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Original article

Hypovitaminosis D in patients after bariatric surgery by Y-Roux and sleeve

Ana Carla de O. Lopes,[1]* Alessandra da R. P. Mulder,[1] Camila F. Lima,[1] Glauciane L. Miranda[2]

Abstract

Introduction: Obesity is a multifactorial chronic disease, resulting from complex interactions between genetic, psychological, environments, lifestyles and emotional facts. Bariatric surgery is the most effective tool in the control and treatment of severe obesity. However, individuals submitted to this surgery may present malabsorption, some degrees of protein-energy malnutrition and hypovitaminoses. Objectives: To evaluate the prevalence of hypovitaminosis D in bariatric patients submitted to BPGYR and to the Sleeve using conventional multivitamins (group with supplementation) or without supplementation. Metodology: A cross-sectional, retrospective analysis of the medical records of female and male patients submitted to BPGYR and Sleeve in the late postoperative period. Data regarding the time after surgery, pre- and post-surgery weight, percentage loss of excess weight and serumlevels of vitamin D, PTH and calcium were analyzed. A total of 93 patients were analyzed, with a mean age of 41.4±7.1 in the SS group and 43.7±10.4 in the CS group. The mean time after bariatric surgery was 52.4±46.4 months in the SS and 46.2±37.1 in the CS, with no difference between groups. Results: Sugery was effective in the weight loss of the patients studied (SS-70.3%±22.6; CS-79.3%±26.8; p=0.19); however, hypovitaminosis D was found (SS-26.4±10.0, CS-24.9±10, p=0.91) even in the group receiving conventional multivitamin supplementation. Conclusion: BPGYR and Sleeve are effective procedures in weight loss; these patients, however, are deficient in vitamin D. Supplementation with multivitamins is not sufficient to avoid hypovitaminosis, so vitamin D supplementation is required.

Keywords: Obesity; Bariatric surgery; Gastric bypass; Vertical gastrectomy.

1. Instituto de Nutrição, Universidade do Estado do Rio de Janeiro. Rio de Janeiro, Brasil.
2. Universidade Federal do Estado do Rio de Janeiro (UFRJ). Rio de Janeiro, Brasil.

***Correspondence address:**
Instituto de Nutrição, UERJ
Rua São Francisco Xavier, 524
Maracanã, Rio de Janeiro, RJ, Brazil.
CEP: 20550-170.
E-mail: anacarlalopesnutri@gmail.com
ORCID: https://orcid.org/0000-0002-9439-3815

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Introduction

Obesity is a public health problem and is considered to be epidemic in the current century. It is closely related to several comorbidities, such as arterial hypertension, type 2 diabetes mellitus, non-alcoholic hepatic steatosis, and even some types of cancer, in addition to having a negative role in the well-being and life expectancy of the patient.[1]

The etiology of obesity is complex and multifactorial, resulting from the interaction of genes, environments, lifestyles and emotional factors.[2] Treatment includes dietary reeducation practices, physical exercises and the use of medication. However, it has been observed that many patients do not respond well to such practices and require a more invasive intervention, namely bariatric surgery.[3]

Bariatric surgery is a procedure that consists of modifying the patient's digestive tract, thereby limiting intake and/or promoting lower nutrient absorption.[4] The surgeries can be classified as: restrictive surgeries, where the only organ modified is the stomach, leading to a decrease in gastric capacity and causing satiety with a smaller volume of food; malabsorptive procedures that reduce the absorption of nutrients at the intestinal level; and mixed interventions, which promote changes in the stomach and intestine. Patients undergoing mixed surgeries, in addition to having a restrictive factor that will be responsible for greater satiety, also have a disabsorptive factor, which is the result of a decrease in the area responsible for absorption of nutrients in the small intestine.[3,5]

Over time, several surgical techniques were developed for the treatment of obesity, including the Roux-en-Y Gastric Bypass, conceived by Fobi-Capella in 1990. This is the most performed technique in Brazil, being characterized as a mixed technique since it is both restrictive and malabsorptive, in addition to promoting

less severe malabsorption than other metods. It is considered safe and presents a low mortality rate.[6] This technique consists of reducing gastric capacity and the remaining region of the stomach while excluding the duodenum and the proximal region of the jejunum from intestinal transit. The gastric reservoir is anastomosed with the jejunal loop.[3]

