ORIGINAL CONTRIBUTIONS



Can Composite Nutritional Supplement Based on the Current Guidelines Prevent Vitamin and Mineral Deficiency After Weight Loss Surgery?

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Abstract

Background Nutritional deficiencies occur after weight loss surgery. Despite knowledge of nutritional risk, there is little uniformity of postoperative vitamin and mineral supplementation. The objective of this study was to evaluate a composite supplement based on the clinical practice guidelines proposed in 2008 regarding vitamin and mineral supplementation after Roux-en-Y gastric bypass. The composite included iron (Fe) and calcium as well.

Methods A retrospective chart review of 309 patients undergoing laparoscopic Roux-en-Y gastric bypass (LRYGB) was evaluated for the development of deficiencies in iron and vitamins A, B₁, B₁₂, and D. Patients were instructed to take a custom vitamin and mineral supplement that was based on society-approved guidelines. The clinical practice guidelines were modified to include 1600 international units (IU) of vitamin D₃ instead of the recommended 800 IU.

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Results The compliant patients' deficiency rates were significantly lower than those of the noncompliant patients for iron (p=0.001), vitamin A (p=0.01), vitamin B₁₂ $(p\approx0.02)$, and vitamin D (p<0.0001). Women's menstrual status did not significantly influence the development of iron deficiency. Conclusions Use of a composite based on guidelines proposed by the AACE, TOS, and the ASMBS appears to be effective for preventing iron and vitamins A, B₁, B₁₂, and D deficiencies in the LRYGB patients during the first postoperative year. Separation of calcium and Fe does not need to be mandatory. Even with simplification, compliance is far from universal.

Keywords Vitamin supplementation · Gastric bypass · Weight loss surgery · Nutritional guidelines

Introduction

Vitamin and mineral deficiencies are common after malabsorptive, restrictive, and mixed weight loss surgical procedures [1–4]. Despite widespread knowledge of the more common nutritional deficiencies, the practice of nutritional supplementation among surgeons varies widely. The available data show that over-the-counter multivitamin formulations do not protect patients from metabolic deficiencies after either laparoscopic Roux-en-Y gastric bypass (LRYGB) or biliary pancreatic diversion with or without duodenal switch (BPD, BPD/DS) [2, 5] and that many deficiencies appear within the first 3 to 6 months postoperatively [2, 6]. Guidelines were proposed in 2008 by the American Association of Clinical Endocrinologists (AACE), The Obesity Society (TOS), and the American Society of Metabolic and Bariatric Surgery (ASMBS) [7]. Updated practice guidelines were released in 2013 [8]. However, adherence requires taking numerous pills



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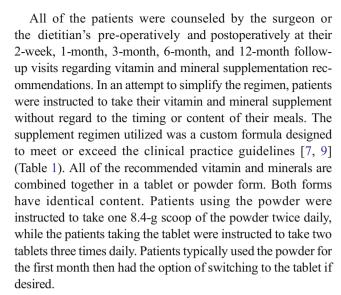
throughout the day. Finding the right pills and scheduling to potentially avoid competitive absorption of iron and calcium make compliance difficult. As a result, several specialty preparations have been offered for the bariatric market. The purpose of this study is to determine whether compliance with such a composite supplement that is based on the above recommendations, without separation of divalent cations, can make compliance simpler and prevent deficiency in post LRYGB patients. The composite supplement exists in either pill or powder form and is prepared based on the 2008 guidelines with a greater amount of vitamin D (1600 IU). In addition to the bariatric-enhanced elements, the composite has the standard components of an everyday vitamin. The simplicity of taking a single compound twice daily is hoped to make adherence easier. As a result, we decided to investigate both the rate of compliance and the development of deficiencies in iron and vitamins A, B₁, B₁₂, and D for patients undergoing LRYGB placed on a composite vitamin and mineral mixture.

