Chapter 177

Vitamin D supplementation in patients after bariatric surgery

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ABSTRACT
Vitamin D acts in the regulation of bone metabolism and plays actions in other tissues, being considered of extreme importance. The causes of its deficiency are multifactorial, its deficiency after bariatric surgery can cause skeletal changes, calcium deficiency, increasing the risk of malignancies (colon, breast, and prostate) and chronic inflammatory or autoimmune diseases, metabolic changes, peripheral vascular disease, muscle weakness and, osteoporosis or osteomalacia. Objective- Given the importance of this nutrient, this study was designed to analyze different types of adequate doses of vitamin D that can help in the treatment of obesity and possible pathologies after bariatric surgery. Methods- For this, it was performed a search in the Pubmed, Scielo, and Science Direct databases, with published articles in Portuguese and English. The search strategy used the keywords individually or in association with "vitamin D", "supplementation", and "bariatric surgery". There was no delimitation as to the year of publication of the articles. Results- 12 articles have been selected The findings confirmed the existence of nutritional vitamin D deficiency in people who underwent bariatric surgery and explain the importance of long-term supplementation for prevention. Conclusion- Therefore, it is concluded that this deficiency in bariatric patients is evidenced in the literature, which elucidates its effects on health, demonstrating the importance of supplementation after bariatric surgery, but there is a need for more specific studies.

Keywords: Bariatric surgery. Vitamin D. Dosages. Supplementation.

1 INTRODUCTION

Obesity is a disease of multifactorial etiology that has become one of the biggest public health problems in the world, reaching the population over 35 years of age, and, according to data from the Brazilian Association for the Study of Obesity and Metabolic Syndrome (ABESO)1, has a prevalence of approximately 17.9% in men and 18.2% in women.

According to data from the Surveillance of Risk and Protective Factors for Chronic Diseases by Telephone Survey (VIGITEL)2, in the last 13 years, there has been a considerable increase in overweight and obesity in the Brazilian population, from 11.8% to 20.3%, between 2006 and 2019. When considering overweight, 55.4% of Brazilians are in this situation. Also, according to this study, according to age group, excess weight tends to increase, being present in 30.4% of young people between 18 and 24 years old and in 59.8% of adults aged 65 years old or more. The research also pointed out the presence of comorbidities,

such as diabetes in 7.4% and hypertension in 24.5%.

Given the sharp increase in obesity in the country, data have shown a significant increase in the number of patients undergoing bariatric surgery. According to the Federal Council of Medicine (CFM)3, candidates for surgical treatment (bariatric surgery) are patients with a Body Mass Index (BMI) greater than 40 kg/m² (grade III) or with a BMI greater than 35 Kg/m² (grade II) associated with comorbidities such as type 2 diabetes, sleep apnea, high blood pressure, dyslipidemia, cardiovascular disease, stroke, depression, among others.

Currently, there are several types of surgeries for weight reduction, however, many seek bariatric surgery as a treatment is known as gastroplasty or stomach reduction surgery, whose objective is to reduce the size of the stomach, and consequently, weight reduction. According to data from the Brazilian Society of Bariatric and Metabolic Surgery (SBCBM)4, throughout 2018, 63,969 bariatric surgeries were performed, 49,521 of which were for supplementary health (health plan), according to data from the National Supplementary Health Agency (ANS), 11,402 by the Unified Health System (SUS) and 3,046 private surgeries. The data also showed that the total number of procedures performed in 2018 was 4.38% higher than in 2017 when approximately 61,283 thousand surgeries were performed by SUS and ANS.

Once the patient intends to undergo this procedure, follow-up examinations of their conditions are ordered. At this stage, it is common to observe nutritional deficiencies, as well as a deficit of vitamins, such as Vitamin D, responsible for stimulating the absorption of calcium by the intestinal mucosa, in the duodenum and jejunum, making the postoperative period even more challenging, due to the implications of bariatric surgery procedures on the patient's nutritional status, which should be specifically restricted to anatomical and physiological changes, which impair absorption pathways and/or food intake 5,6.