Sleeve gastrectomy became more widespread in 1990s; it is a restrictive technique where 70% to 80% of the stomach proximal to the antrum is removed with preservation of the intestine, without compromising the absorption site of some nutrients. This type of technique, although less complex, is irreversible.[3] Compared to the Roux-en-Y Gastric Bypass, it presents a lower probability of nutritional disorders.[7] This technique can induce weight loss in patients by reducing gastric capacity; however, it is characterized by accelerated gastric emptying, allowing a reduction in the feedback mechanism of the feeling of satiety, promoting a feeling of hunger and, consequently, a decrease in the interval between meals. Hormonal changes and high pressure in the gastric tube are involved In this feeling of early satiety.[8]

Sleeve gastrectomy to remove greater curvature (gastric fundus) is also responsible for eliminating one of the main sites of the production of ghrelin, which is an appetite-stimulating hormone and promotes weight gain. Therefore, these patients will experience an abrupt drop in this hormone and, consequently, a reduction in the feeling of hunger.[8,9]

In some sleeve gastrectomy techniques, the antrum is preserved. In this these cases, gastric emptying is unaltered; in addition, preservation of the antrum prevents the triggering of dumping syndrome and gastroesophageal reflux.[8]

Nutritional deficiencies are less frequent in purely restrictive procedures, precisely because they do not present structural changes in the nutrient absorption sites at the intestinal level.[10]

Although bariatric surgery is effective in the treatment of obesity, it is common for operated patients to become exposed to a greater risk of developing nutritional deficiencies. The change in the gastrointestinal tract causes food intake to be limited and, consequently, reduces absorption of macronutrients and micronutrients at the intestinal level. Among the deficiencies that may occur, the shortage of vitamin D stands out.[4]

Vitamin D deficiency is common in obese individuals. This association can be explained by low exposure to the sun because of difficulties in moving outdoors, as well as low intake of food sources and retention of this fat-soluble vitamin in the adipocytes of these individuals, contributing to a reduction in the availability of this vitamin for use by the body and causing nutritional deficiencies. After bariatric surgery, with the change in the conformation of the gastrointestinal tract, the intake of vitamin D is compromised by the decrease in the gastric capacity of the individual, as well as the reduction in the absorption of this micronutrient at the intestinal level by the structural changes resulting from the surgery, further intensifying the condition of nutritional deficit.[11]

The new structure of the gastrointestinal system resulting from the surgical techniques promotes a reduction in the absorption of nutrients, since most such absorption occurs in the first portion of the small intestine (duodenum), which is excluded in the most performed surgical technique. Hypovitaminosis D is related to hypocalcemia, increased parathyroid hormone (PTH) secretion, followed by secondary hyperparathyroidism to normalize serum calcium levels. In addition, muscle relaxation and contraction are also impaired, and are related to muscle pain and weakness, which can lead to falls and fractures, since PTH and, consequently, bone remodeling increase.[12,13,14] The existence of the vitamin D receptor (VDR) in tissues not involved in calcium metabolism and the identification of the 1α-hydroxylase enzyme in extrarenal tissues demonstrate the existence of extraskeletal effects of vitamin D (Figure 1). The main non-skeletal effects studied are the ratio of vitamin D to cardiovascular diseases; antineoplastic actions of vitamin D; and correlation of the vitamin with immunity and autoimmune diseases.[12,15]

Another nutrient that may be affected, especially in patients undergoing Roux-en-Y gastric bypass, is mineral calcium. Found predominantly in bones and teeth, it is absorbed in the small intestine with vitamin D acting on its absorptive metabolism, duodenum and proximal jejunum. Its low absorption is the result of several factors: the reduced absorption site; intolerance of post-surgery source foods; and its association with vitamin D metabolism. In cases of hypocalcemia or hypovitaminosis D, PTH production is stimulated, increasing the excretion of calcium from bones in an attempt to normalize the serum concentration of the mineral. When proper treatment is not introduced in such cases, it can generate bone loss, causing osteoporosis.[7]

