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Review Article

Deficiency and Supplementation of Water-Soluble Vitamins in Obese Patients Undergoing Roux-En-Y Gastric Bypass

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Abstract

Bariatric surgery has become the most efficient treatment for severe obesity. The gold standard Roux-en-Y Gastric Bypass (RYGB) remains the most applied bariatric technique worldwide. After RYGB, there are anatomical changes in gastrointestinal tract that impact on eating behavior and intestinal absorption capacity. The limited food intake and malabsorption that often follow RYGB may worse or aggravate several vitamins deficiencies with local and systemic consequences. This critical revision, done in patients undergoing RYGB, examines the water-soluble vitamins deficiency frequency and supplementation impact. The prevalence of water-soluble vitamin deficiencies after RYGB is high, and can be more than 50% at one postoperative year. Under such deficiencies, relevant health disturbances can occur, including severe and even irreversible neuropathies. Therefore, potential deficiencies of water-soluble vitamins should be screened and properly treated by supplementation. As several obese patients are already vitamin deficient, supplementation should start at preoperative period to avoid or minimize its postoperative aggravation and even to improve the efficiency of its postoperative correction. Following RYGB, multivitamins must be orally supplied immediately after hospital discharge, according to the available clinical guidelines and the postoperative period condition. In addition to adequate medical and nutritional care, vitamins blood tests and assessment of nutritional supplements compliance should be included in RYGB patient monitoring.

Keywords: Bariatric surgery; Obesity; Deficiency; Water-Soluble Vitamins

Introduction

Obesity is an epidemiologic disease that can be accompanied by several comorbidities which may limit life quality and expectance [1,2]. The most effective treatment for obesity and its associated comorbidities is bariatric surgery [3-5]. In a large observational 2-cohort study the bariatric surgery was associated to a significant reduction in mortality related to body weight excess, compared to controls treated with primary health care (without surgery) [6,7].

According to the American Society for Metabolic and Bariatric Surgery last report, in USA, approximately 179,000 bariatric surgeries were performed in 2013 being 32% the Roux-en-Y Gastric Bypass (RYGB) operation. The RYGB is still considered the gold standard technic of bariatric surgery [1,3,4,7-10]. This procedure has a low postoperative mortality ratio, ensures effective and sustainable (for up to 15 years) weight loss, promotes type 2 diabetes mellitus (DM2) remission, and improves cardiovascular disorders and life quality [11-14].

However, RYGB is not free of post-operative complications that include worsening or installation of vitamin and mineral deficiencies [15-18]. This may occur because RYGB involve restrictive and disabsortive procedures that limit the quantity and quality of dietary intake as well as the intestinal surface for micronutrient absorption [3,10,11,13-15]. Approximately 50% of patients undergoing RYGB present early vitamin and mineral deficiencies [17-21].

Deficiency of Water-Soluble Vitamins Following RYGB

Deficiencies of water-soluble vitamins, including B12 (60%), B9 (40%) and B1 (15%), are reported one year following RYGB. Deficiencies of these B vitamins in bariatric patients are difficult to correct and can negatively impacts their health [22-26]. The other water-soluble vitamins (vitamins B2, B6 and C) can also be lacking after RYGB, but do not represent a significant clinical impact because this deficiencies are easily corrected [24,25,27].

Vitamin B1

Vitamin B1, or thiamin, has a major role in brain health, as essential enzymes for brain glucose metabolism use thiamine pyrophosphate as cofactor and 80% of this vitamin is present in nervous system tissues. Between 3 to 20 months after RYGB, about 15% of patients develop thiamine deficiency associated with Wernick encephalopathy (WE) [22,25]. The WE is characterized by neurological complications, including state of confusion, disorientation, ophthalmoplegia, nystagmus, diplopia and ataxia [28,29,30].

According to Fattal-Valevski (2011) and Raziel (2012), 84 patients with WE were recorded between 1991 and 2008, in which 80 (95%) of them had underwent RYGB or other restrictive procedure [21,22].

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Hospital admission by EW occurred within 10 months after surgery in 79 patients (94%) and brain screening revealed a 47% frequency of lesions [21,22]. The main risk factor for WE (achieving 76 patient or 90%) was frequent vomiting with a mean duration of 21 days prior to hospital admission, followed by intravenous glucose administration without thiamine (achieving 15 patients or 18%) [21,22].

