

Bariatric surgery: how and why to supplement

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ABSTRACT

Patients undergoing bariatric surgery are at increased risk of developing nutritional deficiencies from the limited intake and absorption of different nutrients. Thus, a systematic review on PubMed and ISI Web of Science was conducted, including articles from September 1983 to April 2010, to identify literature regarding nutritional deficiencies following bariatric surgery and how treatment is carried out. The keywords used individually or in combinations were: bariatric surgery, obesity, vitamin/mineral deficiencies, protein deficiency, nutrient absorption, and nutrient supplementation. The literature suggests the use of nutritional supplementation to prevent or treat nutritional deficiencies resulting from anatomical changes due to surgical techniques. The success of oral nutritional supplementation in correcting or preventing nutritional deficiencies depends on several factors. Thus, it is very important in clinical practice to understand how the nutrients can be administered. This review aims is to assist in better selecting the nutrients to ensure an appropriate nutrient replacement in patients undergoing bariatric surgery.

Keywords: Nutritional deficiencies; bariatric surgery; gastric bypass; dietary supplements.

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INTRODUCTION

Currently, bariatric surgery is considered the most effective tool in severe obesity control and treatment. The surgery benefits include healing or marked improvement of chronic diseases, such as hypertension, diabetes and hyperlipidemia¹. However, it must be noted that surgical treatment of obesity is not confined to surgery.

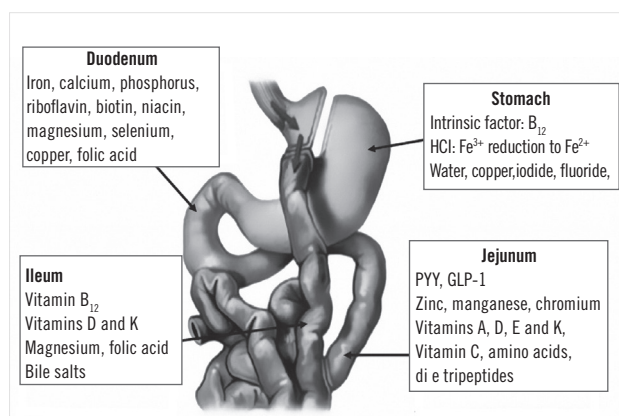
In vivo studies have demonstrated that some nutritional deficiencies encompassing vitamin D²⁻⁴, vitamin A^{5,6} and zinc are concomitantly present in obesity, possibly by playing important role in adiposity regulation or in appetite regulation mechanisms. Thus, a careful planning for clinical-nutritional follow-up is essential. Both pre- and early and late postoperative is extremely important for treatment success¹⁰. In this setting, the phrase “healthy weight loss” has been well applied.

The implications of surgical procedures on the patient's nutritional status are specifically due to anatomical and physiological changes impairing absorption pathways and/or food intake. A good understanding of gastrointestinal tract absorption physiology is very important to understand potential nutritional deficiencies following surgery (Figure 1)^{10,11}.

The main type of bariatric surgery currently performed is the Roux-en-Y gastric bypass (RYGB)¹², a mixed surgical technique by restricting the gastric cavity size and hence the amount of food ingested and by reducing the bowel surface in contact with the food (dysabsorption).

The poor nutrient absorption is one of the explanations for the weight loss reached by using dysabsorptive techniques, such as the biliopancreatic diversion with duodenal switch (BPD), with 25% of protein and 72% of fat no longer being absorbed¹³. Automatically, nutrients depending on dietary fat to be absorbed, such as liposoluble vitamins and zinc, are more susceptible to malabsorption from this kind of procedure¹⁴.

Figure 1 – Roux-en-Y gastric bypass technique and its main metabolic changes. Smaller rectangles show the nutrients and/or hormone production (arrows indicating the main absorption sites and/or production site).



Vitamins and minerals are essential factors and cofactors in many biological processes regulating directly or indirectly the body weight (Table 1). The metabolic benefits of these micronutrients in controlling the weight loss include regulation of appetite, hunger, nutrient absorption, metabolic rate, lipid and carbohydrate metabolism, the functions of thyroid and adrenal glands, energy store, glucose homeostasis, and neural activities among others. Thus, the “adequacy” of micronutrients is important not only for health maintenance, but also for achieving maximum success in maintaining long-term weight loss¹³.

