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Trabajo Original

Obesidad y síndrome metabólico

25-hydroxy vitamin D and syndrome metabolic components in candidates to bariatric surgery

Vitamina D y componentes del síndrome metabólico en candidatos a cirugía bariátrica

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Abstract

Aim: The aim of this study was to assess the prevalence of hypovitaminosis D in candidates to bariatric surgery (BS) and its relationship with risk factors and components of the metabolic syndrome.

Material and methods: Clinical, anthropometric and biochemical parameters were measured in 56 Caucasian patients included in a protocol of BS between January and June 2014. Patients were stratified into three groups according to their vitamin D status: sufficiency (≥ 40 ng/ml), insufficiency (40-20 ng/ml) and deficiency (< 20 ng/ml).

Results: Data showed vitamin D deficiency in 75% of patients. These patients had greater BMI (p = 0.006) and lower PTH concentrations in plasma (p = 0.045). In addition, there were more patients with diabetes mellitus type 2 (DM2) and dyslipidemia (DLPM) in the group with 25 (OH) D < 20 ng/ml levels. Another finding was that 25(OH) D levels were observed to be negatively correlated with fat mass (r = -0.504; p = 0.009), BMI (r = -0.394; p = 0.046) and hypertension (r = -0.637; p = 0.001).

Conclusion: We conclude that vitamin D deficiency is extremely common among candidates to BS, who are associated with DM2 and DLPM.

Although there are limited data regarding the best treatment for low Vitamin D status in BS candidate patients, screening for vitamin D deficiency should be regularly performed in cases of morbid obesity.

Key words:

Vitamin D. Bariatric surgery. Morbid obesity. Metabolic syndrome.

Resumen

Objetivo: el objetivo de este estudio fue evaluar la prevalencia de hipovitaminosis D en los candidatos a cirugía bariátrica (CB) y su relación con factores de riesgo y los componentes del síndrome metabólico.

Material y métodos: los parámetros clínicos, antropométricos y bioquímicos se midieron en 56 pacientes caucásicos incluidos en un protocolo de cirugía bariátrica entre enero y junio de 2014. Los pacientes fueron estratificados en tres grupos de acuerdo al status de vitamina D: suficiencia (≥ 40 ng/ml), insuficiencia (40-20 ng/ml) y deficiencia (< 20 ng/ml).

Resultados: se observó deficiencia de vitamina D en el 75% de los pacientes. Estos pacientes tenían mayor índice de masa corporal (p = 0,006) y concentraciones plasmáticas mas bajas de PTH (p = 0,045). Además, hubo más pacientes con diabetes mellitus tipo 2 (DM2) y dislipemia (DLPM) en el grupo con niveles de 25 (OH) D < 20 ng/ml. Asimismo la 25 (OH) D se correlacionó negativamente con la masa grasa (r = -0,504; p = 0,009), el IMC (r = -0,394; p = 0,046) y la hipertensión arterial (r = -0,637; p = 0,001).

Conclusión: De nuestros hallazgos concluimos que la deficiencia de vitamina D es muy común entre los candidatos a CB y que la misma está asociada con DM2 y DLPM.

Aunque hay pocos datos sobre el mejor tratamiento para el bajo nivel de vitamina D en los pacientes candidatos CB, la detección de la deficiencia de vitamina D debe realizarse de forma rutinaria en estos casos.

Palabras clave:

Vitamina D. Cirugía bariátrica. Obesidad mórbida. Síndrome metabólico.

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INTRODUCTION

Vitamin D in the body comes from the diet and is produced in the skin (1). This vitamin is long known for its essential role in calcium absorption and bone health. More recently, it has been associated with other aspects of health, including cancer prevention, autoimmune diseases, cardiovascular diseases, and other chronic diseases. Given that at least 60 human cell types express the vitamin D receptor, and more than 200 genes have been identified as directly or indirectly responsive to vitamin D, this vitamin is thought to have a wide range of potential functions (2).

It is estimated that more than 50% of the population is vitamin D deficient (1,3). In fact, some authors consider vitamin D deficiency as a pandemia (1,4,5).

Previous studies suggest an inverse relationship between body mass index (BMI) and fat mass, and low 25-hydroxyvitamin D (25 [OH] D) concentrations (3,6-11) also some studies report that obese individuals with vitamin D deficiency are at higher risk of developing metabolic syndrome (3,12-14).

The goal of this study was to assess the prevalence of hypovitaminosis D in candidates to bariatric surgery and its relationship with risk factors and components of the metabolic syndrome.

MATERIAL AND METHODS

A total of 56 Caucasian patients with morbid obesity were included in the protocol of a Bariatric Surgery Unit between January and June 2013 according to the Spanish Society of Obesity Surgery recommended criteria (SECO) (15).

During the preoperative visit, universal variables were registered (age and gender) as well as the presence of co-morbidity in the form of metabolic syndrome (arterial hypertension [HTN], mellitus diabetes type 2 [DM2] and dyslipidemia [DLPM]).

