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Micronutrient Issues in the Bariatric Surgery Patient

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Abbreviations: BMI: Body Mass Index; SG: Sleeve gastrectomy; RNY: Roux-en-Y

Introduction

Currently, more than 36% of adults and 17% of youth in the United States [1] are considered obese with a body mass index (BMI) greater than 30.0kg/m^2. Typically, behavior modification of dietary and physical activity habits is the first line of treatment for obesity. However, the success of this therapy is marginal at best with only a limited number of individuals achieving and sustaining clinically meaningful weight loss of 5-10% after 6-months of treatment. Bariatric surgery is considered the most effective weight loss treatment of severe obesity [2–9] as well as in the treatment and prevention of obesity-related comorbidities [3,10-13].

The three most commonly performed weight loss surgeries are categorized into restrictive, malabsorptive, or a combination of these. Laparoscopic sleeve gastrectomy (SG) is a restrictive procedure. Laparoscopic Roux-en-Y gastric bypass (RNY) and biliopancreatic diversion with duodenal switch (BPD+DS) combine both restrictive and malabsorptive properties. The BPD+DS has the stomach revision similar to sleeve gastrectomy and the stomach empties its contents into the ileum. The SG and RNY are globally the two most frequently performed operations with about 500,000 procedures performed annually with nearly 50% of operations are SG and 43% are RNY [14-16].

Bariatric surgery has been demonstrated as the most successful long-term weight loss intervention with 31.5-39.0% weight loss at 3 years (62% excess weight loss) for RNY [17-19]. Patients experience the maximum weight loss around 18-months post-surgery [20]. Impressively, 90% of patients lost greater than 50% of their excess weight [21]. Unfortunately, not everyone has the same successful response or maintains weight loss as weight regain remains an issue in some patients. A weight regain of 10-20% of minimum weight achieved (i.e. maximum weight loss) has been observed22 in 30-50% of patients by 18-24 months post-surgery [18,20]. Even after 7-10 years of follow-up post-surgery, mean weight regain is only 23-25% of maximum weight loss for RNY [18-23]. Individuals that were most successful in long-term weight loss were those that lost the most weight initially [18].

Nutritional health may be compromised however due to the nature of the surgery. As the gut's anatomy is altered from the surgery, this creates complications that include nutrient deficiencies [24,25]. Development of food intolerances and dietary adjustments recommended post-surgery, such as reduced calorie intake, can also lead to nutrition concerns. These issues are more prominent in patients that do not comply with the post-surgical dietary and supplement recommendations.

Obesity (Pre-Surgery) Nutrient Deficiencies

A significant proportion of bariatric surgery patients are at risk for nutrient deficiencies prior to surgery even in the presence of positive energy balance [26,27]. At pre-surgery, patients should be evaluated to identify and treat nutrient deficiencies. Poor nutritional status prior to surgery can lead to poor surgical and health outcomes. Correction of pre-surgery deficiencies is important as this is a strong predictor of post-operative deficiency [26]. More than 80% of post-surgery patients are deficient in at least one nutrient [28-31].

The prevalence of pre-surgery nutrient deficiencies as assessed by biochemical markers has been reported at 62-71% for vitamin D, 10-30% for vitamin B12, 8% for vitamin A, 25% for folic acid, 20% for iron, 68% for copper, and 74% for zinc [27,32]. Hyperparathyroidism, anemia, and hypoalbuminemia were present in 23%, 14%, and 1% of patients, respectively, prior to surgery. It is thus evident that significant nutritional problems are present in this population.

In examining dietary intake to assess nutritional health, studies show there is extreme variability in energy intake prior to surgery, ranging from less than 1000 to more than 7000kcals per day in obese individuals [33,34]. The range for relative distribution of calories from fat, carbohydrate, and protein ranged from 33-40%, 45-55%, and 14-17% [33,34]. For micronutrients, at least 40% of obese participants scheduled to undergo bariatric weight loss surgery were below recommended dietary intake values for vitamin D (100%), vitamin E (52.9%), vitamin C (41.2%), folate (47.1%), calcium (52.9%), magnesium (58.8%) and potassium (94.1%) [34].

Recommendations for Post-Surgery Nutrition Management

Only a small fraction of pre-surgery patients are being tested for micronutrient deficiencies according to a publication from 21,000 patients in a health insurance database [35]. This is occurring even in the presence of documented nutrient deficiencies in pre-surgery patients and the benefits for recovery and surgery success when nutrient deficiencies are corrected. The most common nutrient assessed was vitamin B12, which occurred in 60% of patients. Less than one-half of patients were assessed for vitamin D, folate, and iron, despite evidence that shows a relative high occurrence of deficiency with these nutrients.