The symptoms of micronutrient deficiency are usually nonspecific in subclinical levels, and the physical exam may not be reliable for an early diagnosis without a laboratory confirmation. Thus, specific clinical signs are only noticeable in a developed phase of the deficiency¹⁵.

Considering the increasing number of bariatric surgeries currently performed and the presence of nutritional deficiencies found in these patients, we will address in this review a few nutrition supplementation forms currently proposed in literature with the purpose of better selecting the nutrients and ensure the appropriate replacement of nutrients.

METHODOLOGY

A systematic review in several data bases, such as PubMed (US National Library of Medicine, Bethesda, MD) and ISI Web of Science (Science Citation Index Expanded) was conducted. The following keywords were used individually or in combinations: bariatric surgery, obesity, gastric bypass, dietary supplement, vitamin deficiencies, mineral deficiencies, and nutrient absorption. Sixty-eight articles, published between September 1983 and April 2010, were selected, including two meta-analysis and two international guidelines for clinical practice in bariatric surgery. Only two studies were not conducted in humans.

NUTRITIONAL SUPPLEMENTATION

Micronutrient deficiencies are the main changes that put the surgical procedure success at risk¹⁶. Prevention of vitamin and mineral deficiencies requires long-term patient's follow-up and understanding of the functions of these micronutrients in human body, in addition to the deficiency signs and symptoms. The long-term nutritional supplementation, although so stressed as an important conduct, still represents a hindrance to success in surgical treatment of obesity¹⁷.

The regular use of a nutritional supplementation has been advocated when appropriately done: at least five times a week¹³. However, only 33% of patients comply with that recommendation, and 7.7% stop using the multivitamins/minerals two years after surgery¹⁸.

The replacement and incorporation of micronutrients from food into the body is the most appropriate way to

Table 1 – Bariatric surgery outcomes warranting nutritional supplementation

Surgical technique outcomes	Nutritional implications
– Gastric capacity restraining	– Lower calory and micronutrient intake and lower HCl production by the stomach
– Exclusion of stomach and bowel from the food transit	– Reduced contact surface for absorption, limited production of factors required for nutrient absorption (e.g., intrinsic factor and digestive enzymes)
– Food intolerance	– Exclusion of food containing sources of key nutrients for health

keep the body stores within the desirable level. However, a few factors warrant the nutritional supplementation in patients undergoing bariatric surgery (Table1). Therefore, the use of an appropriate multivitamin/mineral daily dose is a way to ensure the appropriate nutritional support of micronutrients for a good functioning of processes assisting in body weight regulation¹³.

The concern with micronutrient bioavailability influences on the supplementation efficacy. Accordingly, it is important to consider the quantitative and qualitative composition of marketed supplements. When choosing a supplement, consider:

- pH (acid or alkaline): required gastrointestinal pH to solubilize the nutrient;
- qualitative composition of the supplement: aqueous solution, capsule, powder;
- dependence of gastrointestinal enzymes assisting in some micronutrient absorption;
- bowel integrity and absorption surface;
- administration route: oral, intramuscular or intravenous, according to degree of nutritional deficiency;
- quantity and micronutrient type present in the composition.

With the advent of compounding pharmacies, it is possible to prepare vitamin and mineral formulations in several combinations, using the desired dose and at times with a similar or lower cost than commercial standard multivitamins. When opting for this form of supplementation, the clinician should be aware of the prescription form.