Materials and Methods

Patients undergoing LRYGB from March 1, 2009 to April 1, 2010 in our practice (New Life Center for Bariatric Surgery, TN) were retrospectively reviewed. All patients were treated according to the standard clinical pathway of the practice. IRB approval was received for data collection. The patients were tested 1 month pre-operatively as well as at 6 and 12 months postoperatively for serum levels of iron, and vitamins A, B_1 , and B_{12} , and of total vitamin D. Patients were extensively interviewed to determine their adherence, with compliance being defined as adhering to the composite regimen greater than or equal to 5 days per week. Female patients were further divided into pre- and post-menopausal cohorts.

Statistical analysis to determine whether the observations were independent was evaluated with the Durbin-Watson test. Appropriate tests of significance on all nutrients at the given intervals were performed. Where there were a sufficient number of successes and failures in each compliance group, we utilized the chi-squared two-sample proportion test (vitamin D). In instances where the successes or failures were small (iron and vitamins A, B_1 , and B_{12}], we ran the Fisher exact test.

To determine whether a postsurgical deficiency developed, patients with a pre-operative deficiency were excluded from the analysis. Thus, only patient with normal parameters pre-operatively, for the variable tested, were included for analysis. As a result, there were a different number of subjects available for analysis for each variable investigated.



Patients were considered deficient if their serum iron saturation was <15 % or if their total iron was <40 mcg/dL, vitamin A was <38 mcg/dL, vitamin B_1 was <87 nmol/L, vitamin B_{12} was <200 pg/mL, and total 25-OH vitamin D was <30 ng/mL (Quest Diagnostics Inc.).

 Table 1
 Composite supplement contents

Ingredients	Concentrations in tablet form ^a	Concentrations in powder form ^b
Vitamin A	10,000 IU	10,000 IU
Vitamin C	120 mg	120 mg
Vitamin D	1600 IU	1600 IU
Vitamin E	200 IU	200 IU
Vitamin K	240 mcg	240 mcg
Thiamin	6 mg	6 mg
Riboflavin	8 mg	8 mg
Niacin	40 mg	40 mg
B_6	8 mg	8 mg
Folic acid	800 mcg	800 mcg
B_{12}	600 mcg	600 mcg
Biotin	600 mcg	600 mcg
Pantothenic acid	40 mg	40 mg
Calcium	2000 mg	2000 mg
Iron	40 mg	40 mg
Magnesium	800 mg	800 mg
Zinc	30 mg	30 mg
Selenium	140 mcg	140 mcg
Copper	4 mg	4 mg
Manganese	4 mg	4 mg
Chromium	240 mcg	240 mcg
Molybdenum	200 mcg	200 mcg
Iodine	300 mcg	300 mcg

^a Tablets are taken six pills a day



^b Powder form is consumed two scoops a day (8.4 g/scoop)

Results

There were 309 patients in the study; all of them were constructed ante-colic and ante-gastric, with an 80-cm biliopancreatic limb and a 150-cm alimentary limb. There were no patients lost to follow-up during the study period; however, two patients had inadequate data, thus excluded from the analyses.

Of the 307 subjects available for data analysis, 180 (59 %) reported adherence to the composite regimen. The compliant and noncompliant groups were comparable with regard to patient age, sex, and menstrual status and pre-operative body mass index (BMI) (Table 2).

At 6 months postoperative, there were no meaningful differences between the compliant and noncompliant groups. However, at 12 months, differences were noted in deficiency development for each nutrient. For iron and vitamins A, B_1 , B_{12} , and D, the observations were deemed to be independent (p>0.05) (Table 3).

Iron

Pre-operative iron deficiency was found in 89 patients, leaving 218 (all females) for analysis or 71 %. There was a highly significant (p=0.001) relationship between compliance and a lower probability of developing iron deficiency at 12 months after surgery regardless of the patient's menstrual status. The incidence of menstruation was comparable between the compliant and noncompliant groups (36.5 vs. 42.7 %, respectively. Compliance resulted in an 80 % reduction in odds of developing iron deficiency, with odds ratio (OR) of 20 %. The left-tailed 95 % confidence interval (CI) is (0, 0.53), meaning that it is highly likely that compliance results in a reduction of at least 47 % in the odds of developing iron deficiency following surgery (Table 3). This data indicates that iron (Fe) can be given with Ca, and still effective supplementation is obtained.

