contents. All t values were significant ($p \leq 0.01$), indicating that the means of the sample were significantly ($p \leq 0.01$) different from the proposed value of three.

PARTICIPANTS' ORDERING OF FOOD LABEL'S INFORMATION

The study demonstrated that 44.4 % of participants read first the "calories and energy" contents and 31.3 % of them read the "vitamins and minerals" contents at the end (Fig. 1). The results showed a significant variation between participants selections in the order of the information checked while using the food label.

Table II. Participants' awareness of food labelling

Variables	Frequency	Percent (%)
Reading the products food label		
Yes	232	57.6
No	171	42.4
Is the food label easy to understand		
Yes	210	52.1
No	193	47.9
*Reasons for difficulty in understanding food labels**		
Difference in language	15	3.7
Small size of print and font sizes	95	23.6
Unable to understand the terms	63	15.6
Other	20	5.0
Willingness to buy products without food label		
Yes	152	37.7
No	251	62.3
Importance of reading food labels		
Little	21	5.2
Moderate	145	36.0
High	237	58.8

**Calculation was made upon answering the question "Is the food label easy to understand?" with "no". Data have been represented as frequency and percentage.*

PARTICIPANTS' GENERAL AREAS OF INTEREST FOR FOOD LABEL USE

Results demonstrated that obesity (40.2 %) was the participant's main health worry in case they did not check the food label, followed by diabetes (25.1 %) (Fig. 2A), while high blood lipids (12.7 %), heart diseases (7.9 %) and hypertension (5 %) were the least common health worries. The investigation revealed that around 27 % of participants agreed that lack of time was the main barrier for not using food label information (Fig. 2B), followed by the difference in language (23.6 %). Among the 403 participants, only 2.7 % stated that food label has no use and 46.6 % of them stated that some other barriers are responsible for not using the food label information (Fig. 2B).

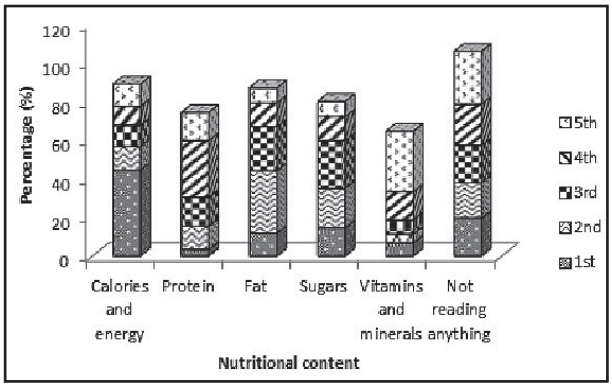

Figure 1.
Participants' ranking of food labels information.

Table III. Participants' opinion and practices in relation to food labels

Variables	Mean ± SD	t	p	Indication
Participants' opinion about food labels				
Reading and understanding food labels is important and beneficial to the consumer	4.56 ± 0.63	49.374	0.001*	Very high
Reading and understanding the nutritional label may prevent some diseases	4.5 ± 0.67	44.945	0.001*	Very high
The nutritional warnings on food labels are honest	3.89 ± 0.96	18.568	0.001*	High
The information on food labels is accurate	3.57 ± 0.99	11.400	0.001*	High
Average mean	*4.13 ± 0.59*	38.548	0.001*	*High*
Participants' practices regarding food labels				
Use of food labels	3.48 ± 1.09	8.793	0.001*	Frequently
Reading the production and expiration date	4.57 ± 0.842	37.330	0.001*	Always
Checking calorie content	3.41 ± 1.195	6.963	0.001*	Often
Checking fat content	3.24 ± 1.234	3.833	0.001*	Often
Checking sugar content	3.33 ± 1.237	5.395	0.001*	Often
Checking and following warning information	3.72 ± 1.203	11.967	0.001*	Frequently
Checking the price of the product before purchasing	4.38 ± 0.978	28.262	0.001*	Always
Checking the name of the manufacturer	3.84 ± 1.198	14.010	0.001*	Frequently
Reading storage conditions	3.59 ± 1.259	9.456	0.001*	Frequently
Average mean	*3.73 ± 0.849*	17.202	0.001*	*Frequently*

*One-sample t test was used to test whether the sample mean is statistically different from a known or hypothesized population mean (= 3). *Significant at p ≤ 0.01.*

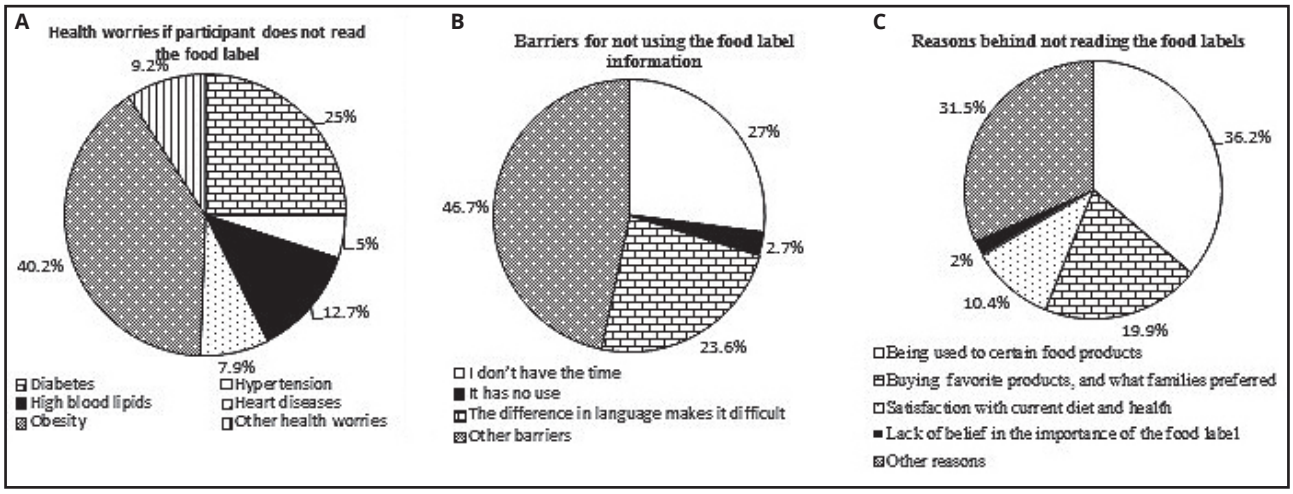

Figure 2.

Participants' general areas of interest for food label use. Results have been expressed in percentages. A. Health worries if the participant does not read food labels. B. Barriers for not using food labels information. C. Reasons behind not reading food labels.

In addition, the reasons given by participants behind not reading the food labels (Fig. 2C) included buying certain food products they used to buy (36.2 %), buying favorite products, and buying what families preferred (19.9 %). On the other hand, 10.4 % of the participants claimed they are satisfied with their current diet and health, and only 2 % did not believe the food label is important.

CORRELATIONS BETWEEN THE MAIN ASPECTS OF FOOD LABEL

Pearson correlations were calculated to investigate the associations between participants' nutrition knowledge, their rating of the importance of reading food labels, their opinions about food labels and their practices in relation to food labels (Table IV). A significant positive correlation ($p \leq 0.01$) was found between participants' nutrition knowledge and their rating of the importance of reading the food labels ($r = 0.175$), their opinion about food labels ($r = 0.178$) and their practices in relation to food labels ($r = 0.242$). In addition, participants' rating of the importance of reading the food label was positively correlated with participants' opinion about food labels ($r = 0.345$) and participants' practices regarding food labels ($r = 0.481$). The correlation between participants' opinion about food labels and participants' practices regarding food labels was the strongest, with a Pearson correlation of 0.503.

PARTICIPANTS' DIFFERENCES IN THE MAIN ASPECTS OF FOOD LABEL BASED ON SEX AND HEALTH STATUS

Results in table V revealed a highly significant ($p \leq 0.01$) difference between male and female participants in nutrition knowledge ($t = -3.851$, $p = 0.000$), rating of the importance of reading the food labels ($t = -4.045$, $p = 0.001$), opinions about food labels ($t = -2.694$, $p = 0.007$) and practices regarding food labels ($t = -6.467$, $p = 0.000$). Moreover, participants who have chronic diseases are more aware of practicing food labels than participants with non-chronic diseases ($t = 3.926$, $p = 0.002$). Other aspects of food labels were not affected by health status.

PARTICIPANT DIFFERENCES IN THE MAIN ASPECTS OF FOOD LABEL BASED ON AGE, BMI, MARITAL STATUS, AND EDUCATIONAL LEVEL

Our study indicated that the age of participants (Table VI) significantly affected their nutrition knowledge ($F = 4.443$, $p = 0.004$), their opinions about food labels ($F = 2.596$, $p = 0.04$) and their practices regarding food labels ($F = 6.090$, $p = 0.000$). All these significant ($p \leq 0.05/0.01$) differences were on behalf of the age category (31-40) as indicated by the Scheffe test. However, participants' rating of the significance of reading the food labels was not affected by participants' age and participants BMI, and they have an insignificant effect on their nutrition knowledge, rating of the importance of reading food labels and their practices in relation to food labels. This variable only affected significantly ($p \leq 0.05$) participants' opinion about food labels ($F = 2.483$, $p = 0.043$). This significant ($p \leq 0.05$) difference was on behalf of the "underweight" category as indicated by the Scheffe test. Marital status has an insignificant effect on participants' nutrition knowledge, rating of the importance of reading food labels, opinions about food labels and practices in relation to food labels. However, results also indicated that the participants' educational level significantly ($p \leq 0.05/0.01$) affected their nutrition knowledge ($F = 2.721$, $p = 0.044$), the rating of the importance of reading food labels ($F = 3.627$, $p = 0.013$), their opinions about food labels ($F = 6.582$, $p = 0.000$) and their practices regarding food labels ($F = 7.800$, $p = 0.000$). All these significant differences were on behalf of the "higher studies" category.

Table IV. Correlations between the main aspects of food labels

Aspects of food labels	Participants' nutrition knowledge	Participants' rating of the importance of reading food labels	Participants' opinion about food labels
Participants' nutrition knowledge	-	-	-
Participants' rating of the importance of reading food labels	0.175* (p = 0.001)	-	-
Participants' opinion about food labels	0.178* (p = 0.002)	0.345* (p = 0.001)	-
Participants' practices regarding food labels	0.242* (p = 0.001)	0.481* (p = 0.003)	0.503* (p = 0.004)

*Pearson's correlation test was used to evaluate the correlation between participants' knowledge, awareness and practices regarding food labels. *Significance at p ≤ 0.01.*

Table V. Participants' differences in the main aspects of food labels based on sex and health status

Aspects of food label	Male (n = 104)	Female (n = 299)	t	p	- Chronic diseases (334)	+ Chronic diseases (n = 69)	t	p
Participants' nutrition knowledge	5.38 ± 1.66	5.93 ± 1.39	-3.85	0.000**	5.71 ± 1.54	5.81 ± 1.47	0.485	0.638
Participants' rating of the importance of reading food labels	2.34 ± 0.71	2.61 ± 0.54	-4.045	0.001**	2.41 ± 0.671	2.56 ± 0.575	1.811	0.073
Participants' opinion about food labels	4.00 ± 0.66	4.17 ± 0.56	-2.694	0.007**	4.03 ± 0.643	4.15 ± 0.574	1.811	0.073
Participants' practices regarding food labels	3.29 ± 1.06	3.88 ± 0.700	-6.467	0.000**	3.37 ± 1.08	3.80 ± 0.78	3.926	0.002**

*Independent-samples t test was used to investigate the difference of participants' knowledge, awareness and practices regarding food labels according to variables of sex and health status. *Significant at p ≤ 0.5. **Significant at p ≤ 0.01.*

Table VI. Participant differences in the main aspects of food label according to age, BMI, marital status and educational level

Aspects of food label	Age		BMI		Marital status		Educational level	
	F	p	F	p	F	p	F	p
Participants' nutrition knowledge	4.443	0.004†	1.138	0.338	0.456	0.713	2.721	0.044*
Participants' rating of the importance of reading food labels	0.882	0.450	0.652	0.626	2.197	0.088	3.627	0.013*
Participants' opinion about food labels	2.596	0.040*	2.483	0.043*	0.75	0.523	6.582	0.000†
Participants' practices regarding food labels	6.090	0.000†	0.889	0.470	1.135	0.225	7.800	0.000†

*One-way ANOVA was used to investigate the difference of participants' knowledge, awareness and practices regarding food labels due to variables of age, body mass index (BMI), marital status, educational level and health status. *Significant at p ≤ 0.05. †Significant at p ≤ 0.01.*

DISCUSSION

This study was aimed to evaluate Saudi consumers' knowledge, awareness, and practices as regards food labels, as well as to explore the effect of sociodemographic characteristics on various aspects of food labels. SFDA exerted extensive efforts in regulating the food labeling in Saudi Arabia, to enhance health awareness among Saudi consumers and to reduce nutrition-related diseases through healthier food choices. This study showed that most participants had moderate knowledge about general nutrition, which is in line with the results of a previous study carried out on Saudi female university students in Riyadh (1). The nutritional label provides information to customers about the available choices and inspires the consumption and production of healthy products. The result recorded around 57.6 % participants read the food labels. Other studies conducted in different parts of the world showed different percentages in reading food labels, for example, in China (28.7 %) (18), South Africa (70 %) (12) and US adolescents (9-16 %) (19). The Ministry of Health of Saudi Arabia has expended considerable effort in delivering public health programs and raising awareness about healthy diet, chronic disease prevention (obesity, diabetes) and the promotion of physical activity, which may be the reason for moderate knowledge about nutrition and reasonable use of food labels in the country (20,21).

Apart from this, positive and significant correlation between participants' nutrition knowledge and consumers' rating of the importance of reading the food label, their opinion about food labels and their practices in relation to food label has been found. Thus, it can be concluded that the knowledge of nutrition motivates the use of food labels. This finding is in agreement with previous studies (1,22). However, this study is contrary to the study performed on undergraduate student in Malaysia, by Nurliyana et al. (23). This inconsistency could be due to variants in the sample size, study time, ethnicity of the examined population, and participants characteristics. The cognitive processing model recommends that consumers with preceding knowledge tend towards using label information more efficiently than those without knowledge (24). So, in order to promote a positive attitude towards the nutrition label, it is immensely vital to upsurge consumers' awareness about health and the importance of nutrition to prevent diseases and promote health. Along with nutrition knowledge, consumers' attitudes toward other aspects related to food products such as taste and economic condition could also affect their use of food labels during the buying process.

It has been observed that participants with high ratings of the significance of reading food labels were more involved in having positive opinions/attitude and good practices regarding food labels. The results of this study showed that the majority of participants preferred to read the food products labels and they were not willing to buy the product without the label. Also, they were aware of the significance of food labels. It became a routine for Indian consumers to purchase prepackaged food after reading the label, so they were familiar with most of the products (25). Participants who find difficulties in understanding food labels mentioned that the causing agent behind this difficulty was the tiny size and font of print and shortage of time, as well as differences in language. This result obtained in the present study is in agreement with Al Barqi et al. (2020) (1) and Jacobs et al. (26). Moreover, Heidarinejad et al. (27) reported that the major causes for not paying attention to food labels include tiny printing of labels, ignorance, and lack of time, interest and motivation. Schupp et al. (28) reported that scarcity of time and interest and availability of previous information about food were the main reasons behind not paying attention to food labels among Americans. Another study revealed that dearth of knowledge and scarcity of interest in nutrition, along with lack of faith on information provided on the labels, small print size, checking the nutrition information only at first instance and scarcity of time were ranked in order of priority as reasons for lack of attention to food labels (29). Graham and Laska (30) reported that clear and colored fonts used on the nutrition label could be more appealing to consumers to read the nutrition label. Participants in the present study firmly believe that reading and understanding the food label is important for the consumer to avoid diseases. Additionally, participants strongly believe that food labels provide accurate nutrition information and the nutritional warnings were honest. These findings indicate that participants have positive attitudes toward using food labels, which in turns positively affects their practices regarding food labels. Al-Barqi's et al. (1) have confirmed similar findings where participants with positive attitudes toward food labels were more likely to use them compared with those with negative attitudes. Ng et al. (31) reported that attitude plays an important role on the customer's decision on food products and purchase. By educating the customer about the concept, importance, and application of food labels, it is possible to influence their desire to choose a healthier food product.

Mahgoub et al. (32) reported that half of the consumers worldwide understand only "partially" the nutritional label available on food packages. They found that lack of understanding was most prevalent among members of Asia Pacific (60 %), followed by Europeans (50 %) and Latin Americans (45 %), while North Americans, followed by Portugueses, Cannadians, and the consumers from New Zealand and Spain were most conversant with food labellings.

In the present study, manufacturing and expiration date, as well as the cost of the product, were read on a regular basis (always) before purchasing, while the manufacturing company name and warning information were frequently checked. Ganbari et al. (33) reported that maximum participants were more interested in production and expiration date of products, while fewer were concerned with the product's nutritional information and information related to additives. Similar findings have been reported earlier in other countries (27,34). A study carried out in Malawi stated that price was the foremost determinant factor to purchase (35). On the contrary, a study in Lesotho (32) showed that instead of price, nutrition information was the major element that influenced consumer's choice to purchase the product. On the other hand, food expiry dates on labels are easy to check and understand, which is very important to ensure food safety (36). Interestingly, calorie, sugar and fat contents were often checked,

which reflects a little interest of participants toward these contents. Wahab (16) observed in his study on Bahraini customers that when buying food for the first time, fat content was the most commonly observed nutrient, followed by sugar and calories. The level of participants' nutrition knowledge, their opinions and the importance of checking food labels may affect their checking of nutrient contents such as calorie, sugar and fat contents. Thus, we can conclude that participants' practices in relation to food labels was positively correlated with these three variables.

However, other factors might affect some aspects of food label usage. Our results indicated that participants' sex affects their nutrition knowledge, rating of the importance of checking food labels, opinions about food labels and practices regarding food labels. Several studies agreed with this finding (16,32) and indicated that sex has a role in persuading food label use. In this study, the highest values recorded in females may be due to the chief role and responsibility of women in grocery shopping for household needs. But it could be also due to females being more concerned about their appearance and fitness than men, which makes them selective and in a mindset to prepare healthy meals (10,32). Nagya (37) reported that many males do not believe that nutritional information is valuable, or that it can help in food choices, or even think about to what extent health is important. By contrast, Aryee et al. (38) demonstrated that males were more likely to understand nutrition labels while other socio-demographic characteristics such as age, educational level, occupation and income were insignificant predictors. Simultaneously, they reported an insignificant connotation between the use of food labels, income and gender. Participants' age has an effect on their nutrition knowledge, opinions about food labels and practices when using food labels. This can be attributed to the restricted diets that their health advisers recommend to prevent them from developing chronic diseases at this age (13). However, BMI was found to have a significant effect on their opinion of food label. This indicates that BMI influences participants attitudes with little impact on their practices and other uses of food label.

Furthermore, results revealed that participants' educational level significantly affects their nutrition knowledge, the rating of the importance of reading food labels, their opinions about food label and their practices when using food labels on behalf of the "higher studies" category. Therefore, highly educated participants are more interested in some aspects of food labels than low educated ones. This is probably because educated consumers read academic journals and academic papers more regularly, so they have more exposure to health-related news and are aware of the connection between diet and health. This finding agrees with Mahgoub's et al. (32), who observed that educational levels have a role in the use of food labels. An educated person can interpret the nutritional information and incorporate it into a healthier diet. Researchers in the United Arab Emirates found a statistical correlation between consumer interest in reading and using food labels and levels of education (39).

The study recorded that most of the participants perceive obesity followed by diabetes, high blood lipid, heart disease and hypertension as the most significant health concerns related to not reading food labels. Similar results have been reported by Wahab (16) in the study carried out on consumers in Bahrain. In addition, results show that participants who have chronic diseases are more aware of checking food labels than participants who do not suffer from chronic diseases. This is a logical finding since individuals with chronic diseases are always at risk and trying to prevent some negative effects of foods contents such as salt, sugar, calories, etc. on their health. Choice the healthy food is acted by an individual to consume food with less sugar and fat and high content of fibers, fruits and vegetables. Nutrition plays a significant role in a healthier life. Since the public is trying to choose healthier food items, so, the health system and food department have a responsibility to provide the public with clear information about food. Finally, marital status has been found to have an insignificant effect on participants' nutrition knowledge, rating of the importance of reading food labels, opinions about food labels and practices in relation to food labels. Arfaoui et al. (40) reported that knowledge about nutrition facts labels and NHC is higher among participants without children and those shopping with their families because respondents have more time available to read food labels than parents and child-care giving parents shopping for household needs.

LIMITATIONS

This study used a valid questionnaire and a substantial sample size (n = 403), representative of the Saudi consumers in Al-Ahsa. However, due to this restriction (Saudi consumers in Al-Ahsa), the current study results cannot be generalized and may not reveal the reality of other Saudi population groups. Thus, further investigation including other Saudi population groups are needed to generalize these results. Moreover, it is crucial to emphasize the significance of nutrition knowledge to instill positive attitudes in Saudi consumers in Al-Ahsa to read the labels on their food products and practice this during purchase, which may reduce the occurrence of diet-related diseases in the Kingdom of Saudi Arabia.

CONCLUSIONS

This study assessed the knowledge, awareness, and practices regarding food labels during purchasing among Saudi consumers in Al-Ahsa. In Al-Ahsa, Saudi consumers' positive attitudes and practices toward food labels, and their emphasis on reading them seem to be influenced by nutrition knowledge, while shortage of time and language differences posed significant barriers. Hence, emphasis on increasing knowledge, awareness, and practices regarding food labels during purchasing among Saudi consumers in Al-Ahsa is required to meet the desired outcomes of the SFDA's policies and regulations. In order to prevent the phenomenon of random food shopping, it is suggested that the SFDA and other Saudi stakeholders develop a policy which should emphasize predetermined health food needs. Also, it needs to be publicized in every setting of the Saudi community

(e.g., schools, universities, etc.). Schools and universities curricula should have nutrition basics, as nutrition knowledge has an impact on some food label aspects. Television, radio and internet programs can significantly improve consumers' knowledge, awareness and practices regarding food labels during purchasing. As such, consumers will learn more about food labels, which will lead to healthier dietary options. And consequently, this will reduce the deterioration in public health, morbidity and the occurrence of multiple diseases.

In contrast, more attention should be paid to barriers such as the difference in languages, print size, and the font used on food labels. So, the goal should be to ensure food labels are easier for consumers to read and comprehend.

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Trabajo Original

Otros

Variabilidad del marcador genético CLOCK rs3749474 y su impacto en investigaciones y pruebas clínicas sobre obesidad y ritmo circadiano

Variability of the genetic marker CLOCK rs3749474 and its impact on research and clinical trials on obesity and circadian rhythm

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Resumen

Introducción: los ritmos circadianos influyen en la conducta alimentaria, siendo el gen CLOCK uno de los encargados de su regulación. El rs3749474T/C del gen CLOCK ha sido asociado a un mayor riesgo de obesidad y quienes portan el alelo T presentan una mayor pérdida de peso ante una dieta baja en carbohidratos y lípidos que quienes poseen la forma CC.

Material y métodos: usando la base de datos 1000 Genomes se obtuvo el genotipo del polimorfismo de nucleótido único (SNP) rs3749474 de 2.504 individuos, abarcando cinco macropoblaciones (África, Este Asiático, Sur Asiático, Europa y Latinoamérica) y 26 poblaciones. CT y TT fueron tratados como genotipos de no riesgo y CC, como de riesgo. Se utilizó la prueba exacta de Fisher para comparar las frecuencias de los genotipos de riesgo y no riesgo.

Resultados: existe una alta diferenciación para la frecuencia de genotipos portadores del alelo T entre las macropoblaciones: África alcanzó solo el 31,47 %; Europa, un 56,86 %; Latinoamérica, un 66,28 %; el Sur Asiático, un 68,3 %; y el Este Asiático, un 81,15 %, con diferencias significativas ($p_{Fisher} < 0,05$) en todas las comparaciones, excepto entre Latinoamérica y Sur Asiático. Se observó una baja heterogeneidad entre poblaciones dentro de cada macropoblación.

Conclusiones: la alta heterogeneidad para las frecuencias genotípicas de CLOCK rs3749474 en las macropoblaciones estudiadas indica que la disminución del consumo de carbohidratos y lípidos tendrá un impacto heterogéneo desde el punto de vista epidemiológico. Esto sugiere incluir la ancestría genética en posteriores estudios de asociación entre ciclos circadianos, conducta alimentaria y obesidad, con el objeto de desarrollar pruebas clínicas personalizadas.

Palabras clave:

Ritmo circadiano. Gen CLOCK. Obesidad. rs3749474.

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Abstract

Introduction: circadian rhythms influence eating behavior, with the CLOCK gene being one of those responsible for its regulation. The rs3749474T/C of the CLOCK gene has been associated with an increased risk of obesity. Those who carry the T allele have greater weight loss on a diet low in carbohydrates and lipids than those who have the CC form.

Methodology: using the 1000 Genomes database, the genotype of the single nucleotide polymorphism (SNP) rs3749474 was obtained from 2,504 individuals, covering five macro-populations (Africa, East Asia, South Asia, Europe and Latin America) and 26 populations. CT and TT were treated as non-risk genotypes and CC as risk. Fisher's exact test was used to compare the frequencies of risk and non-risk genotypes among the five macro populations.

Results: there is a high differentiation for the frequency of genotypes carrying the T allele among the macro-populations: Africa reached only 31.47 %, Europe 56.86 %; Latin America 66.28 %; South Asia 68.3 % and East Asia 81.15 %, with significant differences ($p_{Fisher} < 0.05$) in all comparisons, except between Latin America and South Asia. Low heterogeneity was observed between populations within each macro population.

Conclusions: the high heterogeneity for the genotypic frequencies of CLOCK rs3749474 in the studied macro-populations indicates that the decrease in the consumption of carbohydrates and lipids will have a heterogeneous impact, from the epidemiological point of view. This suggests including the genetic ancestry in later studies of association between circadian cycles, eating behavior and obesity, in order to develop personalized clinical tests.

Keywords:

Circadian rhythm. CLOCK gene. Obesity. rs3749474.

INTRODUCCIÓN

El estado nutricional de un individuo es, principalmente, el resultado de su conducta alimentaria, pero también de sus ritmos circadianos. Estos corresponden a las variaciones periódicas de 24 horas que son controladas por el sistema nervioso central y que regulan los ciclos luz-oscuridad (1).

Entre los genes que están asociados a la regulación de los ritmos circadianos, tenemos al *circadian locomotor output cycles kapu* (CLOCK), el cual sincroniza el ciclo luz-oscuridad con los tiempos de ingesta-ayuno y de actividad-reposo en los individuos (2).

En la actualidad, se ha descrito un gran número de variantes genéticas del tipo polimorfismo de nucleótido único (*single nucleotide polymorphisms* [SNP]) del gen CLOCK, entre las cuales está el rs3749474T/C (3). Los portadores del alelo T de este polimorfismo presentan una mayor obesidad abdominal (circunferencia de cintura), un alto índice de masa corporal (IMC) y un elevado consumo de energía, principalmente a partir de ácidos grasos, en comparación con sujetos homocigotos CC del mismo polimorfismo (4-6).

Por otro lado, se ha establecido que quienes poseen los genotipos TT y TC de rs3749474 tienden a tener una mejor pérdida de peso después de un tratamiento que implica la restricción de grasas en la dieta, en comparación con quienes poseen el homocigoto de tipo CC (7). Además, quienes presentan los polimorfismos en homocigosis o heterocigosis del rs3749474 y suelen tener un hábito de ingesta nocturna de carbohidratos y poseen un IMC más alto que la población general (8). Se ha demostrado que existe una asociación entre el ser portador de los alelos menores de rs3749474 del gen CLOCK y la ingesta de energía, lo cual conllevaría a aumentar el riesgo de desarrollar obesidad (5).

La figura 1 representa el modelo de determinación de los genotipos rs3749474 en relación con el IMC. Mientras que los portadores del alelo T, es decir TT y CT, presentan una asociación directamente proporcional entre consumo de carbohidratos (y lípidos) e IMC, los que presentan el genotipo CC poseen una leve asociación inversa, o bien ausencia de asociación, dependiendo del estudio y la población analizada. La relación causal entre los

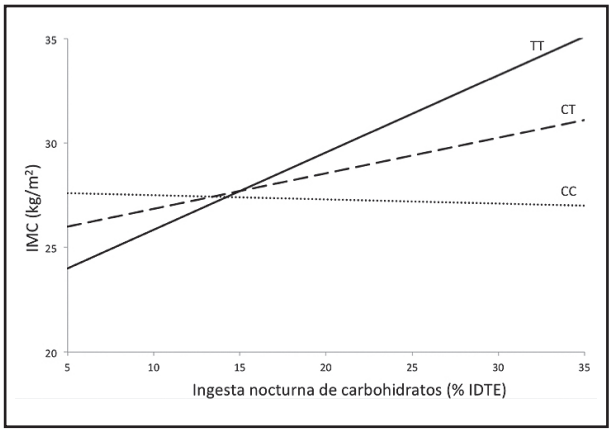

Figura 1.

Modelo de interacción de los genotipos del SNP CLOCK rs3749474 en relación con la ingesta de nutrientes, basado en Camblor y cols. (8). IMC: índice de masa corporal; IDTE: ingesta diaria total de energía.

genotipos portadores del alelo T y el incremento del IMC es, entonces, un factor de riesgo de obesidad. Como consecuencia de lo anterior, los individuos portadores del alelo T presentan una mejor respuesta ante la disminución de carbohidratos y lípidos en la dieta, disminuyendo el IMC (8).

Dado lo anterior, resulta relevante conocer la incidencia de los genotipos portadores del alelo T en diferentes poblaciones. El alelo C es el alelo ancestral, por lo que se espera se presente en mayor frecuencia en poblaciones africanas y en menor frecuencia en otras poblaciones, especialmente las más recientes, como la latinoamericana. No obstante, factores microevolutivos ocurridos en la historia de las poblaciones humanas podrían haber producido diferentes patrones de variabilidad en este marcador genético.

En este estudio analizamos el patrón de variabilidad de los genotipos portadores del alelo T del marcador CLOCK rs3749474 en poblaciones humanas actuales, lo que podría aportar evidencia de base para futuros estudios biomédicos y epidemiológicos, así como para la implementación de pruebas genéticas-clínicas para medidas preventivas e intervenciones clínicas personalizadas.

MATERIAL Y MÉTODOS

Se obtuvo el genotipo del SNP rs3749474 de 2.504 individuos a partir de la base de datos 1000 Genomes (9). Para esto, se descargó el total de la base de datos en su fase 3, para luego extraer los genotipos de rs3749474 para cada individuo usando la herramienta VCFtools. Esta base de datos abarca 2.504 individuos de 26 poblaciones. Los datos de baja cobertura (4x) están presentes para todos estos individuos, así como los de 24 individuos con alta cobertura (50x), con fines de validación. La muestra incluyó las siguientes macropoblaciones: África, Este Asiático, Sur Asiático, Europa y Latinoamérica, abarcando en total 26 poblaciones, cuyo detalle se muestra en la tabla I. El porcentaje de mujeres en la muestra es del 50,9 %. No obstante, variables como la edad y el sexo de los participantes no influyen en los resultados, pues rs3749474 es un marcador genético autosomal.

Tabla I. Información sobre las macropoblaciones y poblaciones analizadas en este estudio

Macropoblación (código)	Población	Código	n
África (AFR)	Caribe-africanos en Barbados	ACB	96
	Ancestría africana en el suroeste de Estados Unidos	ASW	61
	Esan en Nigeria	ESN	99
	Gambianos del oeste	GWD	113
	Luhyas en Webuye, Kenia	LWK	99
	Mendés en Sierra Leona	MSL	85
	Yorubas en Ibadán, Nigeria	YRI	108
			Total: 661
América (AMR)	Colombianos en Medellín	CLM	94
	Ancestría mexicana en Los Ángeles, Estados Unidos	MXL	64
	Peruanos en Lima	PEL	85
	Puertorriqueños en Puerto Rico	PUR	104
			Total: 347
Este Asiático (EAS)	Chinos Dai en Xishuangbanna, China	CDX	93
	Chinos Han en Beijing, China	CHB	103
	Chinos Han del sur	CHS	105
	Japoneses en Tokio	JPT	104
	Kinh en Ciudad Ho Chi Minh, Vietnam	KHV	99
			Total: 504
Europa (EUR)	Utaheño con ancestría del norte y oeste europeo	CEU	99
	Fineses en Finlandia	FIN	99
	Británicos en Inglaterra y Escocia	GBR	91
	Ibéricos en España	IBS	107
	Toscanos en Italia	TSI	107
			Total: 503
Sur Asiático (SAS)	Bengalíes en Bangladesh	BEB	99
	Gujarati en Houston, Texas	GIH	99
	Telugu en Reino Unido	ITU	91
	Punjabi en Lahore, Pakistán	PJL	107
	Sri Lanka Tamil en Reino Unido	STU	107
			Total: 489

ANÁLISIS ESTADÍSTICO

El genotipo CC se codificó como genotipo de riesgo (1), mientras que los otros dos (CT y TT) se codificaron como de no riesgo (0), esto considerando que el alelo T confiere una mejor respuesta a una dieta baja en carbohidratos (8). Se estimó la frecuencia del genotipo de riesgo en las cinco macropoblaciones y se compararon sus frecuencias usando la prueba exacta de Fisher.

Tanto la construcción de la base de datos (disponible como material suplementario) como la estadística descriptiva (estimación de frecuencias) y la estadística inferencial (comparación de frecuencias) se realizaron con el programa R (10).

RESULTADOS

A continuación, se presentan los resultados según distribución de las cinco macropoblaciones relevantes (Fig. 2). La menor frecuencia de genotipos portadores del alelo T se encuentra en África, seguida de Europa, Latinoamérica, Sur Asiático y Este Asiático, en orden creciente. Es notoria la baja frecuencia observada entre África y las otras cuatro macropoblaciones.

Al comparar las frecuencias genotípicas entre todos los pares de poblaciones, se confirma la alta divergencia de África. Además, existen diferencias significativas ($p_{Fisher} < 0,05$) en todas las comparaciones excepto entre Latinoamérica y Sur Asiático (Tabla II).

La figura 3 muestra las frecuencias de genotipos portadores del alelo T en las 26 poblaciones de este estudio. Se destaca la alta homogeneidad de las frecuencias dentro de cada macropoblación. La excepción a este patrón corresponde a Lima, Perú, que muestra una mayor frecuencia de genotipos de no riesgo en relación con las otras poblaciones latinoamericanas ($p_{Fisher} < 0,05$).

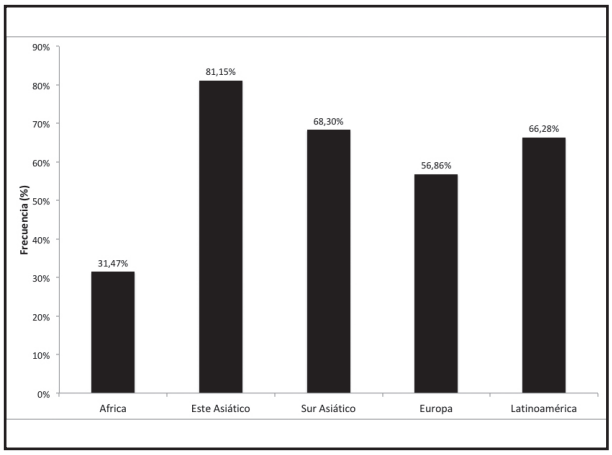

Figura 2.

Frecuencia de genotipos portadores del alelo T (TT y CT) en las cinco macropoblaciones de este estudio.

Tabla II. Prueba exacta de Fisher para la comparación del número de genotipos de riesgo (TT + CT) y no riesgo (CC) entre pares de macropoblaciones

	África	Este Asiático	Sur Asiático	Europa
Este Asiático	$2,2 \times 10^{-16}$			
Sur Asiático	$2,2 \times 10^{-16}$	$3,758 \times 10^{-6}$		
Europa	$2,2 \times 10^{-16}$	$2,2 \times 10^{-16}$	0,0002356	
Latinoamérica	$2,2 \times 10^{-16}$	$1,164 \times 10^{-6}$	0,5497 (ns)	0,006594

ns: no significativo.