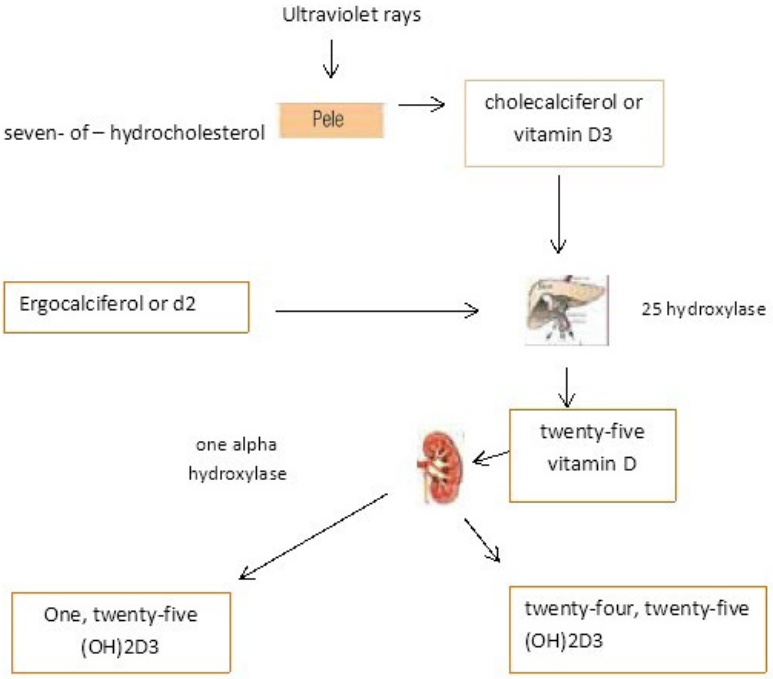

Figure 1. Vitamin D metabolism

Source: Adapted from the Brazilian Society of Endocrinology(SBEM).

In view of the above, it is essential to pay attention to hypovitaminosis D and hypocalcemia, mainly because they are closely related to skeletal health. In their study, Beltrame and colleagues (2002) associate vitamin D deficiency and calcium malabsorption after bypass surgery for morbid obesity with osteomalacia.[16] In this context, the objective of the present study is to investigate the prevalence of hypovitaminosis D in patients after bariatric surgery by Roux-en-Y Gastric Bypass and Vertical Gastrectomy (Sleeve). The patients were treated at the obesity outpatient clinic of the Policlínica Piquet Carneiro.

Methodology

This is a cross-sectional study with a quantitative approach. The sample consisted of patients of both sexes who underwent bariatric surgery and who were followed up at the obesity outpatient clinic of the Piquet Carneiro Polyclinic of the State University of Rio de Janeiro. Data were collected from November 2017 to January 2019. This project was submitted to and approved by the ethics committee.

Data was collected from all available medical records of patients undergoing bariatric surgery who had been treated from March 2010 to January 2019. For inclusion in the research, the following criteria were adopted: patients who had undergone bariatric surgery using the Roux-en-Y gastric bypass technique and/or Vertical Gastrectomy (Sleeve) during this period, since they are the most commonly used techniques in recent times. The exclusion criteria were: patients submitted to unknown surgical procedures and/or those on whom the Roux-en-Y Gastric Bypass technique or Vertical Sleeve Gastrectomy had not been performed. For purposes of sample homogenization, patients with a prior history of vitamin D supplementation after bariatric surgery were excluded to avoid compromising the results.

Information was collected from 93 medical records, of which 7 patients who were already taking vitamin D supplements at time of the first consultation were excluded, leaving a total of 86 patients. After exclusion, these patients were split into two groups: the group that used multivitamin supplements (CS, n=56) and the group that did not use multivitamin supplements

(SS, n=30). Next, 6 patients who did not have vitamin D, PTH and calcium values in their biochemical tests were excluded from the CS group, leaving 50 patients in this group. The same criterion was adopted for the SS group and led to the exclusion of 3 patients, leaving 27 patients in this group (Figure 2).

