CHAPTER 19

VITAMIN AND MINERAL SUPPLEMENTATION AFTER GASTRIC BYPASS

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The principal documented vitamin and mineral deficiencies after gastric bypass are due to lack of iron,vitamin B_{12} and folic acid.Iron deficiency occurs in 50% of patients followed long-term. Vitamin B_{12} deficiency is inevitable in all patients not treated prophylactically. Folic acid deficiency is unusual if patients take multivitamins. Clinical guidelines for preventing and treating vitamin and mineral deficiencies after gastric bypass are reviewed in this chapter.

Prevention of postoperative vitamin and mineral deficiencies after gastric bypass necessitates long-term follow-up of patients and knowledge of how these micronutrients function in the body. Detection of these deficiencies may be further hampered by random and inappropriate ordering of lab tests and not recognizing signs of deficiency.[1] Even in those cases where good diagnostic technique prevails, insufficient experience with vitamin and mineral supplements may prevent their use for all the possible conditions where good nutrition can make an impact. The focus of this paper is to delineate the possible sources of vitamin and mineral deficiencies after gastric bypass and metabolic conditions requiring supplementation. Guidelines are given to help the treating practitioners choose and administer supplements wisely.

AT RISK FOR DEFICIENCY

Late follow-up of patients 25-30 years after subtotal gastrectomy may predict the onset of complications in patients after gastric bypass. Tovey et al[2] found that iron deficiency was the most common nutritional problem by the end of the first decade. Vitamin B_{12} deficiency assumed more importance in the following 10 years. During the third decade both reached equal prevalence, being found in 90% of the female and 70% of the male residual population.

Gastric bypass is functionally a subtotal gastrectomy, and similar nutritional deficiencies prevail. In a study of 150 consecutive patients, Amaral et al[3] found that anemia developed in 37% of patients at a mean of 20 months after surgery, with women being more commonly affected than men. Iron deficiency occurred in 47%, vitamin B_{12} deficiency in 40% and RBC folate deficiency in 18%. Microcytic anemia developed in 18%, normocytic anemia in 12% and macrocytic anemia in 7%. Similar patterns of deficiency have been reported by others.[4,5] The most common problem was the combined iron and vitamin B_{12} deficiencies. The time to development is variable. Iron deficiency manifests within the first 6 months, followed by vitamin B_{12} deficiency within 2 years

after gastric bypass.[3,5] Hemoglobin and MCV are not predictive of these deficiencies. Serum ferritin, serum vitamin B_{12} and serum/RBC folate must be measured to determine iron, vitamin B_{12} and folic acid status, respectively.

Inadequate body reserves,[6] low nutrient intakes, [6,7] insufficient supplementation[8,9] and noncompliance in taking multivitamins have been suggested as factors contributing to these deficiencies. Dietary intakes decrease after gastric bypass due to the reduced size of the gastric pouch, but the total intake of any micronutrient need not be restricted if supplementation is part of the treatment program. Vitamin and mineral supplements have consistently been shown to improve the nutritional status of patients. Supplements providing quantities of micronutrients equivalent to the recommended daily allowance (RDA) were adequate in maintaining normal blood values during the first postoperative year for thiamine, riboflavin, pyridoxine, vitamin E and zinc.[6,9] Multivitamins alone lowered the incidence of folate deficiency but did not prevent iron or vitamin B_{12} deficiencies.[5,10]

Intakes of iron and vitamin B_{12} in ranges much greater than the RDA are needed to help control deficiency.[8,9] Doses of 100, 250, 350 and 600 µg of oral crystalline vitamin B_{12} were effective in maintaining adequate serum vitamin B_{12} concentrations in over 83% of patients, but 350 and 600 µg (300 x RDA) achieved normal levels in 95% of patients.[11] Oral iron taken three times daily (10 x RDA), with the addition of 500 mg vitamin C concurrently, may help in correcting ferritin deficits and anemia more effectively than iron alone.[12] Iron status can be ameliorated by supplementing patients with oral iron immediately after surgery, especially menstruating women.[13]

Persistent vomiting can lead to thiamine deficiency, central nervous system damage and/or peripheral neuropathy designated as *Wernicke-Korsakoff Syndrome.* This complication has been reported after gastric partitioning and gastroplasty[14] and is possible after gastric bypass, especially if anastomotic stenosis occurs. Serum thiamine is not readily measured, so an intravenous dose of 100 mg thiamine given empirically *before* rehydration or glucose administration and continuously thereafter until the cause of vomiting is eliminated can be helpful. Prompt treatment can reverse symptoms of transient mental impairment and rapidly developing peripheral weakness. Delaying therapy is without benefit.