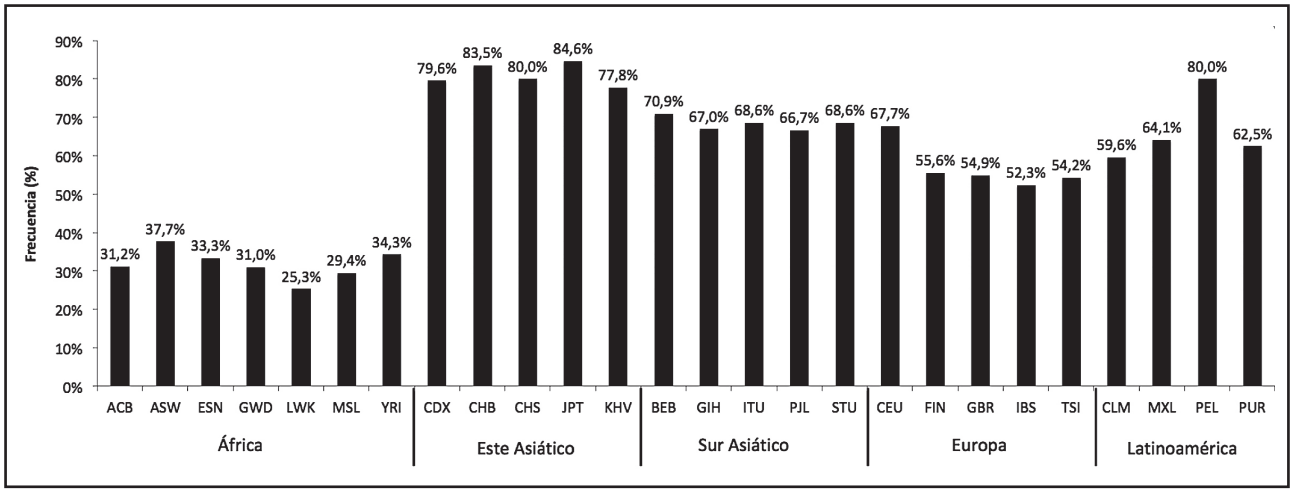

Figura 3.

Frecuencia de genotipos portadores del alelo T (TT y CT) en las 26 poblaciones de este estudio.

DISCUSIÓN

Nuestros resultados muestran una alta divergencia para la frecuencia de genotipos portadores del alelo T en África, en relación con las otras cuatro macropoblaciones. Mientras que en África esta frecuencia alcanza solo el 31,47 %, en las restantes macropoblaciones esta frecuencia varía entre el 56,86 % (Europa) y el 81,15 % (Este Asiático). Por lo tanto, si nos guiamos por los resultados obtenidos por Camblor-Murube y cols. (8), se podría predecir que poblaciones africanas presentarían menor aumento del IMC debido al consumo de carbohidratos y, al mismo tiempo, menor respuesta ante dietas bajas en ellos. Por otra parte, se espera encontrar un patrón inverso para personas del Este Asiático, las cuales presentarían una alta asociación entre IMC y el consumo de carbohidratos y una alta respuesta a dietas bajas en este tipo de nutrientes.

La alta diferenciación de las poblaciones africanas podría ser consecuencia de patrones dietarios ancestrales, probablemente menos dependientes de la ingesta de carbohidratos, lo que es consistente con estudios enfocados en los patrones dietarios en estas poblaciones (11). Así, podría inferirse que la diferenciación observada respondería a los cambios dietarios experimentados durante la última transición alimentaria (12).

La mayor diferencia se observa al comparar macropoblaciones entre sí, puesto que existiría una alta homogeneidad dentro de cada una de ellas (a excepción de la macropoblación latinoamericana, donde la población de Lima, en Perú, destaca sobre el resto). Esta observación se traduce en que la predicción del éxito de dietas bajas en carbohidratos requeriría de la cuantificación de ancestría genética para estas cinco macropoblaciones ancestrales, siendo marginal el efecto de aquellas derivadas de poblaciones locales.

En Chile, es escasa la investigación referente al gen CLOCK, y los estudios que se han realizado en relación con el SNP rs3749474 T/C han contado con tamaños muestrales pequeños y solo han participado sujetos jóvenes. No obstante, los resultados confirman lo encontrado en investigaciones en otras regiones geográficas, asociando un mayor riesgo de obesidad en portadores del alelo T y aportando evidencias de interacción con el SNP rs4864548A (13,14). Dado lo anterior, posteriores investigaciones podrían incluir otras poblaciones latinoamericanas, a fin de contrastar la evidencia aquí reportada y contribuir así a la creación de un perfil de variabilidad a nivel subcontinental para diferentes loci de CLOCK asociados a obesidad y a la respuesta a dietas.

Si bien el presente estudio permite predecir la incidencia del alelo rs3749474 T dentro de las cinco macropoblaciones analizadas, una limitación de este estudio tiene relación con la existencia de particularidades poblacionales que no son aquí abarcadas. Por ejemplo, la existencia de poblaciones de diferentes ancestrías dentro de las macropoblaciones, como es el caso de poblaciones indígenas, que pueden presentar diferenciación genética respecto de sus respectivas macropoblaciones. Otra limitación tiene relación con el hecho de que la muestra con que se creó la base de datos 1000 Genomes corresponde a sujetos voluntarios, por lo que los resultados tienen un sesgo asociado al hecho de ser una muestra intencionada.

Finalmente, este trabajo presenta evidencia que contribuye a la generación de modelos probabilísticos para el éxito de dietas bajas en carbohidratos según las cinco macropoblaciones estudiadas. El tránsito hacia terapias médicas basadas en evidencia genómica personalizada, considerando la ancestría genética como uno de los factores causales, se hace cada vez más factible de incorporar a las decisiones biomédicas, como sería en el caso del gen CLOCK y su relación con ciclos circadianos, susceptibilidad a la obesidad y respuesta dietaria.

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ARÁN

Nutrición Hospitalaria

Revisión

Effectiveness of multicomponent lifestyle intervention programs on adiposity indicators in schoolchildren from vulnerable groups: a review article

Efectividad de los programas multicomponentes de intervención de estilo de vida sobre indicadores de adiposidad en escolares de grupos vulnerables: artículo de revisión

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Abstract

Vulnerable groups are those who, due to their age, sex, race/ethnicity, health status, income level, etc., are at higher risk of poor health. Vulnerable school populations are distinguished by having predisposing factors to overweight and obesity, which results in a greater risk of suffering from the disease and its ravages. Additionally, the effects of the COVID-19 contingency can worsen the situation. Previous reviews of prevention, treatment and control of the disease have focused on schoolchildren from high- and middle-income countries. The objective of this review was to gather the evidence from the studies that evaluate the effectiveness of multicomponent lifestyle intervention programs (MLIP) on adiposity indicators in vulnerable populations. Five electronic databases were searched: PubMed, MEDLINE, Cochrane Library, EMBASE, and Google Scholar. The eligibility criteria were schoolchildren (5 to 12 years old), inhabitants of rural area, with low socioeconomic level and/or belonging to an indigenous community. Randomized and quasi-experimental controlled trials were included. Interventions that included two or more of the following components were considered: physical activity, nutrition, psychology, school meals and/or family/community involvement. Of the 11 interventions included 73 % had significant improvements in at least one variable related to adiposity. The most successful interventions had components of nutrition, physical activity and family/community involvement, the majority (80 %) had a duration of ≥ 6 months and were provided, in 80 % of the cases, by previously trained teachers. In conclusion, there is evidence that MLIPs are effective in improving indicators of adiposity in vulnerable schoolchildren.

Keywords:

Adiposity. Obesity. Child. Ethnic groups. Rural population. Vulnerable populations.

Resumen

Los grupos vulnerables son aquellos que, debido a sus condiciones de edad, sexo, raza/etnia, estado de salud, ingresos, etc., tienen un riesgo mayor de presentar una salud deficiente. Las poblaciones escolares vulnerables se distinguen por tener factores predisponentes de sobrepeso y obesidad, lo que redunda en mayor riesgo de padecer la enfermedad y sus complicaciones. Adicionalmente, los efectos de la contingencia por COVID-19 podrían agravar la situación. Revisiones previas sobre la prevención, tratamiento y control de la enfermedad se han enfocado en escolares de países de altos y medianos ingresos. Esta revisión tuvo como objetivo reunir la evidencia que evalúa la efectividad de los programas multicomponentes de intervención de estilo de vida (PMIEV) sobre los indicadores de adiposidad en poblaciones vulnerables. Se exploraron cinco bases de datos electrónicas: PubMed, MEDLINE, Cochrane Library, EMBASE y Google Scholar. Los criterios de elegibilidad fueron escolares (5-12 años), habitantes rurales, con bajo nivel socioeconómico y/o pertenecientes a comunidades indígenas. Se incluyeron ensayos controlados aleatorizados y cuasi-experimentales. Se consideraron intervenciones con dos o más de los siguientes componentes: actividad física, nutrición, psicología, comidas escolares y/o participación familiar/comunitaria. De las 11 intervenciones incluidas, el 73 % obtuvieron mejoras en al menos una variable relacionada con la adiposidad. Las intervenciones más exitosas incluyeron componentes de nutrición, actividad física y participación familiar/comunitaria, la mayoría (80 %) tuvo una duración ≥ 6 meses y las llevaron a cabo en un 80 % de los casos profesores entrenados. En conclusión, la evidencia indica que los PMIEV son efectivos para mejorar los indicadores de adiposidad en los escolares vulnerables.

Palabras clave:

Adiposidad. Obesidad. Niños. Etnias. Población rural. Grupos vulnerables.

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INTRODUCTION

Childhood overweight and obesity are a global problem that has worsened in recent decades, affecting countries regardless of their income (1). The multiple factors that cause these metabolic diseases have spread throughout societies, reaching economically and socially disadvantaged populations (2). Furthermore, the consequences of the COVID-19 pandemic can trigger higher prevalences of overweight and obesity in children, as poverty worsens, and sedentary lifestyle widens (3).

The World Health Organization (WHO) defines overweight and obesity as an excessive store of fat that can damage health. In the case of boys and girls, diagnoses of overweight and obesity are considered if the BMI for age is +1 and +2 standard deviations above the median established in the WHO child growth standards, respectively (2).

Excess fat during childhood can cause significant physiological and psychosocial damage affecting quality of life. These damages can extend into adulthood and generate an excessive socioeconomic burden for nations (4).

Risk factors for the development of obesity are numerous and of a different nature (5). They arise from genetics, fetal environment, particular aspects of the mother during pregnancy, current and early childhood diet, physical activity (PA) level, sedentary habits, sleep patterns, family, environment, socioeconomic status, and availability and accessibility of food (6-12). Due to the complexity of this disorder, its control is not easy.

Strictly speaking of vulnerable groups or populations, several definitions emerge in the literature. In general, these suggest that individual characteristics such as age, sex, gender, race, ethnicity, displacement, disability, health status, income level, insurance coverage, and lack of a usual source of care, can cause greater vulnerability in people and communities, and lead to poorer health (13). For this review, we adhere to the definition of a vulnerable population that includes economically disadvantaged racial/ethnic minorities, low-income children, rural residents, the elderly, homeless people, people with the human immunodeficiency virus (HIV), and individuals with chronic illnesses, including mental illness (14).

A lifestyle is demarcated by the deliberate decisions about the behavior and daily consumption practices of everyone. However, the choice and maintenance of lifestyle is strongly influenced by the economy, sociocultural and political environment, exerting effects on health and behavior (15).

It has been pointed out that obesity varies according to socioeconomic level (16), as higher rates are found in boys and girls with fewer resources (17-19). Similarly, schoolchildren from vulnerable groups, such as indigenous and rural communities, have a higher risk of being overweight and obese due to changes in diet and increased sedentary lifestyle in a context of poverty and marginalization (20-23). It has been observed that children from households with food insecurity, closely linked to poverty, have higher figures in variables related to adiposity (BMI Z-score and waist circumference) and higher risk of developing overweight or obesity when compared to children from households with food security (24). For their part, the children of migrants and unemployed parents show a higher risk of sedentary behavior (screen time) and less probability of being part of a sports club (25).

A recent systematic review reported that the variables related to an increased risk of childhood obesity were having parents without support networks, with little help from formal and occasional sources, having parents without work, belonging to a minority group or with an immigrant background, suffer from unfavorable experiences (household disintegration, violence and child abuse), having gender imbalances, and belonging to a non-traditional family. The authors proposed that variables associated with childhood obesity, which are also characteristics of vulnerability, are not related to socioeconomic level. However, they indicate that the socioeconomic level plays a very important role since it is capable of exacerbating or lessening the impact that these variables may have on the lifestyle and mental health of schoolchildren. Similarly, they reported conduct, biological, and mental-related mechanisms as conceivable explanatory factors in the relationship between vulnerability and childhood obesity. Hence, dietary intake, physical activity level, sedentary behavior, and sleep pattern are altered by stress and impair mental health due to the status of vulnerability (26).

In order to face the consequences of obesity, previously intervention programs were designed and applied with an isolated approach, which only treated some of the risk factors, and their results were usually partial, with a short-term effect (27-29). Therefore, in recent years, a new perspective has emerged to address the prevention, maintenance and remission of the disease, giving way to the creation and implementation of Multicomponent Lifestyle Intervention Programs (MLIPs) with a more comprehensive approach (30). These are characterized by a combination of varied components, selected according to the objectives and available resources, that seek to mitigate triggers of overweight and obesity, and can reinforce family and community structures (31-33). The most widely implemented interventions are aimed at generating behavioral changes, modifying dietary habits, and increasing physical activity (34), emphasizing that most obesity intervention programs in children do not consider the characteristics of vulnerability and social inequality, which makes them ineffective in the most vulnerable groups (26).

Other reviews have explored the effectiveness of MLIPs in schoolchildren in high- and middle-income countries. However, knowing the results of these interventions in children from vulnerable groups will be very useful to propose and design projects consistent with the needs, characteristics and response of this population (29). Accordingly, this review aims to elucidate whether these interventions are effective in improving adiposity indicators in the selected groups and, if so, which of them are the most effective.

METHODOLOGY

ELIGIBILITY CRITERIA

Population

The interest group for this review were schoolchildren (5 to 12 years old) with characteristics of vulnerability, whether they lived in a rural area, had a low socioeconomic level and/or belonged to an indigenous community or not. Age was established to include boys and girls who attended elementary school or its equivalent, according to the school system of each country. Studies encompassing populations with a broader age range were eligible for inclusion if ≥ 75 % of the participants were within the specified age range. Boys and girls with any BMI classification were included to incorporate intervention programs with preventive and treatment approaches. Studies in which the population was predominantly made up of schoolchildren with chronic illnesses or disabilities were excluded.

Intervention components

The included MLIPs had to contain at least two components, which could be nutrition, PA, psychology, providing school meals, and/or family/community involvement (FCI), regardless of other elements. The intervention programs were analyzed according to their effect on the variables of interest. Without exception, all intervention programs had to be taught in elementary schools or equivalent settings, during class time or at the end of the school day. No restrictions were imposed on the duration of the interventions, nor on the personnel who delivered them.

Comparison

Studies without a control group and studies in which the control group did not receive the program (they continued with the usual classes) or received only one component were included.

Result variables

This review defined, as primary outcomes, variables related to adiposity such as the prevalence and/or incidence of overweight and obesity, as well as indicators of these health conditions (BMI/BMI Z-score, waist circumference, and percentage of body fat). The secondary outcomes were those related with dietary intake (micro and/or macronutrients), knowledge of nutrition, PA and sedentary behavior. Studies reporting at least one outcome of interest were considered.

Study design

Randomized and quasi-experimental controlled trials were selected. All published studies with full text available were eligible. Gray literature was not considered.

SEARCH STRATEGY

The search was carried out in the electronic databases PubMed (interface National Library of Medicine); MEDLINE (OVID interface); The Cochrane Library - Cochrane Central Register of Controlled Trials (CENTRAL) via Cochrane Register of Studies Online (CRSO); EMBASE (Excerpta Medica database) and in Google Scholar, during the months of November and December 2020. The search strategy consisted of entering the combination of keywords: “multi-component program”, “childhood obesity”, “nutrition assessment”, “education”, “ethnic groups”, “health education”, “elementary schools”, “indigenous populations”, “pre-post tests”, “randomized controlled trials”, among others. The search strategy for PubMed is described in table I; for the other databases, modified versions were used according to the controlled language of each search engine (MeSh terms for MEDLINE and Emtree for EMBASE). The search was filtered by date, considering studies published in English, from 2000 to December 19, 2020. In addition, throughout the search, systematic reviews that included possible relevant studies were identified and the references of these reviews were screened in accordance with the Cochrane Handbook recommendations (35).

SELECTION OF STUDIES

The results obtained from the different databases were imported into the EndNote 20 reference software, which helped eliminate duplicate studies and organize references for further screening. Titles and abstracts of potentially relevant studies were reviewed. Subsequently, the full studies were assessed for inclusion. If the vulnerability condition of the population and the application environment of the program was not clearly defined in the summary section, the study was conducted to the full-text evaluation stage. The study selection process is detailed in the PRISMA flow diagram (36) (Fig. 1).

DATA EXTRACTION

Data on the authors, country of application of the program, study design, sample size, age of participants, description of the program, duration and follow-up, description of control, and variables of interest were extracted from the selected studies. With the results reported by the authors, tables were prepared to visually illustrate the most important changes obtained, also, they were explained narratively and a discussion of them was conducted. A meta-analysis was not possible due to the limited data available and the high variability between studies.

RESULTS

SEARCH RESULTS

The systematic search strategy identified 1,473 articles, plus 9 studies obtained from the references of systematic reviews.

Table I. PubMed search strategy, November 17, 2020

Search	Query	Items found
#12	Search: ((#4 AND #8) AND #11)	138
#11	Search: (#8 AND #9)	11,459
#10	Search: ((((body mass index [MeSh Terms])) OR (waist circumference [tiab] OR central obesity [tiab])) OR (((((eating habits[tiab]) OR (Food consumption [tiab])) OR (feeding behavio* [tiab])) OR (diet [tiab]))))) OR ((((screen time [tiab]) OR (sedentary behavio*[tiab])) OR (leisure activit*[tiab])) OR (self-perception [tiab] OR self-esteem[tiab]))	547,961
#9	Search: (randomized controlled trial[Publication Type]) OR cluster randomized controlled trial	533,622
#8	Search: ((#5 AND #6) AND #7)	74,584
#7	Search: (((((physical activity) OR (sport*[tiab])) OR exercise[MeSh Terms])) OR (((diet[MeSh Terms]) OR caloric restriction[MeSh Terms]) OR Healthy diet[MeSh Terms]) OR ((parent-child relations) OR (parental involvement)) OR ((psychological therapy) OR psychotherapy))	1,396,484
#6	Search: school based	1,010,862
#5	Search: (((((intervention[tiab]) OR (treatment[tiab])) OR (program[tiab])) OR (study[tiab])) OR (multicomponent program[tiab]))	11,552,821
#4	Search: ((#1 AND #2) AND #3)	6,044
#3	Search: (((ethnic groups[MeSh Terms]) OR (poverty[MeSh Terms])) OR (rural population[MeSh Terms]))	255,357
#2	Search: ((((obes*[tiab]) OR (overweight[MeSh Terms])) OR (overnutrition[MeSh Terms])) OR (pediatric obesity[MeSh Terms]))	382,038
#1	Search: (((child[MeSH Terms]) OR (students[MeSH Terms])) OR (school age populations[MeSH Terms]) OR elementary schoolchildren)	2,181,957

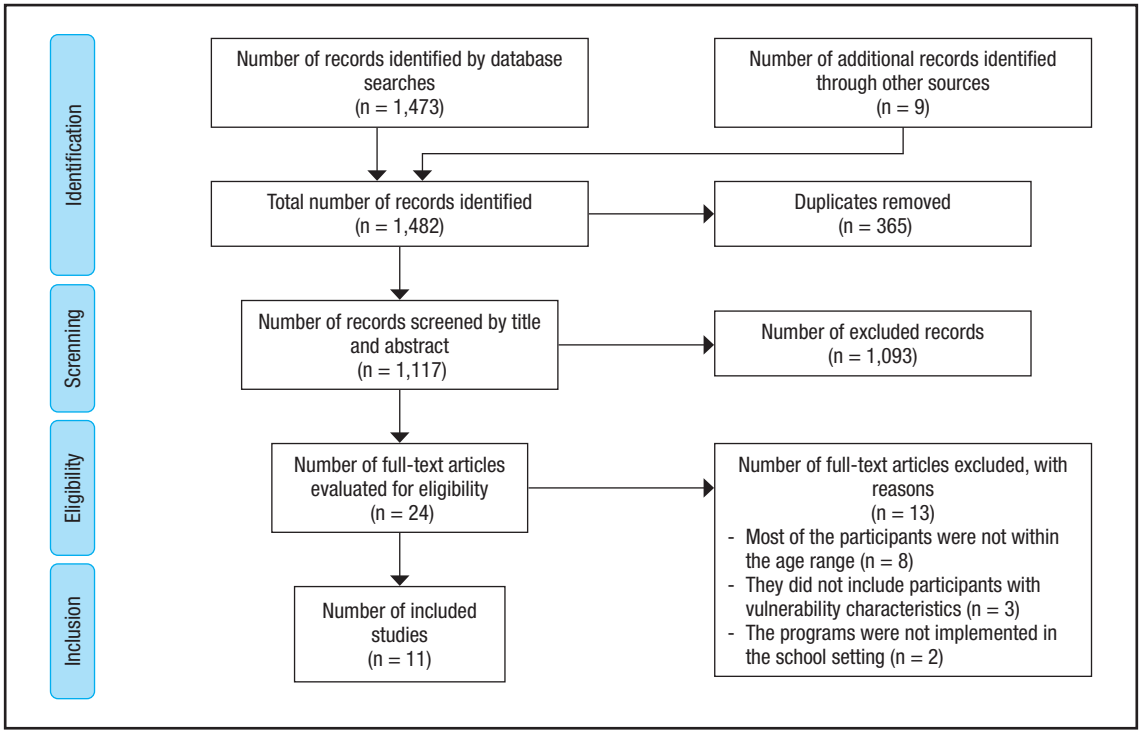

Figure 1.

PRISMA flow chart describing the identification, selection, eligibility and inclusion of studies in this review.

After removal of duplicates, 1,117 titles and abstracts were screened. A total of 11 studies were chosen for inclusion in this review (Fig. 1).

DESCRIPTION OF THE STUDIES

This review considered 11 MLIPs in schoolchildren, made up of two or more components. The studies were conducted in the United States (n = 5), United Kingdom (n = 2), Canada (n = 1), Portugal (n = 1), Taiwan (n = 1) and the Netherlands (n = 1), with publication dates of the articles between 2008 and 2019. The samples of participants were located between 40 and 1,676 children, while the duration of the intervention programs was between 9 weeks and 24 months. The studies included evaluations at different times and only three indicated that there was follow-up, from 6 to 60 months (29,41,45). Most of the studies (n = 6) had a control group, five of them did not receive any intervention component (18,30,37-39) and one received an intervention with partial components (32) (the characteristics of the included studies are in Table II).

Table II. Characteristics of the included studies

References	Study and characteristics of participants	Description of the MLIP	Control description	Variables of interest
El-Rayess et al., United States, *RI Med J* 2017 (19)	Intervention n = 956 Age: 10-12 yrs. Low SES	*Mark, set, go!* is a program that included food and nutrition topics (consumption of fats, sugary drinks, conformation of the food pyramid, among others) and physical activity. Duration: 9 weeks Follow-up: 60 months	No control group	*Primary variables:* BMI, knowledge of nutrition and physical activity. *Secondary variables:* dietary habits and sedentary activity
Lin et al., Taiwan, J *Pediatr N* 2019 (30)	Randomized controlled trial n = 201 Age: 8-10 yrs. Inhabitants of rural area	The NASA mission X program was made up of eight sessions of physical activity (40 minutes long), circuit training and a workshop to improve nutrition knowledge. Duration: 8 months. Follow-up: no	Normal school program	*Primary variables:* BMI. *Secondary variables:* knowledge and behaviors of nutrition and physical activity, interest in NASA and space exploration
Bartelink et al., The Netherlands, *Nutrients* 2019 (32)	Quasi-experimental controlled n = 1676 Age: 4-12 yrs. NSE medium low	*Healthy Primary School of the Future* incorporated two components, the first was to provide a free healthy lunch every day, while the second consisted of structured sessions of physical activity given after lunch. Duration: 24 months. Follow-up: 24 after the end of the program	Control group only received the physical activity component	*Primary variables:* BMI Z-score. *Secondary variables:* time of physical activity, sedentary behavior, active life, dietary intake
Foster et al., United States, *Pediatrics* 2008 (18)	Intervention n = 1349 Age: 9-12 yrs. ≥ 50 % low SES	The School Nutrition Policy Initiative program included of healthy eating and physical activity sessions (50 h/year). The foods provided at school were modified, according to the portion and calorie content recommendations, as well as encouraging the consumption and preparation of healthy snacks. Parents participated by motivating the children to do the 2-1-5 challenge (< 2 hours of television, 1 hour of daily physical activity and eat 5 fruits or vegetables per day). Duration: 24 months. Follow-up: no	Normal school program	*Primary variables:* incidence of overweight and obesity. *Secondary variables:* prevalence and remission of overweight and obesity, BMI Z-score, dietary intake, body dissatisfaction, and hours of activity and inactivity
Choudhry et al., United States, *Prog Community Health Partnersh* 2011 (40)	Pilot study n = 40 Age: 5-12 yrs. African American, low SES	*Power-up* consisted of delivering workshops on nutrition (7 sessions of 1 hour) and physical activity (7 sessions of 1 hour). In addition, there was the participation of parents, who discussed the topics covered weekly, when picking up the children from school and fostering the practice of relevant skills at home. Duration: 14 weeks Follow-up: no	No control group	*Primary variables:* BMI Z-score. *Secondary variables:* blood pressure, dietary intake, health knowledge and beliefs in children and parents

(Continues on next page)

Table II (Cont.). Characteristics of the included studies

References	Study and characteristics of participants	Description of the MLIP	Control description	Variables of interest
Greening et al., United States, *Obesity* 2011 (38)	Intervention n = 450 Age: 6-10 yrs. Inhabitants of rural area	The TEAM Mississippi program incorporated three components: nutrition (an annual session of 45 minutes), physical activity (with two practical sessions per week of 45 minutes) where sports competitions and family participation were promoted, to generate focus groups. Duration: 8 months. Follow-up: no	Normal school program	*Primary variables:* BMI and body fat percentage. *Secondary variables:* waist circumference, physical activity, dietary habits in children and parents, knowledge of nutrition and level of physical condition
Rito et al., Portugal, *Public Health Nutr* 2012 (41)	Intervention n = 266 Age: 6-10 yrs. Low SES	*Obesity Zero* consisted of four nutrition sessions (counseling, a healthy cooking workshop and two extra nutrition education sessions) and physical activity, aimed at parents and children. The program involved families in the process of managing childhood obesity (decrease in adiposity and BMI), addressing the components necessary to achieve behavioral changes at the individual level. The intervention was aimed at achieving five behavioral changes: reducing the consumption of foods rich in fat, salt and sugar; increase the consumption of fruits, vegetables and whole grains; decrease the hours of television; increase levels of physical activity; and increase awareness, positive attitudes about nutrition, healthy diet, and related behavior change. Duration: 6 months. Follow-up: no	No control group	*Primary variables:* BMI, waist circumference, prevalence of obesity and overweight. *Secondary variables:* dietary intake, knowledge and attitudes about nutrition, physical activity, sedentary behavior, sleep
Kulik et al., United States, *Health Educ Behav* 2019 (39)	Quasi-experimental controlled n = 628 Age: Mean of 10 yrs. Low SES	*Building Healthy Communities* purpose was to promote better nutrition through nutrition sessions, as well as to encourage physical activity and a more active life. These activities were carried out through the participation of the school community. Duration: 8 months. Follow-up: no	Normal school program	*Primary variables:* waist-height ratio and BMI. *Secondary variables:* knowledge of health and nutrition
Ronsley et al., Canada, *J School Health* 2013 (33)	Pilot study n = 179 Age: 4-18 yrs. Indigenous	The Healthy Buddies consisted of 21 nutrition and healthy eating lessons and 6 cycles of physical activity (twice a week, lasting 30 minutes). This program also integrates a psychological component, addressing the improvement of self-esteem and body image, healthy development, improvement of social skills, and media awareness. Duration: 10 months. Follow-up: no	Control group (non-participatory)	*Primary variables:* BMI Z-score, waist circumference, and Z-score for blood pressure. *Secondary variables:* physical activity, dietary intake, knowledge of life, health and self-esteem
Sacher et al., UK, *Obesity* 2010 (37)	Randomized controlled trial n = 117 Age: 8-12 yrs. Non-white ethnic origin, low SES	*Mind, Exercise, Nutrition ... Do it!* is a program made up of a nutrition component (8 sessions of 2 hours), where issues of nutrition and healthy eating were addressed. In addition to a physical activity component (8 sessions lasting 1 hour), in which non-competitive games were played and the use of sports facilities (swimming pools) was encouraged by granting free passes. In the psychological component, the objective was to promote behavior change in parents and children (8 sessions). While the family participation consisted of, in addition to receiving all the sessions, being part of the guided visit to the supermarket and collaborating by making healthy recipes. Duration: 6 months. Follow-up: 6 months after the end of the program	Normal school program	*Primary variables:* waist circumference. *Secondary variables:* BMI and percentage of body fat

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Table II (Cont.). Characteristics of the included studies

References	Study and characteristics of participants	Description of the MLIP	Control description	Variables of interest
Smith et al., UK, *BMJ Open* 2013 (42)	Quasi-experimental n = 440 Age: 5-7 yrs. Low SES	*MEND 5-7* consisted of 10 sessions (1 hour and 45 minutes) in which the following components were provided: - Power time (20 minutes) consisted of an exercise in which parents or guardians incorporated healthy food exposure techniques to increase their preference. - Healthy Families (25 minutes) focused on education and the promotion of skills for daily play, active family lifestyles and healthy family eating at home, aimed at parents and children. - Active play was a play session (60 minutes) just for children, which took place while parents/caregivers were in their workshop, focused on active and fun participation. - Workshop for parents/caregivers where psychology issues were discussed to support behavior changes. Duration: 10 weeks. Follow-up: no	No control group	*Primary variables:* BMI. *Secondary variables:* waist circumference, Z-score for waist circumference, psychological symptoms in children, parental self-efficacy, physical activity, sedentary behavior, and portion of fruits and vegetables consumed by parents and children

SES: socioeconomic status; BMI: body mass index.

All of the intervention programs included a PA component, 91 % nutrition, 64 % had FCI, 27 % integrated a psychology component, and 9 % provided school meals. Interventions with three components (55 %) predominated, followed by two (27 %) and four (18 %). Regarding the delivery of the interventions, most of them were provided by health professionals (n = 5) and by trained teachers (n = 4) and only two studies were given by trained peers (Table III). Previously trained teachers and peers were those teachers or students who, before starting the intervention, received training courses by the research team that directed the studies, to provide the intervention in the manner established in the different protocols.

Only three of the 11 included studies investigated the adverse effects of the interventions on the participants (18,32,37). The general features of the components contained in the included MLIPs are described below:

– *PA components:* they consisted of sessions of knowledge and practice of physical activity and a more active lifestyle. With complementary activities such as raffles for sporting goods, non-competitive games, tournaments, free passes to sports facilities.
– *Nutrition components:* they were based on sessions on healthy eating and nutrition. With complementary activities such as nutritional counseling, guided visits to the supermarket, healthy cooking workshops, modifying the school cafeteria menu and playing various games to reinforce knowledge.
– *FCI components:* they consisted of fostering support and motivation for children; in addition to the family receiving the rest of the interventions. The community was also involved in recreational activities.
– *Psychology components:* psychological sessions were provided with a focus on behavior change, self-esteem improvement, body image and social skills.
– *School meal components:* free breakfast, snack and/or healthy lunch delivery.

EFFECTIVENESS OF INTERVENTIONS

Table IV summarizes the findings of the individual studies, categorized according to the results related to adiposity, dietary intake, knowledge of nutrition, PA and sedentary behavior. The statistical significance values (p-values) shown in interventions with a control group refer to the differences between these groups, while the p-values in interventions without a control group show the differences before and after the intervention.

Variables related to adiposity

Eight of 11 studies reported significant effects on at least one variable associated with adiposity (18,19,33,37,38,40-42). These changes occurred in one of two studies made up of physical activity and nutrition (19); in four of five interventions made up of PA, nutrition and FCI (18,38,40,41); in the only study of PA, nutrition and psychology (33), and in the two interventions that included PA, nutrition, FCI and psychology (37,42). Of the interventions lasting ≥ 6 months, five out of eight had a favorable effect on some adiposity variable (18,33,37,38,41) (Table IV).

Table III. Summary of the results of individual studies grouped by characteristics of the MLIP

References	Interventions Components					Imparted by			Duration ≥ 6 months	Secondary Variables with Positive Effects	Positive Results Related to Adiposity
	PA	N	FCI	P	SM	Teacher	Health Professional	Peers			
El-Rayess, et al. *RI Med J* 2017 (19)	√	√	x	x	x	x	x	√	x	Dietary intake, PA and sedentary behavior	BMI
Lin, et al. *J Pediatr N* 2019 (30)	√	√	x	x	x	x	√	x	√	Knowledge of nutrition and PA	
Bartelink, et al. *Nutrients* 2019 (32)	√	x	x	x	√	x	√	x	√	Dietary intake and sedentary behavior	
Foster, et al. *Pediatrics* 2008 (18)	√	√	√	x	x	√	x	x	√		Incidence and prevalence of overweight
Choudhry, et al. *Prog Community Health Partnersh* 2011 (40)	√	√	√	x	x	√	x	x	x		BMI Z-score and prevalence of overweight/obesity
Greening, et al. *Obesity* 2011 (38)	√	√	√	x	x	√	x	x	√	Dietary intake and PA	% BF
Rito, et al. *Public Health Nutr* 2012 (41)	√	√	√	x	x	x	√	x	√	Dietary intake, PA and nutrition knowledge	BMI, WC, prevalence of overweight and obesity
Kulik, et al. *Health Educ Behav* 2019 (39)	√	√	√	x	x	√	x	x	√	Nutrition and PA knowledge	
Ronsley, et al. *J School Health* 2013 (33)	√	√	x	√	x	x	x	√	√		BMI Z-score and WC
Sacher, et al. *Obesity* 2010 (37)	√	√	√	√	x	x	√	x	√	PA and sedentary behavior	BMI and WC
Smith, et al. *BMJ Open* 2013 (42)	√	√	√	√	x	x	√	x	x	PA and sedentary behavior	BMI and WC

PA: physical activity; N: nutrition; FC: family-community involvement; P: psychology; SM: school meals; BMI: body mass index; WC: waist circumference; % BF: percentage of body fat.

Table IV. Results of individual studies grouped according to variables related to adiposity and secondary variables

References	Study details	Results Related to Adiposity	Dietary Intake Results	Nutrition Knowledge Results	PA Results	Sedentary Behavior Results
El-Rayess, et al. *RI Med J* 2017 (19)	*Components:* PA and nutrition *Total participants analyzed:* 787	*BMI:* -0.31 kg/m^2; $p = 0.0183$	*Dietary intake:* -12.3 %; 95 % CI: 0.2 to 0.3; $p < 0.0001$ (juice consumption). -11.8 %; 95 % CI: 0.2 to 0.4; $p < 0.0001$ (consumption of cola drinks in women)		*PA:* + 0.020 h/ week; $p = 0.0347$	*Sedentary behavior:* + 11 %; 95 % CI: 0.1884 to 0.3219; $p = 0.0001$ (participants who watch ≤ 2 hours of screen per week)
Lin, et al. *J Pediatr N* 2019 (30)	*Components:* PA and nutrition *Total participants analyzed:* 197			*Nutrition knowledge:* + 0.62 points; $p < 0.05$ (in the treatment group)	*PA:* + 0.91 points; $p < 0.01$ (in the treatment group)	
Bartelink, et al. *Nutrients* 2019 (32)	*Components:* PA and school meals *Total participants analyzed:* 617		*Dietary intake:* OR 2.63; 95 % CI: 1.7 to 4.0; $p < 0.001$ (fruit consumption). OR 4.39; 95 % CI: 2.7 to 7.2; $p < 0.001$ (vegetable consumption). OR 0.45; 95 % CI: 0.2 to 0.9; $p < 0.027$ (grain consumption). OR 4.52; 95 % CI: 2.9 to 7.0; $p < 0.001$ (dairy consumption). OR 0.19; 95 % CI: 0.1 to 0.3; $p < 0.001$ (butter consumption)			*Sedentary behavior:* - 6.3 min/day; 95 % CI: -31.5 to -6.3; $p = 0.003$
Foster, et al. *Pediatrics* 2008 (18)	*Components:* PA and nutrition. *Total participants analyzed:* 844	*Incidence of overweight:* OR 0.67; 95 % CI: 0.47 to 0.96; $p < 0.05$ (lower in the intervention group). *Overweight prevalence:* OR: 0.65; 95 % CI: 0.54 to 0.79; $p < 0.0001$ (lower in the intervention group)				
Choudhry, et al. *Prog Community Health Partnersh* 2011 (40)	*Components:* PA, nutrition and FCI *Total participants analyzed*: 40	*BMI Z-score:* -1387 units; 95 % CI: 1.053 to 0.809; $p < 0.0001$. *Prevalence of overweight/obesity:* - 6 % (in the group of women)				

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Table IV (Cont.). Results of individual studies grouped according to variables related to adiposity and secondary variables

References	Study details	Results Related to Adiposity	Dietary Intake Results	Nutrition Knowledge Results	PA Results	Sedentary Behavior Results
Greening, et al. *Obesity* 2011 (38)	*Components:* PA, nutrition and FCI *Total participants analyzed:* 450	*% BF:* - 0.56 %; $p = 0.02$ (lower in the intervention group)	*Dietary intake:* -1.38 points; $p = 0.0005$ (higher in the intervention group) (fat consumption)		*PA:* + 0.76 points; $p = 0.04$ (higher in the intervention group)	
Rito, et al. *Public Health Nutr* 2012 (41)	*Components:* PA, nutrition and FCI *Total participants analyzed:* 199	*BMI:* - 0.4 kg/m^2; 95 % CI: - 0.6 to - 0.2; $p < 0.001$. *WC:* -2.0 cm; 95 % CI: -2.7 to -1.3; $p < 0.001$. *Overweight prevalence:* + 1.6 %. *Obesity prevalence:* -9.1 %	*Dietary intake:* + 2.5 g of fiber; 95 % CI: 0.7 to 4.2; $p = 0.005$	*Nutrition knowledge:* + 5.8 points; 95 % CI: 4.6 to 7.1; $p < 0.001$	*PA:* + 0.3 days/ week; 95 % CI: 0.1 to 0.5; $p = 0.008$ (from vigorous physical activity)	
Kulik, et al. *Health Educ Behav* 2019 (39)	*Components:* PA, nutrition and FCI *Total participants analyzed:* 628			*Nutrition knowledge:* + 2.63 points (in the treatment group)	*PA:* + 3.38 points (in the treatment group)	
Ronsley, et al. *J School Health* 2013 (33)	*Components:* PA, nutrition and psychology *Total participants analyzed:* 179	*BMI Z-score:* - 0.06 units; $p = 0.028$ (lower in the intervention group). *WC:* - 2.1 cm; $p < 0.0001$ (lower in the intervention group)				
Sacher, et al. *Obesity* 2010 (37)	*Components:* PA, nutrition, FCI and psychology *Total participants analyzed:* 82	*BMI:* – 1.2 kg/m^2; 95 % CI: – 1.8 to – 0.6; $p < 0.0001$ (lower in the intervention group). *WC:* – 4.1 cm; 95 % CI: – 5.6 to – 2.7; $p < 0.0001$ (lower in the intervention group)			*PA:* 3.9 h/ week; 95 % CI: 0.1 to 7.8; $p = 0.04$ (higher in the intervention group)	*Sedentary behavior:* – 5.1 h/week; 95 % CI: – 9.0 to – 1.1; $p = 0.01$ (lower in the intervention group)
Smith, et al. *BMJ Open* 2013 (42)	*Components:* PA, nutrition, FCI and psychology *Total participants analyzed:* 168	*BMI:* – 0.5 kg/m^2; 95 % CI: - 0.6 to – 0.4; $p < 0.0001$. *WC:* – 0.9 cm; 95 % CI: – 1.3 to – 0.5; $p < 0.0001$			*PA:* + 2.9 h/ week; 95 % CI: 1.2 to 4.7; $p < 0.01$	*Sedentary behavior:* –4.1 h/w; 95 % CI: – 6.1 to – 2.2; $p < 0.0001$

PA: physical activity; FCI: family-community involvement; BMI: body mass index; WC: waist circumference; % BF: percentage of body fat; CI: confidence interval.