According to Azevedo7, the deficiency of some specific micronutrients in the body can impair basic functions and increase the risk of serious illnesses, in addition to the fact that the adequacy of micronutrients is important in maintaining long-term weight loss. Vitamins and minerals are essential factors and cofactors in many biological processes that directly or indirectly regulate body weight. Such deficiencies occur due to restriction of food intake and/or reduction of nutrient absorption areas, decrease in gastrointestinal transit time, and limited food contact with the brush border epithelium8. In this way, it becomes a great challenge for patients to achieve the necessary intake of vitamins and minerals after surgery. In addition, a key element for the incidence of nutritional deficiencies after surgery is the occurrence of frequent vomiting, which leads to malabsorption of nutrients, and the patient's adherence to the nutritional recommendations suggested by nutritionists is also observed9.

In vivo studies have shown that some nutritional deficiencies such as vitamin D, vitamin A, and zinc are concomitantly present in obesity, possibly because they play an important role in adiposity regulation or appetite regulation mechanisms, in addition to the fact that they are absorbed in the duodenum and jejunum proximal. Thus, it is essential to have a care program for the clinical-nutritional follow-up, both pre-and postoperatively, for the success of the treatment5.

Vitamin D is a fat-soluble vitamin, whose main compounds are ergocalciferol (Vitamin D2) and cholecalciferol (D3). Ergocalciferol is found in plants and is the product of ergosterol irradiation by ultraviolet B (UVB) radiation, and is usually consumed in the form of supplements or fortified foods; while cholecalciferol (Vitamin D3) is found in the epithelial cells of the skin and dependent on solar radiation (ultraviolet B - UVB rays) to be converted into vitamin D3. To exert its biological effects, hydroxylation must occur in the liver forming the compound 25-hydroxyvitamin D (25OHD) and another hydroxylation in the kidneys forming the final active metabolite, 1,25-dihydroxyvitamin D10. 10

According to studies, the causes of vitamin D deficiency are multifactorial, and may be related to low exposure to solar radiation, reduced bioavailability of vitamin D concerning the sequestration (storage) of this fat-soluble vitamin in the adipose tissue, which is present in excess, in the case of obesity11, and/or deficiency due to inadequate intake of food and supplements, despite the high overall caloric intake12. In addition, a decrease in the hepatic production of 25-hydroxyvitamin D due to hepatic steatosis and a decrease in the synthesis of vitamin D through the skin can also intervene13.

According to Bittar14, the lack of vitamin D after bariatric surgery can cause skeletal changes, calcium and vitamin D deficiency, increasing the risk of malignancies (colon, breast, and prostate) and chronic inflammatory or autoimmune diseases, metabolic changes, vascular disease periphery, muscle weakness and, osteoporosis or osteomalacia. Also, according to Smith15, calcitriol (1,25-$(OH)_2$D3, active form) is only produced by low serum levels of calcium (stimulated by parathyroid hormone or PTH), while high levels of calcium form 24,25- (OH)2D3 (an inactive form of vitamin D).

Given the above, it is important to analyze the appropriate dosages of vitamin D that can help in the treatment of obesity after bariatric surgery.

2 METHODS

This is a systematic literature review. For this, a search for articles published in the databases of Scielo, Pubmed and Science Direct, and Lilacs was elaborated.

Data collection was carried out with the following keywords individually or in association and their combinations in Portuguese and English: "dosages" (dosage), "suplementação" (supplementation), "vitamin D" (Vitamin D), "bariatric surgery " (bariatric surgery). There was no delimitation regarding the year of publication of the articles. Boolean exclusion operators were applied with the word "AND" or "NOT". There was no delimitation regarding the year of publication of the articles.