Several authors have reported that calcium status is not affected by gastric bypass.[15,16] However, alkaline phosphatase was elevated in 34% of patients after surgery and remained elevated in 15%.[15] In the absence of liver or Paget's disease, an increase in alkaline phosphatase usually indicates osteomalacia, which is associated with an abnormal calcium infusion test and decreased plasma vitamin D activity. The authors suspected that subclinical bone disease could be possible and recommended calcium and vitamin D supplements. Magnesium deficiency on long-term follow-up has been reported.[17] Calcium absorption and bone mineralization may also be compromised by low vitamin D status preoperatively.[18] We evaluated 56 patients for bone mineral status 3-5 years after isolated gastric bypass and found two men and four premenopausal women to be at risk for mild osteoporosis. Elevated parathyroid hormone levels were present in 14%. Decreased bone mineral density was directly related to a very high intake of soft drinks and coffee in one, altered hormone levels in two, genetic predisposition in two, and uncontrollable hyperparathyroidism and hypothyroidism in one. High estrogen levels appeared to protect against osteoporosis (unpublished data).

ABSORPTION AFTER GASTRIC BYPASS

Patients after gastric bypass are particularly vulnerable to malabsorption of iron, B vita-

mins, calcium and vitamin A, because the duodenum and a variable segment of upper jejunum are bypassed—the major sites of absorption (Figure 1). In addition, gastric acid secretion from the small pouch is negligible[19] and absorption of iron,[12] vitamin B_{12},[19] calcium[20] and folic acid[21] are severely limited due to pouch achlorhydria.

Iron absorption is inversely proportional to the size of body stores. Iron in intestinal mucosal cells and storage areas such as the liver, spleen and bone marrow is delivered by transferrin to cells engaged in hemoglobin synthesis. The requirements are 30-35 mg/day. The normal diet provides 15-30 mg/day, and iron must be in the ferrous form. Body iron loss for men is 1.0-1.5 µg/day, but it is 2 to 3 µg/day for women of menstrual age because of menstrual blood loss.

Further malabsorption of these micronutrients may occur if food entering the proximal small bowel is not chewed finely or is not sufficiently warmed. Digestive enzymes are also lacking in the small gastric pouch. We have noted cases of mental fatigue manifesting as difficulty in learning and concentrating, and this may in part be related to decreased absorption of B vitamins. Other micronutri-