Vitamin A

Vitamin A deficiency was not detected in any pre-operative patient; thus, 307 patients were available for analysis. Compliance with the regimen is significantly (p=0.01) related to a lower probability of developing vitamin A deficiency at

 Table 2
 Patient demographics

	Compliant group	Noncompliant group	p value
Age (years)	47.5±11.4	47.5±11.7	0.93
BMI (kg/m ²)	50.5 ± 30.8	47.4 ± 9.6	0.20
Female	140	107	
Male	40	22	

Age and BMI are given in mean and standard deviation

12 months after surgery. The half-life of vitamin A can be as long as 6 months and is longer than vitamin D. As a result, delayed deficiency can occur and this must be monitored past the first year.

Vitamin B₁

Thiamine deficiency was found in only 8 of 307 patients preoperatively. Deficiency was also not common in either group postoperatively. As a result, compliance with the postsurgical regimen was not significant (p \approx 0.09) but did have a lower probability of vitamin B₁ deficiency at 12 months after surgery, with an OR about 17 %. Thiamine has a very rapid half-life and must be administered rapidly in patients with poor oral intake.

Vitamin B₁₂

Deficiency in B_{12} was unusual pre-operatively, 7 out of 307 patients, but did occur following surgery. Compliance resulted in a lower probability of deficiency (p=0.02) at 12 months after surgery, with an OR of 11 %. The left-tailed 95 % CI is (0, 0.75), meaning that it is highly likely that compliance results in a reduction of at least 25 % in the odds of developing vitamin B_{12} deficiency following surgery (Table 3). B_{12} has a long half-life, and stores in the body can present deficiency for a lengthy period of time. As a result, these results are surprising and may indicate a difference in the ability to store B_{12} following gastric bypass.

Vitamin D

Pre-operative vitamin D deficiency was common and found in 134 patients. There was a highly significant (p<0.0001) relationship between the regimen and a lower probability of developing vitamin D deficiency at 12 months after surgery. The probabilities of developing the deficiency, for compliance and noncompliance, are 10 and 34 %, respectively (Table 3). Vitamin D has a half-life of approximately 15 days.

Discussion

An important aspect of aftercare for procedures that alter absorption is vitamin and mineral supplementation. It has become clear that, by themselves, over-the-counter supplements do not meet the recommended thresholds.

Determination of compliance is difficult and complex. To begin, most studies, as does ours, rely on self-reporting. It is also arbitrary as to what constitutes compliance and noncompliance. For these reasons, we believe our study in all probability underestimates the significance of regimen compliance. Self-reporting probably overestimates the compliant population. Also, included in the noncompliant group are patients that occasionally take supplements.



Table 3 Postoperative nutritional deficiencies at 12 months

Vitamin/mineral		Noncompliant group		Compliant group		Difference in the deficiencies	Odds ratio	p value	95 % CI
		n	Deficiencies developed (%)	n	Deficiencies developed (%)	between two groups (%)			
A		127	5.5	180	0.6	4.9	0.10	0.01*	0, 0.611
\mathbf{B}_1		123	3.25	176	0.6	2.6	0.17	0.0942	0, 1.33
B_{12}		124	4.8	176	0.6	4.2	0.113	0.0213	0, 0.75
D		73	34.2	100	10	24.2	0.215	0.0001*	0, 0.45
Iron	Total	89	16.9	129	3.9	13	0.20	0.001*	0, 0.53
	Menstruating females	38	23.7	47	6.3	17.3	0.22	0.02*	0, 0.82
	Non-menstruating females	51	11.8	82	2.4	9.4	0.19	0.04*	0, 0.89

^{*}Indicates statistical significance

Thus it is concerning that with a simplified routine, where the same preparation is taken twice daily, compliance is only 59 %. It would be expected that adherence to a more complex routine would even be lower. In addition, the patients utilized in this study were part of a comprehensive private practice that incorporates nutritional counseling, psychological intervention, and exercise therapy. All patients are required to be part of the multi-disciplinary program that emphasizes compliance. Fortunately, the majority of detected deficiencies rarely caused significant clinical impairment within 12 months of surgery.