Information from the medical records was collected, such as: personal data (patient's name, age, date of birth; identification data: registration number, date of first consultation at the clinic); information about the surgery (type of surgery performed and time since surgery (months and/or years)); medications/ supplements in use at the first consultation; weight history; and biochemical tests (especially serum levels of 25(OH) D, PTH and calcium at the first return visit).

In order to analyze the weight history, preoperative body weight and minimum weight achieved after surgery were collected from patients' charts. The

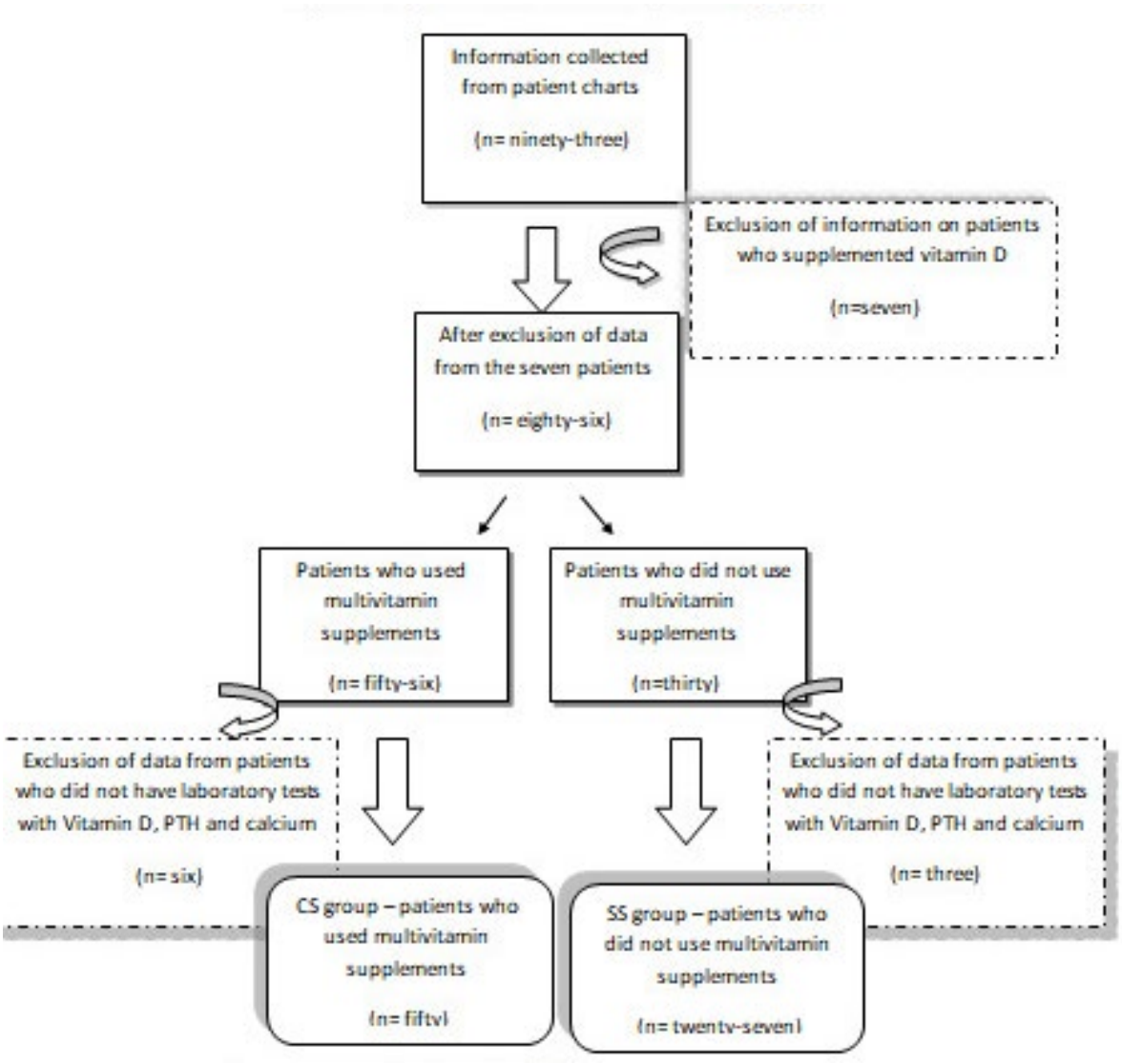

Figure 2. Organizational chart of the separation of groups

Legend: Cs group: used supplements; SS group: did not use supplements.
Source: prepared by the author, 2019.

percentage of weight loss (% PEP) post-surgery was calculated according to the following formula: weight difference preoperative weight in relation to the current weight multiplied by 100/difference of preoperative weight in relation to ideal weight. In this case, the value of 25kg/m[2] was adopted for the body mass index (BMI) in the calculation of ideal weight.

Values of 25-hydroxyvitamin D were used to analyze the serum levels of vitamin D, since it is the most abundant metabolite and considered to be the best indicator of the levels of this vitamin. According to Sempos et al, 2018, a consensus is still needed to determine the values for the definition of hypovitaminosis D. However, in the absence of such values, 25(OH)D values below 12ng ml^{-1} (30 nmol l^{-1}) should be associated with an increased risk of rickets/osteomalacia, while 25(OH)D concentrations between 20ng ml-1 and 50ng mL- (50-125 nmol l^{-1}) appear to be safe and sufficient for general population and skeletal health.[17] The reference values for serum calcium were between 8.4 and 10.2mg/dL and for serum PTH between 10 and 65pg/mL.[6]

Data were tabulated using Microsoft Office Excel 2007 and statistical analysis was performed using GraphPad Prism version 7.03.

