OBES SURG (2013) 23:992–1000
DOI 10.1007/s11695-013-0922-2

REVIEW

Pharmacotherapy Prevention and Management of Nutritional Deficiencies Post Roux-en-Y Gastric Bypass

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Published online: 5 April 2013

Abstract Roux-en-Y gastric bypass is the most commonly performed bariatric procedure. It is associated with nutritional deficiencies due to gastric reduction, intestinal bypass, reduced caloric intake, avoidance of nutrient-rich foods, noncompliance with supplementation and poor food tolerability. Although there are multiple publications on this topic, there is a lack of consistent guidance for the healthcare practitioner caring for the bariatric patient. This article will encompass literature reviewing the pharmacotherapy approach to prevention and management of nutritional deficiencies since the American Society of Metabolic and Bariatric Surgery guidelines were published in 2008.

Keywords Bariatric surgery · Deficiency · Morbid obesity · Roux-en-Y gastric bypass · Malabsorption · Protein · Iron · Vitamin · Trace mineral

Introduction

Bariatric surgeries commonly performed in the United States today include adjustable gastric banding (AGB), vertical sleeve gastrectomy (VSG) and Roux-en-Y gastric bypass (RYGB). AGB works by restricting food intake, while the VSG and RYGB are combination procedures with some food restriction and neurohormonal changes. Additionally, RYGB causes a moderate degree of malabsorption. These surgeries are typically indicated for patients with either a BMI greater than or equal to 40 or 35 kg/m^2 with comorbidities [1]. While the many benefits of bariatric surgeries have been proven in clinical trials [2–4], these surgeries have also been associated with many complications. This article will focus on the RYGB procedure and will encompass recent literature reviewing the pharmacotherapy approach to prevention and management of common nutritional deficiencies. Table 1 will summarize presentation, pathogenesis and diagnosis of these deficiencies.

Nutritional deficiencies may occur in the RYGB procedure due to gastric reduction, intestinal bypass, reduced caloric intake, avoidance of nutrient-rich foods, noncompliance with supplementation and poor food tolerability and may be associated with poor clinical outcomes and severe health complications. Early nutritional complications include protractile vomiting which puts patients at risk for thiamine deficiency, electrolyte imbalance and dehydration. Other early complications include fat malabsorption that may result in deficiencies of fat soluble vitamins (such as vitamin A and D), or zinc deficiency. Furthermore, folate deficiency, cholelithiasis, and dumping syndrome are also seen in the early stages after the bariatric procedure. Protein malnutrition may develop in the early stages following surgery or much later [5–7]. The incidence of calcium and vitamin D deficiencies may lead to increased parathyroid hormone as well as increase in bone turnover and decrease in bone mass as early as 3–9 months post-surgery [2]. Later complications include development of ulcers and vitamin B_{12} deficiency [5, 6, 8]. Iron and copper deficiencies have been reported to develop months to years after bariatric surgery [6, 9–11].

Protein Deficiency

Protein deficiency is most commonly seen after distal RYGB with a Roux limb of more or equal to 150 cm, the

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Table 1 Summary of pathophysiology diagnosis and presentation of nutritional deficiencies post-RYGB [5–8, 10–12, 14, 15, 17, 23–30, 32, 35, 37, 42, 46, 48, 50–52, 54–56]