Prevalence and incidence of overweight and/or obesity

Three of 11 studies reported a reduction in prevalences, one for overweight (18), another for obesity (41), and the third presented decreased for overweight/obesity joint (40). The three studies were made up of PA, nutrition and FCI, two of them lasted ≥ 6 months (18,41). The only intervention that achieved a reduction in the incidence of overweight had the aforementioned characteristics (18).

BMI/BMI Z-*score*

Six of 11 studies showed significant effects on BMI or BMI Z-score (19,33,37,40-42), three of them had a duration of ≥6 months (33,37,41). Such changes were mainly found in interventions that included PA, nutrition and FCI (40,41), and in those that included, in addition to the three previous elements, the component of psychology (37,42).

Body fat percentage

Of all the included studies, one reported a significant reduction in body fat percentage. This consisted of PA, nutrition and FCI and lasted ≥ 6 months (38).

Waist circumference

Four of 11 studies presented a reduction in waist circumference (33,37,41,42), three of them with a duration of six or more months (33,37,41). The interventions that were most effective for this variable were composed of PA, nutrition, FCI and psychology components (37,42).

Result in dietary intake

Four of 11 interventions presented a significant change in dietary intake (micro and macronutrients) (19,32,38,41); three of them with a duration equal to or greater than 6 months (32,38,41). The studies that achieved more consistent changes in this variable, specifically on macronutrients (fats and fiber), according to the components that integrated them were those of PA, nutrition and FCI (38,41).

Nutrition knowledge outcomes

Three of the total of the studies had significant improvements regarding nutrition knowledge (30,39,41). Two of them lasted 6 months or more and consisted of PA, nutrition and FCI components (39,41).

Physical activity results

Seven of 11 interventions reviewed showed favorable changes in physical activity (19,30,37-39,41,42), of which five lasted ≥ 6 months (30,37-39,41). The components of the interventions with the most consistent results were PA, nutrition, and FCI (38,39,41), followed by those that also included psychological aspect (37,42).

Results of sedentary behavior

Four of 11 interventions had improvements in the reduction of sedentary behavior (19,32,37,42), in half of these, the application lasted 6 months or more (32,37). The studies with the best results were made up of PA, nutrition, FCI and psychology components (37,42).

Family/community involvement

It was found that 7 of 11 studies included FCI (18,37-42). These components were part of the most consistent interventions, which also included nutrition and PA components.

DISCUSSION

As a summary of the results, the narrative synthesis suggests that MLIPs integrated by PA, nutrition and FCI components are more effective in achieving changes in variables related to adiposity (prevalence and incidence of overweight and obesity) and in indicators of these conditions, specifically in BMI/BMI Z-score and fat percentage, in schoolchildren from vulnerable groups. In relation to the secondary variables dietary intake, knowledge of nutrition and physical activity, the interventions that include PA, nutrition and FCI also obtained better results.

Around 80 % of the interventions with components of PA, nutrition and FCI, had a duration of ≥ 6 months. This characteristic is favorable for achieving significant changes in the variables associated with adiposity (29). These interventions were also characterized for having been taught mostly (80 %) by teachers who received prior training, which is consistent with what has been reported in other studies (43-45).

The significant improvements in these interventions may be due to the fact that they actively involve parents, who have an essential influence on the acquisition and maintenance of healthy eating habits in children (46). Likewise, it has been described that parental control, attitudes and behavior are closely associated with childhood overweight and obesity (47). One study showed that parental monitoring of children's food choices has been shown to reduce non-nutritious food intake and total caloric intake (48). Therefore, the involvement of the family is an element that must be considered in the MLIP, especially in schoolchildren from vulnerable groups who are additionally affected by the social deficiencies of the parents.

The conjunction of interventions that promote physical activity and a balanced dietary intake confront the fundamental aspects related to the increase in overweight and obesity in schoolchildren, such as the characteristics of the diet, the level of PA and the degree of sedentary lifestyle (49), closely related to dynamic energy balance (50).

The interventions that, in addition to PA, nutrition and FCI, included a psychology component, achieved notable results by improving the BMI/BMI Z-score, waist circumference, PA and sedentary behavior. However, when designing and implementing MLIPs, it is sought not only that they be effective but also that they be efficient, that is, that the best results are achieved with the least amount of resources employed as possible (51). Thus, integrating one more component would entail the use of more physical, material and human resources; consequently, opting for the design of three components (PA, nutrition and FCI) would be more beneficial in all aspects, and would facilitate its replication in different environments, especially in those affected by poverty (51,52).

This is the first review of MLIPs in schoolchildren from vulnerable groups for the prevention, maintenance and remission of overweight and obesity, when evaluating indicators of adiposity. In the particular context of vulnerability that these children live in, a greater increase in the prevalences of the disease is observed compared to the rest of the population (12,21-23). Given the situation, the design and implementation of specific interventions is recommended (52), and the importance of knowing and understanding which interventions work best in these settings is highlighted.

The search strategy did not include gray literature, articles in a language other than English, and a publication date was established as of the year 2000. All the elements mentioned above can cause publication and language biases, and influence the representativeness of the articles that were selected for the review, in relation to the studies that have been performed.

The validity of the findings presented is a function of the methodological quality of the individual studies. Since the risk of bias assessment was not carried through for the different domains (design, performance and presentation of the results), suggested in the Cochrane manual for systematic reviews in interventions (53), it is not possible to classify the quality of the evidence for each study.

In conclusion, the review suggests that MLIPs are effective in preventing and treating overweight and obesity, finding that 73 % of the studies had significant improvements in at least one variable related to adiposity. The most successful intervention programs in schoolchildren from vulnerable groups were made up of nutrition, PA and FCI components, lasting 6 months onwards, and were delivered by trained teachers. The findings of this work should be considered with caution due to reported methodological limitations.

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Revisión

Probiotics in the treatment of infantile colic: a meta-analysis of randomized controlled trials

Probióticos en el tratamiento del cólico infantil: un metaanálisis de ensayos controlados aleatorios

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Abstract

Introduction: infantile colic has always been a problem for caregivers, and research on probiotics in treating and preventing infant colic is still controversial.

Material and methods: trials were performed before November 2021 and retrieved from the PubMed, Web of Science, The Cochrane Library, Medline, and Google Scholar databases. Data extraction and quality evaluation of the trials were performed independently by two investigators. A meta-analysis was performed using Review Manager 5.3. It includes nine randomized controlled trials in 587 infants with colic.

Results: eight of these experiments described probiotics for the prevention and treatment of intestinal colic in infants, with 228 in the probiotics group and 227 in the placebo group, with a total effective rate (RR = 1.88, 95 % CI: 1.61 to 2.19, $p < 0.00001$).

Conclusion: probiotics may improve therapeutic and preventive effects, especially within four weeks of probiotic treatment.

Keywords:

Infantile colic. Probiotic. Placebo. Treatment. Meta-analysis.

Resumen

Introducción: el cólico infantil siempre ha sido un problema para los cuidadores y la investigación sobre los probióticos para tratar y prevenir el cólico infantil sigue siendo controvertida.

Material y métodos: los ensayos se realizaron antes de noviembre de 2021 y se recuperaron de las bases de datos PubMed, Web of Science, The Cochrane Library, Medline y Google Scholar. Dos investigadores realizaron de forma independiente la extracción de datos y la evaluación de la calidad de los ensayos. Se realizó un metaanálisis utilizando Review Manager 5.3. Incluye nueve ensayos controlados aleatorios en 587 lactantes con cólicos.

Resultados: ocho de estos experimentos describieron probióticos para la prevención y el tratamiento del cólico intestinal en lactantes, con 228 en el grupo de probióticos y 227 en el grupo de placebo, con una tasa efectiva total (RR = 1,88, IC del 95 %: 1,61 a 2,19, $p < 0,00001$).

Conclusión: los probióticos pueden mejorar los efectos terapéuticos y preventivos, especialmente dentro de las cuatro semanas posteriores al tratamiento con los mismos.

Palabras clave:

Cólico infantil. Probiótico. Placebo. Tratamiento. Metaanálisis.

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INTRODUCTION

Infantile colic is a behavioral syndrome that manifests as irritable or crying behaviors that are difficult to soothe in healthy babies. It appears for more than three hours a day, lasts for more than three days per week, and lasts for more than three weeks (1). It usually occurs within three months of birth, but approximately 10 % of cases occur after 4-5 months. However, as neurophysiological development occurs, the symptoms of infantile colic will gradually improve, and the symptoms among infants aged three to four months will disappear on their own. In addition, infantile colic can increase the occurrence of psychological distress and depression in caregivers, hinder the development of heathy mother-to-child relationships, and cause infants to suffer accidental injuries and impaired family function (2).

The pathogenesis of infantile colic is unclear. Gastrointestinal motility, lactose intolerance, and psychosocial factors may be involved in the occurrence of infantile colic, but there is no firm evidence (3). Current treatments for infantile colic include dietary adjustments, pharmacological and behavioral interventions, and complementary and alternative therapies, but none of these treatments are effective (4). However, probiotics are viable, nonpathogenic microorganisms that can potentially positively affect a child's body by balancing the intestinal flora. Several beneficial effects of probiotics on the host intestinal mucosal defense system have been identified. These include blocking pathogenic bacterial effects by producing bactericidal substances and competing with pathogens and toxins for adherence to the intestinal epithelium (5-7). The results of research on the treatment and prevention of colic in infants remain controversial. Therefore, this meta-analysis aimed to systematically evaluate the effectiveness of probiotics in preventing and treating infantile colic, to provide evidence-based medical support for clinical practice.

METHODS

DATA SOURCES AND LITERATURE SEARCH

We followed the guidelines of the meta-analysis of observation studies in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). A comprehensive computer search of PubMed, Web of Science, The Cochrane Library, Medline, and Google Scholar databases, collection of published studies on the prevention and treatment of infantile colic as of 2021-11, was performed. Search terms included (probiotic or probiotics or probiotic bacteria) AND (colic or infantile colic or intestinal colic) AND (infant or kid or child and pedia) AND (prevention or treatment or excessive crying or duration of crying or crying time or maternal mental health). The literature was retrieved using the reference backtracking method to avoid missing relevant research as much as possible.

STUDY SELECTION

Inclusion criteria were: a) published randomized controlled study (randomized controlled trials [RCTs]); b) assessed association between probiotics and colic in infants; and c) the experimental group was treated with probiotics, and the control group was treated with placebo. In the data, the titles and abstracts of the searched papers were independently screened by two reviewers, and articles that did not meet the above inclusion criteria were excluded. The third person resolved the differences and contradictions between them. The main data extracted include the first author's last name, year of publication, country of study, indication, sample size, interventions, treatment strategy, duration, and outcomes. The overall details of risk of bias were shown (Figs. 1 and 2). Papers selected for retrieval were assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardized critical appraisal instru-

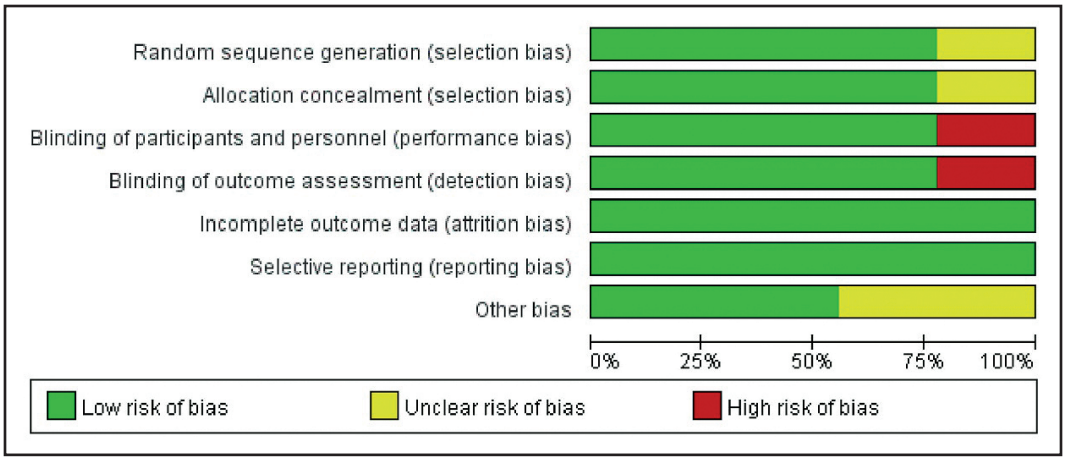

Figure 1.
Risk of bias.

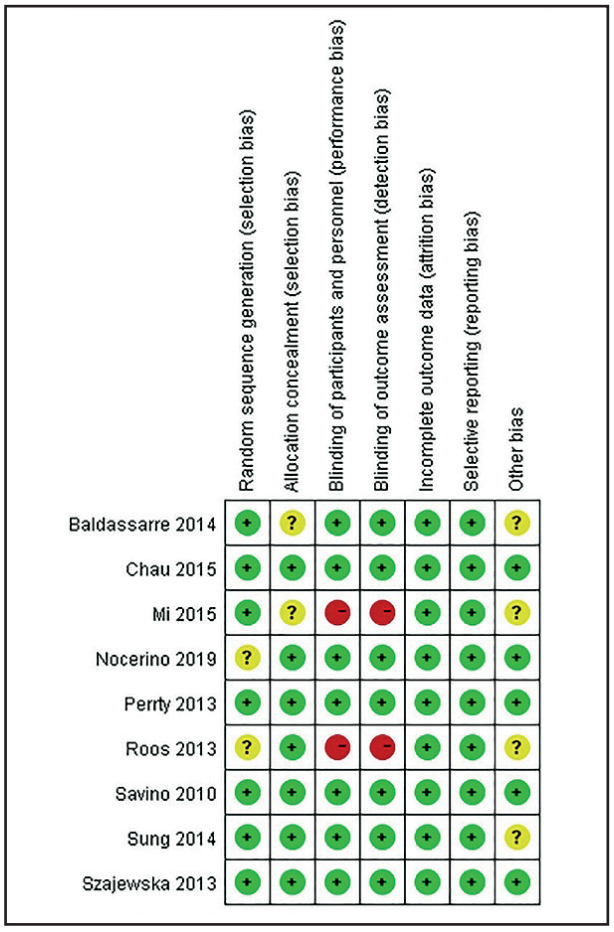

Figure 2.
Risk of bias summary.

ments for RCTs available through The Cochrane Collaboration. Five trials were categorized as being at low risk of bias, three as being at unclear risk of bias and two as being at high risk of bias. All quality measures recorded, and data extracted for meta-analysis, occurred within Review Manager 5.3.

STATISTICAL ANALYSES

Meta-analysis was performed using Review Manager 5.3. The effect of counting data was RR value and 95 % confidence interval (CI). It was estimated by the Cochran Q test and I^2 statistic. Q statistic was considered as significant when the p value was less than 0.10, and the I^2 index was used to quantify the extent of statistical heterogeneity. If $I^2 < 50$ %, $p > 0.05$, it is considered that there is no heterogeneity, and a fixed effect model is used; if $I^2 > 50$ %, $p \leq 0.05$, it is considered that there is heterogeneity, and a random effect model is used for analysis. However, there is heterogeneity between the results of each study, $I^2 > 50$ %, $p \leq 0.05$; the source of heterogeneity needs to be explored, and sensitivity analysis is necessary if necessary. The publication bias was tested using the Begg method, with a test level of $p < 0.05$.

RESULTS

STUDY CHARACTERISTICS

As shown in figure 3, by searching the database, 894 related studies were screened. After reading the title and abstract, 873 studies were excluded. Of the remaining 21 studies, three studies are no quantitative assessment, two studies are no out-

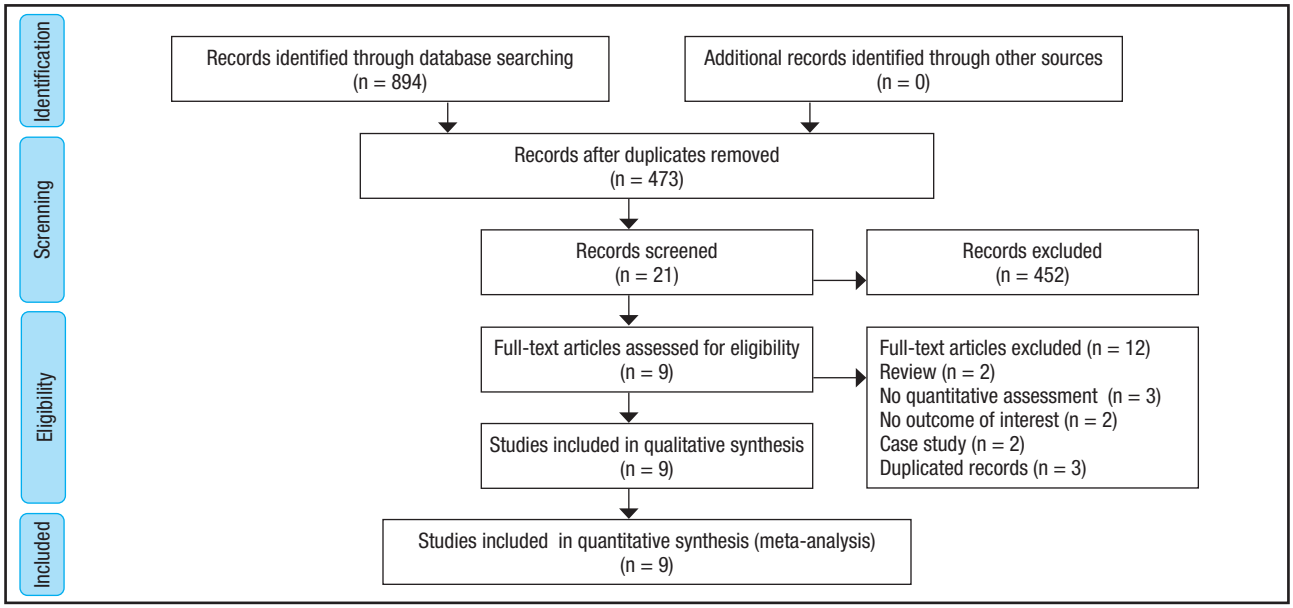

Figure 3.
PRISMA flow diagram of the search result of the meta-analysis.

come of interest, two studies are review, two studies are case study, and three studies are duplicated records, therefore excluded. Finally, the meta-analysis includes nine RCTs between 2010 and 2020 (8-16), and a total of 587 infant patients. Table I summarizes the characteristics of the studies included. Three studies were conducted in Italy (8,14,16) and one in Poland (9), Sweden (10), Australia (11), China (12), Canada (13) and Finland (15), respectively. All included studies provided probiotic species and application metrics, and most provided number of responders.

PRIMARY END POINT

Associations between whole infant colic and the probiotic treatment and prevention

As shown in figure 4, of the nine studies included, eight (8-10,12-16) examined the effectiveness of placebo and probiotics in the treatment and prevention of infantile colic. There was statistical heterogeneity between studies (I^2 = 62 %, p = 0.01), and the analysis was performed using a random effects model. The combined effect size (relative risk [RR] = 1.88, 95 % CI: 1.61 to 2.19, p < 0.00001). The results of the analysis suggest that probiotics are generally beneficial for the treatment and prevention of intestinal colic in infants.

Treatment of infantile colic with probiotics in one month

As shown in figure 5, four of the nine studies included (8,9,12,13) examined the effects of probiotics on infant colic at seven days (RR = 2.47, 95 % CI: 1.40 to 4.36 , p = 0.002); four studies (8,9,12,13) examined the effects of probiotics on infant colic at 14 days (RR = 3.43, 95 % CI: 1.30 to 9.01, p = 0.01); five studies (8-10,12,13) examined the effects of probiotics on infant colic at 21 days (RR = 2.42, 95 % CI: 1.35 to 4.35, p = 0.003); and three studies (9,12,14) examined the effect of probiotics on infant colic at 28 days (RR = 2.48, 95 % CI: 1.28 to 4.80, p = 0.007). The results of the comprehensive analysis suggest that probiotics are more effective than a placebo in treating intestinal colic in infants within seven, 14, 21, and 28 days.

SUBGROUP ANALYSES AND SENSITIVITY ANALYSES

Figure 6 shows the results of a subgroup analysis of the effectiveness of probiotics for treating and preventing intestinal colic in infants. The subgroup analysis examined groups by treatment method. Six studies (8-10,12-14) examined the effects of probiotics on infant colic (RR = 2.08, 95 % CI: 1.45 to 2.98, p < 0.001). There was statistical heterogeneity (I^2 = 74 %, p = 0.002). Two studies (15,16) examined the effect of probiotics on the prevention of intestinal colic in infants (RR = 1.48, 95 % CI: 1.11 to 1.99, p = 0.008), and there was no statistical heterogeneity between studies (I^2 = 0 %, p = 0.84). The results of the subgroup analysis show that probiotics are effective not only in treating infantile colic, but also in preventing infantile colic. Because there was substantial heterogeneity among the studies that examined treatment, a sensitivity analysis was performed on the treatment group. As shown in figure 7, the overall sensitivity analysis results are stable, and the main sources of heterogeneity are the studies by Mi et al. (12) and Chau et al. (13). After excluding the two studies, the combined effect size reduced the heterogeneity (I^2 = 24 %, p = 0.26). However, after excluding any other literature, the heterogeneity did not change significantly.

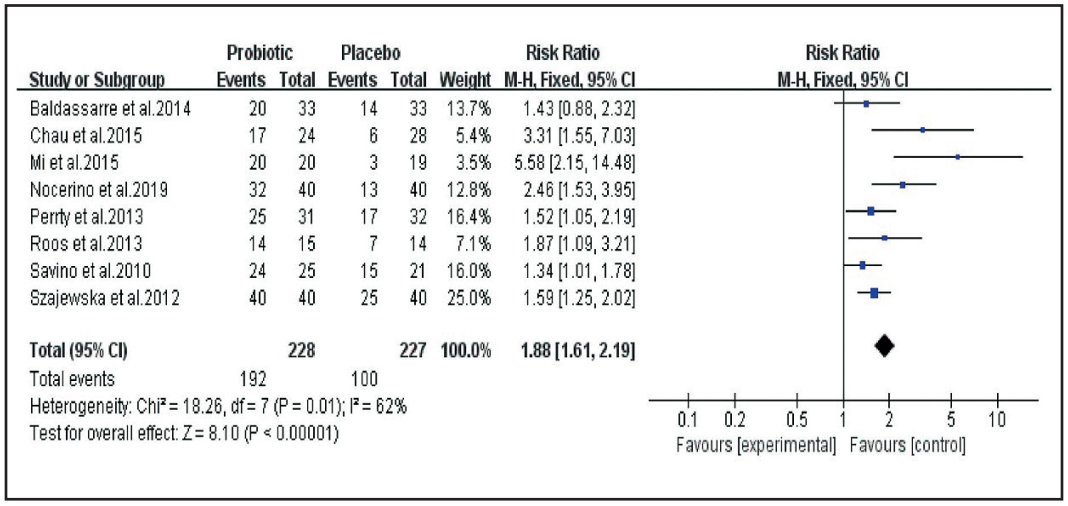

Figure 4.

Total effectiveness of probiotics in preventing and treating infantile colic.

Table I. Characteristics of included studies for the analysis of efficacy

Study	Year	Location	Indication	Sample size (B/G)		Duration of intervention	Intervention	Treatment strategy	Outcomes
				Probiotic	Placebo				
Savino et al. (8)	2010	Italy	Therapy	14/11	15/10	21 days	*L. reuteri* DSM 17938 in a mixture of sunflower oil and medium-chain triglyceride oil	*L. reuteri* at a dose of 10^8 CFU/day for 21 days	Decrease in daily average crying time of < 50 %; infants intestinal microflora; safety
Szajewska et al. (9)	2013	Poland	Therapy	24/16	22/18	28 days	*L. reuteri* DSM 17938	*L. reuteri* at a dose of 10^8 CFU/day for 21 days	Decrease in daily average crying time of < 50 %; parental perceptions of colic severity; family quality of life; safety
Roos et al. (10)	2013	Sweden	Therapy	9/6	7/7	21 days	*L. reuteri* DSM 17938	*L. reuteri* at a dose of 10^8 CFU/day for 21 days	Decrease in daily average crying time of < 50 %; gut microbiota
Sung et al. (11)	2014	Australia	Therapy	37/48	48/34	6 months	*L. reuteri* DSM 17938 an oil suspension	*L. reuteri* at a dose of 0.2×10^8 CFU/day for 1 month	Crying time; parental maternal depression
Mi et al. (12)	2015	China	Therapy	14/7	11/10	28 days	An oil based suspension containing *L. reuteri* DSM 17938	*L. reuteri* at a dose of 10^8 CFU/day for 21 days	Decrease in daily average crying time of < 50 %; parental maternal depression
Chau et al. (13)	2015	Canada	Therapy	14/13	14/14	21 days	10^8 CFU/5 drops of *L. reuteri* DSM 17938 suspended in sunflower oil, medium-chain triglyceride oil, and silicon dioxide	*L. reuteri* at a dose of 10^8 CFU/day for 21 days	Decrease in daily average crying time of < 50 %; safety
Nocerino et al. (14)	2020	Italy	Therapy	22/18	21/19	28 days	lactis BB-12®, DSM 15954 in oil maltodextrin suspension	lactis BB-12® at a dose of 10^9 CFU/day for 28 days	Decrease in daily average crying time of < 50 %; gut microbiota structure and butyrate, beta-defensin-2 (HBD-2), cathelicidin (LL-37), secretory IgA (sIgA) and fecal calprotectin levels were assessed
Perrty et al. (15)	2013	Finland	Prophylaxis	16/15	23/8	2 months	*Lactobacillus rhamnosus* GG (ATCC 53103)	*Lactobacillus rhamnosus* GG (ATCC 53103) 1×10^9 CFU/day in 1 dose from day 1 to day 30 and 1×10^9 CFU twice daily from day 31 to day 60	Decrease in daily average crying time of < 50 %; frequency of stools, consistency of stools

(Continues on next page)

Table I (Cont.). Characteristics of included studies for the analysis of efficacy

Study	Year	Location	Indication	Sample size (B/G)		Duration of intervention	Intervention	Treatment strategy	Outcomes
				Probiotic	Placebo				
Baldassarre et al. (16)	2014	Italy	Prophylaxis	33*	33*	36 weeks gestation to 4 weeks postnatally	High concentration, multi-strain probiotic supplement	900 billion viable lyophilised bacteria of *4 different strains of lactobacilli (L. paracasei* DSM 24733, *L. planetarium* DSM 24730, *L. acidophilus* DSM 24735 and *L. delbrueckii subspbulgaricus* DSM 24734), 3 strains of bifidobacterial (B longum DSM24736, BB breve DSM24732 and B infantis DSM24737) and 1 strain of *Streptococcus thermophilus* DSM 24731	Decrease in daily average crying time of < 50 %; analysis of breast milk for cytokine patterns, secretory IgA in breast milk and stools, fecal lactoferrin

**No specific number of boys and girls reported.*

SECONDARY END POINTS

Impact on parent mental health

Figure 8 shows that two studies (11,12) examined the effects of probiotics on the mental health of pregnant women after treatment and prevention of infant colic (WMD = -1.43, 95 % CI: -2.76 to -0.10, p = 0.04). There was no statistical heterogeneity between the studies (I^2 = 0 %, p = 0.32). The analysis shows that probiotics can make parents feel happy by affecting the baby's intestinal colic.

PUBLICATION BIAS AND SENSITIVITY ANALYSIS

Although the scatter of the funnel plot is slightly asymmetric (Fig. 9), the publication bias was detected by the Begg method. The results showed that the Begg method of the included study was p = 0.063, and there was no evidence of publication bias in the included study.

DISCUSSION

To the best of our knowledge, this is the first meta-analysis examining the effectiveness of probiotics in the treatment and prevention of infantile colic. The results of the meta-analysis show that probiotics are significantly more effective in treating intestinal colic in infants than placebo. Subgroup analysis revealed that probiotics were superior to placebo not only in the treatment of infant colic, but also in prevention. In addition, the use of probiotics to relieve intestinal colic in infants can lead to reduced psychological stress among parents; the results of this study were not found in similar studies.

Infantile colic affects a large proportion of infants. Infants may exhibit symptoms such as uncomfortable crying, painful expressions, high-pitched crying, and curled legs (17). These symptoms are enough to make researchers realize that these infants are in pain. However, in more than 90 % of cases of intestinal colic in infants, the intestinal colic does not need to be treated, but rather, caregivers need to be helped through the challenging period of child growth and development (18). In general, if the symptoms of infantile colic can be relieved and the attention of the caregiver can be appropriately shifted, then infantile colic is not a threat to the baby's body (19). Conversely, an incorrect diagnosis and inappropriate treatment can physically and emotionally harm babies and caregivers unnecessarily (20). Clinicians need to assess caregivers' vulnerabilities, such as depression and lack of social support, and provide sustainable help to the family (21). If attempts to intervene in the baby's intestinal colic are unsuccessful, then it is likely that the caregiver's anxiety and frustration will be increased, eventually impairing the caregiver's ability to comfort the baby and making him/her doubt his/her ability as a caregiver (22).

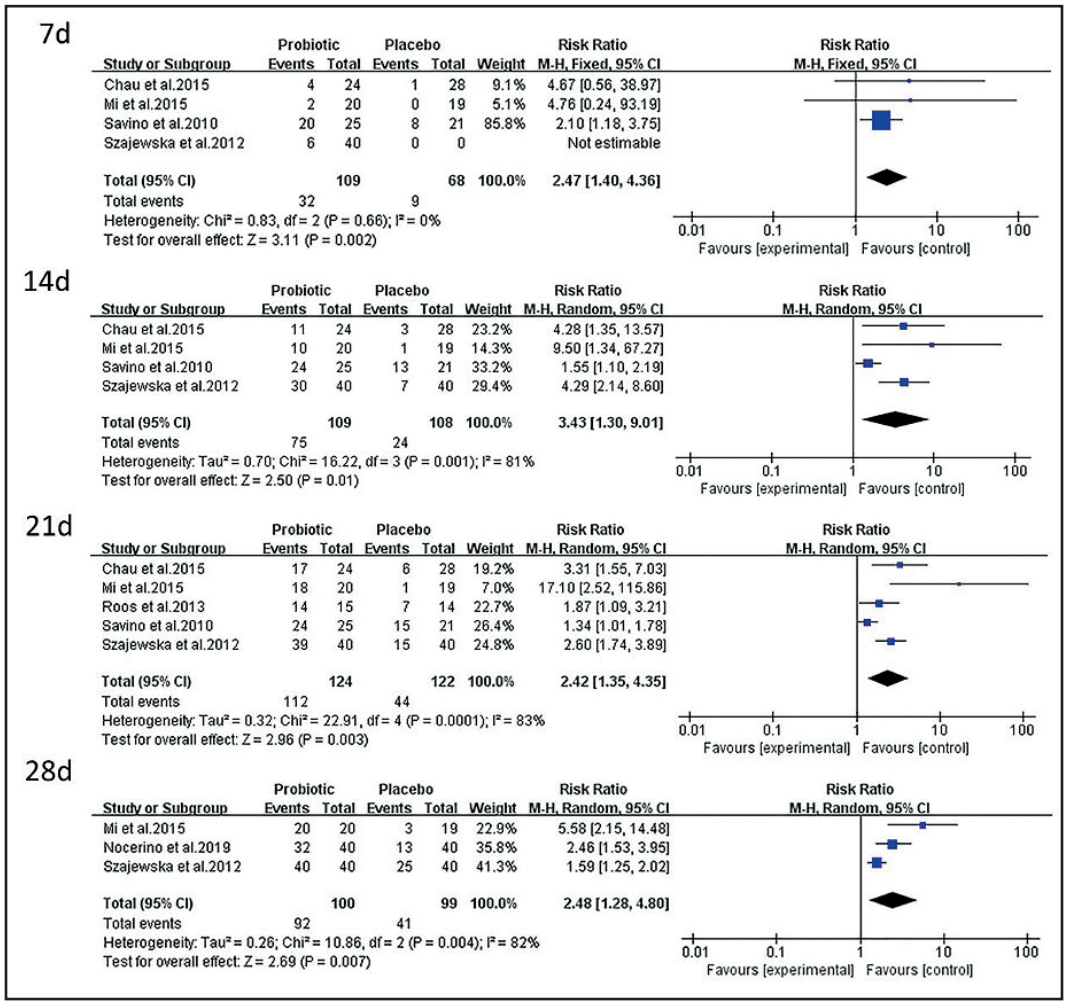

Figure 5.

Effectiveness rate comparison of 7, 14, 21 and 28 days in probiotic groups and the placebo group.

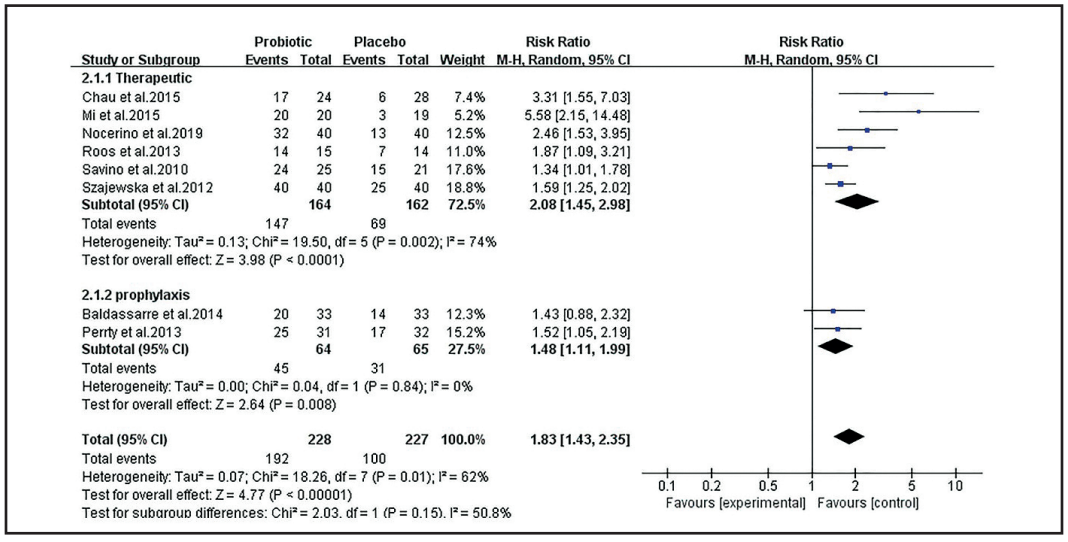

Figure 6.

Subgroup analysis of treatment and prevention groups.