Reduction of gastric pouch following RYGB may favor vomiting episodes and impair the adequate thiamine intake and absorption. Severe vitamin B1 deficiency may early become evident in those RYGB patients experiencing these intercurrences, but about 18% of them may be asymptomatic until postoperative 1 year [16,22]. Other possible factors related to thiamin deficiency include changes in intestinal microbiota composition and function [31,32].

Vitamin B1 deficiency may occur even under its adequate oral supplementation, which should to be initiated until at 2 to 4 months after surgery when its liver storage depletion is concluded [30]. According to the Bariatric Surgery Guideline (2013), patients with severe depletion of thiamin (suspected or confirmed) should receive the intravenous infusion of 500mg/day of this vitamin for 3 -5 days intravenously followed by 250mg/day during more 3-5 days or until symptom remission; while median deficiencies can be treated by 100mg/day of intravenous thiamine for 7-14 days [10].

Vitamin B12

Vitamin B12, or cobalamin, has important role in nervous system function and in growth and proliferation of red blood cells by acting as a cofactor for essential reactions enrolled in transition of methylmalonic acid to succinyl coenzyme A, and of homocysteine to methionine. Postoperative deficiency of cobalamin may affect more than 1 in each 3 bariatric patients and it is commonly associated with RYGB [18]. Intolerance and limited consumption of red meat, the main source of cobalamin, combined with reduced gastric secretion of hydrochloric acid (HCl) and Intrinsic Factor (IF), can contribute to vitamin B12 deficiency and compromise its bioavailability at postoperative RYGB [24,32].

Under normal conditions, vitamin B12 is bound to the protein food of animal origin. In the stomach, protein is cleaved under HCl and pepsin action. Vitamin B12 released from food binds transcobalamin I (TC1), a glycoprotein secreted by saliva and gastric juice responsible for transporting vitamin B12 from stomach to the intestine [33-36].

In the intestinal lumen, TC1 and vitamin B12 are separated, the glycoprotein is degraded by intestinal enzymes, while the B12 binds to intrinsic factor (IF, also called transcobalamin III) and forms a proteolytic-resistant complex. Such complex is carried intact until ileum to be finally absorbed by enterocytes, through Cubam receptors (CR), and carried out for plasma by transcobalamin II (TC2) [33,37-40].

The CR consists essentially of cubilin and Amnionless complex (AMN) or megalin. The cubilin acts as an endocytic receptor that recognizes the complex intrinsic factor/vitamin B12 and is directly involved in the intestinal absorption of this vitamin. However, the absorption mechanism of vitamin B12 also can occurs by passive diffusion (without FI binding) [35,37,38-42].

Vitamin 12 deficiencies after RYGB are associated to lower protein intake and impaired intestinal absorption resulting from its restrictive and disabsortive procedures. The anatomical rearrangement after stomach restriction implies in early satiety, decreased chloridric acid (HCl) and pepsin secretion and loss of exposure to intrinsic factor (IF)-secreting cells [43-46]. In addition, the exclusion of stomach body, duodenum, and proximal jejunum from nutrients flow implies in vitamin B12 malabsorbtion [44].

The role of HCl and IF reduction in vitamin B12 deficiency following RYGB were assessed by studies measuring stomach HCl contend and absorption of free-crystalline B12 and food-associated B12 (measured by urinary excretion) to correct its postoperative deficits. This studies reported significant postoperative decrease in HCl production and in food-bound vitamin B12 absorption, while the absorption of its free-crystalline form was non-significantly decreased, as compared by control subjects [47,48]. In addition to do not require pepsin and hydrochloric acid to be released from food, the free-crystalline form of vitamin B12 is absorbed by passive diffusion, therefore dispensing IF action [47,48].

Postoperative vitamin B12 deficiency was reported to achieve almost 60% of patients submitted to RYGB [49]. Signs and symptoms of cobalamin deficiency include megaloblastic anemia, paresthesia, glossitis, thrombocytopenia, cognitive deficiencies and irreversible neuropathies [13,31,45]. Therefore, vitamin B12 supplementation after RYGB is recommended and can be provided by different strategies.