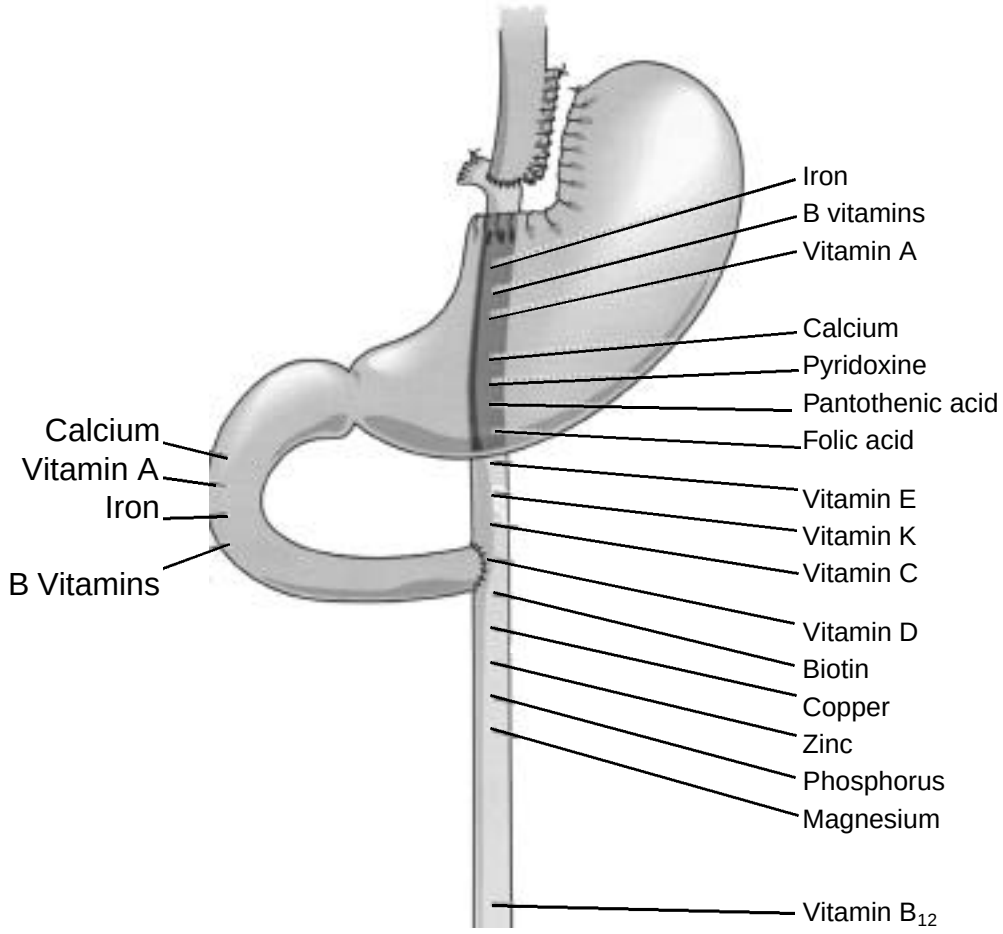

FIGURE 1. Sites of absorption of vitamins and minerals after isolated gastric bypass.

ents are absorbed along the entire length of the small intestine.

Vitamin B_{12} absorption appears to be affected by several factors. While normal absorption of crystalline (unbound) vitamin B_{12} as measured by the Schilling test is preserved, the magnitude of its absorption is altered after surgery.[19] Various authors have suggested causes, including insufficient secretion of intrinsic factor[22] and decreased B_{12}-intrinsic factor complex formation[19] due to poor mixing beyond the jejunojejunal junction or proteolytic destruction of intrinsic factor.

Absorption of vitamin B_{12} from food involves a complex process. It must first be released from protein by the combined action of hydrochloric acid and pepsin in the stomach. The freed vitamin B_{12} attaches to R-binder proteins from the saliva and gastric juice, and in turn is released from these by pancreatic enzymes in the upper small intestine. The vitamin B_{12} molecule is then rapidly bound by intrinsic factor to form a complex that is resistant to proteolysis. The B_{12}-intrinsic factor complex remains intact until it adheres to specific receptors in the distal ileum prior to absorption.

Protein-bound vitamin B_{12} absorption is affected by gastric bypass.[19,23] No method of food preparation was adequate enough to allow for sufficient vitamin B_{12} release from protein foods. Extensive boiling of food,[24] consumption of enzymes with foods to effect release, or incubation of foods with enzymes before ingestion,[23] are not feasible alternatives for providing the vitamin. Therefore vitamin B_{12} must be made available from crystalline sources at doses compatible with passive diffusion rather than dependent on the intrinsic factor mechanism.

OPTIMUM DAILY INTAKES RATHER THAN RDAs

Numerous studies have demonstrated that most North Americans consume nutritionally poor diets. Marginal nutrient deficiencies exist in a substantial portion of the US population. More than 80% consume less than the RDA.[25] These studies indicate the chances of consuming a diet meeting the RDA for all nutrients is extremely unlikely for most people. Theoretically it is possible that a healthy individual can get all the nutrition needed from foods, but most do not even come close to meeting all their nutritional needs through diet alone. While most Americans are deficient in many micronutrients, the level of deficiency is usually not to a point where obvious nutrient deficiencies are apparent. Subclinical deficiencies, where lack of a particular vitamin or mineral is not severe enough to produce a classic deficiency symptom, are thought to be relatively common. In many instances the only clue of a subclinical nutrient deficiency may be fatigue, lethargy, difficulty in concentration, a lack of well-being or some other vague symptom. Severely obese patients have been shown to be at risk for nutrient deficits before surgery as well.[6,18]

The RDAs only focus on the prevention of nutritional deficiencies in groups of people. They do not define optimal intakes for an individual, and special nutritional needs such as those produced by gastric surgery are not covered by the RDAs. A tremendous amount of scientific research indicates that the optimal level for many nutrients may be much higher than their current RDAs. This is clearly evident from our work which indicates that the optimal daily intake for vitamin B_{12} after gastric bypass greatly exceeds current nutritional guidelines for the general population.[23] Decreased food intake, nutrient-depleted foods, altered absorption and biochemical individuality all point to using *optimum daily intakes* (ODI) rather than RDAs as the basis for vitamin and mineral supplementation after gastric bypass.