Quantitative variables were represented by mean and standard deviation and categorical variables were represented by absolute and relative frequencies. The data were distributed normally and two-side tests were performed. To compare the groups, the T Student test was used for quantitative variables, while the chi-square test was used for categorical variables. The level of statistical significance considered was 5% ($p \leq 0.05$).

Results

Table 1 presents the general characteristics of the two groups studied: CS and SS. In this population, a predominance of female patients was observed. Regarding other variables such as gender, age, type of surgery, surgery time (months) and excess weight loss (% EWL) no statistically significant difference was found between the group that used supplementation (CS) and the one that did not use supplementation (SS).

Table 1. General characteristics of the population

Variables	(CS)	(SS)	P value
Genre			
Women (%) N	45 (90.0)	24 (88.8)	-
Men (%) N	5 (10.0)	3 (11.1)	-
Age (Mean ± SD)	43.7 ± 10.4	41.4 ± 7.1	0,425
Type of Surgery			
BPGYR (%) N	44 (88.0)	23 (85.2)	-
Sleeve (%) N	6 (12.0)	4 (14.8)	-
Surgery Time (months) (Mean ± SD)	46.2 ± 37.1	52.4 ± 46.4	0,53
Pre-Surgery Weight (Mean ± SD)	131.4 ± 26.6	128.4 ± 23.2	0,618
Percentage Loss of Excess Weight (Mean ± SD)	79.3 ± 26.8	70.3 ± 22.6	0,196

Source: Prepared by the author (2019).

Table 2 shows that patients in the CS group used vitamin supplements for an average of 46.2 months after undergoing bariatric surgery. Of this group, 54 (96.4%) supplemented with the multivitamin marca 1 in the postoperative period, 3 (5.36%) supplemented with marca 2 (1.78%) and supplemented with marca 3. These patients used an average of 5.4 mcg, that is, 216 IU of cholecalciferol (D3), corresponding to 1 multivitamin capsule per day. This average intake is significantly lower than the recommendations for patients undergoing bariatric surgery techniques. The patients who supplemented with multivitamins also had hypovitaminosis D, with serum levels of 24.9±10, and showed no statistically significant difference from the group that did not use vitamin supplements after surgery (Table 2).

