Current Perspectives

Supplementation in Bariatric Patients: What is Really Important?

Suplementação em Doentes Bariátricos: O Que é Realmente Importante?

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INTRODUCTION

For over two decades, bariatric and metabolic surgery has been recognized as the most effective treatment for severe obesity and type 2 diabetes. However, its metabolic benefits, as well as the promotion of health and quality of life, are sometimes compromised due to possible complications, such as nutritional deficiencies. These require daily attention in the practice of the multidisciplinary team, hence the latent importance of the topic.

THE PAST

Jejunoileal resection for the treatment of obesity is considered the original bariatric surgical technique. Developed in 1952 by the Swedish surgeon Victor Henriksen, it was followed by the

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introduction of jejunoileal bypass without intestinal resection by Kremen in 1954.1 These techniques had a high incidence of early and late complications, including multiple nutritional deficiencies. At the end of the 1970s, the concept of gastric bypass was developed, first in the Billroth II configuration, later modified to Roux-en-Y. This achieved effective weight loss and demonstrated a lower risk of complications, including nutritional deficiencies.

Studies conducted in the 1980s with post-gastric bypass patients demonstrated the presence of anemia and that vitamin B12, folate, iron, and potassium were also commonly found at reduced levels. In addition to this evidence, there were reports from the previous decade of neurological sequelae related to thiamine deficiency, Guillain Barré syndrome, and bone marrow suppression associated with micronutrient deficiencies.2 At that time, it became clear that greater care was needed with vitamin B12 due to stomach reduction and the consequent decrease of intrinsic factor production, as was the case in cancer surgeries that required gastrectomies.

In the 1990s, intervention studies were pursued to demonstrate the feasibility of oral vitamin B12 supplementation, as until then had not been possible to demonstrate satisfactory results in improving the absorption of this B complex vitamin.[3] Prophylactic iron supplementation, especially in young and premenopausal women, was already emphasized.4 Clinical signs and symptoms resulting from vitamin B complex deficiency were evaluated.

In contrast, bone mass reduction was not given priority because its signs and symptoms were late. In a meta-analysis, Sakhae K & Cols. (1999)[5] compared the bioavailability of calcium citrate with calcium carbonate, taken on an empty stomach or administered with meals. They demonstrated that calcium citrate absorption was consistently higher than that calcium carbonate. So, calcium citrate supplementation would be more appropriate due to its bioavailability, considering that the target population is predominantly female. Preventing osteopenia and the development of osteoporosis was already a premise of post-operative care.

THE PRESENT

The evidence accumulated in previous decades led to the publication of the first Clinical Practice Guidelines for Perioperative Nutritional Care in Bariatric Surgery in 2008. Initially, supplementation recommendations emphasized the characteristics of surgical techniques and the importance of monitoring. Over the years, there has been notable progress in this area. In light of new evidence, supplementation recommendations in bariatric and metabolic surgery require personalized nutritional care (Table 1).

Despite the growing development of supplements considered "specialized for bariatric patients" over the last decade, many of them have limitations in terms of their composition, bioavailability and nutrients incompatibility. Examples include: the presence of iron and calcium in the same formulation, inactive forms of vitamin B9 and vitamin B12, retinol instead of ß-carotene, iron content that only meets masculine needs, absence of magnesium, and formulations that are unsuitable for patients above 65 years.

Recently, there have been progressive improvements, such as greater diversity of pharmaceutical forms, more palatable with chewable tablets or sublingual, and sprays.

New technologies allow for greater efficiency in the absorption and bioavailability of micronutrients, in the form of chelated or organic, liposomal vitamins and minerals. Adherence to supplementation remains a considerable challenge, with several determining factors influencing it in the medium and long term. The development of new and more palatable pharmaceutical forms contributes to overcome these challenges (Fig. 1).

There is an inadequate understanding of the importance of continuous supplementation. This contrasts with the ready acceptance of chronic medication when there is a recognized disease. The immediate consequences of vitamin and mineral deficiencies are often difficult to diagnose, leading to an underestimate the seriousness of irregular use or non-use of supplementation.

The classic SOS (Swedish Obese Subjects study) further reinforces the importance of long-term nutritional adherence and monitoring.6 Researchers analyzed significant anemia events and their causes in individuals who underwent bariatric surgery over a 20-year period. The results of the assessment (risk of anemia, association of vitamin B12 or iron deficiency, deficiency of vitamin B12) highlighted the importance to the importance of prevention and early detection of severe nutritional deficiencies, which should be carried out continuously and over the long term.