Deficiency and type	Pathophysiology	Diagnosis	Presentation	Comments
Protein Δmacronutrient	–Malabsorption	↓ Serum albumin	–Alb. < 3.5 mg/dL	–Supplements low in dextrose <100–200 g/day
	–Delayed mixing of proteins with bile and pancreatic enzymes	↓ Serum pre–alb	–Asthenia	–AM consumption stimulates appetite
	–Achlorhydria	↓ Total serum protein	–Hair loss	
	–Persistent vomiting –↓dietary intake/intolerance of protein–rich foods		–Edema	
Vitamin B_{12} (cobalamin)	–Achlorhydria	↑ MCV	–Ataxia	IM injection
	–Decreased secretion of intrinsic factor	↑ RDW	–Optic atrophy	
ΔWater soluble	–Bypass of duodenum	↓ Serum B_{12}	–Memory loss	–Improved compliance
	–↓Food intake	↑Methylmalonic acid	–Mental status changes	
	–Insufficient suppl.	↑ Homocysteine	–Weakness	
			–Myeloneuropathy	
			–Megaloblastic anemia	
			–Thrombocytopenia	
Folate (Folic acid)	–Bypass of upper 3rd of the small intestine	↑ MCV	–Asymptomatic (most cases)	
	–Insufficient dietary intake	↑ RDW	–Glossitis	–ETOH interferes with absorption
ΔWater soluble	–Achlorhydria	↓ RBC folate	–Tiredness	
	–Vitamin B_{12} deficiency	↑ homocysteine	–Diarrhea	
Iron	–Bypass of duodenum/ proximal jejunum	↓ Iron	–Fatigue	–Vitamin C assists absorpt.
ΔTrace element	–Achlorhydria	↓ Transferrin sat.	–Dysphagia	–Take on empty stomach
	–Use of H_2 blockers/PPIs	↓ Ferritin	–Cracks in the corner of the mouth	–Separate from Ca by 2 h
	–Occult blood loss	–Iron deficiency (<40 ng/dL)	–Brittle nails	–Avoid tea
	–Decreased food intake		–Tongue swelling	–Iron toxicity S/S:
	–Red meat intolerance	–Anemia of chronic inflammation (>200 ng/dL)	–Dyspnea	• Nausea
			–Palpitations	• Vomiting
	–Physiological demand>absorption	–Mixed deficiency (40–200 ng/dL)		• Diarrhea
				• HypoTNS
				• Tachycardia
B_1 (Thiamine)	–Bypass of proximal jejunum	↓Serum thiamine erythrocyte transketolase activity assay	Wernicke's encephalopathy	–Vitamin C assists absorption
ΔWater soluble	–Persistent vomiting	MRI	–Visual abnor.	–Poorly absorbed during protein or folate deficiency
	–Reduced food intake		–Confusion	–Avoid coffee and tea
			–Ataxia	–Should be given before glucose
			Korsakoff syndrome	–Foods disrupts thiamine absorption
			–Imp. memory –Confabulation	–Correct hypo Mg
			Dry beriberi	
			–Foods disrupts thiamine absorption	
			–Correct hypo Mg	
			–Burn. sensation	
			–Weakness	
			–Muscle numbness	
			–Loss of reflexes	
			–Pain in extremities	
			Bariatric beriberi	
			–Small intestinal bacterial overgrowth	
Calcium	–Bypass of duodenum	↑ PTH	–Facial spasms	–Only 500 mg elem. Ca can be absorbed at a time
ΔMineral	–Vitamin D deficiency	↑ Alk. phos.	–Paresthesia of lips, tongue, fingers	–>3 g/day not recommended
	–Achlorhydria	↓ 25(OH) vit. D	–Muscle cramps	–Ca citrate is preferred

Table 1 (continued)