Other considerations are important when recommending multivitamins/minerals already marketed (Table 2). Usually folic acid and vitamin B₁₂ are present in lower

Table 2 – Guidelines for choosing preventive nutritional supplementation following bariatric surgery

Supplement/characteristics	Dose
Multivitamin/mineral ^a	1 to 2 tablets/day
Folic acid	> 400 mg
Iron (ferrous fumarate)	> 18 mg
Formulated with zinc and selenium	—

Adapted from AACE/TOS/ASMBS Bariatric Surgery Guidelines, 2008.13. Recommendations for micronutrient deficiency prevention. aThe prevention should start on the first day after hospital discharge. Patients with pre- and postoperative nutritional deficiencies should be treated according to Table 3 for isolated supplementation.

amounts and the formulations contain moderate doses of folate (200 – 400 mcg) and low doses of vitamin B₁₂ (5-50 mcg). All patients undergoing BYGB and BPD should be supplemented with multivitamins/minerals as fully as possible, including liposoluble vitamins and minerals¹⁹.

It is important to remember that some nutrients require a specialized mixture to obtain maximum absorption. For instance, iron is better absorbed in an acid environment and liposoluble vitamins require a lipid source. In addition, certain nutrients are preferentially absorbed at proximal bowel while others at the distal bowel, as demonstrated in Figure 1. Thus, the kind or surgical procedure performed also influence the care in nutritional supplement choice. In Roux-en-Y gastric bypass (RYGB), e.g., there is a prevalence of vitamin B₁₂, iron, and folic acid deficiencies¹⁴. On the other hand, following biliopancreatic diversion/duodenal swich (BPD/DS), only 28% of lipids ingested are absorbed²⁰.

Starting multivitamin/mineral supplementation or isolate iron replacement has been recommended soon after hospital discharge¹³. However, some hospitals have already made such supplementation available in the early postoperative period (48 hours).

Isolate supplementation of vitamins and/or minerals is used in cases of nutritional deficiency diagnosis or when there is a purpose of reducing the interaction with other nutrients that could impair their absorption (Table 3). In this case, the clinician and nutritionist determine whether a multivitamin/mineral supplementation may remain or not concurrently with deficiency therapy. Below we will report studied forms of supplementation after bariatric surgery.

THIAMINE

Thiamine deficiency may occur acutely following any type of bariatric surgery in patients presenting with longstanding vomiting and is associated with severe neurological symptoms that could even be irreversible²¹⁻²³.

Thiamine deficiency following bariatric surgery has been treated together with other B complex vitamins and magnesium to achieve maximum thiamine absorption and appropriate neurological function²⁴.

The first symptoms of neuropathy can often be resolved by oral supplementation with thiamine 20-30 mg/

Table 3 – Guidelines for isolated nutritional supplementation

Supplement	Dose
Thiamine	20-30 mg/day 50-100 mg/day (intravenously or intramuscularly) 100 mg/day (WKS)
Vitamin B ₁₂	≥ 350 mg/day (oral prevention) 500 mg/day (oral treatment) or 1,000 mg/mol (IM) or 3,000 mg/ six-monthly (IM) or 500 mg weekly (nasally or sublingually)
Calcium citrate	1,500 mg/day (AGB) 1,500 to 2,000 mg/day (RYGB) 1,800 to 2,500 mg/day (BPD/DS)
Elemental iron	40 to 65 mg/day (oral prevention) 300 mg/day (oral treatment)
Liposoluble vitamins	10,000 to 100,000 IU / day of vitamin A > 2,000 IU of vitamin D (cholecalciferol) 100 to 400 IU/day

Wernicke-Korsakoff syndrome (WKS), intramuscular (IM) route; AGB, adjustable gastric band (AGB); Roux-en-Y gastric bypass (RYGB); biliopancreatic diversion/duodenal switch (BPD/DS).

day until symptoms subside. When there are signs of a more advanced neuropathy or in the presence of persisting vomiting, 50-100 mg/day intravenously or intramuscularly may be required.

In the presence of the Wernicke-Korsakoff syndrome, a supplementation above 100 mg/day is required²⁵. This syndrome is characterized by signs such as ophthalmoplegia (lateral rectus muscle and conjugate gaze palsy or weakness), ataxia (ambulation or posture impairment and slow gait), and mental and conscience disorders.

Most common risk factors associated with thiamine deficiency are: weight loss percentage, gastric symptoms persistence (nausea and vomiting), non-adherence to nutritional follow-up, the reduction of albumin and transferrin, the presence of jejunioileal bypass²⁶. Many reported cases are related to prolonged vomiting, starvation and, more often, alcoholism²⁶⁻²⁸.