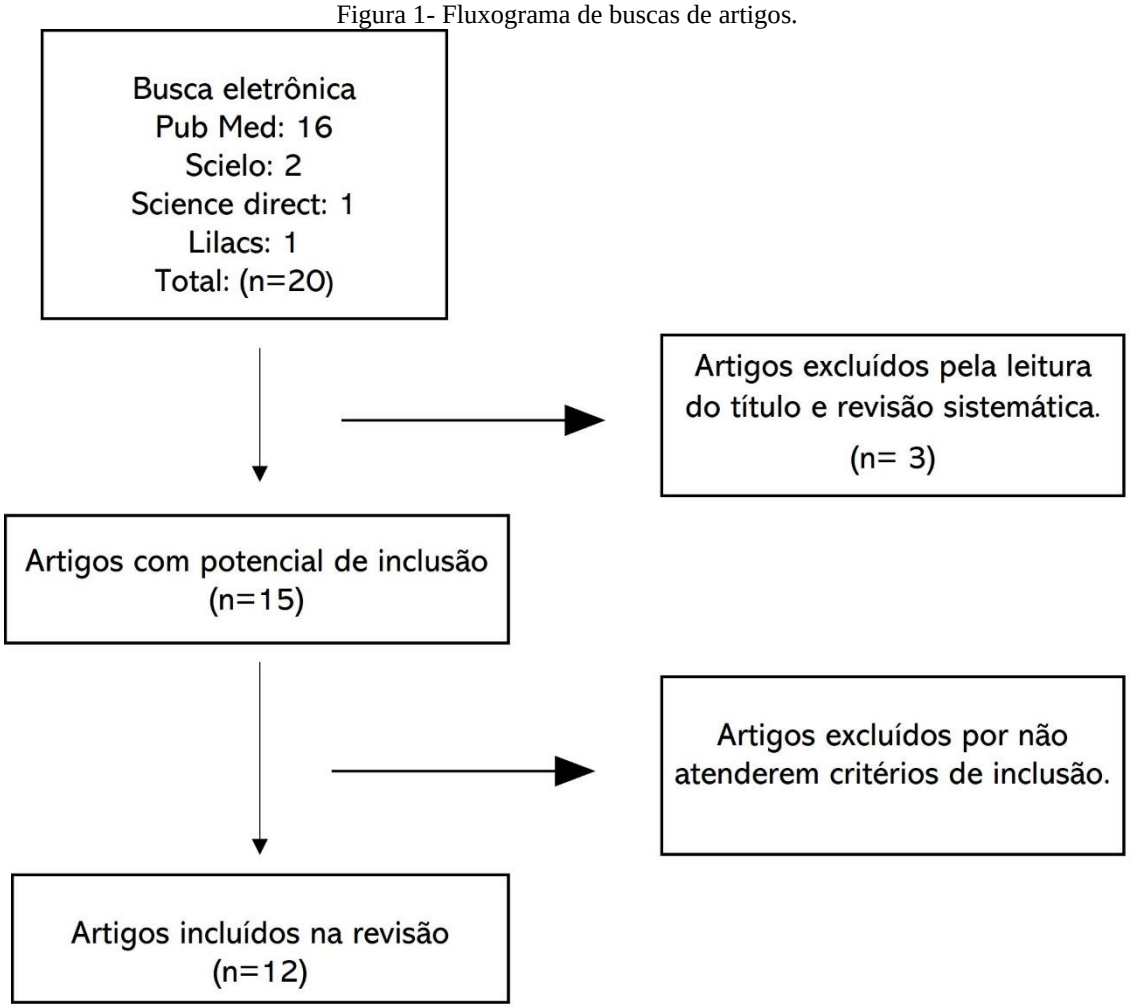
Inclusion criteria were defined as articles containing information on the use of vitamin D, its different dosages, and nutritional deficiencies after bariatric surgery. Exclusion criteria were monographs, systematic reviews, studies with animals, works that did not have a clear methodology, and research without a scientific basis.