Deficiency and type	Pathophysiology	Diagnosis	Presentation	Comments
	–↓Food intake	↓ Ionized Ca	–Weakness	
	–Roux limb>250 cm	↓ Serum Ca	–↓Bone density	–Vitamin D required for absorption
		↓ Urinary Ca in pts with normal renal function	–Bone pain –Osteoporosis	–Separate from iron by 2 h
Vitamin D	–Bypass of duodenum	↓ 25(OH) vit. D (<30 ng/mL)	–Bone pain	–Take with largest meal of the day
ΔFat soluble	–Delayed mixing of dietary fat with pancreatic enzymes and bile salts	↓ Serum phos.	–Muscle weakness	–Exercise
	–↓Food intake	↑ Alk. phos.	–Difficulty arising from chair or ascending a flight of stairs	–Consume diet rich in Ca and Vitamin D
		↑ PTH	– ↑fracture risk	–Moderate sun exposure
				–↓ Caffeine/alcohol
				–Quite smoking
				–Toxicity can develop at doses of 50,000 IU daily×several months S/S of toxicity:
				–N/V
				–Anorexia
				–Weakness
				–Constipation
				–Mental status changes
				–Arrhythmia
Vitamin A	–Bypass of duodenum and 1st portion of jejunum	–Suspect in pts with unexplained vision decline and hx of intestinal surgery	Early S/S:	–Iron and copper deficiency can impair resolution of vitamin A deficiency
ΔFat soluble	–↓Dietary intake	– ↓Vitamin A levels	–Xerosis	–Toxicity may develop at doses of 50,000 IU daily×3 months
	–Low fat diet	–Serum retinol/retinol binding protein ration < 0.8	–Bitot's spots	–S/S of toxicity:
	–↓ Fat absorption		–Poor wound healing	–Early: hair loss, dry scaly skin, mouth sores, vomiting
	–High oxidative stress		–Nyctalopia Advanced S/S:	–Late: hyper Ca, ↑ICP, headache, ↓cognition, hepatomegaly, cirrhosis
			–Corneal damage	
			–Keratomalacia	
			–Retinopathy	
			–Blindness	
Zinc	– Bypass of duodenum and proximal jejunum	–↓Plasma zinc	–Hypogeusia	–Take with iron
ΔTrace mineral	–↓Dietary intake	Δ <0.1 % of whole body zinc	–Poor appetite	–Take on empty stomach
	–Food intolerance	Δlow albumin—correct levels	–Poor wound healing	–Chronic large doses (>50 mg/day×long time) may cause copper deficiency and ↓immune function
	–↓ Fat absorption	–↓Serum zinc	–Hair loss	S/S of acute intox.:
	–Achlorhydria		–Muscle wasting –Skin manifestations	–Nausea/vomiting
Copper	–Bypassing of duodenum, stomach and ileum	–↓ Copper	–Fragile hair	–Avoid exogenous zinc
ΔTrace mineral	–Achlorhydria	–↓ Seruloplasmin	–Skin depigmentation	–↓ Dose in liver and biliary disease
	–Limited intake of vegetable products	–↓ 24 h urine copper excretion	–Osteoporosis	–S/S of toxicity:
	–Excessive zinc	–Abnormal anemia studies	–Myelopathy	–Weakness, diarrhea, peripheral edema, liver tox., behavioral changes
		–Abnormal CBC -Abnormal LFTs	–Paresthesias –↓ Mentation	–Antidotes: D-penicillamine, dimercaprol, edetic acid
			–Anemia	
			–Leukopenia	
			–Neutropenia	
			–Thrombocytopenia	

incidence is 13 % 2 years after and up to 27.9 % ten years post procedure [6, 12, 13]. In patients with shorter limbs the incidence is less than 5 % [12, 13]. Protein deficiency is most commonly seen one to two years after RYGB but may also develop much later [6, 7].

The recommended protein intake per day is approximately 1.0–1.5 g/kg of ideal body weight (IBW) [6, 8, 14, 15]. Daily protein consumption of 1.1 g/kg of IBW was shown to be sufficient at 1 year post-surgery, while 1.5 g/kg may be excessive for a non-complicated patient who is also volume restricted. Excessive protein consumption may preclude other macronutrients from being adequately consumed and lead to increased fracture risk [14, 15]. The adjusted body weight should be used to determine metabolically active tissue to then calculate protein requirement [15]. Patients with protein deficiency may be acutely and chronically managed with oral protein supplementation first, then if necessary, enteral feeding, if a feeding tube can be placed and tolerated. The ideal protein supplement, when used as the only protein source in the diet, should contain a high degree of branched-chain amino acids that are needed to prevent muscle tissue degradation, remain stable in the stomach, be rapidly digested and be lactose-free. Hydrolyzed whey protein may be a good option [6]. In some rare cases, severe refractory deficiency may be corrected with approximately three to four weeks of total parenteral nutrition [7, 13]. In patients who require prolonged parenteral nutrition a surgical intervention may be required to decrease malabsorption [13]. It is imperative for all patients after RYGB to have regular assessment of their protein intake and receive counseling regarding adequate nutrition and supplementation.

Vitamin B_{12}

The incidence of vitamin B_{12} deficiency may range from 26–70 % [16–18]. It is a late complication that can be seen as early as six months but most commonly years after the surgery when the large liver stores are slowly depleted [6, 8, 16, 18]. According to recent data, cobalamin (vitamin B_{12}) assays that are currently used to diagnose clinical vitamin B_{12} deficiency have a failure rate of 22–35 % and clinicians may not recognize the deficiency [19].

Oral absorption of vitamin B_{12} is variable at doses of less than 500 mcg and data suggests that only one percent of free vitamin B_{12} being absorbed therefore higher oral doses are required [8, 20]. The American Academy of Family Physicians recommend a prophylactic dose of 1,000 mcg daily to be used in patients post bariatric surgery [21]. Vitamin B_{12} can be administered either orally or sublingually. A study by Sharabi et al. showed that oral administration of 500 mcg daily was equally effective to the sublingual route [22]. Vitamin B_{12} may also be administered intramuscularly as 1,000 mcg monthly or 3,000 mcg every six months [6, 13, 18, 23, 24]. It was also suggested to administer 1,000 mcg of vitamin B_{12} parenterally as a preventative measure in the pre-operative period [6].