VITAMIN B₁₂

Vitamin B₁₂ deficiency has been often reported following RYGB, with its incidence varying between 12% and 75%²⁹⁻³². Low vitamin B₁₂ levels can be seen at six months postoperatively, but they occur mostly at one year or more when liver storages is found to be depleted³². High prevalence of such a deficiency has also been reported ten years after the surgery³³.

Regarding vitamin B₁₂ absorption, it is important to remember that initially it needs to be liberated from the food source (particularly red meat).

The releasing is facilitated by the presence of gastric acid. Free vitamin B₁₂ then binds to R-protein in the stomach and is cleaved in the duodenum to bind intrinsic factor (IF). The B₁₂-IF complex circulates intact through the gastrointestinal tract to its absorption site (ileum). Marcuard *et al.*³⁴ observed low IF levels in 53% of patients with vitamin deficiency after RYGB.

The frequent absence of symptoms in the presence of vitamin B₁₂ deficiency and the irreversible neurologic damage risk¹³ require a careful decision about supplementing or not the vitamin in a preventive manner. Vitamin B₁₂ is present in the nutritional composition of most multivitamins commercially available, however, the amounts vary widely.

Vitamina B₁₂ deficiency is usually defined as levels below 200 pg/mL. However, about 50% of patients with clear deficiency signs and symptoms show normal levels³⁵. Regarding prevention, a 350 mcg/day oral dose could prevent deficiency in 95% of patients³², and a 500 a 1,000 mcg/day dose has been used to treat the deficiency^{11,18}.

Currently, B₁₂ supplementation is also commercially available as a spray to be applied sublingually. This kind of supplementation is presented as nanoparticles to increase vitamin absorption and bioavailability. Although vitamin B₁₂ deficiency occurs only after a few months from bariatric surgery, a good clinical practice has been preventively administering 1000 mg vitamin B₁₂ parenterally over the preoperative period³⁶.

FOLIC ACID

Folic acid deficiency has been observed mainly after RYGB. It can manifest as macrocytic anemia, leukopenia, thrombocytopenia, glossitis, or megaloblastic bone marrow. Most of the time, folic acid deficiency occurs after bariatric surgery due to reduced intake and not resulting from poor absorption³⁷.

Although less frequent than vitamin B₁₂ deficiency, low levels of folic acid have been reported between 6% and 65% of patients undergoing RYGB^{29,38,39} and can easily be treated by oral supplementation³⁷.

Folic acid absorption occurs preferably in the duodenum, but it can also occur along the entire small bowel length due to a physiological adaptation after surgery. Vitamin B₁₂ is required to convert methyl-tetrahydrofolic acid (inactive) into tetrahydrofolic acid (active). Therefore, vitamin B₁₂ deficiency can result from folic acid deficiency^{30,37}.

In general, folic acid deficiency is treated with 1,000 mg/day of folic acid (orally) for one to two months⁴⁰ and can be prevented with a supplement containing 200% the recommended daily value (800 mg/day). This level can also benefit the fetus in case of an unaware pregnancy in the post-operative phase. A supplementation higher than 1,000 mg/day can “mask” a vitamin B₁₂ deficiency diag-

nosis, thereof the importance of monitoring the vitamin blood levels mostly when high folic acid dose supplementation is adopted¹³.

IRON

Anemia can affect two-thirds of patients undergoing bariatric surgery, usually caused by iron deficiency. In patients undergoing RYGB, the deficiency ranges from 20% to 49%^{32,37,40}. Among superobese patients, anemia is reported in 35-74% and iron deficiency can reach 52% in late post-operative period⁴¹.

In patients undergoing bariatric surgery, the amount of daily intake of elemental iron (ferrous sulfate or ferrous fumarate) should reach 40 to 100 mg/day although the long-term prophylactic treatment efficacy is unknown³².