The study was divided into three phases, the first phase of the process followed the criteria of searches and readings of articles related to the subject of bariatric surgery and vitamin D; the second phase

encompassed the choice of articles and full reading to analyze their effectiveness and descriptive contribution to the present study; while in the third phase, the production of articles, results, and discussions was carried out, according to the criteria used in the previous stages.

After searching the databases, 20 articles were identified. An analysis was performed by title to exclude articles that were repeated or excluded by the abstract. According to the eligibility criteria, 12 articles were selected for this review, where Figure 1 was drawn up, which presents methodological aspects related to the types of studies, sex, age, number of participants, types of surgery, duration of research, and results.

Figura 1- Fluxograma de buscas de artigos.

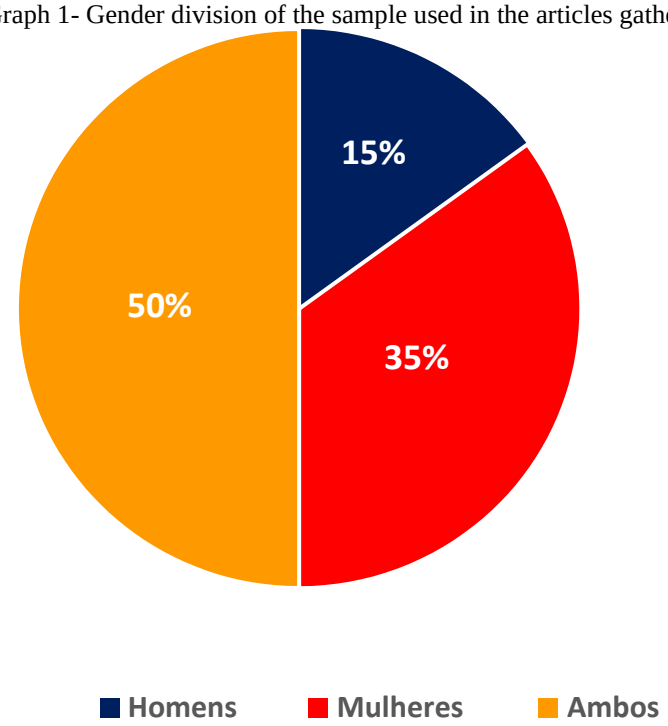


Subtitle: Articles excluded by reading the title and systematic review (n=3)
Articles with potential for inclusion (n=15)
Articles excluded for not meeting inclusion criteria
Articles included in the review (n=12)

3 RESULTS

The systematic literature search resulted in 12 analyzed articles, with the participation of 905 people, with a mean age of 45 years, ranging from men (15%), women (35%), and both sexes (50%). , with the majority including only women (Graph 1).

Graph 1- Gender division of the sample used in the articles gathered.



Subtitle: Men/Women/ Both

These studies were published between 2007 and 2021. Sample sizes ranged from 1 to 222; and among the selected articles, 1 was a case study17, 3 were prospective studies21,22,23 and 4 were a randomized double-blind clinical trial16,18,20,25 (Table 2).

Tabela 2- Características dos estudos avaliados.

Author	Type of study and No. of participants	Sex and age	No. of participants	Type of surgery and time (days)	Types of administration	Vitamin D doses	Objective
Luger et al., 2017[16]	Double-blind, randomized	M F 42	50	OLGB 6 months	-	3 doses de 100.000UI; grupo de intervenção e 3420 UI; grupo controle	To examine whether administering up to 3 oral loading doses at 1 month postoperatively (day 1 and at weeks 2 and 4) followed by an oral maintenance dose in bariatric patients can significantly increase vitamin D levels 24 weeks later surgery compared to a control group receiving placebo followed by the standard daily maintenance dose.
Papanastasiou et al., 2020[17]	Case study	F 45	1	BGYR 3 months	intramuscular	600.000 UI/ 20 days	Evaluate vitamin D deficiency, and