However, it is well known that preventive nutritional supplementation often fails to prevent severe cases of anemia that require intravenous nutritional supplementation, the most effective treatment.

Table 1 – Evolution of nutritional supplementation recommendations in different guidelines for bariatric and metabolic surgery.

Year	Guidelines	Recommendations
2008	ASMBS Allied Health Nutritional Guidelines for the Surgical Weight Loss Patient. doi: 10.1016/j.soard.2008.03.002	AGB, RYGB: 1/3 of the multivitamin and mineral nutrients should be 100% of the RDI. DBP/DS: 2/3 of the multivitamin and mineral nutrients should be 200% of the RDI. Start supplementation on the first day of hospital discharge. Calcium: Consider dietary calcium intake plus calcium supplementation to meet the recommended intake.
	Guidelines for Clinical Practice for the Perioperative Nutritional, Metabolic, and Nonsurgical Support of the Bariatric Surgery Patient. doi: 10.1016/j.soard.2008.08.009.	Minimum nutritional supplementation: 1 to 2 adult multivitamin and mineral supplements containing iron, calcium citrate malate (1200 to 1500 mg/day), and a B-complex vitamin preparation. Fat-soluble vitamins (A, D, E, K): two tablets/day
2013	Clinical Practice Guidelines for the Perioperative Nutritional, Metabolic, and Nonsurgical Support of the Bariatric Surgery Patient--2013 update: Surgery. doi: 10.4158/EP12437.	Gastric sleeve supplementation RYGB and DBP/DS: the recommended nutrient levels are similar.
2014	Interdisciplinary European Guidelines on Metabolic and Bariatric Surgery. doi: 10.1159/000355480.	RYGB: Oral vitamin and micronutrient supplements should be prescribed routinely. BDP/DS: Daily vitamin and micronutrient supplementation for life. Vitamins A, D, E, and K. Parenteral supplementation: Correction of deficiencies, except for Ca
2016	Nutrition Guidelines for the Indian Population. doi: 10.1007/s11695-015-1836-y	Recommendations for vegetarians Iron: minimum recommended doses 28 to 30 mg/day, either ferrous fumarate or glycinate, preferably with the addition of ascorbic acid to increase absorption. Vitamin B12: in severe deficiency, administered intramuscularly (twice/week). Sublingual or nasal administration is recommended only as a maintenance dose. Methylcobalamin. Vitamin A and E: daily, as deficiency is a public health problem.
2017	Integrated Health Nutritional Guidelines for the Surgical Weight Loss Patient 2016 Update: Micronutrients. doi: 10.1016/j.soard.2016.12.018	Calcium: Calcium carbonate should be administered with meals, and calcium citrate can be administered with or without meals. Vitamins A and K: Similar doses for SG and RYGB. Vitamin E: Similar doses for LAGB, SG, RYGB, and BPD/DS. Copper/zinc ratio: 1 mg of copper for every 8–15 mg of elemental zinc to prevent copper deficiency. Copper gluconate or sulfate are the recommended sources of copper for supplementation.
2018	ASMBS Pediatric Metabolic and Bariatric Surgery Guidelines. doi: 10.1016/j.soard.2018.03.019	Adolescence: Caution regarding bone mass is warranted Copper and selenium: should be checked starting at the 6th month postoperatively (SG and RYGB). Vitamin A: pre- and postoperatively. Routine: Vitamin B1 (a common deficiency preoperatively) for at least 6 months postoperatively, sublingual vitamin B12, a multivitamin with iron, and calcium citrate with vitamin D daily.
2019	Clinical Practice Guidelines for the Perioperative Nutrition, Metabolic, and Nonsurgical Support of Patients Undergoing Bariatric Procedures – 2019. Update. doi: 10.4158/GL-2019-0406	Endorsement: Laparoscopic plication, greater curvature, OAGB and OADS (SIPS, SADI-S) OAGB: presence of hypoabsorption, due to a long biliopancreatic limb, OADS (SIPS, SADI-S): possible nutritional and micronutrient deficiencies Calcium: the same levels as SG and RYGB Bone mass: 24-hour urinary calcium excretion at 6 months and then annually. DXA at 2 years postoperatively.
	Pregnancy after Bariatric Surgery: Consensus Recommendations for Periconception, Antenatal and Postnatal Care. doi: 10.1111/obr.12927	Thiamine: 300 mg/day (2 tablets 3x/day) in case of vomiting. Prolonged vomiting: intravenous supplementation of thiamine and vitamin B complex. Folic acid: 0.4 mg/day during preconception and the first trimester, 4–5 mg also for women with diabetes. Vitamin A: convert to beta-carotene form due to the risk of teratogenicity with retinol. Vitamin K: weekly if deficiency is observed with a coagulation defect.
2020	British Obesity and Metabolic Surgery Society Guidelines on Perioperative and Postoperative Biochemical Monitoring and Micronutrient Replacement for Patients Undergoing Bariatric Surgery-2020 update. doi: 10.1111/obr.13087	Iron: Individuals with SG, RYGB, and DBP/DS are recommended to take additional elemental iron. Vitamin A: Must be included in the base multivitamin-mineral supplement. OAGB/MGB: For individuals with a BP of 150 cm, the supplementation recommendations are the same as for RYGB. For individuals with a BP of >150 cm and SADIS, the recommendations are similar to DBP/DS.
2023	Brazilian Guide to Nutrition in Bariatric and Metabolic Surgery. doi: 10.1007/s00423-023-02868-7	Individualization according to the life stage: adolescents, adults, the elderly, pregnant women, and vegetarians Probiotics, prebiotics, and symbiotics: there are still limitations regarding the use of routine supplementation Protein: clean-label whey protein, for both those with and without inflammatory bowel disease, and those undergoing bariatric and metabolic surgery
2025	SICOB Italian Clinical Practice Guidelines for the Surgical Treatment of Obesity and Associated Diseases using GRADE Methodology on Bariatric and Metabolic Surgery. Updates. doi: 10.1007/s13304-024-01996-z	Perioperative supplementation: crucial to prevent and treat iatrogenic deficiencies, mainly: A, B and D