The amount of elemental iron present in most commercial multivitamins is usually small (10 to 20 mg per tablet), which is considered insufficient to prevent iron deficiency in patients undergoing RYGB. The current recommendations include administering 40 to 65 mg elemental iron daily (200-400 mg ferrous sulphate). In women of childbearing age, the recommendations increase to 100 mg elemental iron daily (400 to 800 mg ferrous sulphate)^{10,35,42}. Thus, the anemia clinical course, laboratory value changes, age, gender, and reproductive considerations should be analyzed.

On the other hand, iron deficiency treatment requires supplementation up to 300 mg/day, usually three to four tablets containing 50 to 65 mg elemental iron¹³. When treatment fails or in the presence of severe anemia, intravenous doses of an iron hydroxide-saccharose complex are required (20 mg elemental iron per mL)^{43,44}.

Currently, commercially available multivitamins, mainly in the United States, lack iron in their composition to ensure that this replacement must be performed in isolation and at different times of day. It is important to consider the different absorption characteristics of various iron supplementation types available in the market:

Ferrous fumarate: 33% elemental iron, usually well tolerated by patients and showing good mineral absorption.

Ferrous sulphate: only 20% elemental iron and showing larger gastrointestinal effects.

Ferrouyl: 98% elemental iron. Elemental iron with reduced particles.

Ideally, the iron supplement should be accompanied by vitamin C and fructo-oligosaccharides to prevent constipation, improve intestinal flora, and provide better absorption of the mineral. Other important consideration is related to iron interaction with other elements, such as calcium and phytate⁴⁵, and it is important to supplement it alone and in the fasting state. In addition, copper deficiency can cause anemia, with some authors recommending

supplementation with 900 mg/day copper or an additional supplementation with 50 to 200 mg/day according to the surgical technique used.

CALCIUM AND VITAMIN D

Calcium and vitamin D supplementation has been recommended in most weight loss therapies in order to prevent bone reabsorption⁴⁶. The preferable way of supplementing has been widely discussed in clinical practice. In the presence of a less acid environment, such as the small stomach after a bariatric surgery, calcium carbonate absorption becomes impaired⁴⁷.

A meta-analysis suggests calcium citrate is more bio-available than calcium carbonate, around 22% to 27%⁴⁸. In patients undergoing RYGB, calcium citrate (500 mg/day associated with 125 IU vitamin D₃-cholecalciferol), demonstrated a greater increase in calcium serum levels and greater reduction in parathyroid hormone (PTH) than the same amounts of calcium carbonate supplemented⁴⁹. PTH is the main regulator of calcium homeostasis in mammals and also acts in forming 1,25 (OH)₂D, a metabolite responsible for almost all actions of vitamin D. High calcium levels inhibit PTH release, while low calcium levels leads to increased PTH release by parathyroid glands⁵⁰. Furthermore, calcium absorption occurs in the bowel under vitamin D influence⁵¹.

A vitamin D deficiency after bariatric surgery has been reported among 50-80% of the cases^{14,52-54}. Some studies demonstrated that over 50% of patients that show vitamin D deficiency after bariatric surgery used multivitamins containing 400-800 IU of vitamin D per day.^{14,52,53} Other studies found a postoperative supplementation with 1,200 mg/day calcium carbonate and 400 to 800 IU vitamin D₃ (cholecalciferol) present in multivitamins/minerals was not enough to prevent high levels of PTH and bone reabsorption^{46,55,56}. Thus, over 50% of patients undergoing RYGB showed calcium deficiency in the presence of that supplementation pattern⁵⁷. However, increasing calcium citrate doses from 1000 mg to 1700/day (including 400 IU of vitamin D) could reduce bone loss even in the presence or weight loss⁵⁸. Thus, the current calcium supplementation recommendation in the postoperative phase varies according to the surgical technique applied.

Regarding vitamin D, when a deficiency is present pre-operatively, the supplementation with 5000 IU of oral cholecalciferol once a week for eight weeks is recommended⁵⁹. Postoperatively, the same dose was not enough to treat vitamin D deficiency⁶⁰. Thus, there is no appropriate dose for all patients undergoing bariatric surgery yet. However, doses as high as 5000 IU/day have been found safe and potentially required to treat the secondary hyperparathyroidism present in some patients. We suggest it is appropriate to start supplementation with 2000 IU/day of vitamin D postoperatively, preferably as vitamin D₃ (cholecalciferol).