							osteomalacia accompanied by insufficiency fractures presented 15 years after RYGB for morbid obesity.
Goldner et al; 2009[18]	prospective randomized clinical trial	F M -	45	BGYR 24 months	-	800, 2.000 and 5.000UI/day	Evaluate patients planning to undergo roux-en-Y gastric bypass for one of three doses of vitamin D supplementation to see which is most effective.
Arts et al., 2011[19]	-	F 20-50	14	BGYR -	solubilized oral	50.000 UI/ml	To quantify RYGB-induced changes in intestinal cholecalciferol absorption to serve as a starting point for developing rational and individualized guidelines for dose adjustments to correct postoperative vitamin D deficits.
Dogan et al., 2014[20]	Randomized clinical trial	F M >18	74 74	BGYR 12 months	-	160 UI/day 500 UI/day	Evaluate the efficacy and safety of WLS Forte compared to standard MVS (MVS, commercially available tablets} after RYBG.
Lanzarini et al., 2015[21]	Prospective study	F M 18-60	96 68	LSG RYGB 24 months	-	16.000 UI/day 16.000UI/day	To assess the need for vitamin D supplementation to achieve normal vitamin D levels in morbidly obese patients after bariatric surgery.
Moore et al., 2014[22]	Prospective study	F M 24-63	22	BGYR SG 3 months	pills	2.000UI/day 1.500/ calcium citrate day	Check vitamin D3 and calcium supplementation after gastric bypass and sleeve gastrectomy.
Flores et al., 2015[23]	Prospective study	F M 18-65	176	LRYGB SG	pills	Study1:800UI 1.200	To evaluate the efficacy and

				12 months		UI/ calcium carbonate Study 2: 2.000 UI	safety of achieving vitamin D levels with two supplementation regimens after bariatric surgery.
Nelson et al., 2007[24]	-	F M -	95	BGYR 12 months	multivitamin supplement	710 UI 50.000UI/ weekly	To assess the adequacy of supplementation to correct preoperative and postoperative vitamin D deficiency in patients undergoing RYGB.
Wolf et al., 2015[25]	double-blind, Randomized and placebo-controlled	F M >18	94	BGYR 12 months	-	84 µg/ day dissolved in oil or placebo (pure oil)	To analyze whether vitamin D supplementation in an oily suspension is an effective and safe measure to prevent and achieve sufficiency, minimizing cardiometabolic risk markers.
Flores et al., 2010[26]	Intervention study	F M 44	222	BG 12 months	Combo Chewable Tablets	800 UI 1.200mg/ calcium carbonate day	To evaluate the effect of receiving or not receiving Ca and vitamin D supplementation on the Ca, PTH, and vitamin D axis in patients undergoing GB.

When assessing vitamin D and calcium supplementation after gastric bypass surgery, studies by Flores et al.23,26; and Moore et al.22, showed that both regimens of daily vitamin D3 supplementation were effective, showing that 25(OH) levels increased significantly after 12 months, and certainly since no adverse events were reported.

Studies by Lazanrini et al.21 investigated the effect of vitamin D intake after bariatric surgery. After 24 months, 68% of patients in the intervention group achieved normal vitamin D levels compared to 48% in the no-intervention group. Dogan et al20, on the other hand, demonstrated that despite the daily intake of 160 to 500 IU of vitamin D, 29% of the patients remained insufficient for vitamin D after 12 months.

In the present article, four studies investigated the effect of vitamin D supplementation in bariatric patients. Two publications compared the effects of vitamin D supplementation in patients who underwent Roux-en-Y gastric bypass (BYGB) and laparoscopic sleeve gastrectomy (LSG), and one compared this between patients who underwent BYGB and the style of life.

At the evaluation, the status of serum 25(OH)D levels before and after bariatric surgery were

analyzed. The mean 25(OH)D level before surgery was below 30 ng/ml in 6 studies and 5 of these studies showed mean 25(OH)D levels ≤ 20 ng/ml. Mean 25(OH)D levels remained below 30 ng/ml after bariatric surgery despite various vitamin D replacement regimens, with only a few exceptions.