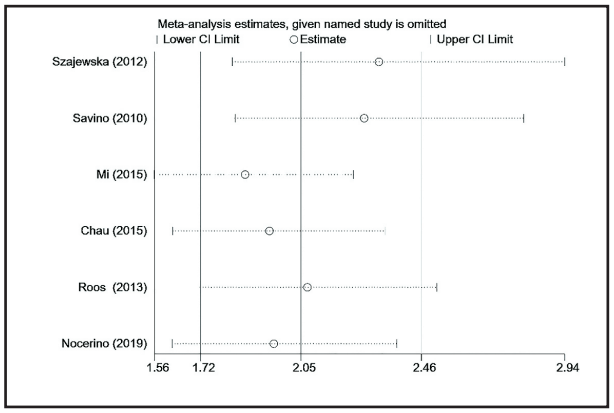

Figure 7.

Sensitivity analysis.

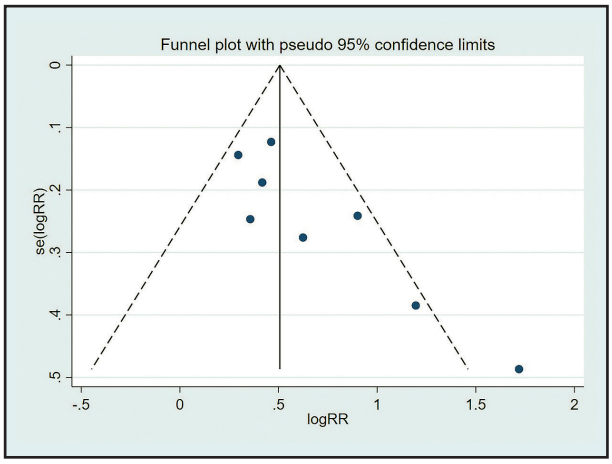

Figure 9.

Funnel diagram of effective probiotics for preventing and treating infantile colic.

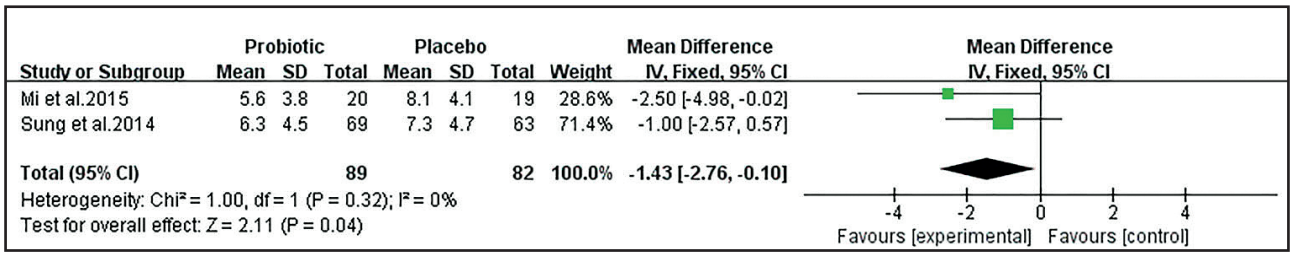

Figure 8.

Compared with the placebo group, the probiotic group can benefit parents' mental health.

In our meta-analysis, eight RCTs produced relatively stable results: probiotics can be used to treat and prevent infantile colic, even at seven, 14, 21, and 28 days. A sensitivity analysis revealed that the studies by Mi et al. (12) and Chau et al. (13) affected the stability of the results. Based on the above analysis, we reached a comprehensive conclusion that probiotics can effectively treat and prevent infantile colic, suggesting that probiotics can play an active role in the treatment and prevention of infantile colic. Gerasimov et al. (23) studied the auxiliary application of *Lacticaseibacillus rhamnosus (L. rhamnosus)* 19070-2 and *Lactobacillus reuteri (L. reuteri)* 12246 in 84 infants with colic. The mean change in cry and fuss time from day 0 to day 28 was 163 ± 99 minutes in the probiotic group and 116 ± 94 minutes in the control group ($p = 0.019$). The findings confirm that *Lactobacilli* can be used to decrease cry and fuss time and to provide dietary support in exclusively breastfed infants with colic. Indrio et al. (24) studied 238 infants who received *L. reuteri* DSM 17938 probiotics for three months. At three months of age, infants in the probiotic group showed a lower mean duration of crying time (38 *vs* 71 minutes; $p < 0.01$), confirming that the use of this probiotic can prevent the incidence of gastrointestinal disorders in infants. In addition, the probiotic strains studied in this paper mainly include *Lactobacillus* (*L. reuteri* DSM17938) and *Bifidobacterium* (*B. lactis* Bb-12), which are currently the best studied probiotics. Some lactobacilli and *Bifidobacterium* strains have proven to be most effective if treatment is introduced early (25). In a study by Chau et al. (13), infants took a daily dose of *L. reuteri* (1×10^8 colony forming units). By 21 days, total average crying and fussing times throughout the study were significantly shorter among infants with colic in the probiotic group compared with infants in the placebo group (29 ± 13 hours *vs* 37 ± 13 hours, $p = 0.028$). Infants given *L. reuteri* DSM 17938 showed a significant reduction in daily crying and fussing times at the end of treatment period compared with those receiving placebo (64 minutes/day *vs* 87 minutes/day, $p = 0.045$). On day 21, a significantly higher proportion of infants in the *L. reuteri* DSM 17938 group responded to treatment with a ≥ 50 % crying time reduction compared with infants given placebo (17 *vs* 6, $p = 0.035$). The results of the study by Nocerino et al. (14) showed that infants treated with lactis BB-12 at a dose of 10^9 CFU/day for 28 days from week 2 had a higher rate of ≥ 50 % reduction in mean daily crying time. After treatment was stopped, no infants relapsed. Mean crying times were reduced in both groups, but the effect was higher in the BB-12 group (-4.7 ± 3.4 *vs* -2.3 ± 2.2, $p < 0.05$). Average daily stool frequency was reduced in both groups, but the effect was significantly higher in the BB-12 group; stool consistency was

similar in both groups. *Bifidobacterium* abundance (significantly associated with reduced crying time), butyrate and increased levels of HBD-2, LL-37, sIgA in the BB-12 group were associated with decreased fecal calcin levels.

Although this study has formulated strict inclusion and exclusion criteria, it still has the following limitations: a) statistical heterogeneity has been detected in the current study (heterogeneity may be due to different probiotic types and different sample sizes); b) some studies did not explain randomization methods, distribution methods, and statistical analysis methods; c) due to language restrictions, only English literature was included, and literature in other languages was excluded; d) the quality of different studies varies, which may lead to bias; and e) different research treatments are different.

The differences in treatments may directly lead to the degree of colic in infants and affect the prognosis. Nowadays, the international community has been working to find a specific probiotic strain with good effect and good safety to better treat infant patients, but it seems to be cautious about probiotics treatment and prevention of infant colic. Therefore, in the future, more rigorous multi-center randomized double-blind controlled trials will further clarify the significance of probiotics in preventing and treating colic in infants.

CONCLUSION

In summary, the meta-analysis has extensively evaluated the existing data, and the results show that probiotics have a certain positive effect on infant colic. Probiotics may improve therapeutic and preventive effects, especially within four weeks of probiotic treatment. However, the conclusions of this study are limited by the heterogeneity of the included randomized controlled trials and require careful consideration. Therefore, we must comprehensively consider the situation of the baby and provide the most appropriate treatment plan under the premise of respecting the wishes of the guardian, improving the treatment effects for the baby, and improving the quality of family life.

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ARÁN

Nutrición Hospitalaria

Revisión

Vitamin D status in irritable bowel syndrome and the impact of supplementation on symptoms: a systematic review and meta-analysis

Estado de la vitamina D en el síndrome del intestino irritable y el impacto de la suplementación en los síntomas: una revisión sistemática y metaanálisis

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Abstract

Background: latest studies have shown that vitamin D deficiency is related to the occurrence of irritable bowel disease (IBS), and taking vitamin D as a supplement can alleviate the symptoms of irritable bowel disease. However, clinical treatment of irritable bowel disease with vitamin D is controversial.

Objective: we conducted a meta-analysis of all clinical trials to evaluate the associations between vitamin D and irritable bowel disease.

Methods: we screened all randomized controlled trials that were published before December 20, 2021 from the following databases: Medline, Web of Science, China National Knowledge Infrastructure (CNKI), Cochrane Central, and Clinical Trial. We used RevMan 5.4.1 and Stata 16.1 to analyze the relevant data. The standardized mean difference (SMD) with 95 % confidence interval (95 % CI) was used to report effect sizes. Serum vitamin D concentration, risk of vitamin D deficiency among patients with IBS, Symptom Severity Score (SSS), and Quality of Life (QoL) score are the main endpoint outcomes in this study.

Results: data from twelve clinical trials with 1331 IBS patients were included. Patients with IBS have relatively low vitamin D levels in their serum. Vitamin D supplementation improves the Quality of Life (QoL) score but has no significant effect on the Symptom Severity Score (SSS).

Conclusions: vitamin D deficiency is associated with the pathogenesis of irritable bowel syndrome. Serum vitamin D levels decreased in patients with irritable bowel syndrome, and vitamin D supplementation could improve patient quality of life.

Keywords:

Vitamin D. Irritable bowel syndrome. Meta-analysis. Gastroenterology.

Resumen

Antecedentes: los últimos estudios han demostrado que la deficiencia de vitamina D está relacionada con la aparición de la enfermedad del intestino irritable (SII) y que tomar vitamina D como suplemento puede aliviar los síntomas de la enfermedad del intestino irritable. Sin embargo, el tratamiento clínico de la enfermedad del intestino irritable con vitamina D es controvertido.

Objetivo: se realizó un metaanálisis de todos los ensayos clínicos para evaluar las asociaciones entre la vitamina D y la enfermedad del intestino irritable.

Métodos: se examinaron todos los ensayos controlados aleatorios que se publicaron antes del 20 de diciembre de 2021 en las siguientes bases de datos: Medline, Web of Science, China National Knowledge Infrastructure (CNKI), Cochrane Central y Clinical Trial. Se utilizaron RevMan 5.4.1 y Stata 16.1 para analizar los datos relevantes. Se utilizó la diferencia de medias estandarizada (DME) con intervalo de confianza del 95 % (IC 95 %) para presentar los tamaños del efecto. La concentración sérica de vitamina D, el riesgo de deficiencia de vitamina D entre los pacientes con SII, la puntuación de gravedad de los síntomas (SSS) y la puntuación de calidad de vida (CdV) son los principales criterios de valoración de este estudio.

Resultados: se incluyeron datos de doce ensayos clínicos en 1331 pacientes con SII. los pacientes con SII tienen niveles relativamente bajos de vitamina D en el suero. La suplementación con vitamina D mejora la puntuación de calidad de vida (CdV), pero no tiene un efecto significativo en la puntuación de gravedad de los síntomas (SSS).

Conclusiones: la deficiencia de vitamina D se asocia con la patogénesis del síndrome del intestino irritable. Los niveles séricos de vitamina D disminuyeron en pacientes con síndrome del intestino irritable, y la suplementación con vitamina D podría mejorar la calidad de vida de los pacientes.

Palabras clave:

Vitamina D. Síndrome del intestino irritable. Metaanálisis. Gastroenterología.

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INTRODUCTION

BACKGROUND AND AVAILABLE EVIDENCE

Irritable bowel syndrome (IBS) is one of the common functional gastrointestinal diseases (1,2). With the deepening of research and the improvement of medical workers' understanding of the disease, the diagnostic rate of IBS has also increased. According to the latest Rome IV standard, irritable bowel syndrome is a non-organic disease characterized by abdominal pain with changes in bowel habits or stool traits (3-5). The prevalence of IBS in Chinese people is about 6.5 % and is on the rise. The possible pathogenesis of IBS includes visceral hypersensitivity, changes in gastrointestinal motility, abnormal regulation of brain and intestinal axis, intestinal flora disorder, mental and psychological factors, and a regulatory mechanism of the nerve-immune-endocrine network that has attracted attention in recent years has been reported (6). Treatment of IBS emphasizes individualized comprehensive treatment, including psychological and behavioral intervention, diet adjustment, and drug therapy, but the overall treatment effect is unsatisfactory, seriously affecting the quality of life of patients, bringing heavy psychological and social burdens. Therefore, it is urgent to explore safe and effective new therapies for IBS treatment (7,8). The main function of vitamin D is to regulate calcium and phosphorus metabolism, but new ideas suggest that vitamin D can inhibit inflammation and regulate immune response (9). Vitamin D deficiency occurs in 30 to 50 % of the global human population and also accounts for a similar proportion in people with gastrointestinal diseases. Recent studies have found that the serum vitamin D level in IBS patients is significantly lower than that in healthy people. Vitamin D deficiency (VDD) has a high incidence in IBS patients, but the relationship between vitamin D and the severity of gastrointestinal symptoms in IBS patients is not clear (10). In recent years, foreign cases and small-sample clinical studies have reported that vitamin D supplementation may alleviate clinical symptoms in IBS patients (11,12). Our initial intention in this review is to synthesize existing studies to provide solid evidence for vitamin D in the treatment of IBD.

VALUE OF THIS REVIEW

In the United States, the medical costs for IBS are as high as $ 20 billion a year. The current treatment regimen is unsatisfactory, seriously affecting the quality of life of patients, bringing heavy psychological and social burdens. Therefore, it is urgent to explore safe and effective new therapies for the treatment of IBS.

METHOD

SEARCH STRATEGY

We selected all randomized controlled trials associated with vitamin D and irritable bowel syndrome from the following databases: Medline, Web of Science, CNKI, Cochrane Central, and Clinical Trial, and any limitations of language were rejected. We also searched the references of earlier meta-analyses related to the selected studies to determine any additional potential studies. The trials were limited to human studies.

STUDY SELECTION

Two independent and trained reviewers screened the title/abstract and full text to determine the included literature. The different opinions between reviewers would be solved by another experienced doctor. The criteria for excluding literature were as follows: 1) the study was performed on randomized controlled trials; 2) participants received at least 3,000 IU of vitamin D per day for 4 weeks; 3) enrollment of patients with no organic digestive diseases; 4) data are complete or available; 5) any conference papers, reviews, case reports, experience summaries, and repeated literature (only the earliest one is retained in the papers published in multiple languages) were also rejected.

ASSESSMENT OF RISK OF BIAS

Two experienced reviewers used Revman 5.4.1 (RevMan; The Cochrane Collaboration, Oxford, UK) to evaluate the publication bias of articles according to the Cochrane Handbook for Systematic Reviews of Interventions. Quality evaluation was generated in the following assessments: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants and personnel; 4) blinding of outcome assessment; 5) incomplete outcome data; 6) selective reporting; 7) other biases. A summary of bias risks is provided in figure 1.

DATA EXTRACTION

Two reviewers assessed and extracted relevant data independently, including demographic characteristics of participants, clinical diagnosis types, treatment duration, type and dose of administration, and sample size. We summarized the curative effect of vitamin D on irritable bowel syndrome (IBS) in the following measures: 1) risk of vitamin D deficiency among patients with IBS; 2) SSS; 3) QoL; 4) serum vitamin D concentration. These outcomes were summarized in figures 2 A-D.

STATISTICAL ANALYSIS

Each outcome was represented by using standardized mean difference (SMD) with a 95 % confidence interval (CI). In addition, a sensitivity analysis was carried out when necessary.

We used the STATA software (Stata Corporation, College Station, TX) to perform forest plot graphics and funnel plots. All statistical tests were bilateral significant levels: p-value was set at 0.05.

Q-statistic and I^2 test were used to calculate the heterogeneity of all studies. When p-value is less than 0.1 or I^2 is bigger than

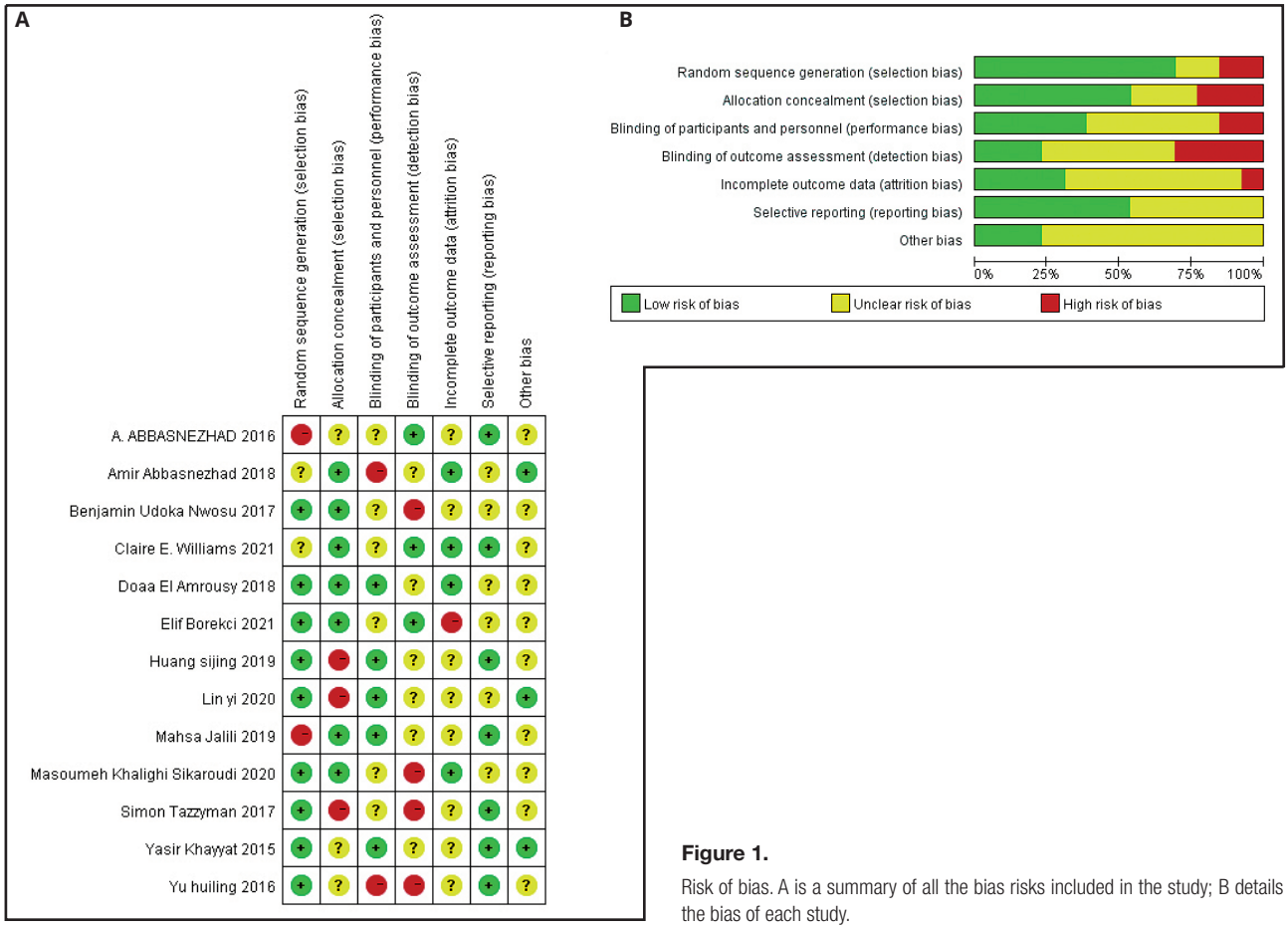

Figure 1.

Risk of bias. A is a summary of all the bias risks included in the study; B details the bias of each study.

40 %, heterogeneity is considered to be significant, and we use a random effects model. On the contrary, when p is bigger than 0.1 or I^2 is less than 40 %, we used the fixed-effect model.

Publication bias was evaluated with a funnel plot, Egger's test, and Begg's test. Egger's and Begg's linear regression tests were used to evaluate asymmetry, and the level of significance was set as $p < 0.05$ (Fig. 3 A-D).

Three researchers (Bin Yang, Lili Yuan, and Kang Liao) independently conducted the screening of titles, abstracts, and the full text of all studies. Study exclusion and inclusion were based on the criteria we set before. Two reviews (Bin Yang, Lili Yuan) extracted the relevant data from included studies: characteristics of participants, outcomes measures, treatment duration, etc., and quality assessments of the studies were performed according to the Cochrane Handbook for Systematic Reviews of Interventions. Any disagreement was reported to an experienced doctor. Another researcher double-checked the consistency between the statistical results converted into software and the data provided in the original literature to avoid any wrong inputs. One reviewer (Bin Yang) performed the statistical analysis using STATA16.1 to obtain the results of each outcome. The whole process was under the guidance of the Cochrane Handbook. All patient data were derived from published literature.

RESULTS

SELECTION OF STUDIES

The literature retrieval strategy is shown in Annex 1. We identified a total of 793 studies associating vitamin D and irritable bowel syndrome (IBS), from which we ultimately included a total of 12 RCTs in 1331 patients, and details of these studies are shown in table I (13-23). Any studies that did not meet the criteria were excluded. We provide a flow chart for the progress of literature retrieval and the inclusion or exclusion of studies in figure 4. The risk of bias of all included trials was assessed using the Cochrane method.

META-ANALYSIS

Risk of vitamin D deficiency among patients with IBS

A total of 974 patients were enrolled in three studies, which provide the risk of vitamin D deficiency among patients with IBS. Data show that people with vitamin deficiency are more likely to suffer from irritable bowel syndrome (relative risk [RR] = 1.78, 95 % CI [1.45, 2.12]). The heterogeneity test for the included studies was done by STATA

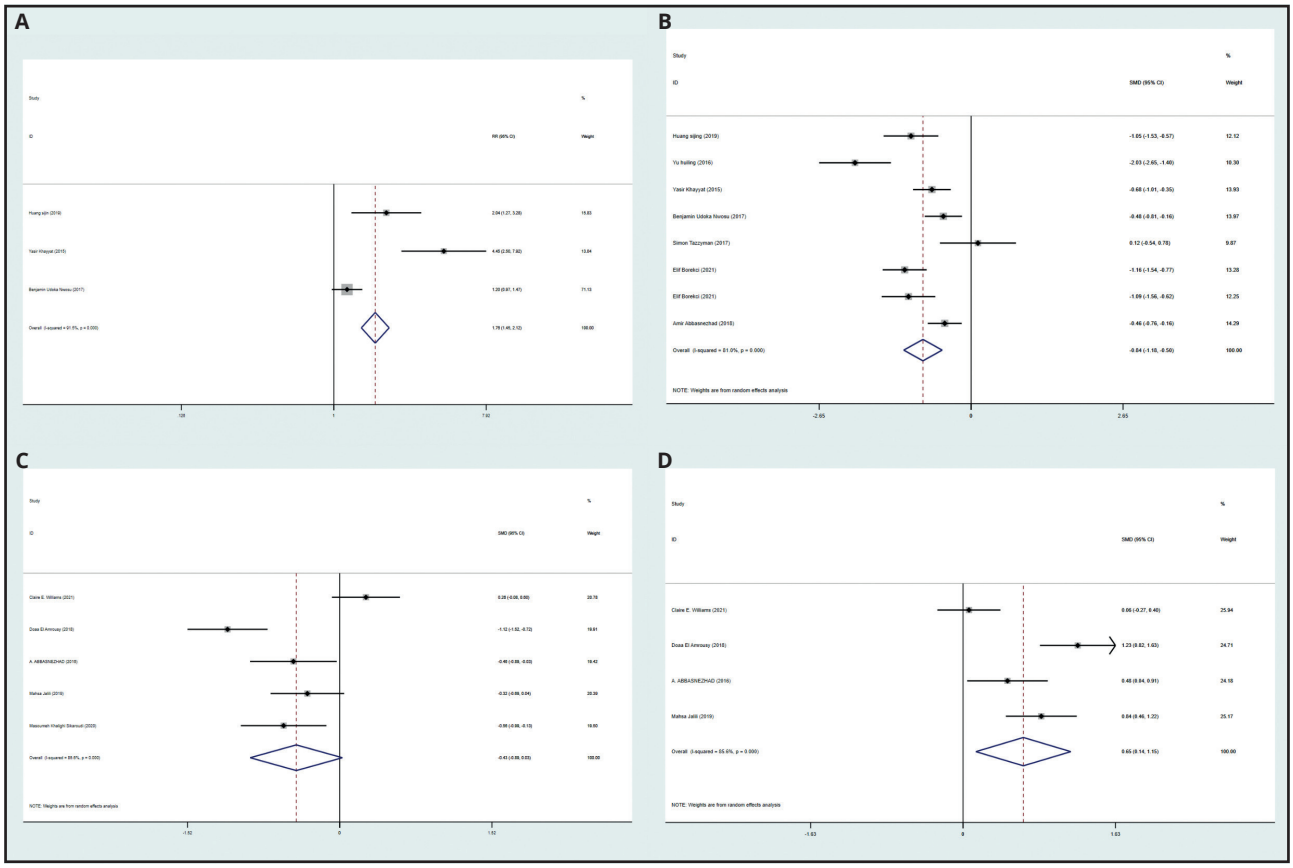

Figure 2.

A. Shows a forest plot that demonstrates the risk of vitamin D deficiency among patients with IBS. Compared with the control group using the random-effect model, people with vitamin D deficiency are more likely to suffer from irritable bowel syndrome. There is also obvious heterogeneity evidence between the experiments. In Meta-analysis, the size of grey squares are proportional to the weight; black lines represent confidence intervals; the virtual line represents the combined effect. Risk factor, RR; p-value is shown in the supplementary material. Shows a forest plot showing serum vitamin D concentrations. The p-value is shown in the supplementary material. C. Shows the forest map showing the changes in the SSS scores of patients after vitamin D treatment. The p-value is shown in the supplementary material. Shows the forest map showing the changes in QoL of patients after vitamin D treatment. The p-value is shown in the supplementary material.

16.1, and results showed $p = 0.000$ and $I^2 = 91.5$ %, a very high heterogeneity, for which we decided to use the random effect model. The results were summarized in figure 2A and the result of publication biases is shown in figure 3A.

Serum vitamin D concentration

Nine studies including 1331 samples reported serum vitamin D levels in patients with irritable bowel syndrome and controls. After summarizing the data, we found that serum vitamin D levels in patients with irritable bowel syndrome were significantly lower than those in the control group (SMD, -0.84, 95 % CI [-0.18, -0.50]). We used STATA 16.1 to test the heterogeneity of 9 studies, and the results showed that $p = 0.000$, $I^2 = 81$ %, indicating high heterogeneity, for which a random effect model is needed. Revman 5.4.1 (Revman 2020) provided a forest plot for each outcome measure. The results were summarized in figure 2B and the result of publication bias is shown in figure 3B.

The SS scores

Five studies enrolling 536 participants reported the effect of vitamin D supplementation on the SS score in patients with IBS. The forest plot showed that vitamin D supplementation had no significant effect on SS score in IBS patients (SMD, -0.43, 95 % CI [-0.89, 0.03]). The heterogeneity test included in the study was carried out by STATA1 6.1, where $p = 0.000$, $I^2 = 85.6$ %, a very high heterogeneity than that we previously set. the source of heterogeneity may be the insufficient number of included studies and small sample size. The publication bias of these 5 studies was done by STATA 16.1. These results are summarized in figure 2 and the result of publication bias is shown in figure 3C.

The QoL score

A total of 448 people in the four studies reported the effect of vitamin D supplementation on QoL scores of patients with IBS.

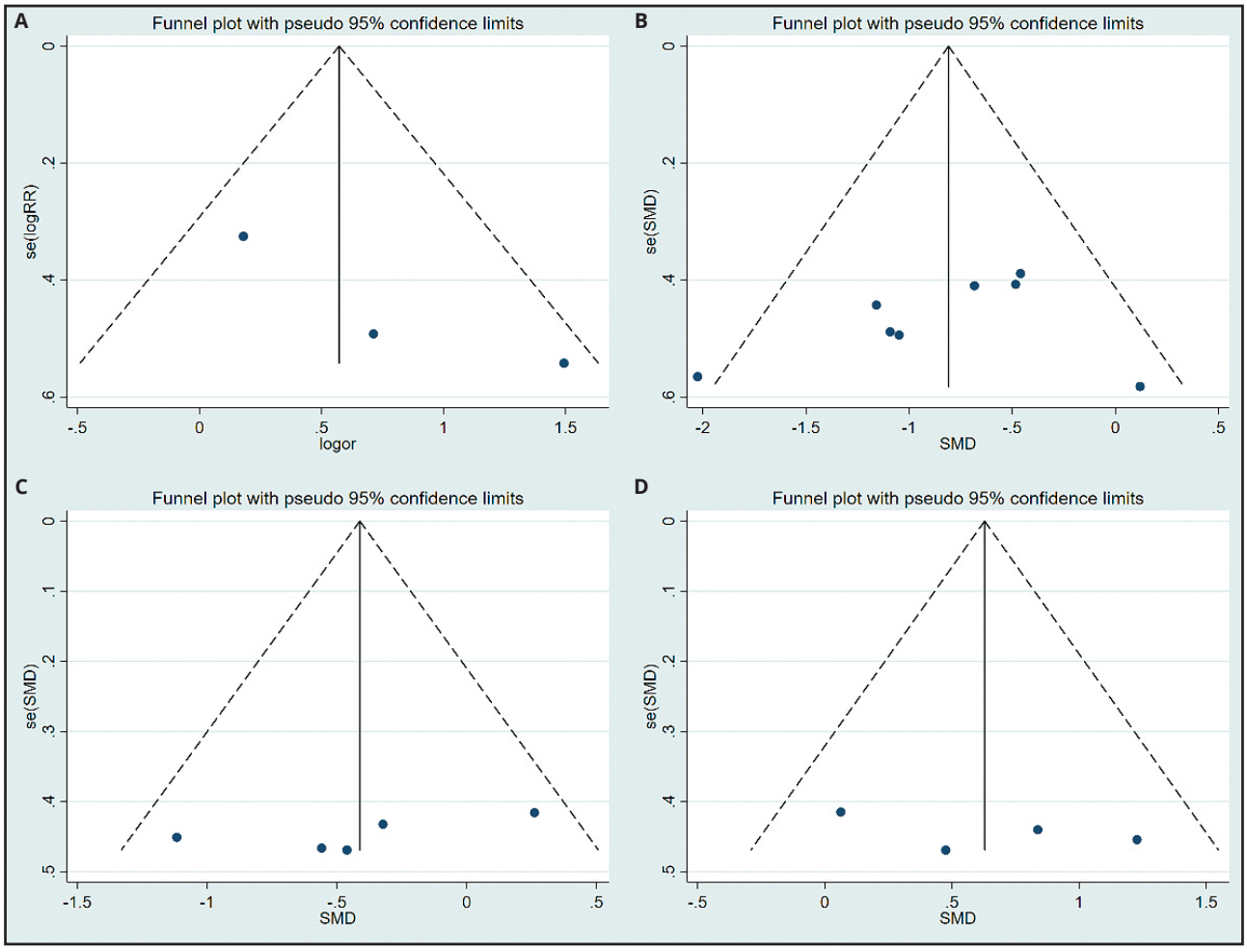

Figure 3.

Publication bias of each outcome. The effect sizes were pooled by using the random-effects model. The standardized mean difference and standard error are described in this funnel plot. The black circles are published literature, and the cone region surrounded by virtual lines on both sides represents the 95 % confidence interval. A. Risk of vitamin D deficiency among patients with IBS. B. Serum vitamin D levels of IBS patients and controls. C. Changes in SSS scores of patients after vitamin D treatment. D. changes in QoL of patients after vitamin D treatment.

The summarized data of four studies show that vitamin D supplementation can significantly increase the QoL score of IBS patients (SMD, 0.65, 95 % CI [0.14, 1.15]), which means that the quality of life of patients is significantly improved. We underwent the heterogeneity test for the 4 studies by STATA 16.1, in which $p = 0.000$ and $I^2 = 85.6$ %, a very high heterogeneity, and for which we decided to use the random effect model. The results were summarized in figure 2D and the result of publication bias is shown in figure 3D.

DISCUSSION

Although the pathogenesis of IBS has not been fully understood, many scholars believe that functional bowel disease is caused by multiple factors. The recognized pathogenesis of IBS is as follows: gastrointestinal motility disorder, visceral sensitivity abnormality, poor food tolerance, intestinal immune system abnormality, and bacterial-intestinal-brain axis dysfunction (25,26). In addition, social-psychological factors, dietary habits, intestinal flora imbalance, intestinal infection, abnormal endogenous cannabinoid system, and vitamin D deficiency are closely related to IBS. Vitamin D deficiency has become a research hotspot (12,27-29).

Vitamin D is an essential vitamin for the human body and belongs to the fat-soluble vitamins group. In addition to the regulation of calcium and phosphorus balance, vitamin D also has anti-inflammatory and immune regulatory effects. Many studies suggest that vitamin D deficiency is widespread in IBS patients (30,31). In addition, a retrospective study of children and adolescents in the United States found that compared with the control group, IBS patients have lower 25(OH)D concentrations. Only 7 % of IBS children and adolescents have sufficient vitamin D.

[Nutr Hosp 2022;39(5):1144-1152]

Table I. Systematic review of RCTs of vitamin D for irritable bowel disease

First author	Country	Sample size				The follow-up time	Course of disease	Gender				Trial group age	Control group age		
		Year	ALL	T	C	-	-	T-male	T-females	C-males	C females	T mean	T SD	C mean	C SD
A. Abbasnezhad (13)	Iran	2016	85	44	41	6 months	-	16	28	12	29	37.45	8.11	38.34	9.85
Benjamin Udoka Nwosu (14)	USA	2017	171	55	116	78 months	9 months	11	44	49	67	16.5	3.1	14.6	4.3
Claire E. Williams (15)	England	2021	135	68	67	28 months	3 months	55	13	51	16	31.1	10.85	28.94	10.03
Doaa El Amrousy (16)	Egypt	2018	112	56	56	24 months	6 months	27	29	24	33	16.4	1.5	16.2	1.1
Elif Borekci (17)	Turkey	2021	154	75	79	-	-	22	53	34	45	43.14	14.18	40.84	10.81
Sijing Huang (18)	China	2019	119	61	58	9 months	-	24	37	25	33	35.61	9.44	37.78	8.97
Mahsa Jalili (19)	Iran	2019	116	58	58	-	1.5 months	-	-	-	-	42.24	12.26	40.06	13.37
Masoumeh Khalighi Sikaroudi (20)	Iran	2020	88	44	44	15 months	-	19	25	22	22	35.07	11.37	35.61	8
Simon Tazzyman (21)	England	2017	51	17+16	18	3 months	-	-	-	-	-	34	14	36	15
Claire Williams (22)	England	2019	80	15	65	3 months	-	-	-	-	-	-	-	-	-
Yasir Khayyat (23)	Saudi Arabia	2015	160	60	100	3 months	-	23	37	11	89	44.2	16	47	14.55
Huiling Yu (24)	China	2016	60	30	30	15 months	-	18	12	16	14	37.4	11.5	35.6	12.4

The 26 trials included in this meta-analysis were randomized controlled trials. They were summarized as participants' country, sample size, gender, and age. Data were reported in means and standard deviations (SD). T: trial; C: control; USA: United States of America.

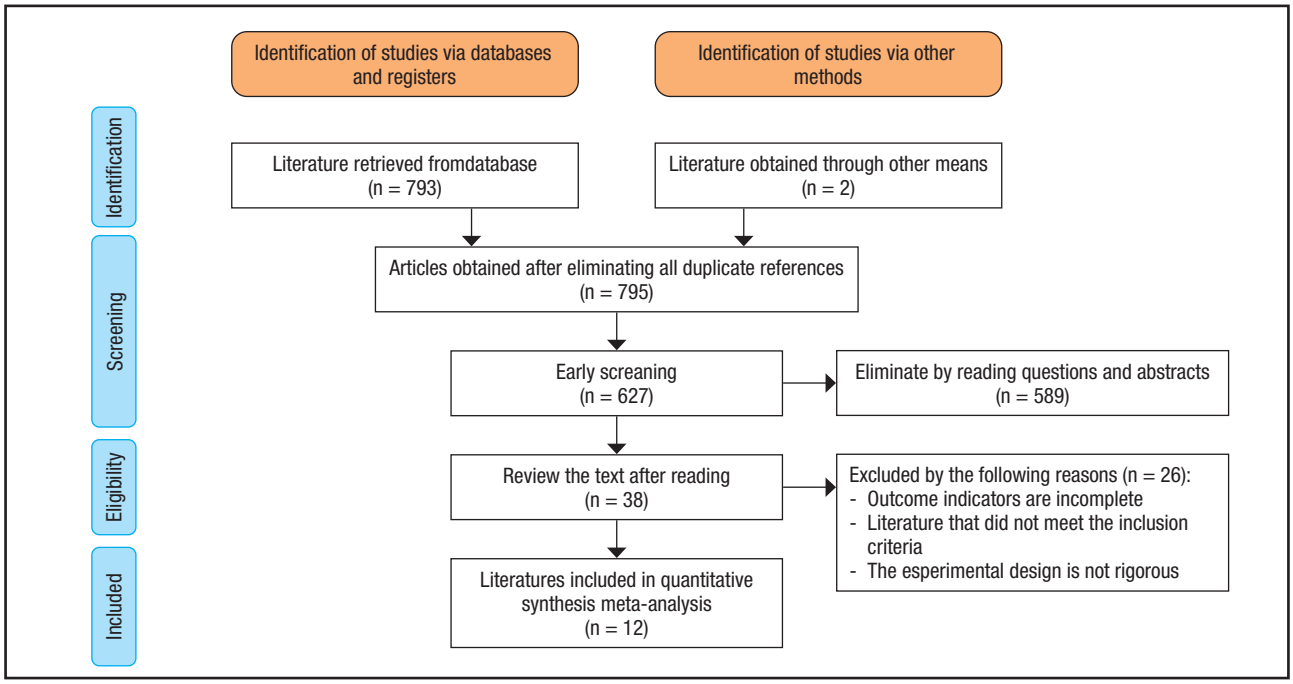

Figure 4.