IMPORTANT ASPECTS OF SUPPLEMENTATION

We have tested numerous nutrient combinations with our patients and believe that the following information could serve as the basis for determining the ODIs after gastric bypass surgery. Our patients responded quickly and positively to these nutrient levels.

1. Choose high potency supplements

Taking a high-quality preparation that provides all of the known vitamins and minerals serves as the foundation of a sound nutritional supplementation program. Choose preparations by companies that manufacture in small frequent batches. Health-food stores tend to carry the better quality brands. Table 1 is a composite listing of the ODI dosages and the best absorbable form for each of the vitamins and minerals. Our core program of supplementation included two preparations which reflect the ODI levels suggested: a high potency multiple vitamin-mineral supplement (minimal amounts of B-complex vitamins + other listed vitamins and minerals), and a B-complex 100 mg timed-release tablet (B_1, B_2, B_3, B_6, B_{12}, folic acid, biotin, B_5, choline). We used Super Vita Vim and B-complex 100 mg timed-release tablets (CE Jamieson & Company Ltd., Windsor, ON, CAN).

2. Timed-release formulas are not always better

Timed-release vitamins are active over an 8-12 hour period and are very effective for water-soluble vitamins. However, absorption of high doses of vitamins may be hampered by the timed-release process in gastric bypass patients. Vitamin B_{12} was better absorbed from two standard 250 µg tablets (total 500 µg) taken once daily than from one 1200 µg as a timed-release preparation. The latter formulas may not dissolve adequately and therefore fail to release their nutrients in time to be absorbed. Encapsulated timed-release supplements may be less unpredictable than hard-coated tablets.

3. Keep quantities of B vitamins balanced

One should not take high doses of a single B vitamin without increasing the amount of all the others. This is important because B vitamins tend to work together, and compete for absorption in the intestines. Once the basic ODI of the B vitamins is established (Table 1), then additional amounts of one or two individual B vitamins can be added to meet particular needs (Table 2). It is safe to take up to 2-3 times the amount of the other Bs being ingested. Side effects may manifest when massive doses (>2000 mg) of any individual B vitamin are consumed.

Folic acid supplementation should always include vitamin B_{12} because folic acid can mask an underlying vitamin B_{12} deficiency. The danger is that while folic acid reverses the macrocytic anemia, it does not prevent or reverse the neurological symptoms of a vitamin B_{12} deficiency. Nerve damage can result that does not respond to vitamin B_{12} supplementation. Vitamin B_{12} is given in a proportionally greater amount to folic acid after gastric bypass because of the surgery's propensity towards low serum vitamin B_{12} levels.

4. Aim for maximum absorption

Look for supplements that dissolve quickly. Nutrients bound up in hard-coated tablets may never make their way into the bloodstream. Loose powder, soft-gel capsules or quickly dissolving tablets are fast-acting forms that permit optimal absorption. Supplements can be cut up into several small pieces or be chewed before swallowing without loss of potency. If the formulations are not timed-release, one should advise breaking the supplement in half and taking half in the morning and the other 8 hours later, in order to get the full benefit of these nutrients over a 24-hour period. B-complex vitamins should be taken early in the day to prevent sleep dif-

TABLE 1. INGREDIENTS IN TWO TABLETS USED IN ROUTINE VITAMIN-MINERAL SUPPLEMENTATION AFTER GASTRIC BYPASS

Supplement	*ODIs*[†]	*Best Absorbed Form*
Vitamin A*	10000 IU	retinol, palm oil carotene
Vitamin D*	400 IU	cholecalciferol
Vitamin C*	200 mg	calcium buffered
Vitamin E*	60 IU	d-α tocopheryl chelate
Thiamine (B_1)**	100 mg	thiamine-HCl
Riboflavin (B_2)**	100 mg	riboflavin-5-phosphate, B_2
Niacin (B_3)**	100 mg	inositol hexaniacinate
Pyridoxine (B_6)**	100 mg	pyridoxal-5-phosphate
Vitamin B_{12}**	100 mg	methylcobalamin
Folic acid**	400 µg	folinic acid
Biotin**	100 µg	biotin
Pantothenic acid (B_5)**	100 mg	pantethine
Choline**	100 mg	bitartrate
Calcium*	140 mg	citrate
Iron*	4 mg	gluconate
Copper*	1 mg	chelate
Iodine*	0.1 mg	kelp, iodine caseinate
Magnesium*	100 mg	citrate
Zinc*	10 mg	citrate
Potassium*	30 mg	chelate
Chromium*	50 µg	picolinate
Selenium*	10 µg	yeast, selenomethionine
Inositol*	100 mg	inositol monophosphate

*High-potency multiple vitamin-mineral supplement
**B-complex 100 mg timed-release supplement
[†]Optimum Daily Intake

ficulties later at night.