Additionally, some anthropometric and biochemical parameters were measured: height and weight were measured with the patients wearing light clothing and no shoes; body mass index (BMI) was calculated as weight in kg divided by the square of height in meters (km/m^2); body fat percentage was evaluated by means of electronic bioimpediantometry (BIA) using the Body Composition Analyzer (TANITA, TBF 300, Tanita Corp of America, Inc, Arlington Heights, Ill) which showed a high correlation with dual-energy x-ray absorptiometry in body fat estimation.

All patients had blood samples taken for hormone assessment (PTH, 25-hydroxyvitamin D) and electrolyte assay. Blood measurements were done in the morning after an 8-h overnight fast. Hormone levels were all assayed in duplicate. PTH was measured using an enzime chemiluminescence immunoassay (Roche products, Modular E, Penzberg, Germany, intra-assay and interassay coefficients of variation were 4.5 and 3.2-6.0%, respectively). Serum levels of 25-hydroxivitamin D were determined by chemiluminiescence immunoassay radioimmunoassay (Liaison; Diasorin, Saluggia. Italy). Intra-assay and interassay coefficient of variations were 4.8 and 7.8%, respectively. Serum calcium and phosphorus were assessed by standard laboratory methods.

Patients were stratified into three groups according to their vitamin 25-hydroxyvitamin D status: sufficiency (≥ 40 ng/ml), insufficiency (40-20 ng/ml) and deficiency (< 20 ng/ml) according to the Endocrine Society recommendations. The study protocol was approved by the Ethical Committee.

STATISTICAL ANALYSIS

Data are expressed as mean ± SD or percentage. Continuous or categorical data were analyzed using ANOVA or χ^2 tests. Levels of 25-OH-D were described by demographic and anthropometric variables and by measures of disease status. Spearman coefficient was calculated to examine the association between 25-hydroxyvitamin D levels and measures of disease status. Data analyses were performed using SPSS for Windows version 17.0. All analyses were two-tailed and $p < 0.05$ was considered significant.

RESULTS

The mean age of subjects was 42.8 ± 10 years, 75% being women. Mean weight was 122 ± 18 kg with 60 ± 11 kg corresponding to fat mass. Mean BMI was 44 ± 9.

DM2 was present in 29%, HTN in 32% and DLPM in 15% of patients.

A significant prevalence of hypovitaminosis was detected in the study group. As many as 75% of subjects presented 25-hydroxyvitamin D levels, corresponding to a deficiency status; 15% presented an insufficient status; only 10% of patients presented levels within normal range. The clinical and biochemical characteristics concerning 25-hydroxyvitamin D levels of the study population are detailed in table I.

The subjects of all groups had a similar age and serum Ca and P concentrations, and the presence of men and women was balanced. However, the subjects in the 25-hydroxyvitamin D -deficient group had greater BMI ($p = 0.04$) and lower PTH concentrations in plasma ($p = 0.04$).

Regarding the metabolic status of patients, there were more patients with DM2 and HTN in the group with 25-hydroxyvitamin D < 20 ng/ml levels than in the group with 25-hydroxyvitamin D > 20 ng/ml levels.

In addition, 25-hydroxyvitamin D levels were found to be negatively correlated with fat mass ($r = -0.504$; $p = 0.009$), BMI ($r = -0.394$; $p = 0.046$) and HTN ($r = -0.637$; $p = 0.001$).

DISCUSSION

The results obtained reveal a high rate of 25-hydroxyvitamin D deficiency in candidates to bariatric surgery. These results are in agreement with those obtained in different cross-sectional studies, which have reported a high prevalence of 25-hydroxyvitamin D deficiency in obese subjects, as well as significantly lower

25-hydroxyvitamin D values in obese as compared to non-obese subjects (7-9). In fact, some of the most recent evidence on the relationship between low vitamin D levels and obesity comes from studies in bariatric surgery patients reporting low preoperative circulating levels of 25-hydroxyvitamin D (9). A recent systematic review of 14 studies with about 1,500 patients undergoing bariatric surgery confirmed that obese individuals have serum 25-hydroxyvitamin D levels below 30 ng/ml preoperatively (16).

Similarly, we observed that the patients with the lowest 25-hydroxyvitamin D levels had greater fat mass and lower PTH levels, as compared to patients with insufficient and normal 25-hydroxyvitamin D levels. Indeed, there is extensive evidence that BMI and fat mass are inversely correlated with serum 25-hydroxyvitamin D levels (4,12,17-19).

Some investigators have suggested that vitamin D sequestration by the adipose tissue contributes to low circulating 25-hydroxivitamin D concentrations in obese individuals. There appears to be increased uptake and storage of vitamin D –which is fat-soluble– by the adipose tissue in obese individuals as compared to that in lean individuals (20-23). Thus, some authors have observed that the expression of 25-hydroxylase and 1-alpha-hydroxylase was low (71% and 49%, respectively) in subcutaneous fat in obese patients (18). Brouwer's study in rats suggested that adipose tissue accumulates vitamin D rapidly but releases it slowly (24).