The flow chart of literature search and data selection. The figure describes the routine for inclusion in the study. Of the 795 studies from databases and other studies, 12 experiments met our inclusion criteria.

More than half of IBS patients have vitamin D deficiency, which may be caused by dietary restriction, sunlight exposure, living habits, gender, hypoproteinemia, and other factors (32,33).

Individuals can acquire exogenous vitamin D from foods rich in vitamin D, but more vitamin D3 (about 70 %) is produced in the skin under ultraviolet light. If the yield from the skin is sufficient, it can even make individuals no longer need to take it from food. The prevalence of vitamin D deficiency in IBS patients may be associated with excessive indoor activity time and sunscreen habits inspired by concerns about the risk of skin cancer caused by exposure to ultraviolet light. These habits affect the normal outdoor activity time of individuals to some extent, resulting in insufficient sources of vitamin D. In conclusion, increasing outdoor activities, ensuring adequate sunshine hours, and appropriate supplementation of vitamin D supplements can provide new ideas for the prevention and treatment of IBS (20,34).

Epidemiological surveys have shown that the prevalence of IBS varies in different regions, different countries, and even within the same country, which may be due to different survey populations and different survey methods. The long course of IBS consumes a lot of medical resources, which seriously affects the quality of life of IBS patients and their families, and causes a serious social burden (35,36). Therefore, it is of great significance for the prevention of IBS to actively carry out an epidemiological investigation and follow-up of IBS for various populations and to promote the health of IBS-related knowledge and health education. Although the pathogenesis of IBS is still unclear, an in-depth study of the pathogenic factors can provide valuable direction for the prevention and treatment of IBS.

We have included four outcome measures from twelve studies and 1331 patients in this review, from which we summarized the following evidence: vitamin D deficiency is a risk factor for irritable bowel syndrome (RR, 1.76, 95 % CI [1.45, 2.12]) and serum vitamin D levels in patients with irritable bowel syndrome are significantly lower than in normal people (SMD, -0.84, 95 % CI [-1.18, 0.50]). In addition, vitamin D supplementation in patients with irritable bowel syndrome can significantly improve their quality of life (SMD, 0.65, 95 % CI [0.14, 1.15]). However, vitamin D supplementation had no significant effect on the SS score of patients with irritable bowel syndrome (SMD, -0.43, 95 % CI [-0.89, 0.03]).

Finally, we concluded that vitamin D deficiency is associated with irritable bowel syndrome: vitamin D deficiency patients are more likely to suffer from irritable bowel syndrome, taking vitamin D can improve the quality of life of patients with irritable bowel syndrome.

Currently, serum 25(OH)D value is used as an indicator of Vitamin D level internationally, for which the universally accepted criteria are that serum 25(OH)D < 20 ng/mL is considered as vitamin D deficiency, serum 25(OH)D between 20 and 30 ng/mL as vitamin D insufficiency, and serum 25(OH)D ≥ 30 ng/mL as vitamin D sufficiency (37). In addition to the IBS studied in this paper, vitamin D levels are also closely related to the skeletal, muscular, and cardiovascular systems. A minimum serum 25(OH)D concentration of 20 ng/mL should be achieved in the general population, and 30 ng/mL should be maintained in high-risk groups to ensure bone health (38). In addition, vitamin D is associated with maintaining muscle function and reducing the risk of cardiovascular diseases, for which the optimal vitamin D levels are not yet clear.

By searching and exploring studies of vitamin D and IBS, future population-based and multicenter prospective studies with larger samples, especially randomized controlled trials, are warranted to verify the causal relationship between vitamin D and IBS. We reviewed the previous literature and suggested at least 4 consecutive weeks of active intervention and up to 6 months of follow-up analysis for IBS patients to continuously validate the effect of the intervention. In the subsequent experiments, the data on vitamin D intake of the subjects need to be obtained using food-recall questionnaires whenever possible to accurately record the intake of each subject. This is particularly critical because some populations, such as patients with severe dietary restrictions and lifestyle choices that limit sun exposure, may have lower concentrations of vitamin D than normal subjects. Therefore, a more objective way is needed for the collection of vitamin D levels, and food-recall questionnaires provide a superior avenue to address this shortcoming. The effect of family history on the relationship between vitamin D and IBS should also be taken into consideration in the later statistical analysis, as this factor is an extremely crucial covariate for model adjustment in association analysis.

CONCLUSIONS

Vitamin D deficiency is associated with the pathogenesis of irritable bowel syndrome. Serum vitamin D levels decreased in patients with irritable bowel syndrome, and vitamin D supplementation could improve the quality of life of patients.

ANNEX 1. THE SEARCH STRATEGY

PubMed Search strategy	
Number	**Items**
#1	irritable bowel syndrome (Mesh)
#2	Irritable Bowel Syndromes (Title/Abstract)
#3	Syndrome, Irritable Bowel (Title/Abstract)
#4	Syndromes, Irritable Bowel (Title/Abstract)
#5	Colon, Irritable (Title/Abstract)
#6	Irritable Colon (Title/Abstract)
#7	Colitis, Mucous (Title/Abstract)
#8	Colitides, Mucous (Title/Abstract)
#9	Mucous Colitides (Title/Abstract)
#10	Mucous Colitis (Title/Abstract)
#11	#1 OR #2 OR #3 OR #4 OR #5 OR # 6 OR # 7 OR # 8 OR # 9 OR 10
#12	Postprandial distress syndrome (Mesh)
#13	#11 AND #12

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ARÁN

Nutrición Hospitalaria

Revisión

Revisión sistemática con análisis de sesgo y calidad de intervenciones en el ambiente alimentario del lugar de trabajo y su impacto en el estado nutricional de los trabajadores

Systematic review with analysis of bias and quality of interventions in the food environment of the workplace and their impact on the nutritional status of workers

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Resumen

Introducción: la exposición de los trabajadores a una alimentación no saludable tiene relación con el aumento del sobrepeso y la obesidad.

Objetivo: esta revisión sistemática tiene como objetivo analizar con análisis de sesgo y calidad el efecto de las intervenciones en el ambiente alimentario del lugar de trabajo en el estado nutricional de los trabajadores.

Métodos: la búsqueda se realizó en tres bases de datos electrónicas de acuerdo a Colaboración Cochrane y fueron incluidos ocho estudios. Los datos se agruparon según tipo de intervención ambiental, se analizó la calidad metodológica y se evaluó la validez con el riesgo de sesgo.

Resultados: de los ocho estudios, tres tuvieron efectos en la reducción del índice de masa corporal (IMC) y peso corporal, pero uno fue considerado como evidencia confiable de efectividad por tener bajo riesgo de sesgo. La mitad de los artículos incluidos fueron evaluados con alto riesgo de sesgo (3/8) y riesgo de sesgo poco claro (1/8) por errores en la selección y la realización y datos faltantes en los resultados.

Conclusiones: se concluye que no hay suficiente evidencia para indicar que este tipo de intervenciones tienen efecto sobre el peso corporal. Para realizar intervenciones efectivas, el diseño de estos estudios tiene que evitar las fuentes potenciales de sesgo, que fueron analizadas en detalle en este estudio. Se debe considerar el entorno alimentario global de los trabajadores y no solo su lugar de trabajo, profundizando la interacción que existe entre factores socioeconómicos y ambientes alimentarios.

Palabras clave:

Alimentación saludable. Trabajadores. Lugar de trabajo. Estado nutricional. Revisión sistemática. Sesgos.

Abstract

Introduction: workers' exposure to unhealthy eating is linked to the increase in overweight and obesity.

Objective: this systematic review aims to analyze with bias and quality analysis the effect of interventions in the food environment of the workplace on the nutritional status of workers.

Methods: the search was conducted in three electronic databases according to the Cochrane Collaboration and eight studies were included. Data were grouped according to type of environmental intervention, and methodological quality and validity with risk of bias was analyzed.

Results: three studies had effects on reducing BMI and body weight, but one was judged to be reliable evidence of effectiveness, as they were at low risk of bias. Half of the included articles were assessed at high risk of bias (3/8) and unclear risk of bias (1/8), due to errors in selection and performance and missing data in the results.

Conclusions: we conclude that there is not enough evidence to indicate that these types of interventions have an effect on body weight. To make effective interventions, the design of these studies has to avoid potential sources of bias, which were analyzed in detail in this study. The global food environment of workers and not just their workplace must be considered, deepening the interaction that exists between socioeconomic factors and food environments.

Keywords:

Healthy eating. Workers. Work place. Nutritional status. Systematic review. Bias.

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INTRODUCCIÓN

Los trabajadores están expuestos a factores de riesgo en su entorno laboral, los cuales afectan directamente a su salud, seguridad y bienestar. Estos riesgos están determinados por las condiciones laborales y, según la Organización Internacional del Trabajo (OIT) y la Organización Mundial de la Salud (OMS), 1,9 millones de personas fallecen en el mundo por accidentes laborales y enfermedades relacionadas con el trabajo (1).

El acceso y la disponibilidad de una alimentación saludable en el lugar de trabajo no están garantizados en Chile y los trabajadores están expuestos a un sistema alimentario con alimentos de alta densidad energética, como hidratos de carbono refinados, grasas saturadas, grasas trans y alimentos bajos en fibra (2). Esta situación representa un factor de riesgo para la salud de los trabajadores, debido a que el consumo de una alimentación no saludable está relacionado con el aumento del sobrepeso y la obesidad, lo que se asocia con un alto riesgo de padecer enfermedades crónicas no transmisibles (ECNT) (3), como las enfermedades cardiovasculares (ECV) y el cáncer, que son las principales causas de muerte en Chile y en el mundo (4,5).

El aumento de la prevalencia de obesidad en las últimas décadas ha provocado un progresivo interés en el entorno alimentario, como un posible factor causal del comportamiento de las personas, en cuanto a su tipo de alimentación, el peso corporal y los resultados de salud (6). Siguiendo esta lógica, el modelo conceptual para el estudio de los ambientes alimentarios en Chile considera que el lugar de trabajo es un ambiente alimentario institucional y organizacional en donde se venden o proporcionan alimentos o comidas a los trabajadores, incluidos casinos y centros de alimentación de diversa índole, como cafeterías, quioscos y máquinas expendedoras de alimentos al interior de las instituciones y organizaciones (7).

Por lo tanto, el lugar de trabajo es un entorno importante para la prevención de la obesidad, ya que existen asociaciones entre los factores ambientales del lugar de trabajo y el comportamiento alimentario de los trabajadores. Aumentar la oferta de alimentos saludables en cafeterías, comedores y máquinas expendedoras se asocia a hábitos alimenticios más saludables y a una disminución del peso corporal. Estos resultados permiten enfatizar que los factores ambientales del lugar de trabajo pueden influir en los hábitos alimenticios de los empleados y en su estado nutricional (8).

El objetivo de este estudio es analizar el efecto de las intervenciones en el ambiente alimentario institucional y organizacional del lugar de trabajo para la prevención del incremento de peso corporal en los trabajadores, por medio de una revisión sistemática. Las intervenciones deben incluir factores ambientales para una alimentación saludable, como son el acceso y la disponibilidad de alimentos saludables y programas de educación nutricional en los espacios físicos destinados a la alimentación.

MATERIAL Y MÉTODOS

TIPO DE ESTUDIO

Revisión sistemática descriptiva de estudios en tres bases de datos bibliográficas: Central, Medline y EMBASE, de acuerdo a Colaboración Cochrane (9).

CRITERIO DE SELECCIÓN EMPLEADO

Los diseños de estudios incluidos fueron ensayos controlados aleatorizados (ECA), publicados entre 2010 y 2020. También se incluyeron aquellos ECA por grupos o conglomerados, donde la unidad de asignación era la organización o el lugar de trabajo (grupo o *cluster*).

Las intervenciones incluidas fueron aquellas que realizaron cambios ambientales en los lugares de trabajo en el acceso y la disponibilidad de alimentos saludables, implementación de programas de educación nutricional o combinaciones de ambos en los espacios físicos destinados a la alimentación de los trabajadores. Además, se incluyeron intervenciones para modificar otros estilos de vida, como la actividad física, el consumo de tabaco, el consumo de alcohol y la salud mental. Las intervenciones fueron realizadas exclusivamente en lugares de trabajo, y la duración total fue de seis meses o más. Se excluyeron estudios con duración inferior a seis meses, por considerarse el tiempo mínimo para tener impacto. Los participantes de las intervenciones incluidas eran de cualquier estado nutricional, con presencia o ausencia de factores de riesgo, con o sin enfermedades crónicas no transmisibles. Respecto a los datos sociodemográficos, los participantes eran mayores de 18 años, de cualquier género, nivel socioeconómico, ocupación o nivel educacional.

Se excluyeron aquellos estudios que tenían como requisito incluir a participantes que fueran de un solo género, que debían tener factores de riesgo o con enfermedades crónicas no transmisibles o sobrepeso y obesidad.

Los lugares de trabajo donde se realizaron las intervenciones eran de cualquier rubro laboral y no existió un requisito del número de trabajadores para poder ser incorporadas en la revisión sistemática.

Los estudios fueron incluidos solo si los efectos de la intervención sobre la reducción o mantención de peso corporal, grasa corporal, índice de masa corporal (IMC) o circunferencia de cintura de los trabajadores eran parte de los resultados primarios o secundarios. Además, las intervenciones podían tener o no, dentro de sus resultados, cambios en el comportamiento alimentario de los participantes.

BÚSQUEDA Y SELECCIÓN DE LOS ESTUDIOS

La estrategia de búsqueda se realizó con palabras clave, con las cuales se realizaron combinaciones y se aplicaron los filtros adecuados, según cada base de datos (Anexo 1). La fecha de búsqueda fue de julio a septiembre de 2020.

Un revisor realizó la búsqueda de los estudios de acuerdo a los títulos y resúmenes, y en una planilla Excel se realizó un listado con los estudios relevantes con un número identificador correspondiente a cada base de datos. Los textos completos de los estudios relevantes identificados fueron descargados para leerlos e identificar el cumplimiento de los criterios de inclusión y exclusión.

Se elaboró el formulario de chequeo de criterios de inclusión y exclusión en formato Excel, definiendo como "incluido" a los estudios que cumplían con todos los ítems y como "excluido" a los estudios que no cumplían con uno o más criterios de inclusión. Luego se realizó una segunda revisión de los estudios incluidos a través del "formulario de características de los estudios incluidos", con lo que se obtuvo la cifra final de estudios.

Los estudios seleccionados luego de las dos revisiones fueron descargados en el gestor de citas bibliográficas Mendeley, donde se pudieron eliminar los archivos repetidos o duplicados, dando por resultado el número total de estudios para la revisión sistemática.

REVISIÓN DE LOS ESTUDIOS

Los datos fueron extraídos por un revisor en forma sistemática, a través de un formulario de obtención de datos en formato Excel, según lo recomienda el Manual Cochrane de revisiones sistemáticas (9). El objetivo fue obtener las características de los estudios incluidos y sus resultados. Se obtuvieron datos referentes a los lugares de trabajo y los participantes de las intervenciones (edad, sexo, grupo étnico, nivel educacional y presencia de comorbilidades), la zona geográfica del estudio, información acerca de los contenidos de las intervenciones, quién las implementa y el formato, el momento de su desarrollo y, finalmente, los resultados de la medida de desenlace de interés.

EVALUACIÓN DEL RIESGO DE SESGO

Para la evaluación de sesgo se utilizó la herramienta recomendada por la Colaboración Cochrane (9), que señala cinco sesgos, con sus dominios: de selección, que tiene cuatro dominios; de realización y de detección, con un dominio cada uno; de desgaste, con dos dominios; y de notificación, con un dominio (Tabla I).

La valoración de esta herramienta permite analizar en cada dominio la existencia de un bajo riesgo de sesgo o un alto riesgo de sesgo y, si no existe información completa para su análisis, se considera un riesgo de sesgo poco claro. En este estudio se consideró que una intervención tiene un riesgo de sesgo bajo cuando en todos los dominios clave existe un bajo riesgo de sesgo, un riesgo poco claro cuando es así en uno o más dominios clave y un alto riesgo cuando para uno o más dominios clave existe un alto riesgo de sesgo.

EVALUACIÓN DE LA CALIDAD DE LOS ESTUDIOS

Se utilizó la herramienta recomendada por la Colaboración Cochrane para evaluar la calidad de los estudios cuantitativos en revisiones sistemáticas de salud pública y promoción de la salud. Se utilizó la Herramienta de Evaluación de la Calidad para los Estudios Cuantitativos (10), que incluye un diccionario que permite realizar la evaluación de una calidad fuerte, moderada o débil según se cumplan los criterios indicados en el documento. Esta herramienta ha demostrado confiabilidad, validez de contenido y constructo y confiabilidad *test-retest* (11).

Los ítems que considera esta herramienta para poder otorgar una puntuación son el riesgo de sesgo respecto a la representatividad de la población objetivo y la cantidad de personas que accedieron a participar del estudio. El siguiente se refiere al diseño del estudio, donde se busca saber si el estudio señala que hubo una asignación aleatoria a los grupos experimentales y si se describe el método de asignación aleatoria. Luego se evalúan los factores de confusión, respecto a si hubo diferencias significativas en la línea base respecto a sus características y si se controlaron o ajustaron los modelos de análisis estadístico por las variables de confusión. Otros ítems de interés son el

Tabla I. Descripción de sesgos y dominios para evaluar el riesgo de sesgo

Sesgos	Descripción	Dominios
Sesgo de selección	Diferencias sistemáticas entre las características iniciales de los grupos que se comparan	Generación de la secuencia Ocultamiento de la asignación Sesgo de reclutamiento (ECA por conglomerados) Desequilibrio basal (ECA por conglomerados)
Sesgo de realización	Diferencias sistemáticas entre grupos en la asistencia que se les entrega o en la exposición a otros factores	Cegamiento de los participantes y del personal del estudio
Sesgo de detección	Diferencias sistemáticas entre grupos en la forma en que se obtuvieron los resultados	Cegamiento de los evaluadores de resultado
Sesgo de desgaste	Diferencias sistemáticas entre grupos en los abandonos del estudio	Datos de resultados incompletos Pérdida de los grupos (ECA por conglomerados)
Sesgo de notificación	Diferencias sistemáticas entre resultados presentados y no presentados	Notificación selectiva de los resultados

ECA: ensayos controlados aleatorizados.

cegamiento de los participantes y evaluadores de resultado, la validez y confiabilidad de los métodos de recolección de datos, los retiros y bajas de los participantes respecto a si se informaron los números y razones y cuántos de ellos lograron terminar el estudio.

Un estudio se denominará con una calidad fuerte en caso de que no tenga ningún ítem del cuestionario calificado como débil; se considerará de calidad moderada si tiene un ítem calificado como débil; y, finalmente, será de una calidad débil si tiene dos o más ítems catalogados como débiles. Se utilizó el segmento del cuestionario que incluye la puntuación para poder calificar los estudios. La parte que incluye integridad de la intervención no fue utilizada, al no poder ser calificada con las categorías antes mencionadas.

ANÁLISIS DE RESULTADOS

Con los datos extraídos de cada estudio, se analizaron los resultados de las intervenciones de manera descriptiva, agrupando la información por tipo de intervención y entregando los detalles respecto a la dirección, estimación y tamaño del efecto en caso de que hayan sido informados por los investigadores.

RESULTADOS

La selección identificó 2.454 estudios en Central, 3.215 en Medline (PubMed) y 233 en EMBASE, con lo que se entregó un total de 5.902 estudios potencialmente relevantes. Después de la revisión de los títulos y resúmenes, se consideraron 150 estudios. Se descargaron los textos completos para su lectura y análisis por cada base de datos y se utilizó el formulario de evaluación de criterios de inclusión y exclusión. Como resultado, quedaron 19 estudios para una segunda revisión, excluyendo cinco de ellos por estar repetidos y seis debido a que no cumplían con los criterios de inclusión. Finalmente, ocho estudios tenían todas las características necesarias para la revisión sistemática. Los resultados de la búsqueda bibliográfica y el detalle del proceso de selección se presentan en la figura 1.

La tabla II muestra un resumen de las características de los ocho estudios: todos fueron aleatorios; siete asignaron al azar los lugares de trabajo para cada grupo de intervención (12-16,18,19) y solamente un estudio utilizó como unidad de asignación a los trabajadores (17).

La unidad de análisis en seis estudios fue el individuo participante de la intervención y en dos el análisis fue a nivel grupal (13,18).

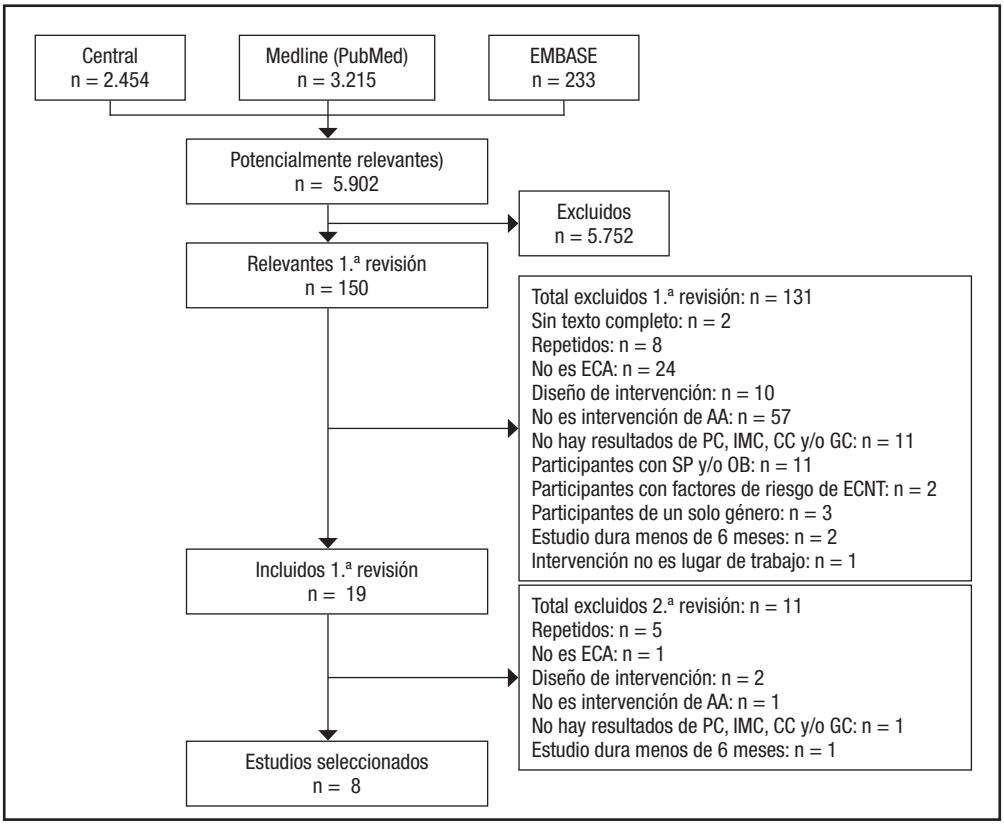

Figura 1.

Diagrama de flujo de la búsqueda y selección de estudios. ECA: ensayo controlado aleatorizado; PC: peso corporal; IMC: índice de masa corporal; CC: circunferencia de cintura; GC: grasa corporal; SP: sobrepeso; OB: obesidad. ECNT: enfermedad crónica no transmisible.

Tabla II. Características de los estudios incluidos

Autor, año	Métodos		Participantes					Intervención		Resultados	
	Diseño	Duración	Ámbito	N.º de participantes	Edad	Género	País	N.º de grupos	Tipo de intervención	Medida de resultado	Puntos temporales
Doran y cols., 2018 (12)	ECA por conglomerados	18 meses	Casas de reposo o de ancianos	98 trabajadores	Mediana: 32 años	Femenino: 89,5 % Masculino: 10,5 %	Estados Unidos	4 G.I. = 2 G.C. = 2	Acceso y disponibilidad de AS + AF + ME	Reducción de factores de riesgo CV: disminución del IMC (resultado primario)	Línea base, postintervención (9 meses) y seguimiento (18 meses)
Fernández y cols., 2015 (13)	ECA por conglomerados	5 años	Empresas de fabricación, investigación y desarrollo	3.799 trabajadores (L.B.: 2.615, P.I.: 1.184)	L.B. = G.I. media: 47,7 años; G.C. media 49 años	L.B. = G.I: Femenino: 31,9 %, Masculino: 68,1 %, G.C: Femenino: 41,2 %, Masculino: 58,8 %	Estados Unidos	10 G.I. = 5 G.C. = 5	Acceso y disponibilidad a AS + EN en espacios de alimentación + AF	Cambios en el IMC promedio y proporción de empleados con sobrepeso y obesidad (resultado primario)	Línea base, postintervención (2 años)
Lemon y cols., 2014 (14)	ECA por conglomerados	2 años	Escuelas secundarias públicas	782 trabajadores	21 - 34 años: 24,3 % (n = 190) 35-44 años: 26,1 % (n = 204) ≥ 45 años: 49,6 % (n = 388)	Femenino: 67 % Masculino: 33 %	Estados Unidos	12 G.I. = 6 G.C. = 6	Acceso y disponibilidad a AS + EN en espacios de alimentación + AF	Prevención del aumento de peso corporal: cambios en IMC y peso corporal	Línea base, postintervención (12 meses), seguimiento (24 meses)
Lemon y cols., 2010 (15)	ECA por conglomerados	3 años	Hospitales	806 trabajadores	18-40 años: 35,2 % 41-50 años: 33,4 % ≥ 51 años: 31,4 %	Femenino: 81 % Masculino: 19 %	Estados Unidos	6 G.I. = 3 G.C. = 3	Acceso y disponibilidad a AS + EN en espacios de alimentación + AF	Prevención del aumento de peso corporal: cambios en el IMC (resultado primario)	Línea base, durante intervención (12 meses), postintervención (24 meses)
Linde y cols., 2012 (16)	ECA por conglomerados	3 años y 2 meses	Colegios y oficinas	1.672 trabajadores	≤ 30 años: 16,8 % 31-40 años: 25,3 % 41-50 años: 31,5 % 51-60 años: 23,1 % > 60 años: 3,3 %	Femenino: 60,7 % Masculino: 39,3 %	Estados Unidos	6 G.I. = 3 G.C. = 3	Acceso y disponibilidad a AS + EN en espacios de alimentación + AF	Prevención del aumento de peso corporal: cambios en el IMC (resultado primario)	Línea base, postintervención (24 meses)
Lowe y cols., 2010 (19)	ECA	18 meses	Hospitales	98 trabajadores (G.I. = 47, G.C. = 49)	Media = 44,2 años	Femenino: 79,5 % Masculino: 18,3 %	Estados Unidos	2 G.I. = 1 G.C. = 2	Acceso y disponibilidad a AS + EN en espacios de alimentación	Cambios en el peso corporal, circunferencia de cintura y grasa corporal (resultado secundario)	Línea base, postintervención (6 meses), seguimiento (12 meses)

(Continúa en página siguiente)

Tabla II (Cont.). Características de los estudios incluidos

Autor, año	Métodos		Participantes				Intervención		Resultados	
	Diseño	Duración	Ámbito	N.º de participantes	Edad	Género	País	N.º de grupos	Tipo de intervención	Medida de resultado	Puntos temporales
Siegel y cols., 2010 (18)	ECA por conglomerados	2 años	Escuelas	413 trabajadores	Media G.C. = 39,5 años Media G.I. = 40 años	G.C.: Femenino: 73,8 % Masculino: 26,2 % G.I.: Femenino: 83,4 % Masculino: 16,6 %	Estados Unidos	16 G.I. = 8 G.C. = 8	Acceso y disponibilidad a AS + AF + ME	Cambios en IMC y en la relación cintura cadera (resultado primario)	Línea base, postintervención (2 años)
Verweij y cols., 2013 (19)	ECA por conglomerados	18 meses	Médicos ocupacionales que prestan servicios a empresas	523 trabajadores	Media = 47 años	Femenino: 37 % Masculino: 63 %	Países Bajos	16 G.I. = 7 G.C. = 9	Acceso y disponibilidad a AS + AF	Cambios en la circunferencia de cintura, peso corporal e IMC (resultado primario)	Línea base, seguimiento (6 meses, 12 meses y 18 meses)

ECA: ensayo controlado aleatorizado; G.I.: grupo de intervención; G.C.: grupo de control; AS: alimentos saludables; AF: actividad física; ME: manejo del estrés; LT: lugar de trabajo; CV: cardiovascular; IMC: índice de masa corporal; EN: educación nutricional; L.B.: línea base; P.I.: postintervención.

La duración de los estudios fluctuó entre 18 meses y cinco años y el ámbito de las intervenciones fueron lugares de trabajo correspondientes a escuelas, hospitales, oficinas y casas de reposo. El país en donde se desarrollaron siete de los estudios fue Estados Unidos y un estudio se realizó en los Países Bajos (19).

Las intervenciones hacían referencia a cambios ambientales en el lugar de trabajo en cuanto a alimentación saludable, actividad física y estrés. Todas incluían el acceso y la disponibilidad de alimentos saludables; una de ellas incluyó solo la actividad física (19); dos agregaron técnicas para el manejo del estrés, más la promoción de actividad física (12,18); cuatro incluyeron la educación nutricional en los espacios físicos de alimentación, más la actividad física (13-16); y solo uno realizó una intervención dirigida al acceso y la disponibilidad de alimentos saludables, junto con educación nutricional en los espacios físicos de alimentación de los trabajadores (17).

Respecto al detalle de las intervenciones, las acciones dirigidas a aumentar el acceso y la disponibilidad a alimentos saludables en el lugar de trabajo son aquellas que se aplicaron en cafeterías y máquinas expendedoras de alimentos, con aumento de la oferta de alimentos saludables (menú semanal y productos en punto de venta) y promociones con reducción de precios. También aparece que los alimentos saludables estaban presentes en reuniones laborales, degustaciones, comidas compartidas y mercados o ferias de agricultores en los lugares de trabajo.

La educación nutricional en los espacios físicos de la alimentación se configuró como información en formato de etiquetas nutricionales, autoadhesivos referentes a guiar una decisión de compra, tarjetas en las mesas y carteles, además de exhibiciones sobre preparaciones saludables. Todo ello fue implementado en cafeterías o en máquinas expendedoras de alimentos.

Las actividades dirigidas al aumento de la actividad física en el lugar de trabajo fueron aquellas que promocionan el uso de las escaleras, rutas peatonales, organización de caminatas grupales, instalación de cintas de correr y elípticas, competencias deportivas y clases de acondicionamiento, gimnasio gratuito e instalación de vestuarios, entre otras. En cuanto al estrés, se realizaron sesiones grupales a los trabajadores para enseñar y reforzar técnicas para el manejo del estrés en el lugar de trabajo durante la jornada laboral.

El desenlace de interés en todos los estudios fue prevenir el aumento de peso corporal de los trabajadores. En siete estudios, el cambio en el IMC fue la medida de resultado primaria. Uno de estos agregó el peso corporal como uno de los resultados primarios (14); otro, el peso corporal y la circunferencia de cintura (19); y un último estudio agregó la relación cintura cadera (18). Solamente un estudio tuvo el peso corporal, circunferencia de cintura y grasa corporal como resultados secundarios de la intervención (17).

ANÁLISIS DE SESGO

Como resultado de la evaluación general del riesgo de sesgo, de los ocho estudios seleccionados, cuatro fueron calificados con un bajo riesgo de sesgo (14-16,19); tres presentan un alto riesgo de sesgo (12,13,17); y uno fue evaluado con un riesgo de sesgo poco claro (18). La evaluación del riesgo de sesgo por cada dominio y evaluación general para cada estudio se resumen en la tabla III.

[Nutr Hosp 2022;39(5):1153-1165]

Tabla III. Evaluación del riesgo de sesgo

Autor, año	Sesgo de selección				Sesgo de realización	Sesgo de detección	Sesgo de desgaste		Sesgo de notificación	
	Generación de la secuencia	Ocultamiento de la asignación	Sesgo de reclutamiento (ECA por conglomerado)	Desequilibrio basal (ECA por conglomerado)	Cegamiento de los participantes y del personal	Cegamiento de los evaluadores del resultado	Datos de resultado incompletos	Pérdida de los grupos (ECA por conglomerado)	Notificación selectiva de los resultados	Evaluación general riesgo de sesgo
Doran y cols., 2018 (12)	Riesgo poco claro de sesgo Falta información de regla de asignación	Bajo riesgo de sesgo	Riesgo de sesgo poco claro	Bajo riesgo de sesgo	Alto riesgo de sesgo Exposición a otra intervención	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	*Alto riesgo de sesgo*
Fernández y cols., 2015 (13)	Alto riesgo de sesgo Se altera asignación aleatoria en 1 grupo	Alto riesgo de sesgo Se conoce asignación para 1 grupo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	*Alto riesgo d e sesgo*
Lemon y cols., 2014 (14)	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	*Bajo riesgo de sesgo*
Lemon y cols., 2010 (15)	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Riesgo de sesgo poco claro	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	*Bajo riesgo d e sesgo*
Linde y cols., 2012 (16)	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	*Bajo riesgo de sesgo*
Lowe y cols., 2010 (17)	Riesgo poco claro de sesgo	Riesgo poco claro de sesgo	No aplica	No aplica	Alto riesgo de sesgo Contaminación entre grupos	Bajo riesgo de sesgo	Alto riesgo de sesgo Alta tasa de deserción (desequilibrio entre grupos)	No aplica	Bajo riesgo de sesgo	*Alto riesgo de sesgo*

(Continúa en página siguiente)

Tabla III (Cont.). Evaluación del riesgo de sesgo

Autor, año	Sesgo de selección				Sesgo de realización	Sesgo de detección	Sesgo de desgaste		Sesgo de notificación	
	Generación de la secuencia	Ocultamiento de la asignación	Sesgo de reclutamiento (ECA por conglomerado)	Desequilibrio basal (ECA por conglomerado)	Cegamiento de los participantes y del personal	Cegamiento de los evaluadores del resultado	Datos de resultado incompletos	Pérdida de los grupos (ECA por conglomerado)	Notificación selectiva de los resultados	Evaluación general riesgo de sesgo
Siegel y cols., 2010 (18)	Riesgo poco claro de sesgo Falta información de regla de asignación	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	*Riesgo poco claro de sesgo*
Verweij y cols., 2013 (19)	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	Bajo riesgo de sesgo	*Bajo riesgo de sesgo*

ECA: ensayo controlado aleatorizado.

Todos los estudios eran de tipo ECA, por lo que el sesgo de selección a través de la generación de la secuencia y el ocultamiento de la asignación se minimiza si el método de asignación al azar se realiza e informa de manera adecuada, evitando prever las asignaciones (9), y en los ECA por conglomerados, si se realiza la asignación estratificada o pareada (20).

En el caso de los ECA por conglomerados, el sesgo de reclutamiento se minimiza cuando el reclutador está cegado o los participantes se seleccionan antes de la asignación al azar, y el desequilibrio basal no ocurre cuando hay asignación pareada o estratificada y en el análisis hay ajuste de las variables de confusión (9).

Cuando los participantes y el personal están cegados, el sesgo de realización es menos probable, y si no es posible el cegamiento, no debe existir contaminación entre grupos. El sesgo de detección se minimiza cuando el evaluador de resultados subjetivos está cegado (no aplica para resultados objetivos). Hay bajas probabilidades de que ocurra sesgo de desgaste cuando no hay pérdidas de participantes o conglomerados durante el seguimiento. Si esto ocurre, no deben presentarse diferencias significativas entre los grupos. Existe un bajo riesgo de sesgo de notificación si los autores informan todos los resultados especificados antes del análisis.

CALIDAD PARA LOS ESTUDIOS CUANTITATIVOS

Según la evaluación realizada con esta herramienta, ningún estudio fue clasificado con una calidad fuerte, ya que todos tenían en común el sesgo de selección. La mayoría de los estudios no tuvo selección aleatoria de los participantes, al ser muestras constituidas por sujetos voluntarios y, en algunos casos, con entrega de incentivos económicos, por lo que no eran representativas de la población objetivo. Un estudio fue la excepción (15), al seleccionar una muestra aleatoria estratificada de participantes, los cuales eran representativos de la población de trabajadores en los lugares de trabajo, pero el porcentaje de personas que accedió a participar fue menor del 60 %, lo que indica que igualmente es débil en esta categoría. De los ocho estudios, uno tuvo una calidad moderada y el resto fueron calificados como débiles. El resumen de la evaluación de la calidad se presenta en la tabla IV.

EFECTO DE LAS INTERVENCIONES EN EL ESTADO NUTRICIONAL

Según el tipo de intervenciones, los estudios seleccionados tuvieron distintos efectos en cuanto a reducción o mantención de peso corporal, grasa corporal, IMC y circunferencia de cintura de los trabajadores.