Self-reported use of micronutrient supplements has been over 90% in a couple of medical chart reviews of patients followed for a mean of 2-3 years [27,28]. Use of individual micronutrient supplements included iron (24.4% of patients), calcium (38.5%), vitamin D (58.2%), and vitamin A (7.5%). Others however found less than 60% of patients reported taking their supplement on the prescribed dosage at 12-months post-surgery [35,36].

The effectiveness of supplements are questioned though as in post-RNY patients followed for 2-years, nutrient deficiencies were common even with standard multivitamin and mineral supplements [30]. When assessed, additional supplements were routinely prescribed when reference values were below the lower point of the reference range. More than 95% of patients at 2-years were prescribed at least one additional supplement besides the multivitamin and mineral supplement. A mean of nearly 3 additional supplements were recommended, with the most common being vitamin B12 (80%), iron (60%), calcium and vitamin D (60%) and folic acid (45%).

Recommendations for nutritional supplements start as early as day 1 after hospital discharge from RNY and BPD+DS patients with taking a high potency multivitamin and mineral supplement containing at least 200% of the daily value for more than two-thirds of the micronutrients in [25]. Use of specialized bariatric formulations is desired as they do not have the enteric coating or are time-released.

Post-Surgery Nutrient Concerns and Supplement Guidelines

Mechanisms for nutrient deficiencies in post bariatric surgery patients are multifactorial, depending on the surgery type. In the RNY procedure, the reduction in stomach volume to 30ml, and bypass of duodenum and proximal jejunum causes not only restriction and malabsorption, but also importantly alterations in incretin secretion, gut hormone release, and microbiome [37-39]. In addition to low food intake and dietary restrictions, the exclusion of the inferior stomach decreases acid production needed for vitamin B12 and cation absorption (ex. calcium, iron, copper, zinc), malabsorption from exclusion of portions of the small intestine, particularly the duodenum as it is the primary location for the absorption of a number of macro and micronutrients [31,40]. Furthermore, the degree of malabsorption of nutrients is affected by different points of anastomosis (proximal, distal, and intermediate) in RNY procedures. Presence of anemia was higher postoperatively in individuals with a more distal connection [41]. Other biochemical indicators of metabolic deficiency were observed for vitamin A, vitamin D, calcium, and protein in distal vs. proximal limb anastomosis [41]. Support for this was also observed in a swine model that compared nutrient digestion between SG and Roux-en-Y procedures [42]. The investigators showed that protein, calcium, fat, and ash digestibility was lower for RNY than SG.

The high prevalence of iron deficiency and anemia in obese individuals and in bariatric pre-surgery patients is affected by the chronic pro-inflammatory state on iron absorption. This is evident in that in obese patients prior to bariatric surgery anemia was present in 5-22% and iron deficiency was found in up to 50% of patients [26,43-49]. The increased activity of the immune system disturbs iron homeostasis. Hepcidin, an adipose tissue cytokine that is increased during inflammation, blocks intestinal iron absorption [50-52]. Normally, iron deficiency leads to a decrease in hepcidin and a subsequent increase in iron bioavailability. However, the chronic inflammatory condition and raised hepcidin present in obesity reduces iron absorption. Importantly, perioperative anemia is linked with increased postoperative morbidity and mortality [49].

The impact of bariatric surgery on iron deficiency is inconsistent as some research indicates that weight loss reduces inflammation and thus improves iron homeostasis through its effect on hepcidin [52,53]. However, more frequently, prevalence of iron deficiency and anemia does not improve and likely worsens [49,50] based on a number of factors, including the prolonged inflammatory state of the surgical procedure, intestinal anatomical changes that diminishes gastric acid secretion and absorptive area of the

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duodenum, and from food intolerances, including avoidance of high iron source foods such as red meat [49]. Complicating the issue is that a frequent biomarker measured for iron deficiency, serum ferritin, is an acute phase protein and is elevated with systemic inflammation, and thus may mask the presence of iron deficiency [54-56]. In a recent report, biomarkers of iron status (iron binding capacity, serum ferritin, and hemoglobin) were worse post-surgery than pre-surgery, and these had not returned to pre-surgery levels even after 4 years of follow-up [22]. Others showed that over a short post-surgery follow-up period, serum ferritin remained normal, but more than one-third of patients had low ferritin at 5 years post-surgery56. Over an extended follow-up, new onset anemia at 3-months was present in 34.6% patients and this increased to 80.6% of patients at 4-years [27].