Table 3 presents the biochemical parameters of the patients studied. The 25-hydroxyvitamin D, PTH and serum calcium of the CS and SS groups were analyzed. With regard to 25-hydroxyvitamin D, the values found are at the lower limit of the suggested values, which are between 20 ng mL^{-1} and 50 ng mL- (50–125 nmol l^{-1}), both in the CS and SS groups. The PTH values in both groups are within the normal range, but are at the maximum limit of the recommended values. With regard to serum calcium values, both groups are within the recommendation, without hypocalcemia. No statistically significant difference was found between the CS and SS groups (Table 3) in the three parameters under analysis.

Discussion

In the present study, an elevated rate of hypovitaminosis D was found in the two groups analyzed: CS and SS who underwent RYGB and Sleeve techniques on average four years after the procedure. This result confirms findings of vitamin D deficiency in post-bariatric patients. Such nutritional deficiencies after bariatric surgery are common, and occur in about 50% to 80% of all cases.[18] Even with the use of nutritional supplements, some patients still have deficiencies, especially in micronutrients.[19]

Table 2. Types and daily intake of supplements

	Supplementation	(%)N
Product	brand 1	54 (96.4)
	brand 2	3 (5.3)
	brand 3	1 (1.7)
Daily IU intake (mean ± SD)		216.0 ± 88.9

Legend: UI: International Unit; N= number of patients; Mean ± Standard Deviation.
Source: Author (2019).

Table 3. Biochemical parameters of the studied patients

Parameters	CS	SS	P value
25(OH)D (ng/mL)	24.9 ± 10.0	24.6 ± 10.0	0,916
PTH (pg/mL)	56.2 ± 28.2	57.7 ± 18.1	0,852
Calcium seric (dL)	9.1 ± 0.9	9.3 ± 1.6	0,574

Legend: ng: nanogram; pg: picogram; mg: miligram; mL: mililiter.
Source: Author (2019).

A meta-analysis involving 15 articles with 3867 obese individuals and 9342 healthy individuals of Asian and European-American origin established a positive relationship between obesity and vitamin D deficiency.[20] A study that analyzed the serum levels of 25(OH)D in women undergoing RYGB three years after surgery found an average of 28.9ng/mL, a result similar to the present study, which found an average of 24.9g/mL, and is consistent with post-surgery hypovitaminosis D.[10]

Post-bariatric surgery hypovitaminosis D occurs due to food restriction and/or decreased nutrient absorption area. In addition, it can occur either because of the exclusion of the duodenum and jejunum or the decrease in the amount of time food remains in contact with the intestinal mucosa. Food intolerances acquired at that time, as well as the non-use of supplements can contribute to an inadequacy of nutrients. Furthermore, it is well known that dietary sources of vitamin D are scarce and little consumed by the Brazilian population.[21,22]

Youssef and colleagues, in a prospective study of 193 women, assessed 25(OH)D levels two years after RYGB. The presence of hypovitaminosis D was observed, with low values (<20ng/mL) of vitamin D.[23] Another study followed patients at 6 and 12 months after RYGB and compared the prevalence of hypovitaminosis D (defined as serum 25(OH)D below 20ng/mL). The prevalence found was 53% at baseline and 71% in the following six months. In the case of hypovitaminosis D (defined by serum 25(OH)D <30ng/ml), the prevalence was 70% at baseline and 71% in the following six months.[24] Other findings of hypovitaminosis D were also found in a study, in which 24 months after RYGB surgery, 61.1% of patients had vitamin D deficiency.[25] These findings in the literature corroborate the data found in the present study, in which patients suffer from hypovitaminosis D after undergoing bariatric surgery.