Los dos estudios que realizaron intervenciones dirigidas a aumentar el acceso y la disponibilidad de alimentos saludables con iniciativas para promocionar la actividad física y el manejo del

Tabla IV. Evaluación de la calidad de cada estudio

Autor, año	Sesgo de selección	Diseño de estudio	Confusores	Cegador	Recopilación de datos	Retiros y bajas	Evaluación general
Doran y cols., 2018 (12)	Débil	Fuerte	Fuerte	Débil	Fuerte	Débil	*Débil*
Fernández y cols., 2015 (13)	Débil	Fuerte	Fuerte	Moderado	Fuerte	Débil	*Débil*
Lemon y cols., 2014 (14)	Débil	Fuerte	Fuerte	Moderado	Débil	Moderado	*Débil*
Lemon y cols., 2010 (15)	Débil	Fuerte	Fuerte	Débil	Fuerte	Moderado	*Débil*
Linde y cols., 2012 (16)	Débil	Fuerte	Fuerte	Débil	Débil	Fuerte	*Débil*
Lowe y cols., 2010 (17)	Débil	Fuerte	Fuerte	Moderado	Débil	Débil	*Débil*
Siegel y cols., 2010 (18)	Débil	Fuerte	Fuerte	Moderado	Fuerte	Débil	*Débil*
Verweij y cols., 2013 (19)	Débil	Fuerte	Fuerte	Fuerte	Fuerte	Moderado	*Moderado*

estrés en el lugar de trabajo tuvieron, en el primer estudio, una disminución significativa en el IMC, pero no en la relación cintura-cadera en el primer estudio (18) y sin cambios significativos del IMC en el segundo estudio (12).

De los cuatro estudios que realizaron intervenciones de acceso y disponibilidad a alimentos saludables, educación nutricional en espacios de alimentación y promoción de la actividad física en el lugar de trabajo, el primer estudio (13) presentó una disminución significativa del IMC y de la proporción de empleados con sobrepeso y obesidad y el segundo estudio (14), una disminución significativa en el IMC y peso corporal a los 24 meses de seguimiento. En cambio, en los estudios tercero (15) y cuarto (16) no hubo cambios significativos en el IMC.

Un estudio (19) realizó intervenciones de acceso y disponibilidad a alimentos saludables y promoción de la actividad física en el lugar de trabajo, pero sin resultados con diferencia significativa en circunferencia de cintura e IMC entre grupo intervenido y control.

El único estudio con intervenciones de acceso y disponibilidad a alimentos saludables y educación nutricional en espacios físicos de alimentación en el lugar de trabajo (17) no mostró cambios significativos en el peso corporal, la circunferencia de cintura ni la grasa corporal en el grupo intervenido.

En resumen, desde el punto de vista de la efectividad de las intervenciones, solo tres ensayos lograron tener efecto en la disminución del IMC (13,14,18) y del peso corporal (14). Estos resultados se presentan en la tabla V.

Tabla V. Efecto de las intervenciones

Autores	Medida de resultado	Punto temporal	Línea base *vs.* PI	Diferencia línea base *vs.* PI en y entre grupos	Significancia estadística*
Doran y cols. 2018 (12)	Reducción de IMC (kg/m^2)	18 meses	G.I.: 31,29 *vs.* 30,71 G.C.: 29,86 *vs.* 26,67	G.I.: -0,58 G.C.: -3,19	p = 0,045†
Siegel y cols. 2010 (18)	Reducción de IMC (kg/m^2)	2 años	G.I.: 28,54 *vs.* 28,40 G.C.: 27,56 *vs.* 27,98	G.I.: -0,14 G.C.: +0,42 DM: -0,561	p = 0,047
	Reducción de la relación cintura-cadera	2 años	G.I.: 0,86 *vs.* 0,87 G.C.: 0,87 *vs.* 0,87	G.I.: +0,01 G.C.: 0	p = 0,565
Fernández y cols. 2015 (13)	Reducción de IMC (kg/m^2)	2 años	G.I.: 28,85 *vs.* 28,31 G.C.: 28,55 *vs.* 28,43	G.I.: -0,54 G.C.: -0,12 DM: -0,42	p = 0,02 p = 0,73 p = 0,33
	Reducción de % de trabajadores con SP y OB (%)	2 años	G.I.: 78,0 *vs.* 74,3 G.C.: 75,1 *vs.* 80,0	G.I.: -3,7 G.C.: +4,9 DM: -8,6	p = 0,07 p = 0,1 p = 0,02

(Continúa en página siguiente)

Tabla V (Cont.). Efecto de las intervenciones

Autores	Medida de resultado	Punto temporal	Línea base *vs.* PI	Diferencia línea base *vs.* PI en y entre grupos	Significancia estadística*
Lemon y cols. 2014 (14)	Reducción de IMC (kg/m^2)	2 años	NI	DM: -0,48	p = 0,05
	Reducción del peso corporal (libras)	2 años	G.I.: 173,9 *vs.* 172,6 G.C.: 173,9 *vs.* 176,1	DM: -3,03	p = 0,04
Lemon y cols. 2010 (15)	Reducción de IMC (kg/m^2)	2 años	G.I.: 28,4 *vs.* 28,9 G.C.: 29 *vs.* 29,4	β: +0,276	p = 0,38
Linde y cols. 2012 (16)	Reducción de IMC (kg/m^2)	2 años	NI	G.I.: +0,32 G.C.: +0,19 DM: +0,13	p = 0,36
Verweij y cols. 2013 (19)	Reducción de IMC (kg/m^2)	18 meses	G.I.: 27,6 *vs.* 27 G.C.: 28 *vs.* 27,4	β: + 0,1	IC 95 %: -0,3-0,5
	Reducción del peso corporal (kg)	18 meses	G.I.: 86 *vs.* 84,6 G.C.: 87,5 *vs.* 86,7	G.I.: -1,4 G.C.: -1,2 β: +0,3	IC 95 %: -1,0-1,6
	Reducción de circunferencia de cintura (cm)	18 meses	G.I.: 94,5 *vs.* 93,3 G.C.: 98 *vs.* 96,8	G.I.: -1,2 G.C.: -1,2 β: +1,2	IC 95 %: -0,6-2,9
Lowe y cols. 2010 (17)	Reducción del peso corporal (kg)	12 meses	G.I.: 85,5 *vs.* 80,2 G.C.: 78,7 *vs.* 80,2	G.I.: -5,3 G.C.: +1,5	p = 0,44
	Reducción de grasa corporal (%)	12 meses	NI	NI	NI
	Reducción de circunferencia de cintura (cm)	12 meses	NI	NI	NI

*IC: intervalo de confianza; PI: postintervención; GI: grupo de intervención; GC: grupo de control; DM: diferencia de medias; SP: sobrepeso; OB: obesidad; NI: no informado; β: coeficiente de correlación. *p < 0,05. †Efecto en dirección inesperada.*

DISCUSIÓN

El proceso de búsqueda, selección y análisis de los estudios incluidos en esta revisión sistemática permitió conocer aquellas intervenciones en factores ambientales del lugar de trabajo que fueron efectivas y que entregaron evidencia confiable para prevenir el incremento de peso corporal de los trabajadores.

Respecto a un análisis confiable del efecto de las intervenciones en los ECA (9), de los ocho estudios publicados entre los años 2010 y 2018, cuatro fueron evaluados con un bajo riesgo de sesgo (14-16,19) y, por lo tanto, la mitad de los estudios incluidos presentaron validez interna. De ellos, solo una intervención tuvo efecto en la reducción del IMC y el peso corporal (14), utilizando el acceso y la disponibilidad de alimentos saludables, promoción de la actividad física y educación nutricional en los espacios físicos de alimentación.

Los otros estudios presentan sesgos o errores importantes en el diseño, al alterar la secuencia de asignación aleatoria (13) y no informar el método de asignación al azar (12,17,18), generando sesgo de selección. Hay fallas relevantes en la realización respecto al cegamiento de los participantes, al existir contaminación entre individuos de diferentes grupos de tratamiento y exposición a intervenciones alternativas (12,17). Se produjeron errores en la etapa de análisis de los resultados por datos incompletos debido a la alta tasa de abandono, lo que generó desequilibrio entre los grupos de tratamiento (17). Todos estos sesgos afectan directamente a la credibilidad de los resultados de efectividad, ya que alteran la comparabilidad de los grupos de tratamiento y no permiten conocer el verdadero efecto de la intervención en los participantes seleccionados.

La evaluación de calidad de los estudios indica que este tipo de intervenciones carece de validez externa, ya que presentan problemas en la etapa de diseño del estudio. Esto ocurre porque la selección de los lugares de trabajo y de los participantes no fue realizada al azar desde la población objetivo, por lo que sus resultados no se pueden generalizar.

Estos resultados son similares a los de una revisión sistemática de Fernández y cols. (21), cuyo objetivo era analizar las intervenciones ambientales en el lugar de trabajo y su efecto en la prevención y control de la obesidad. El análisis indicó que solo la mitad de los estudios incluidos tuvo un bajo riesgo de sesgo y el efecto sobre las medidas de peso y grasa corporal fue escaso y, a veces, en una dirección inesperada. Los sesgos que afectaron principalmente la validez de los estudios fueron fallas en la aleatorización de los grupos y problemas en el desequilibrio basal.

El objetivo de la revisión sistemática de Allan y cols. (22) fue evaluar la efectividad de intervenciones ambientales en el lugar de trabajo en el peso corporal, el IMC y la grasa corporal en ECA. Sus análisis concuerdan con esta revisión, en la que hubo un solo estudio que tuvo efecto modesto sobre la disminución del peso corporal e IMC y que fue evaluada con un alto riesgo de

sesgo por errores en el sesgo de selección. Además, el resto de los estudios tenían un alto riesgo de sesgo y un riesgo de sesgo poco claro, por informar de manera deficiente las intervenciones.

Las revisiones de Verweij y cols. (23) y Engbers y cols. (24) al analizar el efecto de intervenciones ambientales en lugares de trabajo sobre el peso corporal de los trabajadores coinciden en que los problemas recurrentes de las investigaciones son la inadecuada o poco clara descripción del proceso de asignación aleatoria. Además, los efectos de la intervención sobre peso corporal, IMC y grasa corporal están relacionados con estudios de calidad moderada y baja (23). Se estimó que la mayoría de los estudios tenían una calidad pobre o débil, y no hubo evidencia de que este tipo de intervenciones tuvieran efecto sobre el IMC y la grasa corporal.

Respecto a las fortalezas, el presente estudio utilizó el Manual Cochrane de revisiones sistemáticas (9) como guía fundamental para poder realizar un análisis completo y sistemático de los ECA y los aleatorizados por conglomerados. Esto permite tener una evidencia clara de los errores más frecuentes en el diseño, la implementación y el análisis de las intervenciones ambientales para la prevención del incremento de peso corporal de los trabajadores, que afectan la credibilidad de los resultados de efectividad. Esto fue posible gracias a un exhaustivo análisis de sesgo. Además, la inclusión de la evaluación de calidad permitió conocer la falta de validez externa de este tipo de estudios. Otras dos revisiones con objetivos similares (21,23) utilizaron la misma herramienta para evaluar la validez interna a través del riesgo de sesgo, junto con otras herramientas para la evaluación de la calidad metodológica.

Las debilidades indican que la búsqueda de ensayos controlados aleatorizados estuvo restringida al excluir aquellos estudios que solo consideraban a hombres o solo a mujeres, o a personas con sobrepeso y obesidad.

La cantidad de intervenciones ambientales en el lugar de trabajo que miden la efectividad en resultados de impacto, como los cambios en el peso corporal, son escasas y, además, la evidencia que existe, en general, no es confiable. Por ello, se recomienda aumentar el desarrollo de ensayos controlados aleatorizados por conglomerados o individuales en este tema, pero con un diseño adecuado para evitar los problemas que afectan la validez interna. Las intervenciones deben realizar una correcta aleatorización de los grupos y participantes e informar adecuadamente este proceso, así como controlar el alto número de abandonos a lo largo del estudio y la contaminación entre participantes de los grupos o la exposición a otros factores, como las intervenciones alternativas que se entrecruzan con la intervención de interés.

A su vez, la falta de efectividad permite considerar que los hábitos alimenticios y su impacto sobre el peso corporal no solo están condicionados por el aumento en la oferta de alimentos saludables y educación nutricional en el lugar de trabajo, ya que existen contextos mayores que pueden estar influyendo. El lugar de trabajo es parte de un ecosistema conectado con otros ambientes alimentarios por los cuales transitan los trabajadores y realizan sus conductas alimentarias (7), por lo que existe una interacción con el nivel socioeconómico de los individuos (25). Esto hace necesario considerar el contexto en el que viven al momento de desarrollar intervenciones en la población trabajadora (26).

Por lo tanto, los estudios deben comprender los factores sociales, económicos y culturales que afectan las elecciones de alimentos y los patrones de alimentación de los trabajadores (26) que identifiquen la realidad de la alimentación laboral y su asociación con el peso corporal y el estado de salud. Para tener una descripción de la situación actual, se requiere desarrollar intervenciones en los lugares de trabajo que consideren los distintos ambientes alimentarios por los que transitan los trabajadores y sus distintas realidades socioeconómicas, ya que estos elementos pueden generar distintos efectos sobre las elecciones de estilos de vida (7).

Este estudio confirma la escasa evidencia confiable de efectividad de estudios anteriores y no permite afirmar que este tipo de intervenciones son efectivas para el control del peso corporal de los trabajadores. Además, sus efectos no son generalizables a la población. Esto requiere realizar más estudios que consideren los requisitos de validez y sesgo descritos en esta revisión sistemática y el entorno alimentario global de los trabajadores, y no solo su lugar de trabajo, profundizando en la interacción que existe entre factores socioeconómicos y ambientes alimentarios.

ANEXO 1. ESTRATEGIA DE BÚSQUEDA

I. Búsqueda en Central

Fecha de búsqueda: 28 de julio, 2020

Palabras clave y combinaciones:

#1: (healthy food access):ti,ab,kw OR (healthy food availability):ti,ab,kw OR (food environment):ti,ab,kw OR ("workplace health promotion"):ti,ab,kw (word variations have been searched)

#2: (cafeteria):ti,ab,kw OR (food vending machine):ti,ab,kw OR (food service):ti,ab,kw OR (food carts):ti,ab,kw OR (beverage vending machine):ti,ab,kw (word variations have been searched)

#3: (nutritional information):ti,ab,kw OR (nutritional education):ti,ab,kw OR (nutritional assistance):ti,ab,kw OR (nutritional standards):ti,ab,kw OR (nutritional intervention):ti,ab,kw

#4: (worksite):ti,ab,kw OR (workplace):ti,ab,kw OR (workers):ti,ab,kw OR (employees):ti,ab,kw

#5: (weight gain):ti,ab,kw OR (obesity prevention):ti,ab,kw OR (eating behavior):ti,ab,kw (word variations have been searched)

Combinación: #1 OR #2 AND #3 AND #4 AND #5

(Continúa en página siguiente)

ANEXO 1 (Cont.). ESTRATEGIA DE BÚSQUEDA

II. Búsqueda en Medline

Esta búsqueda se realizó a través de PubMed, ya que permite acceder de manera libre al contenido de Medline.

Fecha de búsqueda: 7 de agosto, 2020

Palabras clave:

((((((((((((((((((food environment[Title/Abstract]) OR (healthy food access[Title/Abstract])) OR (healthy food availability[Title/Abstract])) OR (healthy food[Title/Abstract])) OR (nutritional education[Title/Abstract])) OR (nutritional program[Title/Abstract])) OR (health promotion[Title/Abstract])) OR (cafeteria[Title/Abstract])) OR (canteens[Title/Abstract])) OR (food machine[Title/Abstract])) OR (food policies[Title/Abstract])) OR (food servicie[Title/Abstract])) AND (workplace[Title/Abstract])) OR (worksite[Title/Abstract])) OR (workers[Title/Abstract])) OR (employees[Title/Abstract])) OR (obesity prevention[Title/Abstract])) OR (weight gain[Title/Abstract])) OR (overweight[Title/Abstract]))

Filtros aplicados:

Abstract, Free full text, Full text, Randomized controlled trial, in the last 10 years, English, Spanish, Female, Male, Medline, Adult: 19+ years, Young adult: 19-24 years, Adult: 19-44 years, Middle aged + aged: 45+ years, Middle aged: 45-64 years.

III. Búsqueda en EMBASE

Fecha de búsqueda: 8 de septiembre, 2020

Palabras clave:

#1: 'healthy food'/exp OR 'food environment'/exp OR 'work environment'/exp OR 'health promotion'/exp OR 'food access'/exp OR 'food availability'/exp OR 'food policy'/exp
#2: 'workshops'/exp OR 'cafeteria' OR 'canteen'/exp OR 'catering service'/exp OR 'vending machine'/exp OR 'food intake'/exp
#3: 'nutrition education'/exp OR 'nutrition labeling'/exp OR 'nutrition standards' OR 'nutrition programs'/exp
#4: 'workplace'/exp OR 'worksite' OR 'worker'/exp OR 'employee'/exp OR 'workforce'/exp
#5: 'body weight gain'/exp OR 'obesity prevention and control'/exp OR 'body weight control'/exp
#6: #1 OR #2 OR #3 OR #5
#7: #6 AND 'randomized controlled trial'/de
#8: #4 AND #7
#9: #8 AND (2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py)
#10: #8 AND (2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py) AND ([adult]/lim OR [aged]/lim OR [middle aged]/lim OR [young adult]/lim)

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ARÁN

Nutrición Hospitalaria

Grupo de Trabajo SENPE

Proceso de tratamiento médico nutricional

Process of medical nutrition therapy

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Resumen

El tratamiento médico nutricional es de gran utilidad en el mantenimiento y recuperación de la salud de los pacientes con desnutrición relacionada con la enfermedad, aunque su implementación puede ser compleja y no está exenta de riesgos. Se entiende por proceso aquel conjunto de actividades que están mutuamente relacionadas o que interactúan para transformar elementos de entrada en resultados. Desde el Grupo de Trabajo de Gestión de la SENPE presentamos el Proceso de Tratamiento Médico Nutricional (PTMN), que tiene por objetivo facilitar la gestión de la nutrición clínica, pensando en un equipo de soporte nutricional multidisciplinar de atención al paciente hospitalizado.

En este documento se describen los siete subprocesos que constituyen el PTMN, además de un subproceso previo de cribado nutricional. Cada subproceso se divide en una primera sección con una ficha técnica en la que se detallan sus aspectos generales, mientras que en la segunda sección se proponen objetivos clave, indicadores de calidad y estándares para su evaluación.

Palabras clave:

Calidad. Gestión por procesos. Indicador de calidad. Estándar de calidad.

Abstract

Medical nutrition therapy is a very useful tool in maintaining and recovering the health of patients with disease-related malnutrition, although its implementation can be complex and is not without risks. Quality processes are understood as sets of activities that are related or interact to transform input elements into results. From the SENPE Management Work Group we present the process of medical nutrition therapy (PMNT), which aims to facilitate the management of clinical nutrition of a multidisciplinary nutrition support team in a hospital setting.

This paper describes the seven sub-processes PMNT is comprised of, in addition to a previous nutritional screening sub-process. Each sub-process is divided into a first section with a technical sheet detailing its general aspects, while a second section proposes key objectives, quality indicators, and standards for their evaluation.

Keywords:

Quality. Process management. Quality indicator, Quality standard.

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INTRODUCCIÓN

La desnutrición relacionada con la enfermedad (DRE) supone un problema sanitario de primer orden, particularmente en los hospitales, debido a los costes en términos humanos y económicos que supone. El estudio PREDyCES demostró que uno de cada cuatro pacientes hospitalizados en España presenta desnutrición según la herramienta *Nutritional Risk Screening* (NRS-2002) y que, en aquellos en los que esta aparece durante el ingreso, la estancia se dobla y los costes aumentan en un 50 % (1,2). Más recientemente, en el estudio SeDREno se demostró una prevalencia similar (29,7 %), según los criterios GLIM (3).

El tratamiento médico nutricional (TMN), que incluye el uso de suplementos orales, la nutrición enteral y la nutrición parenteral, es de gran utilidad en el mantenimiento y recuperación de la salud de los pacientes hospitalizados, aunque su implementación puede ser compleja y no está exenta de riesgos. Por otra parte, la progresiva incorporación de técnicas de cribado sistemático de la DRE para la posterior aplicación de una TMN precoz ha demostrado ser una medida coste-efectiva (4,5).

En gestión se entiende por proceso aquel conjunto de actividades que están mutuamente relacionadas o que interactúan para transformar elementos de entrada en resultados. Aplicado a la nutrición clínica, el proceso tendrá como entrada al paciente que precisa una valoración y, posiblemente, un tratamiento nutricional, mientras que la salida se corresponde con la finalización de dicho tratamiento. El propio proceso a su vez se divide en varios subprocesos que se van encadenando hasta llegar al resultado final (6).

El presente documento supone la actualización de una acción sinérgica entre la Sociedad Española de Nutrición Clínica y Metabolismo (SENPE) y la Sociedad Española de Farmacia Hospitalaria (SEFH), realizada en 2014 (7), que tiene por objetivo facilitar la gestión de la nutrición clínica. El actual proceso de tratamiento médico nutricional (PTMN) enlaza con los de la alimentación hospitalaria, publicado con anterioridad (8), y el de atención nutricional ambulatoria, pendiente de elaborar (Fig. 1). Aunque se puede aplicar a otros ámbitos de la atención sanitaria, casi en su totalidad se ha desarrollado pensando en un equipo de soporte nutricional multidisciplinar que atiende a pacientes hospitalizados.

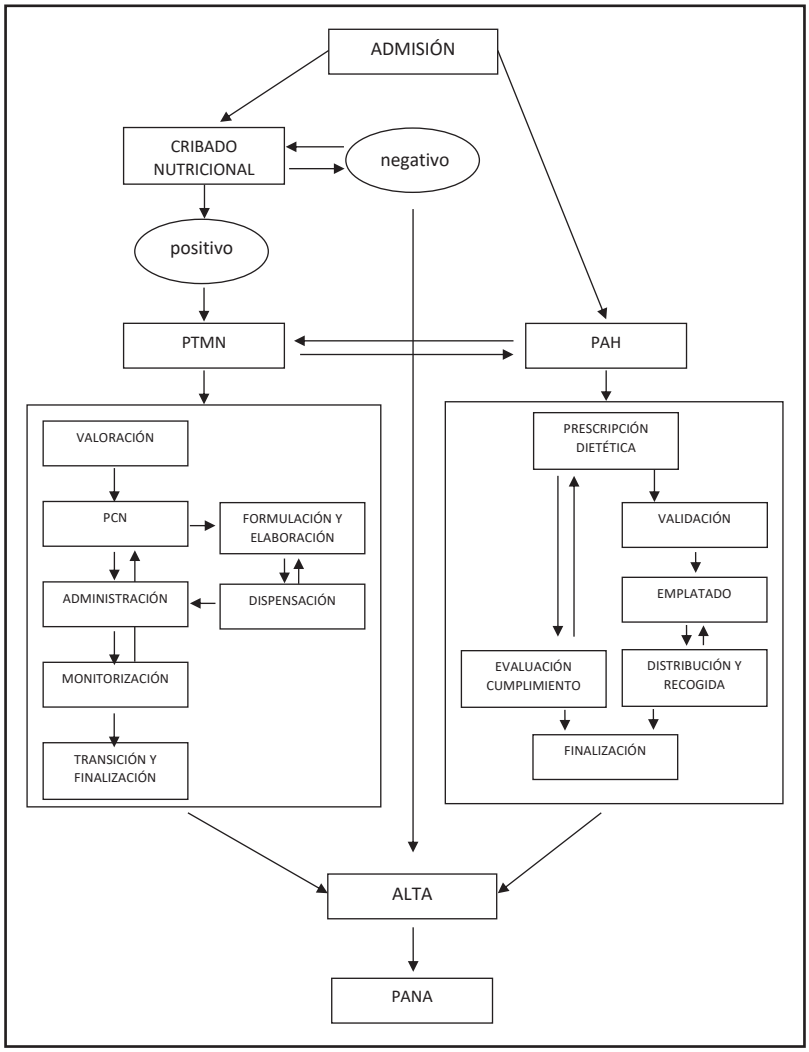

Figura 1.

Procesos clínico-asistenciales en nutrición clínica. PTMN: proceso de tratamiento médico nutricional; PAH: proceso de alimentación hospitalaria; PANA: proceso de atención nutricional ambulatoria. Las flechas en ambos sentidos indican la necesidad de repetir ciclos mientras dure el ingreso (repetición de cribado nutricional negativo, formulación y elaboración-dispensación, emplatado-distribución y recogida), o bien la interrelación entre subprocesos (PTMN-PAH, monitorización-PCN, evaluación del cumplimiento-prescripción dietética).

La responsabilidad asistencial en el ámbito de la nutrición clínica en España puede recaer, según la organización, sobre diferentes servicios, unidades y profesionales, a menudo con diversas denominaciones, que van desde las unidades de nutrición clínica o de soporte nutricional a los equipos más o menos numerosos de personas pertenecientes a uno o varios servicios (9). Los profesionales implicados son igualmente de variada procedencia, como lo son sus relaciones de dependencia y su situación en el organigrama de la organización. Dado que en la mayoría de los casos se trata (o debiera tratarse) de un equipo de profesionales dedicado al manejo de pacientes con DRE o en riesgo de desarrollarla, se ha usado la denominación genérica "equipo de soporte nutricional" (ESN), de un modo meramente descriptivo. Por otro lado, se desea destacar la trayectoria y experiencia acumulada durante muchos años en las unidades de nutrición clínica y dietética, que representan un modelo ejemplar de gestión por su carácter multidisciplinar e integrador. Por este motivo se ha usado la expresión "equipo de soporte nutricional/unidad de nutrición clínica y dietética (ESN/UNCYD) a lo largo de todo el texto. Corresponderá a cada institución hacer uso de esta o de cualquier otra denominación que se adapte mejor a su realidad.

En esta misma línea, aunque el presente documento está concebido como herramienta para evaluar el PTMN, no se ha diseñado el proceso en sí, al entender que esta labor debe llevarse a cabo en cada centro, teniendo en cuenta sus particularidades. Así, los diversos actores y las acciones que se describen pueden no corresponder a la situación en una institución determinada, ya que es imposible recoger en un único documento todas las posibles variantes. Para evitar que se interprete este trabajo de una forma dogmática, y con la intención de evitar constricciones, se han usado expresiones como "u otro organismo designado por la dirección". De este modo se deja abierta la puerta a cualquier modelo, pero sin renunciar al objetivo de fomentar la práctica adecuadamente organizada de la nutrición clínica.

Además de los siete subprocesos que constituyen el PTMN (Fig. 1), se ha distinguido un subproceso previo, de cribado nutricional (CN), que debería incluirse en el macroproceso de hospitalización de todos los centros. Cinco de los siete subprocesos propios del PTMN constituyen su eje principal (valoración, planificación de cuidados, administración, monitorización y transición y finalización), mientras que los dos restantes discurren de forma paralela a este eje (formulación y elaboración y dispensación).

La descripción de cada subproceso se dividide en dos secciones: la primera es una ficha técnica en la que se detallan aspectos generales, mientras que en la segunda se proponen indicadores de calidad para su evaluación. En la ficha técnica, tras la justificación del subproceso, se hace una definición funcional que explica sus objetivos. A continuación se exponen sus criterios de calidad, es decir, las características que debe tener la labor realizada para ser considerada de calidad. Otros elementos incluidos en la ficha técnica vienen detallados en la tabla I.

En la segunda parte de cada subproceso se proponen objetivos clave relacionados con los criterios de calidad anteriormente expuestos, junto con indicadores para medir su logro. Para cada indicador se plantea una fórmula para su obtención (en el caso de los indicadores numéricos) y se propone una metodología de medición. Corresponde a cada institución, dependiendo de la situación en la que se encuentre, la priorización y selección de los objetivos clave más convenientes en cada fase de su proceso de mejora continua.

Para la mayoría de los indicadores numéricos se propone una medición anual, habitualmente mediante muestreo de pacientes atendidos en un periodo de tiempo, aunque esto se debe adaptar a las posibilidades y necesidades de cada centro. Es posible que inicialmente sea conveniente una medición más frecuente, sobre todo si se han implantado medidas de mejora.

En otro tipo de indicadores se plantea la elaboración de protocolos, actuación relativamente sencilla de llevar a cabo y que supone el primer paso en la mejora continua de la asistencia (10).

En cada indicador se proponen estándares a partir de los cuales su cumplimiento se considera aceptable. En la presente actualización se han incorporado algunos estándares basados en un reciente estudio realizado por el Grupo de Trabajo de Gestión de SENPE (11). Sin embargo, en la mayoría de los casos, los autores se han visto obligados a proponer objetivos de cumplimiento que no están basados en datos reales debido a la falta de información disponible. Por este motivo se insiste en la necesidad de la puesta en marcha de iniciativas para compartir experiencias en este campo, que sirvan para enunciar estándares más realistas y a la vez para estimular a otros centros en su mejora continua.

Finalmente, durante el desarrollo de la guía se han identificado los recursos necesarios para el buen funcionamiento del PTMN (Tabla II). En la ficha técnica de algunos subprocesos se añaden recursos adicionales específicos.

Tabla I. Ficha técnica de los subprocesos del PTMN

Propietario del proceso	Persona cuya actividad está relacionada con el desarrollo del proceso, responsable de su gestión sistemática y mejora continua.
Entrada y salida	Acciones que suponen el inicio y la finalización de cada subproceso (habitualmente la salida de un subproceso supone la entrada del siguiente).
Proveedor	Personas o estructuras organizativas que proporcionan la entrada al subproceso.
Participantes	Personas o unidades que realizan las actividades del subproceso.
Destinatarios	Personas o estructuras organizativas sobre los que la salida del proceso tiene impacto y que, por tanto, van a exigir que todo haya funcionado correctamente.

Tabla II. Recursos generales necesarios para el buen funcionamiento del PTMN

Dirección del centro sensibilizada y comprometida en la erradicación de la desnutrición en el medio sanitario.
Política y estrategia del centro orientada a la eficiencia, la prevención de riesgos y la mejora continua de la calidad.
Personal sanitario sensibilizado y formado en los diversos aspectos que se incluyen en este proceso.
Comisión de nutrición activa, independiente y respaldada por la dirección.
Unidad de nutrición clínica o equipo de soporte nutricional multidisciplinar, con dotación suficiente, integrado por personal cualificado y reconocido.
Estandarización y diseño de protocolos.
Comunicación fluida con servicios proveedores de pacientes.

SUBPROCESO DE CRIBADO NUTRICIONAL (TABLAS III A VI)

JUSTIFICACIÓN

La desnutrición o la situación de riesgo de desarrollarla se relacionan con un incremento de la fragilidad, la incidencia de complicaciones, la tasa de ingresos hospitalarios y la duración de la estancia hospitalaria, así como de la mortalidad y los costes sanitarios (12-16). Con una detección precoz se pueden reducir estos problemas de forma coste-efectiva (4,5,17-19).

DEFINICIÓN FUNCIONAL

El CN debe ser el primer paso del proceso de atención nutricional en el ámbito sanitario. Se trata de la aplicación conjunta y rápida de actuaciones clínicas y técnicas analíticas, orientada a identificar precozmente a aquellos pacientes con DRE o en riesgo de desarrollarla y que se beneficiarían de una intervención nutricional adecuadamente planificada (20-25).

Tabla III. Subproceso de CRIBADO NUTRICIONAL

Criterios de calidad	*CN.1. Realizar un CN inicial y repetirlo periódicamente en caso de resultado negativo.* *CN.2. Comunicar el resultado del CN.* *CN.3. Establecer un plan de actuación en pacientes con resultado positivo en la prueba de CN.*
Propietario	Designado por la comisión de nutrición u organismo delegado por la dirección del centro.
Entrada	Admisión del paciente en el ámbito asistencial que proceda (atención ambulatoria, centros sociosanitarios, hospitalización).
Proveedor	Servicio o unidad asistencial de acogida.
Salida	Alta del paciente o test de cribado positivo.
Destinatario	Servicio o unidad asistencial de acogida, atención primaria, unidad de nutrición, servicio de admisiones y documentación clínica.
Participantes	Totalidad del equipo asistencial (con especial implicación del personal de enfermería).
Recursos específicos	Campo específico disponible para el CN en la historia clínica. Básculas y tallímetros accesibles.

Tabla IV. Objetivos clave relacionados con el criterio de calidad CN.1 (realizar un CN inicial y repetirlo periódicamente en caso de resultado negativo) (22,31)

CN.1.A. Determinar el peso y la talla de los pacientes	
Indicador	(nº de pacientes con determinación de peso y talla mediante métodos directos o indirectos) / (nº de pacientes atendidos) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana (H, AA) o mediante control transversal (CCS).
Fuente	Historia clínica.
Población	Todos los pacientes incluidos en el programa de CN del centro.

(Continúa en página siguiente)

Tabla IV (Cont.). Objetivos clave relacionados con el criterio de calidad CN.1 (realizar un CN inicial y repetirlo periódicamente en caso de resultado negativo) (22,31)

CN.1.B. Disponer de una herramienta de CN	
Indicador	Selección, por parte de la comisión de nutrición o el organismo delegado por la dirección del centro, de una herramienta de cribado validada[1], adecuada a las posibilidades de la institución, teniendo en cuenta el ámbito sanitario y el tipo de paciente al que se presta asistencia.
Estándar	Sí.
Medición	Control cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.
CN.1.C. Realizar el CN en los grupos de riesgo de desnutrición[2]	
Indicador	(nº de pacientes pertenecientes a grupos de riesgo de desnutrición sometidos a test de cribado) / (nº de pacientes pertenecientes a grupos de riesgo de desnutrición) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana (H, AA) o mediante control transversal (CSS).
Fuente	Historia clínica.
Población	Pacientes en grupos de riesgo de desnutrición
CN.1.D. Realizar el CN precozmente	
Indicador	(nº de pacientes con test de cribado realizado precozmente[3]) / (nº de pacientes pertenecientes a grupos de riesgo de desnutrición) * 100.
Estándar	100 %.
Medición	Frecuencia: anual, en una muestra de pacientes atendidos a lo largo de una semana (H, AA) o mediante control transversal (CSS).
Fuente	Historia clínica.
Población	Pacientes en grupos de riesgo de desnutrición.
CN.1.E. Repetir el CN en pacientes con resultado previo negativo	
Indicador	(nº de pacientes cribados con la periodicidad recomendada[4]) / (nº de pacientes pertenecientes a grupos de riesgo de desnutrición y con CN anterior negativo) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana (H, AA) o mediante control transversal (CSS).
Fuente	Historia clínica.
Población	Pacientes en grupos de riesgo de desnutrición ingresados durante más de una semana (H), con más de seis meses de estancia (CSS) o con sospecha de desnutrición sostenida durante más de seis meses (AA).

AA: atención ambulatoria; CSS: centros sociosanitarios; H: hospitalización. [1]Herramientas de cribado: H: Nutrition Risk Screening 2002, MUST, CIPA, filtros electrónicos; CSS: MNA; AA: MUST, MNA (ancianos). [2]Grupos de riesgo de desnutrición: H: pacientes de oncología, cirugía mayor, ancianos, con enfermedades del aparato digestivo, respiratorias y cardiovasculares, entre otros; CSS: todos los residentes; AA: pacientes con sospecha clínica de desnutrición por pérdida involuntaria de peso o de tejido muscular o adiposo; falta de apetito persistente; problemas con la ingesta, deglución, digestión o absorción de nutrientes; pérdida de nutrientes (por ejemplo vómitos o diarrea prolongada); enfermedad intercurrente prolongada. [3]CN precoz: H: primeras 24 horas; CSS: primera semana; AA: en la primera valoración. [4]Frecuencia de cribado recomendada en pacientes con CN negativo: H: semanal; CSS y AA: semestral o antes si hay cambios significativos del estado clínico del paciente.

Tabla V. Objetivos clave relacionados con el criterio de calidad CN.3 (comunicar el resultado del CN positivo) (32)

CN.2.A. Comunicación del resultado del CN positivo al equipo asistencial	
Indicador	(nº de pacientes con CN positivo comunicado a su equipo asistencial) / (nº de pacientes con CN positivo) * 100.
Estándar	100%.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana (hospitales y atención ambulatoria) o mediante control transversal (centros sociosanitarios).
Fuente	Historia clínica.
Población	Pacientes con CN positivo.

AA: atención ambulatoria; CSS: centros sociosanitarios; H: hospitalización.

Tabla VI. Objetivos clave relacionados con el criterio de calidad CN.2 (establecer un plan de actuación en pacientes con resultado positivo en la prueba de CN) (17,22,25)

CN.3.A. Realizar una valoración nutricional en pacientes con CN positivo	
Indicador	(nº pacientes con CN positivo en los que se ha realizado valoración nutricional) / (nº de pacientes con CN positivo) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana (H, AA) o mediante control transversal (CSS).
Fuente	Historia clínica.
Población	Pacientes con test de cribado positivo.

AA: atención ambulatoria; CSS: centros sociosanitarios; H: hospitalización.

SUBPROCESO 1: VALORACIÓN NUTRICIONAL (TABLAS VII A XIV)

JUSTIFICACIÓN

La valoración nutricional (VN) tiene como objetivo caracterizar el estado nutricional de los pacientes con sospecha o riesgo de desnutrición, con el fin de establecer un plan terapéutico.