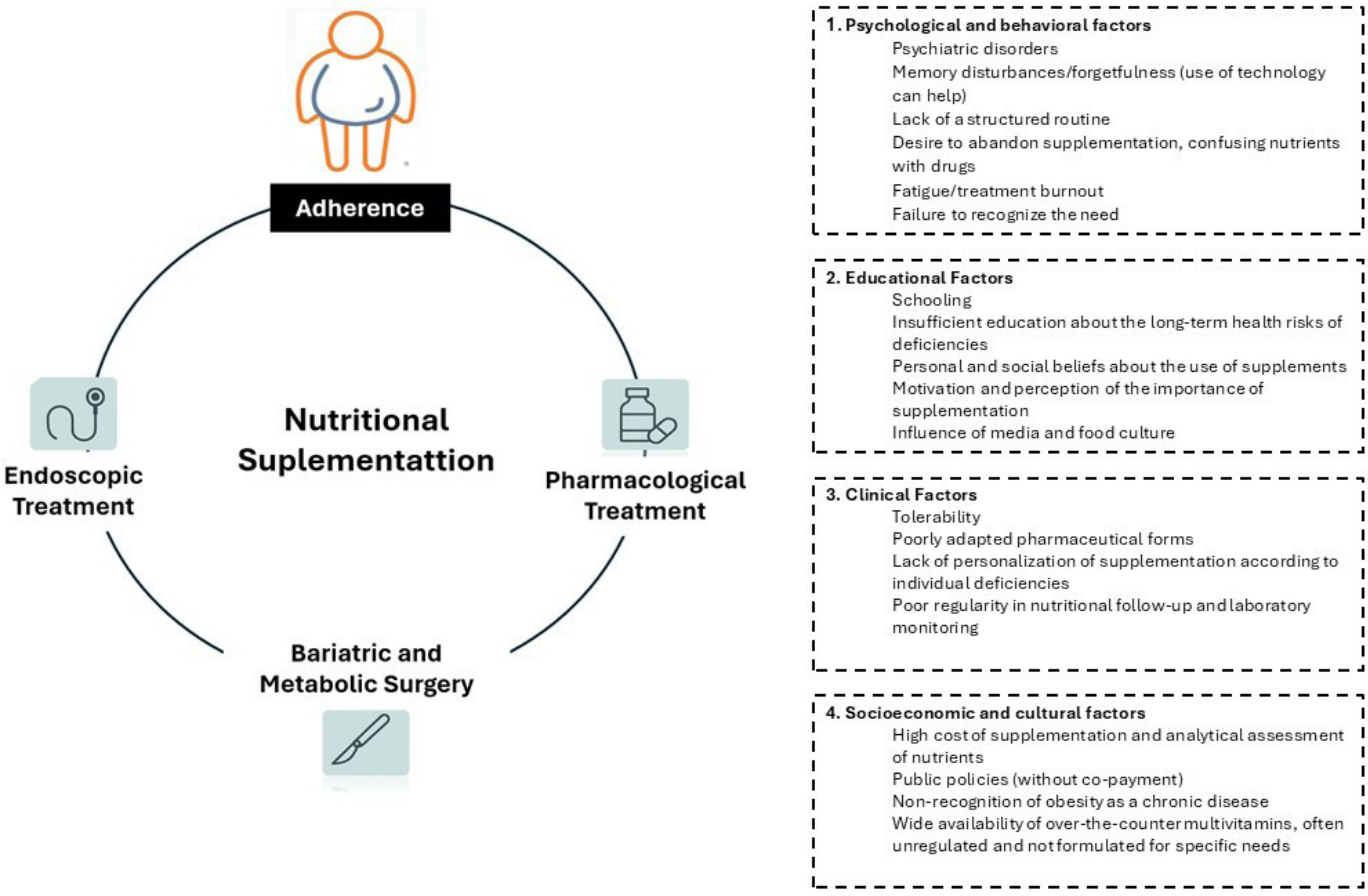

Figure 1 – Determining factors in medium- and long-term adherence to nutritional supplementation in the multimodal treatment of obesity.

THE FUTURE

When nutritional deficiencies are found following surgical treatment of obesity and diabetes, there is a wide variety of individual responses. It is therefore essential to understand the mechanisms and factors involved in this process to provide accurate medical and nutritional intervention.

Considering this scenario, precision medicine and nutrition, guided by biomarkers (genomics, proteomics, metabolomics, lipidomics, microbiomics and immunology) will have a decisive role in this process of personalized interventions. Integrated artificial intelligence tools will also be of utmost importance to create algorithms capable to assist doctors and nutritionists decisions. Examples include key genes that impact nutrient metabolism, such as MTHFT (folate metabolism) and the VDR (vitamin D receptor gene). The MTHFR gene influences the levels of the active form of folic acid (5-MTHF) and vitamin B12. Patients undergoing bariatric and metabolic surgery who may have variations in this gene will be strongly recommended to use methylated forms of folate (5-MTHF) and vitamin B12, thus preventing deficiency and maintaining serum levels as recommended. The VDR gene controls the activation and absorption of vitamin D, as well as calcium metabolism, both of which are crucial for maintaining bone mass and preventing osteoporosis. The ability to effectively absorb vitamin D may be limited by polymorphisms in the VDR, and thus higher doses of this vitamin will be necessary, in combination with vitamin K2, to promote bone and cardiovascular health.[7]

It is also necessary to highlight the decisive role of the gut microbiota in vitamin synthesis, mineral absorption and immunometabolism. Nutritional transcriptomic analysis, by differentiation between good and bad responders, may help to better understand nutritional deficiencies, allowing interventions to be tailored to improve individual clinical response after bariatric and metabolic surgery.[8]