At least partial cobalamin levels correction can be achieved by intramuscular (from 1000μg/month to 1000-3000μg each six months, and then each year, according to the deficiency grade), intranasal (500μg/week) and oral supplementation [10]. Oral supplementation of vitamin B12 is preferred to provide its free-crystalline form, but the ideal dose for this purpose is lacking. When testing different doses of oral free-crystalline vitamin B12 (100μg, 250μg, 350μg and 600μg/day) during the 6 months after RYGB, Rhode et al. (1995) found better corrections (more than 90%) when providing 350 a 600μg/day [50].

Free-crystalline vitamin B12 absorption seems to occur in terminal ilium in a similar mechanism to that FI-dependent and was reported to correct vitamin B12 levels in 81% of patients submitted to RYGB [15,23,51]. According to Xanthakos & Inge (2006), it is not clear if nasal and sublingual forms of vitamin B12 are better absorbed than its oral form, but postoperative supplementation of this nutrient by other than oral pathway is currently preferred. In addition, even facing evidences that other non-oral supplementation can be efficient to restore postoperative deficits of vitamin B12, such as nasal supplementation, muscular pathway has been considered the better option for this purpose in clinical practice [23,51-53].

Vitamin B9

Postoperative deficiency of vitamin B9, also known as folic acid or folate, is frequently related to the vitamin B12 deficiency, because this acts as a main enzyme which converts folate in its active form [54,55]. Vitamin B9 deficiency after RYGB can be also induced by the decreased consumption of its food sources and decreased absorption due the stomach reduction and intestinal deviation that excludes its

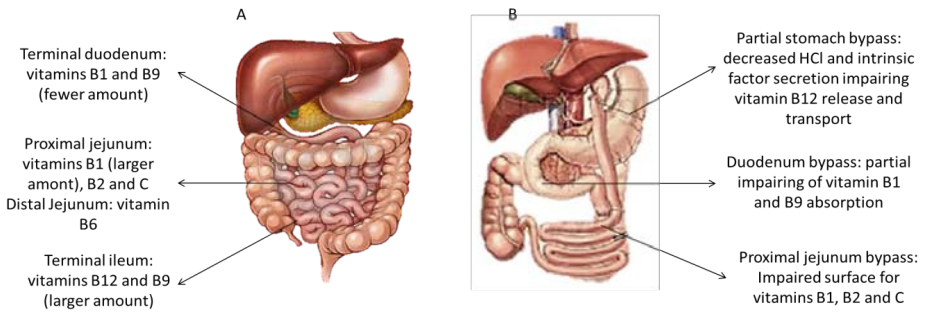

Figure 1: Anatomical changes induced by Roux-en-Y gastric bypass (RYGB) surgery and its impact on water soluble vitamin absorption: absorption of water soluble vitamin by intact gastrointestinal tract (a) and after the anatomic arrangement of gastrointestinal tract following RYGB (b).

digestive flux and absorption site, respectively. In normal conditions, absorption of vitamin B9 occurs under low pH at proximal jejunum, but following bariatric surgery it seems to be absorbed throughout all small intestine by a physiologic adaptive mechanism [17,26,56].

The lack of continuous folic acid supplementation combined to the vitamin B12 deficit can lead to its fast depletion and deficiency. Vitamin B9 deficiency can be reflected by megaloblastic anemia, leucopenia, glossitis and increased homocysteine levels [11,26], and seems to be avoided by its adequate oral supplementation (800µg/dia a 1000 µg/dia) following RYGB [50]. In addition, folic acids deficits can also indicate a lack of multivitamin intake [42,57].

Vitamins B_2, B_6 and C

Vitamin B_2, or riboflavin, acts as an enzyme by participating in cobalamin, folic acid, pyridoxine and niacin metabolism and has in liver its major storage (about a third of total contend) [9,28,58]. Currently, several natural flavins are recognized to participate in various essential metabolic processes, mainly those related to energy production through the respiratory chain [59,60]. Riboflavin deficiency after RYGB occurs mainly due the low intake of food sources for a period exceeding three months after surgery and its low body storage [61-63].

Vitamin B_6, or piroxin, can be found as three different forms (pyridoxal, pyridoxine and pyridoxamine) and all of it can be phosphorylated [32,64]. The pyridoxal 5'-phosphate (PLP) is the biologically active form of vitamin B_6 and acts as a cofactor for over 140 enzymes. The PLP can synthetize vitamin B_3 by converting tryptophan to niacin [65-67].