Acute management of vitamin B_{12} deficiency includes administering 1,000 mcg of intramuscular vitamin B_{12} weekly for eight weeks [6, 14, 17]. A more aggressive therapy with 1,000 mcg parenteral vitamin B_{12} administered daily for five days, followed by monthly injections for life may be recommended for patients who develop neurological symptoms. These symptoms do not always improve with repletion but may get stabilized [25]. Data suggest that in patients lacking intrinsic factor, high oral daily doses of 1,000–2,000 mcg are believed to be equally effective as a parenteral regimen due to sufficient absorption by passive diffusion in the ileum that is independent of intrinsic factor [20, 23]. Sublingual 2,000 mcg of vitamin B_{12} daily for 7 to 12 days may be recommended for patients who are unable to tolerate oral therapy due to diarrhea or vomiting and who refuse parenteral route [9]. Following repletion, all patients should continue taking vitamin B_{12} supplementation for life [14].

Folate Deficiency

Folate deficiency affects about 9–38 % of patients and especially women who become pregnant after the surgery [23, 26]. Neural tube closure defects have been reported in infants born to mothers who underwent RYGB [27]. The human body has small stores of folate and therefore the deficiency usually occurs in the very early stages post procedure. However, recent reports indicate that patients may present with increased rather than decreased levels of folate due to regular vitamin supplementation and increased bacterial folate synthesis, which occurs in the upper small intestine in the presence of achlorhydria [22, 24].

For prevention, it is recommended to take 800–1,000 mcg of folic acid orally daily post-RYGB [6, 14, 23]. Monitoring and supplementation is especially necessary during pregnancy.

For therapy, a dose of 1,000 mcg of folic acid is administered orally daily for about 1 to 2 months [6]. Doses up to 5,000 mcg/day may be required in severe malabsorption [14].

Iron Deficiency

The incidence of iron deficiency is 6–52 % which may occur as early as two months or at any point in life post-RYGB [6, 9, 11]. Incidence may be higher in menstruating females and those who become pregnant after the procedure [8, 28].

The recommended iron intake for patients post-RYGB is 36–65 mg elemental iron daily [6, 14, 18]. Menstruating women and those at high risk for anemia such as patients with peptic ulcer disease should be taking 100 mg of elemental iron daily [6, 11, 18, 23]. Iron deficiency is sometimes difficult to correct post-surgery. Therefore, it is recommended to evaluate iron status in all patients pre-operatively and if warranted correct iron deficit with about 100–200 mg of elemental iron daily [27].

In case iron deficiency develops post-surgery, doses of up to 300 mg of elemental iron orally may be required to replete iron stores and in some cases of severe refractory deficiency intravenous iron might be warranted [6, 14]. For example, menstruating women may have a more resistant deficiency and may require intravenous iron [11]. von Drygalski et al. [26] has recommended an iron tolerance test with 100–150 mg of oral elemental iron along with small amount of orange juice to be used to identify patients who may require intravenous therapy. Patients with normal absorption should have a 100 % increase in serum iron 2–3 h following ingestion.

Thiamine Deficiency

Thiamine deficiency post-RYGB occurs in about 1 % of patients as an early complication, developing within six months or earlier post-surgery especially in patients with prolonged vomiting [23, 25, 29]. The deficiency is also common in patients pre-operatively and can occur in up to 29 % of bariatric candidates putting them at higher risk of developing deficiency after the procedure [7].

The American Society of Metabolic and Bariatric Surgery (ASMBS) guidelines recommend patients after RYGB to take a daily multivitamin that contains 3 mg of thiamine [14]. However, in order to prevent acute Wernicke's Encephalopathy (WE), a prophylactic oral daily dose of 25–50 mg in addition to multivitamins starting as early as 6 weeks after surgery might be recommended for malnourished patients [23]. Post operatively, if patients develop gastrointestinal symptoms such as nausea, vomiting and diarrhea without neurological signs, prophylactic administration of thiamine is warranted [25].