In terms of technology and the development of pharmaceutical forms, transdermal nutritional supplementation is an

ambitious modality in current clinical research, with broad potential for expansion if we consider its applicability in public health. The inherent potential benefits (hepatic pharmacokinetics, reduced gastrointestinal effects, stable release rate over a long period, high convenience of administration, painless for patients, improved adherence) create challenges for the development and effectiveness of this micronutrient administration technique.[9] Nevertheless they present an opportunity to improve the efficiency of nutritional supplementation in bariatric surgery patients as well as in patients in general.

CONCLUSION

It is essential to highlight the need to develop public policies that make supplementation available to this population. Adherence is equally decisive in optimizing the results of bariatric and metabolic surgery, amplifying the gains in health and quality of life of those who benefit from it.

This article provides an opportunity to reflect on supplementation in bariatric and metabolic surgery, historically, currently and in perspective. Based on the evidence and recognized developments in this field, "supplementation" remains and will remain an important component of treatment. Nowadays, the management of obesity and diabetes is multimodal as it may begin with other or isolated therapeutic approaches, such as pharmacological or endoscopic therapy. This means that people under these treatments may also benefit of the improvements in nutritional supplementation, even in the absence of surgery. It is our duty to implement this intervention ethically, guided by scientific evidence and the individual characteristics of each patient.

It is essential to promote public policies that ensure access to supplementation in this population. Adherence to supplementation is pivotal for maximizing the advantages of bariatric and metabolic surgery, improving the health and quality of life gains for those who benefit from it.

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