Fat-soluble vitamins (A, D, E, K) and essential fatty acids (flaxseed oil) (Table 2) require fat for proper assimilation. Dry- or water-soluble forms are available for people where fat ingestion is not advised. Two processes, emulsification and micellization, reduce the size of fat droplets and greatly enhance absorption. Emulsified and particularly micellized vitamins become nearly as absorbable as water-soluble vitamins.

Most supplements are best taken with meals to promote better absorption and tolerance, as in the case of oral iron. On an empty stomach water-soluble vitamins can leave as quickly as 2-3 hours after ingestion, while fat-soluble vitamins remain in the body for about 24 hours, with excess amounts being stored in the liver longer.

Certain long-term medications can prevent absorption or utilization of nutrients. The H_2-receptor blockers used for treating stomal ulcers after gastric bypass interfere with vitamin B_{12} absorption. An extra dose of a specific vitamin or mineral may be needed to compensate for the drug's effect.

5. Use chelated minerals

Minerals are best absorbed from the digestive tract in their chelated form where they are bound to other substances. There are many chelation vehicles on the market with a wide

TABLE 2. INDIVIDUAL VITAMIN AND MINERAL SUPPLEMENTS ADDED TO CORE PROGRAM FOR TREATING CONDITIONS AFTER GASTRIC BYPASS

Condition	***Additional Vitamins + Minerals***
Low serum ferritin	Ferrous gluconate 300 mg tid[12] Vitamin C 500 mg tid[12]
Iron-resistant anemia	Ferrous gluconate 300 mg tid Vitamin C 500 mg tid Zinc chelate 15 mg qd Copper chelate 1 mg qd Vitamin E 400 IU qd
Low serum vitamin B_{12}	Vitamin B_{12} 500 µg qd[11]
Low RBC folate	Folic acid 400 µg qd Vitamin B_{12} 500 µg qd
Poor wound healing	Vitamin C 2,000 mg qd Vitamin E 400 IU qd Selenium 200 µg qd Zinc chelate 50 mg qd
Low calcium intake/osteopenia	Elemental calcium 200 mg 4x qd* Elemental magnesium 100 mg 4x qd* Vitamin D 400 IU qd** Vitamin A 5,000 IU qd**
Hair loss	Zinc chelate 15 mg qd Copper chelate 1 mg qd Silica 20 mg qd Vitamin C 2,000 mg qd Flaxseed oil 15 cc qd Vitamin A 5,000 IU qd**
Extreme fatigue	Vitamin C 2,000 mg qd Vitamin E 400 IU qd Selenium 200 µg qd Zinc chelate 15 mg qd Copper chelate 1 mg qd Elemental calcium 200 mg 2x qnite* Elemental magnesium 100 mg 2x qnite* Vitamin D 400 IU qd** Vitamin A 5,000 IU qd** Flaxseed oil 15 cc qd

*Calcium and magnesium combined in one supplement

**From North Atlantic fish oil source

variation in absorption. The ones with the highest absorption efficiencies are malate, ethanolamine phosphate, ascorbate, citrate, fumarate, peptonate, succinate, lysinate, glycerate, picolinate and acetate. Moderately high efficiency absorption vehicles are amino acid chelate, aspartate, chloride, sulfate, gluconate and phosphate. The lowest absorption efficiency vehicles and the least expensive are carbonate and oxide.

6. Monitor vitamin A and D intakes

Vitamins A and D have the potential for toxicity. Up to 1,000 IU of vitamin D and 15,000 IU of vitamin A (dietary and supplement sources combined) can be taken safely. Vitamin D is best utilized when taken with vitamin A in natural sources such as fish oils. The food industry fortifies milk products, cereals, grain products, as well as animal feed, with synthetic vitamin D_2 (ergocalciferol). Those individuals who regularly consume vitamin D-fortified foods should avoid supplemental vitamin D and should diminish their consumption of fortified foods and find whole food alternatives when possible.

7. Check mineral ratios in supplements

Zinc and copper antagonize each other. To maintain good health, keep the ratio between zinc and copper at 10:1 or 15:1. Calcium and magnesium should be present in supplements in a 2:1 ratio. Magnesium taken in a 1:1 ratio to calcium could cause diarrhea in susceptible individuals. Vitamin D should be taken with calcium supplements to promote absorption.