Early symptoms of neuropathy can be treated with 20–30 mg a day of oral thiamine until symptoms disappear [6]. For more advanced symptoms and for patients with protractile vomiting, it is recommended to give 100 mg of thiamine parenterally for seven days, then 50 mg orally daily along with other water soluble vitamins until complete recovery [14]. It is recommended to treat patients with neurological manifestations due to WE more aggressively with doses of 500 mg parenterally three times daily for 2 to 3 days, then 250 mg parenterally daily until improvement is seen, followed by 50–100 mg orally three times a day until patient no longer continues to have nausea, vomiting and diarrhea [25]. After repletion, supplementation with 30 mg of oral thiamine twice a day should then be continued for several months and in some cases for life [30]. In the acute setting, oral therapy should not be used due to decreased gastrointestinal absorption. Thiamine should be given intravenously or intramuscularly [25, 29]. Because thiamine is short acting, more frequent dosing (twice to three times a day) may be more efficient [29]. However, the most effective frequency is yet to be established. Korsakoff syndrome responds poorly if at all to thiamine supplementation [30].

Metabolic Bone Disease

A direct casual relationship was found between any type of bariatric surgery and metabolic bone disease, which may develop at any time between eight weeks to 32 years after surgery. As a result, all patients following RYGB should undergo lifelong screening for the presence of metabolic bone disease. This includes the evaluation for calcium and vitamin D deficiencies, for markers of altered bone turnover and for levels of parathyroid hormone (PTH) and albumin. The following symptoms should trigger clinicians to look for vitamin D and calcium deficiencies: proximal weakness, deep dull poorly localized bone pain, increased difficulty rising from chair or ascending a flight of stairs, frequent stooling, steatorrhea or kidney stones [15].

The incidence of calcium deficiency after distal RYGB is about 10 % at 2 years post-surgery [2, 12]. The incidence of vitamin D deficiency post-surgery has been reported as high as 50–80 % [6, 31]. Moreover, vitamin D deficiency was seen in 84 % of obese individuals before surgery [32]. There is also a direct correlation between increased BMI and increased PTH [33]. The incidence of elevated PTH was found to be 48 % in pre-operative patients [34]. It is therefore imperative to assess patients' vitamin D (25 OH-D) status and intact PTH levels before surgery to identify and treat patients at high risk for bone loss after surgery.

Calcium Deficiency

The optimal daily calcium intake for patients post-RYGB is yet to be defined but it is essential to attempt to optimize calcium ingestion specifically during rapid weight loss [15]. Some sources recommend doses of 1,200–2,000 mg of elemental calcium daily for asymptomatic patients after RYGB [5, 6, 14, 35]. It was suggested that a daily dose of 1,700 mg of calcium citrate was able to ameliorate but not prevent bone loss in overweight post menopausal women during weight loss [6]. According to Carlin et al. [36] a daily

dose of 1,500 mg of calcium citrate with 800 IU of vitamin D was not sufficient for prevention of vitamin D depletion, bone resorption and hyperparathyroidism in post-operative patients. Following surgery, specifically during rapid weight loss, it is recommended to supplement with a higher calcium intake of 1,700–2,000 mg from both diet and supplementation in addition to adequate vitamin D [14]. Patients should be encouraged to consume foods that are a significant source of calcium. Calcium citrate is the preferred form due to a better absorption in a non-acidic environment created after RYGB. Patients should be counseled on the appropriate consumption of calcium as doses higher than 500–600 mg of elemental calcium are not sufficiently absorbed. This may be challenging for patients as doses must be taken multiple times a day. Also, calcium should be separated from iron supplements by at least 2 h.