DEFINICIÓN FUNCIONAL

Procedimiento por el que, mediante un enfoque integral a partir de un uso conjunto de técnicas (historia clínica, dietética y farmacológica, examen físico, valoración antropométrica y morfofuncional, y determinaciones analíticas) se investigan las enfermedades, trastornos o mecanismos subyacentes que pueden estar causando un deterioro nutricional, se determinan los requerimientos energéticos, proteicos y de micronutrientes y, se establece el diagnóstico nutricional de un individuo, proporcionando la base para un TMN apropiado (21,22,25,26,32).

Tabla VII. Subproceso 1 (VALORACIÓN NUTRICIONAL)

Criterios de calidad	*1.1. Obtención de un diagnóstico nutricional en los pacientes valorados.* *1.2. Documentación del diagnóstico nutricional.*
Propietario	Responsable de la unidad de nutrición clínica y dietética, equipo de soporte nutricional u organismo o servicio designado por la dirección del centro.
Entrada	Resultado positivo en test de cribado, solicitud de consulta al ESN/UNCYD o sospecha de riesgo de desnutrición por parte del equipo asistencial.

(Continúa en página siguiente)

Tabla VII (Cont.). Subproceso 1 (VALORACIÓN NUTRICIONAL)

Proveedor	Servicio o unidad asistencial de acogida.
Salida	Caracterización nutricional del paciente.
Destinatario	Servicio o unidad asistencial de acogida.
Participantes	Miembros del servicio o unidad asistencial de acogida y del ESN/UNCYD.
Recursos específicos	Equipamiento para realización de antropometría y estudios analíticos. Cuestionarios estructurados de valoración de la ingesta dietética. Dinamómetro. Bioimpedanciómetro. Ecógrafo. Hojas estructuradas de recogida de datos o espacios específicos en la historia clínica.

Tabla VIII. Objetivos clave relacionados con el criterio de calidad 1.1 (obtención de un diagnóstico nutricional en los pacientes valorados)

1.1.A. Disponer de un protocolo para hacer la VN	
Indicador	Existencia en el centro de un protocolo que describe el procedimiento de VN (Tabla IX) y define los criterios para establecer el diagnóstico de desnutrición (Tabla X), su gravedad (Tabla XI) y su categoría etiológica (Tabla XIII).
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.
1.1.B. Cumplimiento del protocolo de VN	
Indicador	(nº de pacientes con valoración realizada según el protocolo) / (nº de pacientes valorados) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes atendidos por el ESN/UNCYD.

Tabla IX. Parámetros que podrían ser incluidos en un protocolo de VN (25-28,35-40)

Historia clínica	Existencia de trastornos y tratamientos con repercusión sobre el estado nutricional. Alteraciones del apetito, la alimentación y la función digestiva.
Valoración dietética	Métodos retrospectivos: recordatorio de 24 horas, frecuencia de consumo de alimentos. Métodos prospectivos: registro dietético, escalas visuales.
Antropometría	Peso, talla (real o estimada) e índice de masa corporal. Porcentaje de pérdida involuntaria de peso durante un intervalo de tiempo. Relación peso actual/peso habitual. Pliegues cutáneos: tricipital, bicipital, subescapular, suprailíaco. Circunferencia braquial. Circunferencia muscular del brazo. Circunferencia de la pantorrilla. Perímetro de cintura y cadera.
Estudio morfofuncional	SARC-F (despistaje de sarcopenia). Test de levantarse de la silla. Dinamometría de la mano (fuerza muscular). Bioimpedanciometría (BIA). Ecografía nutricional. Índice de Barthel. *Timed up and go test.* Velocidad de la marcha (4 m). SPPB.

(Continúa en página siguiente)

Tabla IX (Cont.). Parámetros que podrían ser incluidos en un protocolo de VN (25-28,35-40)

Cuestionarios estructurados	Valoración global subjetiva. Mini Nutritional Assessment (ancianos).
Estudio de la disfagia	*Eating Assessment Tool*-10 (método de despistaje). Método de exploración clínica de volumen-viscosidad. Fibroendoscopia y videofluoroscopia de la deglución.
Análisis	Hemograma. Proteínas plasmáticas (albúmina, prealbúmina, proteína ligadora de retinol, transferrina). Marcadores inflamatorios (proteína C-reactiva, fibrinógeno, ferritina, interleuquina 6). Cociente proteína C-reactiva/prealbúmina. Glucemia y perfil lipídico. Funciones renal y hepática. Iones y minerales en plasma y en orina. Vitaminas y oligoelementos.

SARC-F: strength, assistance with walking, rising from a chair, climbing stairs and falls; *SPPB:* short physical performance battery.

Tabla X. Criterios de desnutrición según la Global Leadership Initiative on Malnutrition (GLIM) (25)

Criterios fenotípicos[1]		
Pérdida de peso	**Bajo IMC**	**Reducción de la masa muscular[2]**
< 5 % en > 6 meses. < 10 % en > 6 meses.	< 20 si < 70 años (Asia < 18,5). < 22 si > 70 años (Asia < 20).	Reducción con métodos de medida de composición corporal validados.
Criterios etiológicos[1]		
Ingesta o absorción de nutrientes reducida.[3,4]	*Inflamación.*	
≤ 50 % de los requerimientos energéticos > 1 semana o cualquier reducción > 2 semanas.	Enfermedad o daño agudo.[5,8]	
Presencia de enfermedad GI crónica que afecte a la absorción.	Relacionada con enfermedad crónica.[7]	

[1]Se requiere al menos 1 criterio fenotípico y 1 criterio etiológico para el diagnóstico de malnutrición. [2]Por ejemplo, el índice de masa libre de grasa (FFMI) mediante DXA o los correspondientes estándares, usando otros métodos de composición corporal como BIA, TAC o RMN (Tabla XII). Cuando no esté disponible o por preferencia regional, se pueden usar el examen físico o medidas antropométricas como la CMB o la CP. Los umbrales deben adaptarse a la raza (Asia). Las valoraciones funcionales como la dinamometría de la mano pueden considerarse como una medida de apoyo. [3]Considerar los síntomas gastrointestinales como marcadores que dificultan la ingesta o la absorción (disfagia, náuseas, vómitos, diarrea o dolor abdominal). Valorar su severidad, intensidad, frecuencia y duración. [4]La reducción de la asimilación de comida/nutrientes se asocia a enfermedades malabsortivas como el síndrome de intestino corto, la insuficiencia pancreática o la cirugía bariátrica. También con trastornos como la estenosis esofágica, la gastroparesia y la pseudoobstrucción intestinal. La malabsorción es un diagnóstico clínico que se manifiesta como diarrea crónica, esteatorrea o alto débito por ostomías. Usar el juicio clínico o estudios adicionales para valorar la severidad en base a la frecuencia, duración o cuantificación de la grasa fecal y/o el volumen de las pérdidas. [5]La inflamación aguda grave generalmente aparece en pacientes con infección grave, quemaduras, trauma o TCE cerrado. El resto de las situaciones de daño/enfermedad aguda deben considerarse moderadas o leves. [6]La inflamación grave generalmente no aparece en situaciones de cronicidad. La inflamación crónica o recurrente, de intensidad leve a moderada, generalmente ocurre en pacientes con enfermedad maligna, enfermedad pulmonar obstructiva crónica, insuficiencia cardiaca congestiva, enfermedad renal crónica o en cualquier enfermedad con inflamación crónica o recurrente. Nótese que la inflamación transitoria de intensidad leve no sobrepasa el umbral de este criterio etiológico. [7]La proteína C-reactiva puede usarse como medida de laboratorio de apoyo.

Tabla XI. Gravedad de la DRE según los criterios GLIM (25)

	Criterio fenotípico[1]		
	% pérdida de peso	**IMC (kg/m²)[2]**	**Reducción de masa muscular**
Estadio 1 (moderada)	5-10 % en < 6 meses 10-20 % en > 6 meses	< 20 si < 70 años < 22 si ≥ 70 años	Leve-moderada
Estadio 2 (severa)	> 10 % en < 6 meses > 20 % en > 6 meses	< 18,5 si < 70 años < 20 si ≥ 70 años	Severa

[1]Se establece en base a los criterios fenotípicos (los criterios etiológicos sirven para contextualizar el caso, guiar la intervención nutricional y anticipar los resultados). [2]Se necesitan más estudios para establecer límites consensuados de IMC para la población asiática.

Tabla XII. Ejemplos de límites recomendados para el diagnóstico de masa muscular reducida o sus marcadores alternativos (26,27)

	Hombres	Mujeres
Índice de masa magra apendicular (ALMI) o índice de músculo esquelético apendicular (ASMI), kg/m^2 (BIA)	< 7	< 5,7
Índice de masa magra (FFMI), kg/m^2 (BIA)	< 17	< 15
Circunferencia de pantorrilla, cm	< 33	< 32

Se debe ajustar el valor obtenido en función del IMC, sumando 4 cm (IMC < 18,5) o restando 3 cm (IMC 25-30), 7 cm (IMC 30-40) o 12 cm (IMC > 40).

Tabla XIII. Categorías diagnósticas según la causa subyacente (25)

Desnutrición secundaria a:
- Enfermedad crónica con inflamación. - Enfermedad crónica con inflamación mínima o no percibida. - Enfermedad o daño agudo con inflamación severa. - Inanición, incluyendo hambre o escasez de comida por factores socioeconómicos o ambientales.

Tabla XIV. Objetivos clave relacionados con el criterio de calidad 1.2 (documentación del diagnóstico nutricional) (40)

1.2.A. Registro en la historia clínica de la VN	
Indicador	(nº de pacientes con VN registrada en la historia clínica) / (nº de pacientes valorados) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes atendidos por el ESN/UNCYD.
1.2.B. Inclusión en el informe de alta del diagnóstico nutricional	
Indicador	(nº de pacientes con diagnóstico nutricional codificado (Tabla XV) en el informe de alta) / (nº de pacientes valorados) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Informe de alta.
Población	Pacientes atendidos por el ESN/UNCYD.

SUBPROCESO 2: PLAN DE CUIDADOS NUTRICIONALES (TABLAS XV A XVIII)

JUSTIFICACIÓN

El concepto de cuidado nutricional incluye varios aspectos diferentes que deben ser manejados adecuadamente para garantizar que cada paciente recibe el soporte nutricional adecuado, y en el momento y lugar correctos. En todo paciente con desnutrición o en riesgo de desnutrición se debe establecer un plan de cuidados nutricionales basado en sus requerimientos nutricionales y preferencias (20). La terapia nutricional es un proceso complejo en el que intervienen diversos factores que pueden comprometer la consecución de los objetivos marcados. Por ello, una planificación clara y ordenada de los cuidados nutricionales puede minimizar la aparición de errores y maximizar su eficacia.

DEFINICIÓN FUNCIONAL

Es un procedimiento mediante el que se diseña el tratamiento nutricional de cada paciente, optimizando su eficiencia y seguridad, para un adecuado conocimiento de este por el equipo a cargo del paciente. En el plan de cuidados nutricionales (PCN) se incluye información sobre: requerimientos de energía, nutrientes y fluidos, objetivos nutricionales a corto y largo plazo, instrucciones para la implementación del tratamiento, su ruta y método de administración, una revisión de la medicación si estuviera indicado, un plan de monitorización, la duración estimada de la terapia y las medidas necesarias para asegurar su continuidad en el tiempo cuando sea necesario. (21,33).

Tabla XV. Subproceso 2 (PLAN DE CUIDADOS NUTRICIONALES)

Criterios de calidad	*2.1. Prescripción basada en la valoración nutricional del paciente.* *2.2. Plan de cuidados nutricionales (PCN) basado en el uso de protocolos clínicos.* *2.3. Estandarización de la prescripción.*
Propietario	Responsable del ESN/UNCYD u organismo designado por la dirección del centro.
Entrada	Indicación de tratamiento nutricional.
Proveedor	Profesional que indica el tratamiento nutricional.
Salida	Registro del plan de cuidados nutricionales (PCN).
Destinatario	Profesionales responsables de la formulación, elaboración y administración del preparado nutricional. Personal a cargo del paciente.
Participantes	ESN/UNCYD.

Tabla XVI. Objetivos clave relacionados con el criterio de calidad 2.1 (prescripción basada en la valoración nutricional del paciente) (21)

2.1.A. El PCN se establece en pacientes con VN previa	
Indicador	(nº de pacientes con VN previa) / (nº de pacientes con tratamiento nutricional) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con tratamiento nutricional.

Tabla XVII. Objetivos clave relacionados con el criterio de calidad 2.2 (plan de cuidados nutricionales basado en el uso de protocolos clínicos) (21,23,33,41-44)

2.2.A. Disponer de un protocolo para diseñar el PCN	
Indicador	Existencia en el centro de un protocolo para la prescripción del tratamiento nutricional[1].
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.
2.2.B. Cálculo de requerimientos energéticos y proteicos en función de la situación clínica y el estado nutricional	
Indicador	(nº de pacientes con cálculo de requerimientos[2]) / (nº de pacientes con tratamiento nutricional) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con tratamiento nutricional.
2.2.C. Indicación de ostomías en pacientes con nutrición enteral (NE) prolongada	
Indicador	(nº de pacientes con ostomías de alimentación) / (nº de pacientes con NE por sonda durante más de seis semanas[3]) * 100.
Estándar	> 70 %.

(Continúa en página siguiente)

Tabla XVII (Cont.). Objetivos clave relacionados con el criterio de calidad 2.2 (plan de cuidados nutricionales basado en el uso de protocolos clínicos) (21,23,33,41-44)

2.2.C. Indicación de ostomías en pacientes con nutrición enteral (NE) prolongada	
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con NE.
2.2.D. NE precoz por sonda en pacientes críticos	
Indicador	(nº de pacientes críticos que reciben NE precoz[4]) / (nº de pacientes críticos con indicación de NE por sonda) * 100.
Estándar	> 90 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes críticos con indicación de NE.

[1]Protocolo de prescripción de cuidados nutricionales: debe incluir como mínimo métodos para la estimación de los requerimientos nutricionales, la selección de la vía de administración y la fórmula nutricional, así como los cuidados relacionados con la terapia nutricional (referencia). [2]Los requerimientos calóricos se calculan de manera más exacta mediante la calorimetría indirecta. Al no disponerse habitualmente de este método, se suele hacer una estimación mediante el uso de ecuaciones predictivas. Los requerimientos proteicos dependen de la situación de estrés y otras variables clínicas. Definir la idoneidad de cada método en las diversas situaciones clínicas excede el objetivo de este documento. Se recomienda la revisión de la bibliografía especializada antes del diseño del correspondiente protocolo. [3]Se excluyen pacientes en estado terminal o con contraindicación para la ostomía. [4]NE precoz: dentro de las primeras 48 h de a partir del ingreso en la unidad.

Tabla XVIII. Objetivos clave relacionados con el criterio de calidad 2.3 (estandarización de la prescripción) (42,45)

2.3.A. Disponer de un protocolo para la planificación de cuidados nutricionales	
Indicador	Existencia en un protocolo[1] de PCN.
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.
2.3.B. Adherencia al protocolo de PCN	
Indicador	(nº de pacientes con constancia en la historia clínica del PCN) / (nº de pacientes con tratamiento nutricional) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con tratamiento nutricional.

[1]El protocolo de PCN debe incluir como mínimo: cálculo de requerimientos nutricionales, vía de administración y composición de la fórmula, método de administración y cuidados relacionados con el tratamiento. Esta información debe constar en la historia clínica.

SUBPROCESO 3: FORMULACIÓN Y ELABORACIÓN (TABLAS XIX A XXII)

JUSTIFICACIÓN

La correcta selección, elaboración y almacenamiento de las fórmulas de nutrición enteral y parenteral permite administrar un TMN eficaz y seguro. Especialmente la elaboración de la nutrición parenteral (NP) constituye un proceso complejo susceptible de contaminación y errores que pueden comprometer la seguridad del paciente y la efectividad del tratamiento (46,47).

DEFINICIÓN FUNCIONAL

Procedimiento por el cual se seleccionan y/o elaboran las fórmulas de nutrición enteral y parenteral seguras y efectivas, que quedarán listas para su dispensación y administración al paciente (47).

Tabla XIX. Subproceso 3 (FORMULACIÓN Y ELABORACIÓN)

Criterios de calidad	*3.1. Selección apropiada de fórmulas y nutrientes.* *3.2. Elaboración y conservación adecuadas de las fórmulas de nutrición enteral/parenteral.* *3.3. Personal elaborador de la NP formado y evaluado.*
Propietario	Designado por la comisión de farmacia.
Entrada	Prescripción de la nutrición enteral/parenteral.
Proveedor	Profesional que prescribe la nutrición enteral/parenteral.
Salida	Fórmula de nutrición enteral/parenteral elaborada y lista para su dispensación.
Destinatario	Profesionales responsables de la dispensación y administración del preparado nutricional. Personal sanitario a cargo del paciente. ESN/UNCYD.
Participantes	Integrantes del área de elaboración del servicio de farmacia.
Recursos	Infraestructura adecuada para la elaboración de estériles: cámara de flujo laminar (CLF) y salas limpias. Espacio para el almacenamiento, elaboración y distribución de las fórmulas de nutrición enteral/parenteral. Personal sanitario formado y evaluado periódicamente.

Tabla XX. Objetivos clave relacionados con el criterio de calidad 3.1 (selección apropiada de fórmulas y nutrientes) (33)

3.1.A. Disponer de un catálogo de fórmulas y nutrientes para TMN	
Indicador	Existencia de un catálogo de fórmulas y nutrientes (con indicaciones generales de uso de estas) adaptado a la población atendida en el centro[1,2].
Estándar	Sí.
Medición	Cada 2 años.
Fuente	Documentación de las comisiones de farmacia y de nutrición.

[1]El personal de la institución más involucrado en el soporte nutricional debe participar de manera directa en el proceso de selección. [2]Se recomienda la elaboración de un algoritmo de selección de las fórmulas nutricionales adaptado a las características asistenciales de la organización, basado en la evidencia, actualizado, consensuado y accesible a los prescriptores.

Tabla XXI. Objetivos clave relacionados con el criterio de calidad 3.2 (elaboración y conservación adecuadas de las fórmulas de nutrición enteral y parenteral) (33,46,47)

3.2.A. Gestión eficiente del stock de fórmulas de NE	
Indicador	(Nº de envases retirados por caducidad) / (nº de envases adquiridos) * 100.
Estándar	< 5 %.
Medición	Control anual.
Fuente	Registros del servicio de farmacia.
3.2.B. Elaboración de la NP en CLF ubicada en sala limpia	
Indicador	(nº de NP elaboradas en CLF ubicada en sala limpia) / (nº de NP administradas) * 100.
Estándar	100 %.
Medición	Auditoría anual.
Fuente	Registro de prescripciones de NP recibidas en el servicio de farmacia.
Población	Pacientes con NP.

(Continúa en página siguiente)

Tabla XXI (Cont.). Objetivos clave relacionados con el criterio de calidad 3.2 (elaboración y conservación adecuadas de las fórmulas de nutrición enteral y parenteral) (33,46,47)

3.2.C. Disponer de un protocolo de limpieza y desinfección del área de elaboración de estériles	
Indicador	Existencia de protocolo de limpieza y desinfección.[1]
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación del servicio de farmacia.
3.2.D. Registro de limpieza de CFL y salas limpias	
Indicador	(nº de registros de limpieza firmados) / (nº de días hábiles de limpieza) * 100.
Estándar	100 %.
Medición	Control mensual.
Fuente	Registros de limpieza.
3.2.E. Plan de mantenimiento ambiental de CFL y salas limpias	
Indicador	Existencia de un plan de mantenimiento ambiental de CFL y salas limpias.[2]
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación del servicio de farmacia.
3.2.F.1. Adherencia al plan de mantenimiento ambiental de CFL y salas limpias (1)	
Indicador	(nº de registros de presiones) / (nº de días hábiles de elaboración) * 100.
Estándar	100 %.
Medición	Control mensual.
Fuente	Planilla de registro de presiones.
3.2.F.2. Adherencia al plan de mantenimiento ambiental de CFL y salas limpias (2)	
Indicador	Registro de verificación ambiental de CFL y salas limpias.
Estándar	Sí.
Medición	Anual (y siempre que se produzcan cambios en la ubicación de la CFL).
Fuente	Documentación del servicio de farmacia.
3.2.G. Plan de control microbiológico ambiental de CFL y salas limpias	
Indicador	Existencia de un plan de control microbiológico ambiental de CFL y salas limpias.[3]
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación del servicio de farmacia/medicina peventiva.
3.2.H. Resultados del control microbiológico de CFL y salas limpias dentro de los límites establecidos	
Indicador	(nº de muestras con resultados microbiológicos dentro de los límites establecidos) / (nº total de muestras) * 100.
Estándar	> 75 %.
Medición	Control semestral.
Fuente	Resultados de controles microbiológicos.

(Continúa en página siguiente)

Tabla XXI (Cont.). Objetivos clave relacionados con el criterio de calidad 3.2 (elaboración y conservación adecuadas de las fórmulas de nutrición enteral y parenteral) (33,46,47)

3.2.I. Normas de higiene del personal y empleo de técnica aséptica	
Indicador	Existencia de normas de higiene del personal y empleo de técnica aséptica.[4]
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación del servicio de farmacia.

[1]El protocolo debe contemplar como mínimo: retirada de residuos, técnicas de limpieza de mobiliario, suelos, paredes, techos de CFL y salas, selección de desinfectantes y material de limpieza, frecuencia de limpieza. [2]El plan de mantenimiento debe incluir, como mínimo: medida diaria de presiones, cambio de filtro y prefiltros con periodicidad establecida, verificación ambiental anual de CFL (recuento de partículas, ensayo de humo, velocidad del aire, integridad de filtros) y salas (recuento de partículas, tasa de renovación del aire). [3]El plan de control microbiológico debe incluir, como mínimo: localización de las muestras, método de recogida, frecuencia de muestreo, volumen y número de muestras, momento del día en relación con la actividad, niveles de acción. [4]Las normas deben contemplar, como mínimo: normas de higiene, colocación de la indumentaria, circuitos de circulación del personal, circuitos de circulación del material, documentación y producto final, técnicas de trabajo en CFL.

Tabla XXII. Objetivos clave relacionados con el criterio de calidad 3.3 (personal elaborador de la NP formado y evaluado) (46,47)

3.3.A. Formación del personal elaborador de NP	
Indicador	Existencia de un procedimiento de formación y evaluación de la competencia del personal elaborador[1].
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación del servicio de farmacia.
3.3.B. Verificación de la competencia	
Indicador	(nº de elaboradores con evaluación de la competencia, incluyendo lista de adecuadas prácticas y test de simulación del proceso) / (nº total de elaboradores) * 100.
Estándar	75 %.
Medición	Control anual.
Fuente	Documentación del servicio de farmacia.

[1]El plan de formación para las nuevas incorporaciones incluirá, al menos: lavado de manos, limpieza de la CFL, colocación de la indumentaria, mantenimiento de las condiciones ambientales en la CFL, mantenimiento de las condiciones ambientales del espacio de elaboración de NP, empleo de la técnica aséptica, medida de volúmenes y secuencia de aditivación, manejo de dispositivos y equipos, conservación de envases parcialmente usados, conservación de fórmulas elaboradas, inspección de producto final.

SUBPROCESO 4: DISPENSACIÓN (TABLAS XXIII A XXIV)

JUSTIFICACIÓN

La dispensación es el acto farmacéutico asociado a la entrega y distribución del medicamento o producto sanitario, con las consecuentes prestaciones específicas, entre ellas la preparación de la dosis a administrar y la información al paciente. En el caso de la TMN, la dispensación individualizada constituye el método de elección (46).

DEFINICIÓN FUNCIONAL

Conjunto de actuaciones farmacéuticas orientadas a proporcionar al paciente la TMN de forma individualizada, para procurar su correcta administración y utilización, y minimizar los errores de este tipo de terapéutica.

Tabla XXIII. Subproceso 4 (DISPENSACIÓN)

Criterios de calidad	*4.1. Dispensación segura e individualizada.*
Propietario	Responsable designado por el servicio de farmacia.
Entrada	Fórmula de nutrición enteral/parenteral elaborada.
Proveedor	Servicio de farmacia.
Salida	Fórmula de nutrición enteral/parenteral dispensada lista para su administración.
Destinatario	Servicio o unidad asistencial de acogida del paciente. ESN/UNCYD.
Participantes	Servicio de farmacia.

Tabla XXIV. Objetivos clave relacionados con el criterio de calidad 4.1 (dispensación segura e individualizada) (45,46,48)

4.1.A. Disponer de un protocolo para la dispensación de la nutrición enteral / parenteral	
Indicador	Existencia en el centro de un protocolo que detallan las características específicas de la dispensación de la nutrición enteral/ parenteral[1].
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.
4.1.B. Dispensar las presentaciones de NP "listas para su uso" con los micronutrientes en la mezcla	
Indicador	(nº de NP "listas para su uso" con los micronutrientes en la mezcla) / (nº NP "listas para su uso" administradas) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Registros de elaboración. Observación directa.
Población	Pacientes con NP.
4.1.C. Identificación del paciente en las bolsas de nutrición parenteral	
Indicador	(nº de preparaciones de nutrición parenteral con correcto etiquetado[2]) / (nº de preparaciones de nutrición parenteral administradas[3]) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Registros de elaboración. Observación directa.
Población	Pacientes con nutrición parenteral.

[1]Aspectos que pueden ser incluidos en el protocolo de dispensación: horarios de recepción de la prescripción y de salida de las unidades de nutrición enteral/ parenteral, características que debe cumplir el procedimiento para que sea eficaz y seguro. [2]La etiqueta debe estar estandarizada y contemplar: identificación del paciente (número de historia, nombre y apellidos), localización del paciente (unidad, habitación, cama), volumen y composición, fecha de elaboración, fecha de administración, fecha de caducidad, vía y modo de administración. [3]Se contemplan las bolsas de NP, incluidas las "listas para su uso".

SUBPROCESO 5: ADMINISTRACIÓN (TABLAS XXV A XXVIII)

JUSTIFICACIÓN

La correcta administración del soporte nutricional es determinante para que el aporte se corresponda con lo prescrito, evitando complicaciones e interacciones con medicamentos.

DEFINICIÓN FUNCIONAL

Procedimiento mediante el que se suministran las fórmulas de nutrición enteral/parenteral, por vía digestiva en la nutrición enteral y por vía intravenosa en la nutrición parenteral, acorde con la prescripción y la tolerancia del paciente, procurando prevenir la aparición de complicaciones y las interacciones entre medicamentos y nutrientes (33).

Tabla XXV. Subproceso 5 (ADMINISTRACIÓN)

Criterios de calidad	*5.1. Uso de protocolos de administración.* *5.2. Administración segura y eficaz.* *5.3. Minimización de interacciones medicamento-nutriente.*
Propietario	Responsable del ESN/UNCYD u organismo designado por la dirección del centro.
Entrada	Fórmula de NA dispensada y lista para su administración.
Proveedor	Servicio de farmacia.
Salida	Finalización del tratamiento con NA.
Destinatario	Personal sanitario a cargo del paciente. ESN/UNCYD.
Participantes	Personal de enfermería a cargo del paciente. ESN/UNCYD.
Recursos específicos	Equipamiento: bombas, catéteres, sondas, filtros, etc.

Tabla XXVI. Objetivos clave relacionados con el criterio de calidad 5.1 (uso de protocolos de administración) (11,41,42,45)

5.1.A. Disponer de un protocolo para la administración de la nutrición enteral y parenteral	
Indicador	Existencia en el centro de un protocolo que detallan las actuaciones necesarias para una administración segura y eficaz de la nutrición enteral/parenteral[1].
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.
5.1.B. Cumplimiento del objetivo calórico	
Indicador	(nº de pacientes que alcanzan el objetivo calórico) / (nº de pacientes con TNM) * 100.
Estándar	> 85%.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con TNM.

[1]Aspectos que pueden ser incluidos en el protocolo de administración de nutrición enteral/parenteral: utilización y mantenimiento de las bombas de infusión, cuidados de las vías de acceso, prevención de complicaciones (mecánicas, digestivas, infecciosas y metabólicas), normas para la administración de medicación.

Tabla XXVII. Objetivos clave relacionados con el criterio de calidad 5.2 (administración segura y eficaz) (11,42,49-52)

5.2.A. Confirmar la correcta posición del acceso enteral antes de iniciar la NE	
Indicador	(nº de pacientes con comprobación[1] de la correcta posición de la sonda antes de iniciar la NE) / (nº de pacientes con NE por sonda nasoentérica) * 100.
Estándar	> 90%.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con NE.
5.2.B. Minimizar la incidencia de obstrucciones de los accesos de NE	
Indicador	(nº de episodios de obstrucción del acceso enteral) / (nº de pacientes con NE por sonda x días de NE) * días de NE.
Estándar	< 10 episodios/100 días de NE (paciente hospitalizado). < 10 episodios/1000 días de NE (paciente no hospitalizado).
Medición	Frecuencia anual, en una muestra representativa de pacientes atendidos en el centro.
Fuente	Historia clínica.
Población	Pacientes con NE.
5.2.C. Minimizar la incidencia de sepsis por catéter en pacientes con NP	
Indicador	(nº de episodios de sepsis por catéter en pacientes con NP) / (número de pacientes con NP) * días de NP.
Estándar	< 2 episodios/100 días de NP.
Medición	Frecuencia anual, en una muestra representativa de pacientes atendidos en el centro.
Fuente	Historia clínica.
Población	Pacientes con NP.
5.2.D. Administrar la NE por sonda gástrica con el paciente en posición semiincorporada	
Indicador	(nº de pacientes en posición semiincorporada[2]) / (nº de pacientes con NE) * 100.
Estándar	> 90 %.
Medición	Control de pacientes atendidos en tres días diferentes del año.
Fuente	Estándar.
Población	Observación directa.
5.2.E. Minimizar la incidencia de neumonías en pacientes con NE	
Indicador	(nº de episodios de neumonía en pacientes con NE) / (nº de pacientes con NE) * días de NE.
Estándar	< 10 episodios/100 días de NE (paciente hospitalizado). < 10 episodios/1000 días de NE (paciente no hospitalizado).
Medición	Frecuencia anual, en una muestra representativa de pacientes atendidos en el centro.
Fuente	Historia clínica.
Población	Pacientes con NE.

[1]La técnica de referencia para comprobar la correcta posición de la sonda es la radiológica. No se precisa en sondas colocadas bajo control radiológico o endoscópico. [2]Torso a un ángulo igual o superior a 30° respecto al plano horizontal. Se mantendrá durante la administración de la NE y una hora después de su finalización.

Tabla XXVIII. Objetivos clave relacionados con el criterio de calidad 5.3 (minimización de interacciones medicamento-nutriente) (42,45,47)

5.3.A. Disponer de información sobre la correcta administración de fármacos en pacientes con nutrición enteral / parenteral, accesible para todo el personal asistencial	
Indicador	Existencia de un documento con información detallada relativa a la correcta administración de fármacos en pacientes con nutrición enteral/parenteral[1].
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.
5.3.B. Administrar los fármacos en pacientes con nutrición enteral/parenteral siguiendo las recomendaciones correspondientes	
Indicador	(nº de fármacos administrados correctamente) / (nº de fármacos administrados en pacientes con nutrición enteral/parenteral) * 100.
Estándar	> 90 %.
Medición	Control de pacientes atendidos en tres días diferentes del año.
Fuente	Observación directa y entrevista con personal al cuidado del paciente.
Población	Pacientes con nutrición enteral/parenteral.

[1]Aspectos que deben ser contemplados en el documento: principio activo, nombre comercial y presentación, forma farmacéutica recomendada para su uso en pacientes con nutrición enteral/parenteral, compatibilidad para su coadministración con la nutrición enteral/parenteral, modo de preparación antes de la administración, observaciones específicas del principio activo.

SUBPROCESO 6: MONITORIZACIÓN (TABLAS XXIX A XXXII)

JUSTIFICACIÓN

Durante el soporte nutricional especializado se pueden presentar diversas complicaciones que pueden condicionar su eficacia terapéutica e incrementar la morbimortalidad. La adecuada monitorización de la nutrición artificial es decisiva para su éxito.

DEFINICIÓN FUNCIONAL

Conjunto de actuaciones dirigidas a asegurar que el tratamiento nutricional se administra de forma suficiente y adecuada, y a la detección precoz y manejo de sus complicaciones (21,23).

Tabla XXIX. Subproceso 6 (MONITORIZACIÓN)

Criterios de calidad	*6.1. Seguimiento regular del PCN.* *6.2. Manejo adecuado de las complicaciones asociadas a la NA.* *6.3. Ajuste evolutivo del PCN.*
Propietario	Responsable del ESN u organismo delegado por la dirección del centro.
Entrada	Prescripción del PCN.
Proveedor	Prescriptor del PCN.
Salida	Alta del paciente.
Destinatario	Personal sanitario a cargo del paciente, ESN.
Participantes	ESN.

Tabla XXX. Objetivos clave relacionados con el criterio de calidad 6.1 (seguimiento regular del PCN) (21,23,34,42)

6.1.A. Disponer de un protocolo de monitorización de la TMN	
Indicador	Existencia en el centro de un protocolo en el que se describen las actuaciones necesarias para el adecuado seguimiento de pacientes con TMN[1].
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.
6.1.B. Cumplir el protocolo de monitorización de la TMN	
Indicador	(nº monitorización realizada según el protocolo) / (nº de pacientes con TMN) * 100.
Estándar	> 90 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con NA.
6.1.C. Registrar los efectos adversos de la TMN	
Indicador	(nº de pacientes con registro de efectos adversos) / (nº de pacientes con TMN) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con TMN.

[1]Aspectos que incluir en el protocolo de monitorización: evaluación clínica de la tolerancia y eficacia de la TMN, determinaciones analíticas (incluyendo frecuencia de determinación en función de la situación del paciente), valoración del cumplimiento de los requerimientos nutricionales, medidas a tomar ante la aparición de complicaciones.

Tabla XXXI. Objetivos clave relacionados con el criterio de calidad 6.2 (manejo adecuado de las complicaciones asociadas a la TMN) (53-60)

6.2.A. Disponer de protocolos específicos para el manejo de las complicaciones de la TMN	
Indicador	Existencia en el centro de protocolos en los que se describen las actuaciones diagnósticas y terapéuticas a realizar ante la aparición o sospecha de complicaciones (diarrea, estreñimiento o vómitos en pacientes con NE, sepsis por catéter en pacientes o alteraciones metabólicas en pacientes con NP, etc.).
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.
6.2.B. Hacer un seguimiento de las complicaciones asociadas a la TMN según su protocolo	
Indicador	(nº de pacientes en los que se ha aplicado el protocolo de manejo de la complicación) / (nº de pacientes con TMN que han presentado una complicación específica, p.e. pacientes con diarrea asociada a la NE) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con TMN.

(Continúa en página siguiente)

Tabla XXXI (Cont.). Objetivos clave relacionados con el criterio de calidad 6.2 (manejo adecuado de las complicaciones asociadas a la TMN) (53-60)

6.2.C. Control de la hiperglucemia en pacientes con NP	
Indicador	(nº de controles de glucemia > 180 mg/dL) / (nº de pacientes con NP) * días de NP.
Estándar	< 10 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con NP.
6.2.D. Minimizar las hipoglucemias	
Indicador	(nº de controles de glucemia < 60 mg/dL) / (nº de pacientes con NP) * días de NP.
Estándar	< 1 %
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con NP.

Tabla XXXII. Objetivos clave relacionados con el criterio de calidad 6.3 (ajuste evolutivo del PCN) (41,61)

6.3.A. Hacer un cálculo periódico de los requerimientos nutricionales.	
Indicador	(nº de pacientes con cálculo periódico de requerimientos nutricionales) / (nº de pacientes con TMN durante más de una semana) * 100.
Estándar	> 90 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con TMN.

SUBPROCESO 7: TRANSICIÓN Y FINALIZACIÓN (TABLAS XXXIII A XXXVII)

JUSTIFICACIÓN

La restitución de la vía fisiológica de alimentación y la interrupción de la TMN, en sus distintas modalidades, constituyen situaciones en las que pueden darse complicaciones que pueden poner en riesgo el estado nutricional del paciente y alterar su evolución.

Por otra parte, cuando es necesario mantener la terapia nutricional a largo plazo, el tránsito entre niveles asistenciales puede comprometer su continuidad. Finalmente, en determinadas circunstancias la interrupción de la TMN en ocasiones tiene connotaciones éticas que deberán ser tenidas en cuenta (33,42).

DEFINICIÓN FUNCIONAL

Conjunto de actuaciones que permiten, de una manera eficaz, segura y teniendo en consideración los valores fundamentales de la bioética, realizar el tránsito entre las distintas modalidades de TMN, finalizarlo o mantener su continuidad entre niveles asistenciales.

Tabla XXXIII. Subproceso 7 (TRANSICIÓN Y FINALIZACIÓN)

Criterios de calidad	*7.1. Transición entre nutrición enteral/parenteral y alimentación oral protocolizada.* *7.2. Transición entre nutrición enteral/parenteral y alimentación oral eficaz y segura.* *7.3. Interrupción de la TMN por limitación del esfuerzo terapéutico (LET) considerando aspectos éticos.* *7.4. Facilitar la continuidad del TMN entre niveles asistenciales.*
Propietario	Responsable del ESN/UNCYD u organismo delegado por la dirección del centro.
Entrada	Decisión de iniciar la alimentación oral, de finalizar la nutrición enteral/parenteral o de derivar al paciente a otro nivel asistencial.
Proveedor	Profesional que decide iniciar la alimentación oral, mantener la TMN en otro nivel asistencial o finalizar la nutrición enteral/parenteral.
Salida	Finalización de la TMN o continuidad del tratamiento nutricional en otro nivel sanitario.
Destinatario	Personal sanitario a cargo del paciente, ESN.
Participantes	ESN.