Attention should be given to other factors such as patients taking anticonvulsants, glucocorticoids, heparin, or cholestyramine with a higher risk for bone disease.

VITAMIN A AND VITAMIN E

Yearly monitoring of liposoluble nutrients should be obtained after disabsorptive procedures. The recommendation of 50,000 IU of vitamin A every other week has been suggested to correct most deficiency cases¹⁹. In their study, Sugerma *et al.*⁶¹ reported that supplementation of 10,000 IU of vitamin A was sufficient to prevent any deficiency. Actually, the doses used in treating vitamin A deficiency vary according to the signs and symptoms presented. In the absence of corneal changes, the supplementation with 10,000 to 25,000 IU/day is recommended until there is clinical improvement of symptoms (normally between 1 and 2 weeks); in the presence of corneal changes, 50,000 to 100,000 IU/day (intramuscularly) for 2 weeks are required¹³. It is also important to assess iron and copper deficiency, as it can hamper the resolution of vitamin A deficiency.

Regarding vitamin E, there is no therapeutic recommendation considered ideal or clearly defined. The potential antioxidant effects of vitamin E can be achieved with supplementation of 100 to 400 IU/day¹³.

PROTEINS

Protein deficiency is the most often reported among macronutrients. It is observed mainly after disabsorptive or mixed surgical techniques (DBP/DS and RYGB)¹³. Only 57% of the ingested protein is estimated to be absorbed after bowel bypass^{10,62}.

The hypoalbuminemia (albumin < 3.5 g/dL) after RYGB may vary from 13% two years after the surgery⁶³ to 27.9% after ten years³³ or it might even be absent in the first months⁶⁴⁻⁶⁶.

Some experts recommend 70 g/day of protein during caloric restriction to lose weight⁶⁷. However, many bariatric surgery programs recommend 60 to 80 g/day of protein or 1.0 to 1.5 g/kg of optimum body weight, although the exact requirements have not been defined yet. The patient should be instructed to use high biological value powder protein supplements 48 hours after the surgery.

Meat, poultry, fish, eggs, milk and dairy should be encouraged still in the first postoperative months according to the diet evolution protocol. Protein intake should be periodically evaluated in each nutritional visit. In the presence of clinical or subclinical protein deficiency, even in the absence of vomiting or food intolerance, the patients must be treated with hyperproteic diet⁶⁸.

Protein modules are widely available on the market. However, factors such as flavor, texture, solubilization, absorption, and cost are considered important when choosing the supplements. The amine acid profile should be given

priority when the supplement is the only protein source in the diet. Whey protein can be an excellent choice, since it has high level of branched-chain amine acids, which are important to prevent muscle tissue degradation, remain stable in the stomach, are rapidly digested, and lactose-free. Currently, there is a hydrolyzed whey protein product which reduces allergenicity and improves absorption.

CONCLUSION

There are no absolutely appropriate recommendations to prevent or treat most nutritional deficiencies after bariatric surgery yet; however, it is clear that preventive supplementation has been increasingly important in this setting.

Many factors are involved in causing such deficiencies. Even before any surgical intervention, obesity can be associated with subclinical nutritional deficiencies that could be aggravated after the anatomical and physiological changes caused in gastrointestinal tract. In addition, there is a limitation and/or change in the dietary intake. Therefore, nutritional supplementation becomes a necessary alternative therapy, contributing to weight loss in a healthy manner and, in most cases, it should be evaluated individually.

The preventive use of multivitamins/minerals should compound the care protocol in all patients undergoing bariatric surgery, mainly in those undergoing techniques involving a certain degree of dysabsorption. The treatment of these patients' nutritional deficiencies should consider micronutrient megadoses due to lower bioavailability resulting from physiological changes provided by the surgical techniques. Further studies are required to establish an effective dose to treat nutritional deficiencies following bariatric surgery.

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