Vitamin D Deficiency

Post operatively, the common recommendation is to supplement with 800–2,000 IU of cholecalciferol (vitamin D_3) daily to ameliorate bone loss during rapid weight loss [14, 15, 37]. However, despite adequate supplementation vitamin D levels are frequently insufficient for proper bone metabolism, and more aggressive supplementation may be warranted especially in patients with vitamin D levels of less than 30 ng/ml [7, 31, 36, 38]. Mahlay et al. [38] evaluated the efficacy of ergocalciferol (vitamin $D_{2)}$ dose of 50,000 IU weekly started in the sixth week after surgery and continued for 12 weeks in patients with vitamin D levels of less than 32 ng/ml. The dose was followed by prophylactic 800 IU of D_3 in conjunction with 1200 mg calcium taken daily. Authors found that 45 % of patients continued to be vitamin D deficient despite therapy. They concluded that after repletion higher prophylactic doses of 1,000–2,000 IU D_3 daily with additional 50,000 IU D_2 every 1, 2, or 4 weeks might be required to prevent further vitamin D depletion. Similar results were shown by Carlin et al. [36] who detected vitamin D deficiency in 44 % of patients with vitamin D levels of less than 20 ng/ml treated with 50,000 IU D_2 weekly together with daily 800 IU D_3 and 1,500 mg calcium. Authors suggested that 50,000 IU of D_2 taken once weekly indefinitely in addition to daily 2,000 IU of D_3 and 1,500 mg of calcium is a reasonable prophylactic dose for patients post-RYGB. In their study, this regimen was not associated with toxicity, although, authors still recommended to monitor levels of serum 25(OH) vitamin D every 6 to 12 months. Goldner et al. [31] found a higher prophylactic dose of 5000 IU of D_3 daily to be safe and more effective than 800 IU and 2000 IU in increasing serum vitamin D levels. However, results of this study showed that such a high dose was still insufficient to maintain an adequate vitamin D levels in all patients. Authors suggested that all patients post operatively should be taking at least 2000 IU of D_3 daily. Williams [15] suggested that after acute repletion, patients should be maintained on 50,000 IU of ergocalciferol one to three times weekly. It is not clear how long patients must be maintained on such a high dose. To date, the most effective and the safest prophylactic dose of vitamin D is yet to be found, it is therefore implied that further research is needed to find such a dose. A patient's vitamin D status should be evaluated soon after surgery and vitamin D levels should be repleted aggressively before giving standard supplementation.

According to ASMBS guidelines [14], acute vitamin D deficiency is treated with 50,000 IU of D_2 administered either orally or intramuscularly weekly for 8 weeks. This dose might not be sufficient to correct vitamin D deficiency in all patients. Some sources suggest that doses of 50,000 IU of D_2 taken as frequently as three times per week may be required to treat the deficiency and in cases of severe malabsorption, doses as high as 50,000 to 150,000 IU daily for 1 to 2 weeks may be needed [7, 13, 15, 37]. Some sources suggested that ergocalciferol and vitamin D analogs are unable to show the same efficacy as cholecalciferol in normalizing blood values, while a study by Holick et al. [15, 39] have demonstrated vitamin D_2 and D_3 to be equally effective. More research is still needed to compare these two forms of vitamin D in patients post bariatric surgery. In order to confirm successful repletion, serum 25(OH) vitamin D levels should be re-checked 2 months after repletion [24].

Vitamin A Deficiency

According to study by Clements et al. [40], the incidence of vitamin A deficiency was reported to be about 11 %. Eckert et al. [41] reported that almost 70 % of patients in their study had decreased night vision, 33 % had new onset of persistently dry eyes and 39 % experienced subjective decline in visual acuity post-RYGB. Vitamin A deficiency was found to be directly related to low serum concentration of prealbumin. Therefore, deficiency should be suspected in patients who present with protein-calorie malnutrition [42].

Currently, ASMBS guidelines do not recommend an additional prophylactic vitamin A post-RYGB [14]. Most over-the-counter multivitamins contain approximately 3,500 IU of vitamin A, which accounts for about 70 % of the recommended daily intake [41]. Brolin and Leung [43] reported that vitamin A found in multivitamins failed to prevent deficiency in up to 10 % of patients with distal Roux-en-Y gastric bypass after 2 years. Moreover, a study by Pereira et al. [44] suggested that a supplemental dose of daily 5,000 IU of retinol acetate failed to prevent vitamin A

deficiency. Authors have also emphasized the importance of pre-operative screening for vitamin A deficiency. Clearly, a stronger supplementation may be required in order to prevent visual and other consequences of hypovitaminosis A after gastric bypass procedure, but no definitive data is currently available on the optimal supplementation. Therefore, studies are needed to evaluate the most effective dose of vitamin A supplementation.

According to the ASMBS guidelines, patients without corneal changes should be treated orally with 10,000–25,000 IU daily until clinical improvement, which may take approximately 2–3 weeks. Patients with corneal changes may be treated with 50,000–100,000 IU intramuscularly daily for 3 days and then 50,000 IU intramuscularly daily for two additional weeks [14].

Zinc Deficiency

A study by Madan et al. [45], found abnormal zinc levels in 30 % of obese patients prior to surgery and the incidence increased by 6 % after one year post operatively. The deficiency may develop in very early stages post-surgery because functional reserves or body storage of zinc is lacking [46]. According to Ruz et al. [47], the absorption of zinc is significantly decreased starting 6 months post-surgery and persists at least until 18 months after the operation.