The relationship between vitamin D and the adipose tissue does not seem to be limited to a mere storage function; the adipocytokines and inflammatory mediators produced in the adipose tissue may have an important role (11).

It has not been elucidated yet whether it is visceral or subcutaneous fat which is involved in lower vitamin D values (25,26). Obese patients have been observed to have lower serum vitamin D levels after sun exposure to UV-B radiation and after supplementation, as compared to non-obese subjects (12,27,28), which highlights the role of subcutaneous fat in vitamin D storage. However, other authors have found that visceral fat is more relevant than BMI in determining vitamin D values (25).

In addition, vitamin D may play a role in insulin-resistance related diseases such as obesity, mellitus diabetes type 2 and hypertension (12). The results obtained in this study revealed a grater prevalence of DM2 and HTN in patients with 25-hydroxyvitamin D levels below 20 ng/ml. In fact, there is accumulating evidence that there is an independent relationship between hypovitaminosis D, obesity and metabolic syndrome components (hypertension, mellitus diabetes type 2 and hyperlipidemia) (3,12,13,18,26). Furthermore, 25-hydroxyvitamin D does not only stimulates insulin-receptor expression, but it also regulates calcium homeostasis, which is essential in insulin-mediated intracellular processes (27).

Ferreira et al. suggest that vitamin D deficiency is associated with insulin resistance, regardless of dietary calcium, intracellular calcium levels and serum parathyroid hormone, calcium and calcitriol (29).

On the other hand, low 25-hydroxyvitamin D levels are associated with lower HDL cholesterol levels (13), higher triglyceride levels and increased waist circumference (14,30,31). The inverse correlation between 25-hydroxyvitamin D and triglyceride levels might be associated with the vitamin D-mediated activation of a lipoprotein lipase of the adipocyte (14,30).

Although analyzed intervention studies reported that the consumption of calcium and vitamin D may be beneficial in preventing and treating T2DM (32), there is scant evidence to support the influence of vitamin D supplementation on the metabolic syndrome (31,33).

When hypovitaminosis occurs in candidates to bariatric surgery preoperatively, it is conceivable that a compromised vitamin D status might adversely affect clinical outcomes after surgery, although this aspect has not been thoroughly studied.

Table I. Clinical and biochemical characteristics according to study groups

	25-hydroxyvitamin D- deficiency (n = 42)	25-hydroxyvitamin D-insufficiency (n = 8)	25-hydroxyvitamin D-sufficiency (n = 6)	p
Age (years): mean ± SD	42.7 ± 10	44.9 ± 5	42.3 ± 8	0.93
Sex (female/male)	29/13	6/2	4/2	0.56
BMI (kg/m^2):mean ± SD	45.3 ± 5	42.0 ± 4	41.9 ± 6	0.04
Fat mass (%)	63 ± 6	59 ± 5	57.5 ± 4	0.03
25-hydroxyvitamin D (ng/ml) mean ± SD	9 ± 4	24 ± 5	41 ± 6	0.01
Syndrome metabolic component:				
DM (%)	14	1	1	0.03
HTA (%)	15	2	1	0.01
DLPM (%)	7	1	1	0.63
Ca (mg/dl) mean ± SD	8.5 ± 3	7.9 ± 5	8.2 ± 3	0.78
P (mg/dl) mean ± SD	3.2 ± 0.9	3.0 ± 1.5	2.9 ± 2	0.84
PTH (pg/ml) mean ± SD	62.3 ± 17	43.6 ± 13	43.3 ± 15	0.04

Some studies report that vitamin D supplementation has beneficial effects on plasma vitamin D levels one year after surgery (18,19-21). However other retrospective studies that supplemented their patients during the postoperative period only with low doses of calcium and vitamin D (500 mg and 400 IU, respectively) proved no efficacies to correct and prevent vitamin D deficiency that occurs in obese and which is aggravated after surgery (34). However, there are limited data on how best to treat low vitamin D status in bariatric surgery patients. Unfortunately, procedure-specific guidelines are not available.

To the extent of our knowledge, there are no studies assessing the usefulness and security of systematic preoperative vitamin D prescription. Thus, further intervention studies are necessary to better understand its effects.

There are potential limitations to our study. First, factors influencing skin synthesis of vitamin D such as ultraviolet exposure, screen use and dietary consumption of vitamin D were not assessed in this study. Second, the cross-sectional design of our study limited our ability to examine the causal relationship between 25 (OH) D levels and the metabolic syndrome.

In this study, candidates to bariatric surgery often present deficient vitamin D levels. Additionally, lower 25-hydroxyvitamin D levels are associated with DM2 and HTN.

Although there are limited data regarding the best treatment for low Vitamin D status in BS patients, screening for Vitamin D deficiency should be regularly performed in cases of morbid obesity.

Nevertheless, long-term observation is needed to asses the advantages and potential side effects of systematic Vitamin D supplementation.

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