Papanastasiou et al.17 found a patient who presented anemia deficiency in the admission laboratory test; vitamin B12 deficiency, vitamin D deficiency (25 OH D), and hyperparathyroidism, consistent with the diagnosis of osteomalacia due to severe vitamin D and calcium deficiency due to malabsorption. Treatment was started with intravenous iron and calcium gluconate and intravenous infusion of alpha-calcidiol, at the same time with calcium citrate, it was observed that one month later, calcium and phosphate levels returned to normal, PTH decreased and the vitamin D became 8.1ng/ml, with skeletal muscle and weakness mobilized. After 2 months, hyperparathyroidism and vitamin D status improved, and BTM (Basal Metabolic Rate) was increased.

In another study, Goldner et al.18 evaluated a lower dosage of vitamin D3 in two groups, one of intervention and the other of a placebo, in which it was divided into 3 doses each: 1 or 2 days, 2 weeks, and 4 weeks in the postoperative until the 6-month visit. Until the 4th week

postoperatively, it was observed that the concentration remained below 75nmo/L, showing differences between the analyzed groups after 2 months and 6 months, with the intervention group reaching a maximum concentration of 25(OH)D of 75.7 nmol/ L at 4.7 months. The control group demonstrated a Cmax of 67.5 nmol/L at 4.2 months for the duration of the study.

4 DISCUSSION

Obesity is a chronic disease characterized by excessive accumulation of adipose tissue in the body, with an increase in its prevalence over the last decade26. The main findings show that the obesity epidemic is one of the greatest public health, social and economic challenges of the 21st century22, so that bariatric surgery ends up being an effective alternative in weight loss, improving the metabolic profile, quality of life, and, consequently, reducing the mortality rate18,19.

The main findings in this study show that bariatric surgery can cause alterations in the anatomy of the gastrointestinal tract23,25, causing malabsorption of essential vitamins (folate, vitamin B12, and vitamin D) and micronutrients (for example, iron, and calcium), as well as abnormalities in bone metabolism16,20,25.

As mentioned above, the study by Dogan et al20 observed the effectiveness of a multivitamin supplement specifically designed for patients who underwent Roux-en-Y gastric bypass (RYGB) surgery through a triple-blind randomized clinical trial. After laboratory blood tests, 29% of the observed patients were identified with a vitamin D deficit after 12 months, which was corrected with solubilized oral cholecalciferol 50,000 IU/mL. During the observation period, patients received 1500 mg of calcium carbonate and 1200 IU of vitamin D daily as a standard postoperative protocol.

Other studies found a high incidence of vitamin D deficiency (34% –73%) after RYGB, however,

the exact mechanisms of postoperative vitamin D deficiency are still not completely understood, as evidenced in the study by Wolf et al25, Therefore, a daily intake of 2,000 IU of vitamin D is recommended, in addition to 1,500 to 2,000 mg of calcium per day30. However, the study by Lanzarini et al21 mentions that postoperative vitamin D supplements should vary between 320IU and 2000IU per day, with a calcium intake of 1000 to 1500mg per day.31

Corroborating with the aforementioned authors, according to the study by Papanastasiou17, regular oral supplementation with high doses of vitamin D together with calcium is necessary. However, the study by Carlin et al32 demonstrated that, despite the daily intake of 800 IU of vitamin D, 44% of the population that undergoes this type of surgical procedure remained with a deficit of vitamin D in the body.

In his study, Papanastasiou17 reported on severe vitamin D deficiency osteomalacia after bypass surgery for morbid obesity. The patient had iron and vitamin D deficiency anemia and secondary hyperparathyroidism. Furthermore, due to vitamin D deficiency and calcium malabsorption, she was diagnosed with Osteomalacia. The treatment was based on ergocalciferol intramuscularly, 600,000 IU every 20 days, and 500g of calcium citrate 4x a day. The study showed that such medications provided improvement about three months after treatment, in the clinical and biochemical aspects.