The intake of the patients in the study is similar to the recommendations for healthy adults without a history of bariatric surgery, in which the RDA is 5mcg or 200 IU.[2]

A consensus already exists that multivitamin supplementation for this group should be performed after the procedure and throughout life. (4,14,26) However, vitamin D dosages must be adequate and compatible with the recommendations established for this at-risk group . According to the literature, the recommended supplementation for patients undergoing bariatric techniques requires the ingestion of 7000 IU per day, which is equivalent to 175mcg of cholecalciferol, or 50,000 IU, equivalent to 1250mcg, once a week for 6 to 8 weeks. After this time, patients should receive 400 IU equivalent to 10mcg at 2000 IU or 50mcg daily for maintenance.[4,12]

Another recommended supplementation schedule is supplementation with 6000 to 10,000 IU per day, to be performed 2 to 3 times a week, followed by a daily maintenance dosage of 3000 to 6000 IU.[27] The response to treatment varies from individual to individual. In more severe cases, the values of plasma levels of vitamin D should ideally be assessed after loading doses.[12] A randomized study conducted by Goldner and colleagues analyzed patients who had undergone the Roux-en-Y Gastric Bypass technique and who received daily supplements of 800, 2000 and 5000 IU and 2000mg of calcium for a period of 6, 12 and 24 months. At the end of 24 months, 67%, 50% and 78% of the groups that received daily supplements of 800, 2000 and 5000 IU achieved serum 25(OH)D levels above or equal to 30.[18]

Hypovitaminosis D causes a reduction in calcium absorption at the intestinal level, with subsequent hypocalcemia and, through a compensatory mechanism, an increase in parathyroid hormone (PTH) secretion (secondary hyperparathyroidism), which will be responsible for inducing greater reabsorption. bone in order to normalize serum calcium levels.[28] Calcemia normalization occurs through some reactions at the renal level, in which PTH promotes the increase of 1,25(OH)D through the stimulation of the enzyme. In bones, 1,25(OH)D acts in conjunction with PTH to mobilize calcium and phosphorus, by inducing the differentiation of precursor cells into osteoclasts, which are responsible for bone resorption. In the intestine, 1,25(OH)D is responsible for the absorption of calcium in the duodenum and phosphorus in the jejunum and ileum.[29]

The current study found high incidences of PTH values, although still at the upper limit of the normal range. Similar results were also found in the study conducted by Youssef and colleagues, in which they evaluated PTH levels in 193 obese women 24 months after RYGB. The incidence of PTH levels (>65pg/mL) was 53.3%.[23] A study by Munhoz and colleagues evaluated 47 post-bariatric patients using the RYGB technique, with a mean time of 33.3 months. The results showed a 41.7% prevalence of secondary hyperparathyroidism (>67pg/mL). In the present study, hypocalcemia was not found in patients, which is consistent with the literature, since

patients with increased PTH values have serum calcium values within the normal range.[30]

Elevated levels of PTH promote an increase in bone resorption in order to release calcium into the bloodstream. If bone resorption is maintained for a long time, by reducing the levels of either calcium or vitamin D, significant loss of bone mass may occur, since PTH when secreted continuously has a catabolic effect and the individual consequently becomes more susceptible to the development of fractures.[30] In children, these changes can lead to inadequate bone mineralization: the bones continue to widen, although inappropriately. In adults, bone growth no longer occurs, but vitamin D deficiency, with a decrease in calcium absorption and an increase in PTH, causes problems in bone mineralization, leading to osteomalacia.[31]

The impact of low levels of vitamin D is not limited to skeletal-level complications. It is now known that reductions in the serum levels of this vitamin are related to the development of other complications, including cardiovascular disorders, autoimmune disease, and cancer. It is even more important to collect data related to the prevalence of hypovitaminosis D in this population at risk, in order to avoid new extraskeletal complications.[12]

Conclusion

The need for vitamin and mineral supplementation after bariatric surgery is already a consensus in the literature. The current study shows that most patients who had their medical records analyzed used commercial multivitamin supplements after the procedure. However, the amount of supplementation was lower than that recommended by the literature and, according to analyses, insufficient to prevent hypovitaminosis D in these patients.

From these data, it can be said that, in order to avoid nutritional deficiencies, post-bariatric supplementation based solely on the use of commercial multivitamins should not be adopted as a treatment after the bariatric procedure, since most of these vitamin supplements do not have the necessary and recommended amounts of vitamin D for daily ingestion by this high-risk group.

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