Anemia is caused not only by iron deficiency, but also by low levels of copper, folate, and vitamin B12. Both folate and vitamin B12 deficiencies cause macrocytic anemia and are frequently present in bariatric surgery patients prior to the procedure, and persists post-surgery. Reduced intrinsic factor from stomach resections, lower acid production, and decreased food intake in post-surgical patients leads to vitamin B12 deficiencies [27]. Since it takes 3-4 years to deplete vitamin B12 stores and reduce blood levels, continued monitoring of vitamin B12 levels is important.

Physiologic and anatomic changes from bariatric surgery can lead to copper deficiency in bariatric surgery patients. The reduction in gastric acid from stomach resection and bypassing the duodenum reduce copper bioavailability. About one in five RNY patients were copper deficient at 24-months post-surgery [57]. Complicating assessment of copper status is that serum copper and ceruloplasmin, both biomarkers for copper status, are elevated with inflammation [58].

There is a decrease in circulating vitamin D levels in obesity. Possible mechanisms for this includes reduced synthesis in the kidney, less sun exposure, inability to use sunlight to initiate vitamin D synthesis, reduced intestinal absorption, and sequestration of vitamin D in adipose tissue [59,60]. Up to 90% of these individuals have vitamin D insufficiency [26,27,61]. Globally, there is a 2.4 times greater odds of vitamin D insufficiency in obese vs. nonobese [62]. Vitamin D has a role in calcium metabolism, regulating insulin action, immune function, and cell proliferation [63]. As fat mass decreases with weight loss, this mobilizes vitamin D from adipose tissue and subsequently temporarily increases circulating vitamin D [31]. However, long-term studies still demonstrate vitamin D deficiency in post-surgery patients [27,64-65]. The prevalence of low vitamin D levels decreased from 63.2% in pre-surgery patients to 24.3% at 5 years of follow-up [27]. Whereas total bone loss was observed in a cohort following bariatric surgery, bone mineral density was maintained, thereby keeping risk of osteoporosis low66. Supplementation with both calcium and vitamin D at daily dosages of 1200-1500mg of calcium and >3000 IU vitamin D may attenuate bone loss following bariatric surgery [24].

Low levels of fat-soluble biochemical markers show compromised status prior to surgery. After both restrictive and malabsorptive procedures, vitamin A insufficiency worsened compared to pre-surgery values, but this may be dependent upon duration of follow-up. Prevalence of insufficient vitamin A levels was 7.9% pre-surgery, and by 3-months post sleeve gastrectomy, nearly 30% of patients had insufficient levels27. However, at 2 years post-surgery, prevalence of insufficient vitamin A levels returned to pre-surgery values. More severe vitamin A status was not apparent throughout a 5-year follow-up in these patients.

Current guidelines also suggest that in patients with BPD+DS that lifelong supplementation with fat and selected water-soluble vitamins are necessary due to malabsorption of these nutrients [66-67]. Slater et al. [68] showed in a 4-year follow-up that after BPD+DS, low serum vitamin A was observed in 52% of patients at year 1, 58% in year 2, 69-70% in years 3 and 468 [68]. In this same study, low vitamin K was seen in 13-21% of patients during years 1-3, but by year 4, 68% of patients had low levels of vitamin K. Low levels of vitamin D were also seen in 46-63% of the patients during this 4-year follow-up. In a study that compared RNY with BPD+DS, individuals were followed for 12-months post-surgery. BPD+DS patients had lower biomarkers for vitamin A and vitamin D and a faster rate of decline in vitamin B1 than RNY69. Vitamin K is at risk for deficiency in post-surgery patients due to abnormally low bile and pancreatic secretions, especially in BPD+DS procedures, and alteration of gut micro flora which provides a significant amount of the body's vitamin K70 [69-70].

Conclusion

Nutrient concerns are evident in pre-bariatric surgery patient. Assessing and then addressing these nutrient deficiencies with dietary modifications and supplements improves surgical outcomes. Nutrient deficiencies are seen post-bariatric surgery patients, with the anatomical and physiological changes associated with the various bariatric surgery procedures underlying the mechanism for these observations. It is important to correct these deficiencies and monitor developing deficiencies through life-long monitoring of nutritional health and encouraging life-long vitamin and mineral supplementation.

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