In the context of the above, the study by Collazo-Clavell et al33 points out that since 2004 the effectiveness of using aggressive calcium (1.8 g per day) and vitamin D supplementation (ergocalciferol 50,000 IU per day) has been reported to correct vitamin D deficiency and osteomalacia after gastric bypass surgery.

Moore22 in his study demonstrated that vitamin D deficiency in women who underwent bariatric surgery decreased from 60.6% preoperatively to 26.1% after 3 months of dietary intake of vitamin D and calcium with the use of 2,000 international units (IU) of vitamin D3 and 1,500 mg of calcium citrate, significantly increasing 25 (OH) D concentrations. However, some patients remained with vitamin D deficiency, suggesting more aggressive supplementation.

By analyzing the efficacy and safety of a vitamin D forced dosage regimen and its interventional effects in patients with liver fibrosis, Luger et al16 conclude that vitamin D has been proposed as a potential therapeutic option for liver fibrosis due to its metabolic effects, anti-inflammatory and antifibrotic agents in hepatocytes and liver cells. Results showed that the vitamin D3 loading dose regimen was the only one effective in increasing 25(OH)D concentrations in patients with significant liver fibrosis over the 6 months in contrast to the conventional regimen using the same dose of vitamin D3. maintenance.

Evaluating 14 morbidly obese premenopausal women before and 4 weeks after laparoscopic RYGB, Aarts et al19 point out that for the normalization of vitamin D levels due to malabsorption induced by surgery, cholecalciferol (type of Vitamin D) was used. , with a single oral dose of 50,000 IU of the solubilized vitamin, which reduced peak cholecalciferol levels by about 25% after RYGB.

In this same context, Avioli et al34 point out that the correction of vitamin D deficits after surgery is complex because the necessary dose adjustments to overcome malabsorption are currently not known.

This lack of knowledge makes it difficult to develop rational guidelines to correct postoperative calcium and vitamin D deficits. Therefore, the development of further studies to verify this specific analysis are recommended.

Nelson et al24 presented evidence that vitamin D deficiency was effectively corrected after RYGB surgery with 710 IU of vitamin D per day or 50,000 IU weekly (doses applied in two different groups). The author further points out that current supplementation practices do not appear to optimize serum 25(OH)D levels and need to be examined more closely with further studies.

With a similar objective to the aforementioned author, Goldner18 demonstrated that more aggressive vitamin D supplementation tends to increase 25OHD levels. Vitamin D replacement up to 5,000 IU/day is safe and necessary in many patients to treat vitamin D deficiency after Roux-en-Y gastric bypass.

Flores et al26, in their review study on the efficacy and safety of achieving 25-hydroxy VD (25 (OH) D) levels ≥75 nmol/L with two regimens of VD supplementation after LYRGB in a period from 2009 to 2011, showed that the standard doses of 800 IU of VD were enough to reach the levels of VD satisfactorily in 4 months, therefore, it was verified that the daily supplementation of VD3 in high and fixed doses, proved to be effective and safe in clinical practice, showing improvements in patients with vitamin D deficiency.

Despite presenting relevant improvements, and its importance in bone metabolism and calcium homeostasis, the study by Arunabhs et al35 comments on the relationship between vitamin D and obesity. An association between adiposity and serum 25-hydroxyvitamin D [25(OH)D] levels, the relevant marker of low vitamin D status, was found in adults and children. In adults, an inverse relationship has been reported between fat mass and circulating 25(OH)D concentrations.

5 CONCLUSION

The results of this review showed that vitamin D supplementation in most publications improved serum levels of vitamin D. However, further intervention studies are needed to determine the optimal dose of vitamin D supplementation and replacement in individuals undergoing bariatric surgery, as patients with other pathologies may interfere with the effects of supplementation.

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