It was reported that compared to normal weight patients, obese individuals have lower serum levels of zinc. This may be explained by zinc sequestration in fat and therefore its reduced bioavailability [46]. In fact, up to 28 % of patients were found to be zinc deficient prior to bariatric surgery [48]. This together with other factors that decrease zinc bioavailability and absorption places patients at an increased risk for severe zinc deficiency early after the surgery. Therefore, adequate zinc supplementation may be warranted in the early stages post-surgery. Currently, there are no guidelines for zinc supplementation and patients are being instructed to only take a multivitamin that contains zinc [14]. Most multivitamin formulations however contain very small amounts of zinc. According to Gasteyger et al. [49] a standard multivitamin preparation that contained 5 mg of zinc was unable to prevent zinc deficiency. Moreover, Ruz et al. [47] have suggested that supplementation with 9.5 mg of zinc would not be sufficient to prevent zinc deficiency. Therefore, much higher doses of prophylactic zinc may be required to prevent the deficiency. Some sources suggest that patients might require up to 60 mg of zinc daily during malabsorptive states [46, 47]. More aggressive supplementation is essential during pregnancy when requirements are particularly high for fetal and maternal tissue development. Zinc deficiency was associated with maternal hypertension, low birth weight, preterm delivery, and congenital abnormalities [46]. More research is still needed to identify the optimal prophylactic zinc supplementation dose and regimen.

The recommended treatment dose of zinc deficiency is 60 mg of elemental zinc taken orally twice a day until the deficiency resolves [14]. High doses of zinc may deplete copper levels and lead to copper deficiency, therefore, patients should be evaluated for copper deficiency and copper supplementation may be warranted when high zinc doses are used.

Copper Deficiency

Although copper deficiency is relatively uncommon, an increasing number of case reports have been found in the literature due to the rising number of bariatric surgeries [50–52]. Recently Gletsu-Miller et al. [10] have reported the incidence of copper deficiency to be 18.8 % and in contrast to other case reports that reported copper deficiency to occur several years post-surgery, they suggested that copper status may become impaired within months following surgery and that patients may be at risk at any time period after the procedure.

Currently, recommendations regarding prophylactic dose of copper after RYGB are missing. Because copper deficiency that might result in irreversible neurologic sequelae becoming more common and better recognized in the bariatric patient population, studies are warranted to assess whether prophylactic doses are required post bariatric surgery and what those doses should be.

It is suggested that copper deficiency may be corrected with 6 mg of elemental copper orally daily for one week, followed by 4 mg daily for another week followed by maintenance dose of 2 mg daily thereafter [25]. If oral therapy fails to correct deficiency, an elemental copper dose of 2 mg administered intravenously over 6–12 h for approximately five days was reported in case reports to correct copper deficiency [51, 53]. However, in severe cases, longer therapy may be warranted. After correction, multivitamin supplementation that contains 2 mg of elemental copper daily is suggested to be sufficient to prevent the development of deficiency. Copper supplementation may result in a rapid resolution of hematological abnormalities, but neurological manifestation may not be resolved completely leading to an irreversible long-term decline [10, 53].

Conclusion

Nutritional deficiencies are common after the RYGB procedure. The prevention strategy for every patient should

include at least 200 % of the daily recommended value for a chewable or liquid multivitamin that contains 400 mcg of folic acid and 18 mg of elemental iron. Ideally, multivitamins should also contain sufficient amounts of vitamin A, zinc, and copper. Additionally, it is recommended to consume 1,000 mcg of vitamin B_{12} and 1,700–2,000 mg of calcium with at least 1000–2000 IU of vitamin D daily. Some bariatric patients may require additional supplementation of one or more of these and other vitamins and minerals. Patients should be monitored carefully and frequently because nutritional deficiencies may lead to severe consequences if not promptly diagnosed and treated. Each member of the healthcare team should be actively involved in the bariatric patient's care including counseling on the importance of proper nutrition and compliance with supplementation.

Conflict of Interest Disclosure Statement Radmila Levinson, PharmD, BCPS—no conflict of interest
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Jon B. Silverman, BS, PharmD—no conflict of interest
Hina Jolin, PharmD—no conflict of interest
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Kellene Isom, MS, RD, LDN—no conflict of interest

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