Iron

It has been shown that after weight loss surgery heme iron absorption is interfered with much more than is the absorption of non-heme iron that is found in supplements [10].

Pre-operative iron deficiency rates of 44 % have been reported after LRYGB [11]. This incidence is consistent with our results, as 39 % of the noncompliant group and 51 % of the compliant group were iron-deficient pre-operatively and were therefore excluded from the iron arm of this study. Aasheim et al. found that separate iron supplement use declined after surgery and that only 25 % of LRYGB patients were compliant with their iron supplementation 1 year after surgery [12]. Postoperative iron deficiency rates have been reported to be 25–39 % after LRYGB [11, 13]. These rates do not appear to be different than the rate of deficiency preoperatively; however, it is not clear whether those patients who are deficient pre-operatively are the same patients who are deficient postoperatively.

In this study, the compliant patient cohort had a significantly lower risk of developing iron deficiency after LRYGB compared to the noncompliant group regardless of the menstrual status of the patient (p=0.001). The patients took their supplement, containing both iron and calcium, without regard for the timing or content of their meals, which allowed simplification

of the postoperative supplementation regimen. The ability to combine iron and calcium in the same tablet is consistent with Roughead et al.'s study finding that calcium supplementation did not significantly interfere with the absorption of non-heme iron [14]. There has been much made of the competition between iron and calcium for absorption in the small bowel [14, 15]. This competition appears to occur primarily due to calcium's inhibitory effect on heme iron absorption in the small bowel [15]. Calcium does not as significantly inhibit the absorption of non-heme iron present in supplements, and most of the studies published looking into this have been performed on the unaltered gastrointestinal tracts of healthy subjects [14, 16–18]. It would be of interest to determine whether surgically induced malabsorption or a deficiency of iron might influence this competition, a subject that warrants further study. In this study, the presence of calcium and iron together in the supplement resulted in low rates of iron deficiency in the compliant cohort. With compliance rates already low, we believe that any regimen that improves simplicity is advantageous.

Vitamin A

The incidence of vitamin A deficiency after LRYGB has been reported to be as high as 12.5 % [4, 19], but the incidence of symptoms such as night blindness has been rare (only four reported cases [19]). The incidence of vitamin A deficiency was significantly lower in our compliant patients, with less than 1 % developing a deficiency at 12 months (p=0.01). None of the deficient patients at 12 months had symptoms associated with the laboratory abnormalities.

Vitamin B₁

The consequences of thiamine deficiency postoperatively have been the topic of expanded discussion. When it occurs, deficiency can result in permanent neurologic abnormalities [20, 21].



Our study shows that deficiency is rare pre-operatively and rarely develops postoperatively unless there are factors that limit or prevent adequate food intake. This means that deficiency is acquired following surgery. As compared to other vitamins, thiamine has a very short half-life; thus, it must be supplemented rapidly in patients that develop postsurgical intake issues.

This water-soluble vitamin is readily absorbed orally. Additionally, in the absence of gastrointestinal symptoms, deficiency post-surgery is unusual. As a result, the incidence of deficiency in our study was lower in the compliant group, but did not reach significance (p=0.09). The primary symptom associated with B_1 deficiency in our patients was nausea, which resolved with B_1 replacement. Chang et al. also found an exceedingly low incidence of vitamin B_1 deficiency following LRYGB [22].