Tabla XXXIV. Objetivos clave relacionados con el criterio de calidad 7.1 (transición entre nutrición enteral/parenteral y alimentación oral protocolizada) (42,62)

7.1.A. Disponer de un protocolo para la transición entre nutrición enteral/parenteral y alimentación oral	
Indicador	Existencia de un protocolo de transición entre modalidades de nutrición enteral / parenteral y alimentación oral[1].
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.
7.1.B. Cumplir el protocolo para la transición entre nutrición enteral/parenteral y alimentación oral	
Indicador	(nº de pacientes en los que se ha usado el protocolo de transición) / (nº de pacientes en los que se ha finalizado la nutrición enteral/parenteral[2]) * 100.
Estándar	100 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con nutrición enteral/parenteral.
7.1.C. Controlar la ingesta durante la transición a la alimentación oral	
Indicador	(nº de pacientes con valoración de la ingesta oral) / (nº de pacientes en los que se ha finalizado la nutrición enteral/parenteral[2]) * 100.
Estándar	> 50 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con nutrición enteral/parenteral.

[1]Se considerará el paso de NP a NE, además de la transición a la alimentación oral. Se tendrán en cuenta: nivel de alerta y capacidad deglutoria (transición a alimentación oral), posibilidades de uso del aparato digestivo, aporte calórico con la modalidad nutricional de destino. La transición es especialmente importante en pacientes desnutridos, ancianos y con enfermedad oncológica, neurológica y cirugía de cabeza y cuello. [2]Se excluyen los casos en los que la interrupción de la nutrición enteral/parenteral se hace de forma urgente o por LET.

Tabla XXXV. Objetivos clave relacionados con el criterio de calidad 7.2 (transición entre nutrición enteral/parenteral y alimentación oral eficaz y segura) (42)

7.2.A. Evitar la necesidad de reiniciar la nutrición enteral/parenteral tras su suspensión	
Indicador	(nº de pacientes con necesidad de reiniciar la nutrición enteral/parenteral[1] / (nº de pacientes en los que se ha finalizado la nutrición enteral/parenteral) * 100.
Estándar	< 10 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes con nutrición enteral/parenteral.
7.2.B. Evitar la neumonía por aspiración durante la transición a alimentación oral	
Indicador	(nº de pacientes que desarrollan neumonía por aspiración o dificultad respiratoria durante la introducción de la alimentación oral) / (nº de pacientes en los que se ha iniciado la alimentación oral) * 100.
Estándar	< 5 %.
Medición	Frecuencia anual, en una muestra de pacientes atendidos a lo largo de una semana.
Fuente	Historia clínica.
Población	Pacientes que inician la alimentación oral.

[1]Sin mediar causas que puedan hacer considerar la situación como un nuevo proceso (p. ej., una intervención quirúrgica).

Tabla XXXVI. Objetivos clave relacionados con el criterio de calidad 7.3 (interrupción del SNE por limitación del esfuerzo terapéutico considerando aspectos éticos) (33,63-65)

7.3.A. Cumplir con las debidas consideraciones éticas en caso de suspender la TMN por limitación del esfuerzo terapéutico (LET)	
Indicador	(nº de pacientes con interrupción de la TMN por LET que cumplen los requisitos éticos[1]) / (nº de pacientes con interrupción de la NA por LET) * 100.
Estándar	100 %.
Medición	Frecuencia anual.
Fuente	Historia clínica.
Población	Pacientes con TMN interrumpida por LET.

[1]Una decisión de LET cumple con los requisitos éticos si se hace con: respeto a la autonomía del paciente, concordancia con las posibilidades evolutivas del caso, consenso del equipo asistencial, información y consulta a los familiares. Se recomienda consultar con el comité ético del centro en caso de duda.

Tabla XXXVII. Objetivos clave relacionados con el criterio de calidad 7.4 (facilitar la continuidad del TMN entre niveles asistenciales) (33)

7.4.A. Disponer de un protocolo para facilitar la continuidad de la TMN entre niveles asistenciales	
Indicador	Existencia de un informe protocolizado de cuidados nutricionales al alta hospitalaria[1].
Estándar	Sí.
Medición	Cada tres años.
Fuente	Documentación de la comisión de nutrición u organismo delegado por la dirección del centro.

[1]El informe protocolizado de cuidados nutricionales al alta hospitalaria podrá incluir: diagnóstico nutricional, recomendaciones de alimentación oral; productos nutricionales a administrar, su dosis y vía de administración; duración estimada del tratamiento, objetivos del tratamiento, plan de seguimiento, profesional responsable y medios para contactar.

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Carta al Director

HACIA LA ELABORACIÓN DEL PROTOCOLO DE INVESTIGACIÓN Y SU REGISTRO

Sr. Editor:

Hace un tiempo fue publicado el manuscrito denominado*: "A propósito de las revisiones sistemáticas, los metaanálisis y los resúmenes de revisiones sistemáticas"* (1), el cual nos hace un brevísimo recordatorio sobre las definiciones de los diseños secundarios de investigación mencionados previamente. Posterior a ello, se cita el Manual Cochrane de revisiones sistemáticas de intervenciones, capítulo 22, para plasmar las diferencias metodológicas existentes entre una revisión sistemática y un resumen de revisiones sistemáticas, también denominado *"overview"*. Este análisis se basa principalmente en las diferencias metodológicas existentes en los siguientes puntos: a) objetivos; b) criterios de selección; c) búsqueda; d) obtención de los datos; e) evaluación de las limitaciones; e) calidad de la evidencia y f) análisis. Si bien es cierto que estos apartados metodológicos son el eje medular de estos diseños de investigación sumados a otros ítems, no debemos olvidar que tanto las revisiones sistemáticas como los metaanálisis y los *overviews* deben ser elaborados sobre la base previa de un *protocolo de investigación (PI)*, el cual debe describir la justificación de la revisión, incluido el enfoque metodológico y analítico, con anterioridad a su realización (2). Sin embargo, actualmente pocas revisiones que se encuentran publicadas informan sobre su PI.

La existencia de un PI y su registro tiene repercusiones positivas tanto para el equipo elaborador de una revisión (EER) como para quien decide leer el trabajo en cuestión. Para el EER, el PI va a asegurar que el trabajo se planifique de forma cuidadosa y obliga a que los investigadores plasmen todos los ítems metodológicos que se lleven a cabo de forma previa al inicio del trabajo de investigación. Por tanto, trabajar con un PI promueve la responsabilidad, integridad y transparencia de todo el proceso de una revisión. También debemos considerar que reduce la arbitrariedad al momento de tomar una decisión (extracción de datos, uso de la información contenida en los estudios analizados), debido a que esta planificación brindará una gran oportunidad para que todo el EER se pueda anticipar a diversos inconvenientes que podrían surgir. Por otro lado, cuando una revisión presenta el registro de su PI, permite al lector identificar la existencia de algún cambio o desviación de los métodos que habían sido planificados previamente y también identificar si existe algún sesgo en la interpretación de los resultados y sus conclusiones.

No hay que olvidar que uno de los primeros pasos, cuando se tiene en mente la realización de una revisión, es determinar lo siguiente: a) si hay otras revisiones sobre el mismo tema de interés o temáticas similares; B) cuándo se realizaron o si aún se encuentran en proceso de elaboración, y c) qué métodos fueron los que se utilizaron para realizar las revisiones existentes (3).

Es bastante complejo dar respuesta a lo expuesto previamente, debido a que no todos los recursos electrónicos presentan este tipo de información. Si bien es cierto que muchas revistas mencionan que es tan importante el registro como la publicación del PI, ello no siempre llega a ser una exigencia para los autores. En el año 2011, el Instituto Nacional de Investigaciones en Salud desarrolló "PROSPERO" (3). La base de datos PROSPERO (https://www.crd.york.ac.uk/prospero/) actualmente proporciona un lugar para que diversos autores logren publicar y registrar su PI de forma oficial; con ello, el resto de los autores podrán tener conocimiento de la existencia del proyecto y así evitar las duplicaciones, minimizar el sesgo y aumentar la transparencia de las revisiones (2,4). Para poder llevar a cabo este proceso es fundamental fortalecer la transparencia, precisión e integridad de los informes que deben contener los PI. Por tanto, la utilización de una plantilla que logre indicar todos los apartados que deben considerarse permitirá a los autores crear un manuscrito claro y completo donde se plasmen de forma previa todos los procedimientos metodológicos a realizar, lo que va a facilitar el proceso de registro en PROSPERO (4). Esta guía o plantilla se denomina PRISMA-P (5) *(ítems de referencia para publicar protocolos de revisiones sistemáticas y metaanálisis: Declaración PRISMA-P 2015).* La definición y el objetivo de PROSPERO y de PRISMA-P se detallan en la tabla I.

Conflictos de intereses: los autores no tienen conflictos de intereses.

Tabla I. PROSPERO y PRISMA-P

	Definición y objetivo
PROSPERO	Es un portal de internet a través del cual se registra la intención de llevar a cabo una revisión sistemática, con resultados relativos a la asistencia sanitaria, antes de su inicio. Uno de los principales objetivos de PROSPERO es dar a conocer la intención de realizar una revisión sistemática previa antes de su inicio para reducir las duplicaciones imprevistas de revisiones sistemáticas. Además, al requerir la documentación de los métodos de la revisión sistemática antes de su inicio, el registro facilita una mayor transparencia del proceso de revisión, dado que permite, a los lectores de las revisiones sistemáticas, la comparación de los métodos, los resultados y los análisis realizados con aquellos previamente planificados y decidir si estos cambios influyen en los resultados de la revisión.
PRISMA-P	Son directrices que orientan a los autores en la preparación de protocolos para la planificación de revisiones sistemáticas y metaanálisis, a través de un conjunto mínimo de ítems de inclusión en el protocolo. El objetivo de un protocolo es proporcionar, de antemano, tanto la justificación de la revisión como el enfoque previamente planificado de la metodología y el análisis de la revisión. Los investigadores deben preparar un protocolo de la revisión con antelación a su registro en PROSPERO, de manera que los detalles que necesiten mayor consideración dispongan de la reflexión previa necesaria, lo cual evita la necesidad de múltiples rectificaciones en la información del registro. Los ítems de PRISMA-P derivan en gran medida de la lista de verificación de PRISMA y de los ítems del registro PROSPERO, a fin de facilitar un proceso de registro fluido.

Fuente: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P), 2015 (5).

A modo de conclusión, debemos tener presente que la elaboración y el registro de un PI es fundamental debido a que va a promover la responsabilidad, integridad y transparencia del proceso de revisión, y a su vez reduce la arbitrariedad al momento de tomar una decisión. Sin embargo, cuando tenemos claridad sobre qué revisión vamos a efectuar, siempre debemos revisar si esta cuenta con su PI registrado, debido a que de esta forma se podrá identificar la existencia de algún cambio en los apartados metodológicos previamente planificados.

Al momento de elaborar el PI, se recomienda utilizar PRISMA-P, debido a que esto facilitará el proceso para su posterior registro en PROSPERO.

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Carta al Director

DIFERENCIAS METODOLÓGICAS ENTRE UNA REVISIÓN SISTEMÁTICA CON METAANÁLISIS Y UNA REVISIÓN SISTEMÁTICA CON METAANÁLISIS EN RED

Sr. Editor:

Hace un tiempo fue publicado en su prestigiosa revista el manuscrito titulado: ¿Revisión sistemática? ¿Metaanálisis? ¿Resumen de revisiones sistemáticas? (1). El artículo logra plasmar de una forma bastante simple el concepto de "revisión" (revisión sistemática sin metaanálisis, revisión sistemática con metaanálisis, revisión narrativa y resumen de revisiones sistemáticas). Posteriormente, y como complemento al manuscrito citado, se publicó: "A propósito de las revisiones sistemáticas, los metaanálisis y los resúmenes de revisiones sistemáticas" (2), donde se explican las diferencias metodológicas existentes entre una revisión sistemática y un resumen de revisiones sistemáticas (para más detalles, se recomienda leer previamente ambos manuscritos).

El propósito del presente manuscrito es generar una comparación entre los aspectos metodológicos presentes en una revisión sistemática con metaanálisis y una revisión sistemática con metaanálisis en red.

Antes de continuar, debemos recordar que las revisiones sistemáticas corresponden a un tipo de investigación secundario donde la unidad de análisis no son los pacientes sino más bien los diferentes estudios disponibles en los distintos recursos electrónicos (3). Por tanto, existen dos tipos de revisiones sistemáticas (cualitativas o cuantitativas o también denominadas con metaanálisis) (1). Las revisiones sistemáticas sin metaanálisis o cualitativas presentan la evidencia científica de una forma totalmente "descriptiva" (sin presentar un análisis estadístico) (1). Las revisiones sistemáticas con metaanálisis o cuantitativas también pueden presentar la evidencia de una forma descriptiva, pero la gran diferencia radica en el uso de técnicas estadísticas para combinar "numéricamente" los resultados frente a un estimador puntual (1).

Tanto las revisiones sistemáticas sin metaanálisis como aquellas otras con metaanálisis presentan un análisis tradicional basado en comparaciones directas entre una intervención y un comparador (tratamiento A *vs.* tratamiento B), con el fin de poder analizar de forma cuantitativa los resultados disponibles referentes a la intervención de interés (4). Basado en lo plasmado en el párrafo anterior, estos diseños metodológicos se han logrado consolidar en la última década como una herramienta metodológica indispensable a la hora de tomar una decisión clínica. Sin embargo, estos diseños no están exentos de limitaciones debido a que, metodológicamente, no pueden comparar múltiples tratamientos a la vez, lo que puede dificultar la toma de la decisión clínica en las situaciones donde existen varias opciones de tratamiento que compiten entre sí. Por tanto, no brindan información sobre los efectos relativos de todas las intervenciones de forma simultánea. Por otro lado, hay situaciones en las cuales no existen estudios clínicos aleatorizados que incluyan la comparación de forma directa de dos o más intervenciones. Es por tal motivo que surge el concepto de revisión sistemática con metaanálisis en red o "network meta-analysis" (5,6). Este diseño de investigación principalmente llegó para ampliar el alcance que presenta una revisión sistemática, analizando de forma simultánea la evidencia proveniente tanto de comparaciones directas como de comparaciones indirectas (basados en un comparador común) (7). La tabla I presenta las diferencias existentes entre una revisión sistemática con metaanálisis y una revisión sistemática con metaanálisis en red.

Conflictos de intereses: los autores no tienen conflictos de intereses.

Tabla I. Diferencias entre una revisión sistemática con metaanálisis y una revisión sistemática con metaanálisis en red

	Metaanálisis	Metaanálisis en red
Número de intervenciones para comparar	Dos intervenciones	Tres o más intervenciones
Análisis	Comparación directa	Comparación directa e indirecta (mixta)
Objetivos	- Sintetizar e integrar los resultados de varios estudios individuales. - Analizar las diferencias entre los resultados de los estudios. - Aumentar el poder de detectar un efecto de interés. - Mejorar la precisión en la estimación de los efectos. - Evaluar los efectos en análisis de subgrupos. - Determinar si se requieren nuevos estudios para un tema en concreto. - Recolectar toda la información disponible respecto a un tema en particular e identificar las bases para ese conocimiento obtenido. - Reportar de forma comprensiva los resultados y el proceso para obtenerlos, con el fin de que los métodos y las asunciones sean de libre escrutinio por el lector.	- Sintetizar la evidencia disponible sobre múltiples intervenciones y permitir realizar comparaciones indirectas entre aquellas intervenciones que no se hayan reportado en la literatura, basándose en un comparador común. - Sintetizar la evidencia disponible sobre múltiples intervenciones y permitir realizar comparaciones indirectas entre aquellas intervenciones que no se hayan reportado en la literatura, basándose en un comparador común. - Establecer estimados del efecto de tratamiento. - Jerarquizar la efectividad de las intervenciones. - Mostrar de forma transparente la metodología empleada y los métodos estadísticos con el fin de permitir al lector someter a escrutinio la evidencia arrojada.

Fuente: How to interpret systematic review with multiple comparisons or network meta-analysis (4).

A modo de conclusión, debemos recordar que una revisión sistemática con metaanálisis no es lo mismo que una revisión sistemática con metaanálisis en red. Por tanto, ambos diseños de investigación presentan diferencias metodológicas al momento de su elaboración. Las revisiones sistemáticas con metaanálisis analizan la evidencia de forma directa, mientras que las revisiones sistemáticas con metaanálisis en red analizan múltiples intervenciones (directas y mixtas).

Queremos agradecer a la revista *Nutrición Hospitalaria* la generación de estas instancias donde se pueden difundir aspectos metodológicos existentes en los distintos diseños de investigación clínica, considerando que son herramientas que podrán ayudar a los clínicos, los investigadores y los organismos gubernamentales en la toma de decisiones clínicas.

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Carta al Director

RESULTS OF LIFESTYLE DURING CONFINEMENT FOR COVID-19 IN SCHOOLCHILDREN AGED 8 TO 12 YEARS

Dear Editor,

Due to the recent publication of "Estado nutricional y niveles de ansiedad durante la pandemia de COVID-19" (1) and "Conducta alimentaria y su relación con el estrés, la ansiedad, la depresión y el insomnio en estudiantes universitarios" (2), where the authors have reported higher probabilities of anxiety due to the consumption of sugary drinks, fast food and pastries, we would like to complement this information approaching another study population. The main effects of confinement have been shown because of reduced mobility, generating greater physical inactivity and mostly sedentary behavior (3,4); at the same time, changes in eating habits occurred, as evidence suggests fewer proper diets during confinement, as well as an increase in screen time, a situation that may lead to irregular sleep problems, leading to mental health issues that generated anxiety and depression alerts, and effects on the overall health of children (5). That is why we analyze the changes in physical activity (PA) during confinement for COVID-19 and their relationship with eating habits and anxiety in schoolchildren aged 8 to 12 years.

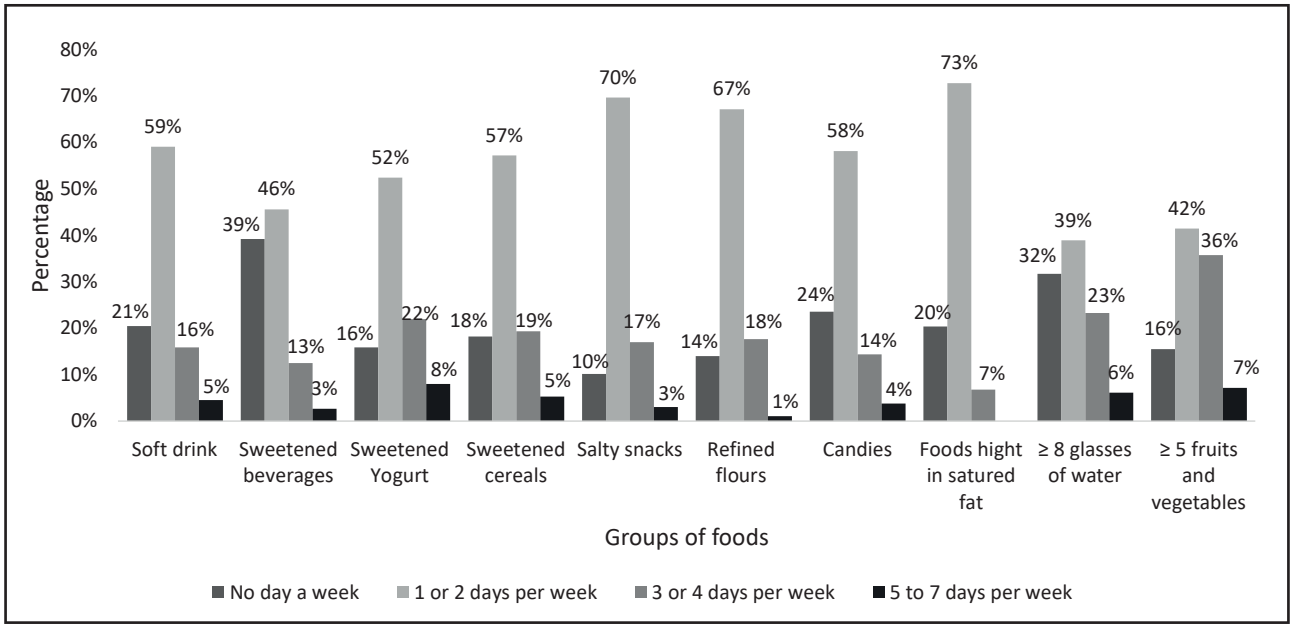

Figure 1.

Percentage of consumption of the different food groups.

Conflict of interest: the author declare no conflict of interest and no economic support.

The tutors of 278 children answered questions about PA, anxiety, frequency of feeding, and data such as sleep and screen time. The results show an inverse correlation was found between screen time and minutes of PA during confinement ($r = -0.175$, $p < 0.001$) and changes in the time of PA before-during confinement ($r = -0.181$, $p = 0.003$). It did present an inverse correlation with screen time ($r = -0.168$, $p = 0.006$). The frequency of food consumption was not related to PA levels or PA time as carried out before and during confinement ($p > 0.05$); those who consumed soft drinks from 3-4 and 5-7 days a week ($\tilde{x}$= 240 min, IQR = 180 min; $\tilde{x}$ = 300 min, IQR = 270 min, respectively), who consumed salty snacks from 3-4 and 5-7 days a week ($\tilde{x}$ = 240 min, IQR = 180 min; $\tilde{x}$ = 270 min, IQR = 270 min, respectively), who consumed candies from 5-7 days a week ($\tilde{x}$ = 480 min, IQR = 225 min), and who consumed foods rich in saturated fat 1-2 days a week ($\tilde{x}$ = 180 min, IQR = 120 min) had more screen time compared to those who usually do not report consuming any of these foods per week ($\tilde{x}$ = 180 min, IQR = 150 min for soft drinks; $\tilde{x}$ = 180 min, IQR = 195 min for salty snacks; $\tilde{x}$ = 180 min, IQR = 210 min for candies; $\tilde{x}$ = 180 min, IQR = 148 min for foods rich in saturated fat [$p < 0.05$]).

Concerning anxiety, those who consumed refined flours 5-7 days a week ($\tilde{x}$ = 7, IQR = 1) had a higher anxiety score ($p < 0.05$) than those who consumed 1-2 times a week ($\tilde{x}$ = 2, IQR = 5) and those who did not consume them any day of the week ($\tilde{x}$ = 3, IQR = 4); in addition, those who consumed salty snacks 5-7 times a week ($\tilde{x}$ = 6, IQR = 5) compared to those who consumed them 1-2 times a week ($\tilde{x}$ = 2, IQR = 4) and those who reported not consuming them at all per week ($\tilde{x}$ = 2, IQR = 2). A considerable decrease in PA levels and an increase in sedentary lifestyle were found in schoolchildren aged 8 to 12, mainly in those schoolchildren who feel that someone will tell them that they are doing everything wrong. Likewise, a relationship was observed of screen time with anxiety and unhealthy eating.

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Carta al Director

LA NECESIDAD DE UN PROGRAMA MULTIDIMENSIONAL PARA PACIENTES CON OBESIDAD, COMO MEDIDA PREVENTIVA ANTE UNA NUEVA OLA DE COVID-19 EN CHILE

Sr. Editor:

En el artículo de Martínez y colaboradores (2021) (1) se aborda el desarrollo de la enfermedad COVID-19 según el estado metabólico previo al contagio. En dicho estudio se estableció que factores como el metabolismo de los lípidos y el de los glúcidos están relacionados con mayor estancia hospitalaria y riesgo de mortalidad en los pacientes con obesidad.

Durante la pandemia hubo un cambio en los hábitos de alimentación, donde aumentó la ingesta de comida rápida con un menor consumo de frutas y verduras, y una priorización de la compra de alimentos de larga conservación y fácil preparación (2,3), que por lo general suelen ser ricos en sales, grasas y azúcares.

La obesidad suele ir acompañada de resistencia a la insulina, diabetes de tipo 2 (DM2) e hipertensión arterial (HTA); en algunos casos, estas condiciones se vuelven más complejas cuando las personas no realizan ejercicio físico y no presentan adherencia a los programas farmacológicos y de alimentación. En Chile, al igual que en gran parte del mundo, la pandemia produjo una disminución de la cobertura de prestaciones, por lo que un gran número de pacientes dejaron sus tratamientos (4), lo que implica que actualmente existe una población de riesgo que se encuentra descompensada y que además ha retrocedido en sus tratamientos de pérdida de peso.

Los pacientes con DM2 tienen una probabilidad 2,2 veces mayor de ingresar en unidades de cuidados especiales; por su parte, quienes presentan HTA tienen una expresión de gravedad y mortalidad 2,27 y 3,48 veces mayor que los de la población normal (5). Ambas condiciones, sumadas a la obesidad, los hacen sujetos prioritarios de atención.

Un aspecto relevante es que los pacientes obesos y con DM2 suelen presentar una alteración del perfil inmunitario de las células T, lo que se puede traducir en un retraso de la respuesta inflamatoria, presentando signos y síntomas más leves de la enfermedad de COVID-19 en un primer periodo; pero, una vez que el proceso inflamatorio se presenta, este suele ser mucho mayor

Tabla I. Condiciones previas al contagio de la COVID-19 y sus consecuencias en pacientes obesos

Estado basal previo al contagio	Condiciones adicionales en la unidad de cuidados intensivos	Condiciones adicionales posteriores al contagio
- Resistencia a la insulina - Grasa visceral aumentada - Desordenes musculoesqueléticos - Inflamación sistémica de bajo grado - Lípidos sanguíneos elevados - Apnea del sueño y patrón restrictivo	- Alteración cerebral - Fibrosis pulmonar - Arritmias y pericarditis - Sarcopenia - Resistencia a la insulina	- Estrés postraumático - Alteración de la función pulmonar - Alteración metabólica de la glucosa - Disminución de la masa muscular - Alteraciones neuromotoras - Alteración de la capacidad funcional

Adaptación (9).

Conflicto de intereses: los autores declaran no tener conflictos de intereses.

que el esperado, agravando la evolución y generando mayores secuelas funcionales, tales como el síndrome de distrés respiratorio y la fibrosis pulmonar (6-8).

Si a este grupo de pacientes obesos que se encuentran descompensados, con tratamientos interrumpidos y con aumento de peso, sumamos a aquellos que llegaron a una unidad de cuidado intensivos y que actualmente presentan estrés postraumático y alteraciones de la función pulmonar entre otras consecuencias, además de su situación de obesidad basal (9) (Tabla I), nos situamos ante una proyección poco auspiciosa frente a una posible nueva ola de COVID-19 en Chile.

Es necesario por tanto implementar, como una prioridad en Chile, programas multidisciplinares que incluyan una reeducación nutricional y programas de ejercicio y asistencia psicológica de manera que se puedan recuperar y mejorar, dentro de lo posible, las condiciones de los pacientes de este grupo prioritario y así prevenir un nuevo aumento de casos.

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Carta al Director

SALUD MENTAL EN NIÑOS Y ADOLESCENTES COMO FACTOR AGRAVANTE EN LA PANDEMIA DE COVID-19

Sr. Editor:

En el artículo de Delgado-Floody y colaboradores (1) se señala que los escolares obesos tienen menor capacidad física y un mayor riesgo de presentar hipertensión arterial. Es un hecho que las alteraciones fisiológicas y morfológicas causadas por la obesidad son un factor agravante de la evolución de la COVID-19 (2). Durante la pandemia se observó que la población infantil y adolescente desarrolló trastornos en su salud mental de diferentes intensidades (3); muchos de estos trastornos suelen estar asociados con una mayor ingesta de alimentos, por lo que el riesgo de generar obesidad y sus problemas derivados también aumenta.

Entre las alteraciones fisiológicas más importantes que provoca la obesidad se encuentran el exceso de tejido adiposo, la resistencia a la insulina (IR) y la hiperactividad del sistema renina-angiotensina-aldosterona (RAAS). El aumento de la secreción de la enzima convertidora de angiotensina 2 (ACE2), producto de la hiperactividad del sistema RAAS, es un factor de riesgo debido al mecanismo de infección de la COVID-19, uniéndose el virus a esta enzima ARA2 para infectar las células. La mayoría de los pacientes con IR son obesos, por lo que tienen una mayor cantidad de células adiposas en las que encontramos una mayor concentración de ACE2 (4). El aumento de peso que se pudo generar debido a los diferentes trastornos mentales sufridos por los niños y adolescentes dado el confinamiento los convierte en un nuevo grupo de riesgo ante una nueva ola de COVID-19, ya que los hábitos alimenticios compulsivos o emocionalmente compensatorios es muy probable que se estén manteniendo aun cuando el confinamiento ha terminado en muchos países.

La ansiedad, la depresión y el estrés fueron los principales trastornos que se desarrollaron durante la pandemia; todos ellos están asociados a una mayor ingesta alimentaria y a disminución de la actividad física, lo que permite el desarrollo o la agudización de las alteraciones de la imagen corporal y el estado nutricional (5-7), en especial en la población más joven, que es la que ha presentado los mayores índices de trastornos de salud mental durante y después del confinamiento (8).

La actividad física durante la pandemia se vio deteriorada por el confinamiento indicado por la Organización Mundial de la Salud (OMS) para tratar de controlar los contagios (9). Tanto niños como adolescentes disminuyeron su actividad física y aumentaron las horas frente a las pantallas de diferentes dispositivos (10). Estos nuevos hábitos pudieron generar un círculo vicioso centrado en aspectos psicológicos como, por ejemplo, la autoimagen, que conllevan cambios nutricionales relevantes y que pueden tener permanencia en el tiempo.

Dado todo lo ya mencionado, se hace imperativo retomar los planes y programas destinados a combatir la obesidad y el sedentarismo desde un punto de vista psiconutricional, incorporando políticas que aborden la problemática de salud mental que está presentando la población infantil y adolescente, incluyendo a los actores comunitarios y no solo a los colegios y al núcleo familiar. Los planes deben proporcionar espacios que promuevan un sistema de asistencia acorde a la realidad local, para generar intervenciones con un sentido de pertenencia y pertinencia.

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Carta al Director

¿QUÉ TANTO HA AFECTADO LA PANDEMIA AL ESTADO NUTRICIONAL DE LOS NIÑOS CHILENOS?

Sr. Editor:

Leímos la publicación realizada por Muros y colaboradores en el año 2016 (1), donde se señala que los niveles de sobrepeso y obesidad en los niños son alarmantes en Chile. Han pasado ya cinco años y la situación claramente no ha mejorado. En Chile, la Junta Nacional de Auxilio Escolar y Becas (JUNAEB), responsable de los programas de alimentación escolar en los colegios dependientes del Estado, publica cada año el Mapa Nutricional, que da un reporte estadístico del estado nutricional de la población escolar (2). El aumento casi constante de la obesidad y de la obesidad severa entre 2009 y 2019 (Tabla I) nos indicaba claramente que estábamos perdiendo la batalla contra la obesidad.

El sobrepeso y obesidad infantil en Chile se han asociado a una amplia gama de complicaciones graves para la salud, como la hipertensión y la sensibilidad insulínica en edad temprana (3-5). La baja condición física que presentan los estudiantes se

Tabla I. Evolución de los estados nutricionales entre 2009 y 2020 en estudiantes chilenos según datos de la JUNAEB

Año	Desnutrición	Sobrepeso	Obesidad	Obesidad severa	Malnutrición por exceso	Normopeso
2009	2,1 %	26,8 %	12,3 %	4,8 %	43,9 %	54,1 %
2010	2,3 %	26,9 %	13,1 %	5,3 %	45,3 %	52,5 %
2011	2,3 %	27,4 %	13,5 %	5,8 %	46,8 %	50,9 %
2012	2,4 %	27,0 %	13,5 %	5,9 %	46,4 %	51,2 %
2013	1,7 %	28,2 %	14,6 %	6,3 %	49,1 %	49,2 %
2014	2,0 %	27,8 %	14,8 %	6,9 %	49,4 %	48,6 %
2015	2,0 %	28,1 %	15,1 %	6,5 %	49,6 %	48,4 %
2016	2,1 %	28,0 %	15,2 %	6,5 %	49,7 %	48,3 %
2017	1,8 %	27,5 %	14,8 %	6,1 %	48,4 %	49,9 %
2018	1,9 %	28,7 %	16,8 %	6,2 %	51,7 %	46,4 %
2019	1,8 %	28,7 %	17,1 %	6,4 %	52,2 %	46,0 %
2020	2,6 %	28,7 %	17,8 %	7,6 %	54,1 %	43,3 %

Fuente: creación propia a partir de los datos disponibles en https://www.junaeb.cl/mapa-nutricional.

Conflictos de intereses: los autores declaran no tener conflictos de intereses.

asocia a un mayor riesgo de tener enfermedades cardiovasculares (5). En el informe del año 2019 del Mapa Nutricional se había llegado a un 52,2 % de niños con malnutrición por exceso, lo cual ya era alarmante. Durante el año 2020, que fue el primero de confinamiento en Chile, se cerraron colegios, se estableció el trabajo remoto entre otras medidas y se llegó al nivel más alto de obesidad severa con un 7,6 % (un 1,2 % por sobre el año anterior). Este aumento era esperable, pero el aumento de los niños con desnutrición con respecto al año anterior, de un 0,6 %, no lo era. Para explicar este aumento podríamos hacer varios supuestos, como la suspensión por varios meses de los programas de alimentación que entregaba la JUNAEB a los niños de los quintiles más bajos. Muchas familias perdieron su fuente de trabajo y, en otras, los adultos tuvieron que concentrar toda su atención en el teletrabajo; en ambos casos, procurar una buena alimentación a los niños pasó a segundo plano. El estrés por el confinamiento entre los niños también pudo jugar un papel en sus hábitos de alimentación, pues en vez de estimular la ingesta los llevó a cuadros de inapetencia. Estos supuestos, lógicamente, deben ser corroborados o refutados a partir de investigaciones en profundidad.

El manejo preventivo de las alteraciones de los hábitos de alimentación en los niños no solo debe vincular a los colegios sino que debe integrar al sector productivo para crear ambientes de comida saludable, siendo el gobierno el responsable de crear políticas que tengan como fin último disminuir las inequidades sociales para así favorecer hábitos de vida saludables, todo esto apoyado por los medios de comunicación (6). La pandemia nos está dejando una nueva realidad en cuanto a los hábitos y estados nutricionales de los niños y es necesaria una pronta intervención que se concrete en la creación de programas de promoción de estilos de vida saludables a largo y corto plazo que no solo se centren en la obesidad sino en la salud nutricional integral.

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In Memoriam

Carmen Villares García (1937-2022)

Ha fallecido en León, el 7 de septiembre de 2022, a los ochenta y cinco años, Carmen Villares García. Carmen Villares fue desde 1976 jefa del Servicio de Farmacia en el Hospital Princesa Sofía y, tras la fusión en 1990 con el Hospital Virgen Blanca, del Complejo Asistencial Universitario de León. Lo fue hasta su jubilación en 2007.

Carmen fue socia fundadora de la Sociedad Española de Nutrición Parenteral y Enteral (SENPE) en 1979. Junto con Domingo García Rodríguez y Milagros Anaya Turrientes, ambos del Hospital Universitario Ramón y Cajal, constituyeron un núcleo de farmacéuticos muy activo en la sociedad. Tuvo parte muy destacada en la organización de los congresos de SENPE en León en 1995 y el congreso conjunto de SENPE y SEN en 2002, y colaboró muy activamente en el congreso de A Coruña en 1989 junto a Alfredo García Iglesias y Francisco Javier Pallares Machuca.

Carmen Villares leyó la tesis doctoral en la Universidad de Salamanca en el año 2000 con la máxima calificación. Era, además de Licenciada y Doctora en Farmacia, Licenciada en Ciencias Biológicas por la Universidad de Salamanca y profesora asociada de esta universidad. Además fue autora o coautora de más de sesenta artículos científicos originales y de varios capítulos de libros.

Carmen Villares fue vocal de la junta Directiva de SENPE durante varios periodos y también miembro de su Comité Científico Educacional. Decidió que sus colaboradores fueran también doctores consiguiendo que el número de doctores entre los miembros de su Servicio de Farmacia fuera de los más altos del país.

Consciente de la importancia de la vinculación del hospital con la Universidad de León, apoyó decididamente el Instituto de Biomedicina (IBIOMED). Sus buenas relaciones con la industria farmacéutica le permitieron vehiculizar importantes sumas de dinero al IBIOMED para patrocinar ayudas de investigación, proyectos y becarios, y lo mismo hizo con los cursos de microcirugía.

Fue presidenta de Comité Ético de Investigación de León desde que se constituyó hasta su jubilación en 2007.

Era miembro de número de la Cofradía Internacional de Investigadores de Toledo.

A sus tres hijas, Mamen, Ana y Cristina, y a sus yernos y nietos trasladamos nuestro más sentido pésame.

Descanse en paz.

Jesús M. Culebras

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Carmen Villares en 1985, flanqueada a su derecha por Abelardo García de Lorenzo, ex-Presidente de SENPE de 2000 a 2012, y Jesús Culebras, Presidente de Honor de SENPE.

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