Moreover, vitamin B_6 is closely involved in the nervous system function and in protein, fat and carbohydrate metabolism. The amino acid metabolism occurs under the action of enzymes that use PLP as cofactor or prosthetic group [34,35]. In agreement to all complex B vitamins, a large part of vitamin B6 is accumulated at brain, muscles, plasma and erythrocytes [65,68,69].

Vitamin C, or ascorbic acid, exert important antioxidant function, participate in enzymatic and non-enzymatic reactions, in collagen, carnitine and norepinephrine synthesis, in vitamin E recycling, and improves the nonheme iron absorption [70,71]. The mechanism responsible for ascorbic acid storage is not yet fully elucidated, but vitamin fractions are deposited in various human tissues [72]. Due to lack of specific biomarkers for determining vitamin C deficiency in clinical practice, its signs and symptoms (escorburto, perifollicular petechiae, ecchymosis, keratosis, poor wound healing, gingivitis and glossitis) are widely used for diagnosis [73].

Vitamins B_2, B_6 and C are reported to achieve 13.6%, 17.6% and 34.5% of obese patients at 1 year postoperative of RYGB, respectively [60,63]. The real prevalence of these vitamins deficiency in association to clinical signs and symptoms following RYGB is still unknown, but can be adequately prevented or attenuated by providing multivitamin [26,29-31,74].

Final Comments and Conclusion

A significant number of obese patient's candidates for RYGB can experience micronutrient deficiencies even before surgery. The habitual consumption of high fat diets and sweetened beverages is associated to decreased dietary intake of fiber, vitamins A, C and D, calcium and folate and may at least partially explain such preoperative deficits [75]. In 2013, the main American societies related to the obesity care joined efforts to publish a Clinical Practice Guidelines for the Perioperative Support of the Bariatric Surgery Patients that highlighted the importance in accessing serum micronutrient levels before and after RYGB in order to identify and treat micronutrients deficits (Grade A of recommendation) [10].

Therefore, potential deficiencies of water-soluble vitamins should be screened and properly treated by supplementation already at preoperative to avoid or minimize it postoperative extension and even to improve the efficiency of its postoperative correction [54,76]. Regarding postoperative supplementation, multivitamins must be supplied immediately after hospital discharge, at doses two to three times greater than those recommended for healthy individuals (Recommended Dietary Allowance, RDA). Specifically for water-soluble vitamins ASBMS recommends 150% (1.65 mg), 300% (7.2 µg), 150% (1000 µg) and 200% (120 mg) of RDA to daily supplement vitamins B1, B12, B9 and C, respectively [10].

A major drawback is that most commercially available multivitamins are not specifically designed for bariatric patients and has insufficient concentration of water-soluble vitamins to achieve its recommended daily intake. Therefore, in clinical practice is usual to provide more than one capsule of multivitamin to compensate this failure, but it may oversupply certain vitamins and imply in adverse effects [15,73]. For instance, overdose of pyridoxine (B6) was reported to result in toxicity, emesis, diarrhea and headache[66].

In other hand, hypovitaminosis (including those water-soluble) is also a prevalent postoperative complication, achieving 50% of bariatric patients 1 year after surgery and associated to relevant side effects [54,76]. The best choice is therefore to supplement vitamins after RYGB according to existing clinical guidelines, which can vary according to the postoperative period experienced [49,77,78]. As the digestive process is compromised after RYGB it should be preferred to perform multivitamin supplementation in liquid or chewable form or even by intravenous and intramuscular pathways to allow greater micronutrient use [49,76,79,80].

Overall, deficiencies in water soluble vitamins can be aggravated or raised after RYGB not only due its decreased consumption but also due the anatomical rearrangement of gastrointestinal tract induced by this procedure, as shown in Figure 1.

In conclusion, the RYGB is a safe and effective treatment for obese patients by promoting significant weight loss and obesity-related comorbidities remission when compared to non-surgical techniques. However, long-term postoperative clinical follow-up shows a frequent micronutrient deficiency, including water-soluble vitamins with central role for health maintaining. These undesirable side effects can be minimized by frequent plasma levels monitoring of water-soluble vitamins and providing it adequate supplementation in a continuous and multidisciplinary approach at pre and postoperative periods.

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