Vitamin B₁₂

The incidence of vitamin B_{12} deficiency after LRYGB has been reported to be 12--36 % [1, 9]. B_{12} deficiency may lead to macrocytic anemia, megaloblastosis of the bone marrow, leukopenia, thrombocytopenia, glossitis, and neurologic derangements [23, 24]. The incidence of deficiency was much lower in this study, and glossitis was the only symptom that manifested itself (two patients). There was a significant $(p \approx .02)$ reduction in the incidence of deficiency between the cohorts in favor of the compliant group.

Vitamin D

Vitamin D is the most common vitamin deficiency in the obese and weight loss surgery patient [25, 26]. Deficiency may lead to musculoskeletal dysfunction, secondary hyperparathyroidism, metabolic bone disease, and autoimmune and cardiac dysfunction [27]. In Carlin et al.'s investigation, patients taking the recommended 800 IU of vitamin D daily after LRYGB had an unacceptably high incidence of hypovitaminosis D (44 %) [28]. An international panel recently suggested that the US Food and Drug Administration (FDA) recommendation for the daily requirement of Vitamin D is too low [27, 29]. The 2008 AACE, TOS, and ASMBS clinical practice guidelines are based on these FDA recommendations. For these reasons, the amount of vitamin D recommended to our patients was increased to 1600 IU of vitamin D₃/day (of note, updated 2013 guidelines recommend 3000 IU vitamin D/day [8]). The incidence of hypovitaminosis D was significantly decreased in the compliant patient group (p < 0.0001). In the noncompliant group, the incidence of developing hypovitaminosis D was 33 %. The practical implication is that compliance resulted in a 24 % reduction in the probability of developing vitamin D deficiency (Table 3). For iron and vitamins A, B₁, B₁₂, and D, the observations were deemed to be independent (p>0.05).

Study Limitations

The present study has limitations that deserve comment. This retrospective review was not blinded, controlled, or randomized. The patient's compliance was self-reported, and no attempt to count tablets of vitamins to confirm compliance was performed. The patient's education level and support group attendance was not recorded and may have an impact on compliance. Finally, the short duration of follow-up means no comment can be made regarding the efficacy of the clinical practice guidelines for preventing deficiencies in the LRYGB patient after 12 months. Further study is needed on this important subject.

Conclusions

Even simplified, vitamin regimen compliance, is modest at best. Our study suggests that adherence to supplementation that is based on the modified clinical practice guidelines proposed in 2008 appear to be effective for preventing the development of deficiencies in iron, vitamin A, and vitamin B_{12} in postoperative LRYGB patients during the first postoperative year. The amount of vitamin D recommended in the clinical practice guidelines may not be adequate [24, 27, 29]; thus, it was increased to 1600 IU vitamin D in our study. This resulted in a low incidence of hypovitaminosis D in our compliant cohort that was significant (p<0.0001) without any incidence of vitamin D toxicity. Our study suggests that supplements may be taken without separating the iron and calcium allowing simplification of the postoperative regimen and, hopefully, increasing patient compliance.

Finally, a significant number of patients have pre-existing deficiencies. This highlights the fact that those patients with high BMIs are not super nourished or have higher reserves. They have excess fat and are frequently poorly nourished. This fact combined with inadequate compliance of even a simplified routine highlights the need for improved techniques that ensure the majority or patients get the required supplementation.

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Conflict of Interest SB is the owner of Bari Life bariatric supplements. He also reports personal fees from Ethicon Endo-surgery Inc.

RG, KC, and JC declare no conflicts of interest.

MR is a teaching consultant for Johnson & Johnson Incorporated and Covidien Ltd. where he receives compensation. He is also in the scientific advisory board at SurgiQuest and ValenTx and has stocks options in them.

Ethical Approval All procedures performed in this study were according to the standard clinical protocol. IRB approval was obtained prior to data collection.



Informed Consent For this type of study, formal consent is not required.

Grants Information None.

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