8. Monitor vitamin-mineral combinations

Iron fumarate and sulfate destroy vitamin E. It is not affected by iron chelated to gluconate, fumarate or citrate. Vitamin C taken concurrently with vitamin B_{12} destroys its activity. Zinc is required to utilize vitamins A and B. Bioflavonoids (vitamin P) are essential for the proper absorption of vitamin C. Selenium improves vitamin E activity considerably. High coffee, soft drink and sugar intakes deplete B vitamins, zinc and calcium.

Less prominent but equally important micronutrients are not commonly added to multivitamin preparations. Their absence may play a vital role in degenerative conditions arising after gastric bypass. Sulfur is found in insulin and works with B vitamins for nerve health. Dietary sulfur can be found in eggs, meat, fish and dairy products. Manganese helps in the utilization of B vitamins and is important for blood formation and sex hormone production. Best food sources are whole grain cereals, eggs, nuts, seeds and green vegetables. Vitamin K is necessary for clotting factor manufacture and building healthy bones. Dark green leafy vegetables, broccoli, lettuce, cabbage, spinach and green tea are rich sources of vitamin K.

9. Synthetic versus natural preparations

Most vitamins are synthetic even if their labels say "natural". The cost of "all natural" vitamins would be prohibitive. The body recognizes and uses molecules of most synthetic vitamins. One notable exception is vitamin E. Synthetic vitamin E, the dl form, has very little vitamin E activity. Use the d form only (Table 1). Synthetic fat-soluble vitamins are difficult for the liver to utilize properly. Use natural North Atlantic fish oil sources free from heavy metal residues to provide vitamins A and D to treat impaired health, especially in sun-starved climates (Table 2).

10. Do not adjust supplement dosages without supervision

Some practitioners advocate periodically discontinuing or at least reducing the dosages of vitamin and mineral supplements for 1-2 days per week during leisure time, and for one or more weeks every 3-4 months, especially when on vacation or in a quieter, cleaner, less stressful environment. This may not be possible with the high nutrient requirements demanded of the gastric bypass. We noted that continuous therapy with oral vitamin B_{12} was

necessary, since serum vitamin B_{12} values declined rapidly over a 3-month period in patients off treatment.[11] A highly significant incidence of iron deficiency anemia approximating 50% was present in our population 2 years after initial follow-up for iron status.[12] Others have noted similar declines.[8,10] Suggesting once to patients that they modify their vitamin/mineral intakes may be interpreted as a long-term event, and in light of the rapid decline in serum values, could precipitate a deficiency if continuous patient follow-up is not maintained. Changing instructions may also be confusing to some patients. We keep our patients on oral iron long enough to see their serum ferritin values increase satisfactorily into the normal range and then discontinue treatment to avoid iron toxicity. This fluctuation in instructions may cause confusion and probably contributes to the high frequency of iron deficiency anemia.[12]

Once conditions requiring high intakes of vitamin C (2,000 mg) and zinc (50 mg) are resolved, further doses should be tapered gradually and discontinued to prevent imbalance (Table 2).

11. Consider essential fatty acid supplementation

Experts estimate that 80% of our population consumes an insufficient amount of essential fatty acids. Research indicates that over 60 health conditions benefit from essential fatty acid supplementation. We have used organic, unrefined flaxseed oil with patients under emotional and physical stress (Table 2).

12. Oral versus injectable preparations

Oral vitamin therapy is more reliable, less burdensome for patients and less costly than the parenteral form, but does require compliance on the part of patients. Some will require parenteral iron or vitamin B_{12} because of intolerance or diminished intestinal absorption. Severely depleted patients unable to take oral vitamin B_{12} responded more favorably when small amounts (100 µg) of vitamin B_{12} were administered subcutaneously each week over a 3-month period and then at 1,000 µg doses each 3 weeks (unpublished data). Intramuscular iron as Jectofer (50 mg/cc) was administered weekly (1 cc each buttock, total 100 mg/wk) for 10 consecutive weeks. This proved to be effective treatment in patients with iron deficiency anemia resistant to oral therapy.

CONCLUSION

Optimal health after gastric bypass is possible if nutrition is a major focus of treatment. Because of specialized needs due to decreased absorption of some vitamins and minerals, a well-balanced supplementation program is needed. The importance of full participation in health decisions by patients is important if noncompliance is to be eliminated. Prescribing the best forms of vitamins and minerals will ensure better assimilation and, in the long run, will be more cost-effective for the patient.

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