Clinical nutrition: 6. Management of nutritional problems of patients with Crohn's disease

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Case

Ms. C is a 40-year-old woman with Crohn's disease involving the terminal ileum who complains of lower abdominal cramps and diarrhea after eating a normal meal. The pain starts within 30 minutes of the meal and is followed by 3–4 loose stools some 1½–2 hours later. These symptoms, which began about 2 years ago, are associated with reduced appetite and weight loss. Over the past year, she has lost about 9 kg, including about 1 kg in the last 2 weeks. Her current weight is 52 kg and her height, 1.62 m. Apart from her weight loss, the patient has no signs of clinical wasting. She has not been taking medication that could have caused some of her symptoms. How would you assess and treat Ms. C's nutritional problems?

Crohn's disease is a chronic, segmental, transmural inflammation of the gastrointestinal tract. It most frequently involves the terminal ileum and the colon. The incidence of Crohn's disease has been rising steadily since the 1950s and is now about 6 per 100 000 population per year in North America. Even when their disease is inactive, patients with Crohn's disease suffer from a variety of nutritional deficiencies, including protein wasting and vitamin and mineral deficiencies (Table 1).[1] Reduced serum carotene has been described in 90% of patients with inactive disease, and reduced serum zinc, selenium, magnesium and vitamin C in 50%.[1] The main cause of nutritional deficiency in patients with Crohn's disease is anorexia,[2] which is probably the result of high levels of activity of tumour necrosis factor-α and other cytokines. However, in most patients, a combination of factors including malabsorption; bowel obstruction; excessive loss from the gut of fluids, electrolytes, plasma and blood; and drug–nutrient interactions combine with anorexia to aggravate malnutrition (Table 2).

This article describes a simple approach to assessing malnutrition in patients with Crohn's disease, then enumerates useful strategies for managing these problems.

Nutritional assessment

The nutritional problems of patients with Crohn's disease can be divided into those that concern macronutrients (protein, energy) and those that concern micronutrients (vitamins, minerals and electrolytes). The easiest and most useful way to assess the protein and energy status of patients is with the subjective global assessment (SGA), which is a qualitative assessment of the severity of a patient's malnutrition based on the history of gastrointestinal symptoms, sustained inadequate food intake, weight loss and poor functional status, coupled with a physical examination focused on the identification of muscle wasting, fat loss and edema.[3,4] In the history-taking, recent and continuing weight loss, poor dietary intake and the persistence of conditions that propagate these are assigned the greatest importance. From this assessment, a judgement can be made as to whether nutrient assimilation has been restricted because of decreased food intake, maldigestion or malabsorption, whether any effects of malnutrition on organ function and body composition have occurred and whether the patient's disease process influences nutrient requirements. Most important is a history of recent and

Review

Synthèse

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continuing weight loss, poor dietary intake and the continuous presence of conditions that limit food intake. The aim of SGA is to categorize a patient as being (A) well-nourished, (B) moderately malnourished or (C) severely malnourished. Baker and colleagues[3] and Detsky and colleagues[4] found that the use of SGA in evaluating hospital inpatients gives reproducible results with better than 80% agreement when 2 independent observers assessed the same patient.

For example, a person with a 10% weight loss from her usual body weight over the previous 8 months, but who has recently regained weight and has good functional status and no loss of muscle or fat, would fall into the SGA A category. However, Ms. C's condition would be classified as SGA B, because she has an acute exacerbation of Crohn's disease with 10% weight loss within the previous 2 weeks, while ingesting mostly liquids to avoid gastrointestinal discomfort. She is ambulatory, but off work, and has slight loss of subcutaneous tissue (reduced buccal fat pad and loose skinfolds over the arms). Whereas, if the patient had minimal food intake for 3 months, 15% weight loss and continuing weight loss, marked muscle weakness and fatigue, lacked subcutaneous tissue, and had hollow temples, deltoid muscle wasting and mild pitting edema, her condition would be classified as SGA C. More details about SGA and the assessment of protein–energy malnutrition are given in an earlier paper in this series by L. John Hoffer.[5]

Micronutrient (vitamin and mineral) deficiencies are very common in Crohn's disease, and especially common in patients who are in SGA classes B and C. These deficiencies require hematologic and biochemical assessment (Table 1).

Anemia is common, and when it is not caused by chronic disease, it is most often the result of iron deficiency. The diagnosis of iron deficiency can be a problem. Microcytosis occurs with iron deficiency but is also seen with other conditions such as thalassemia. Raised iron binding capacity with reduced serum iron is an index of deficiency. However, low serum iron levels can occur with chronic illness. Low ferritin levels are diagnostic of iron deficiency but, because ferritin is an acute phase reactant, when inflammation is present, a low normal serum ferritin concentration does not exclude iron deficiency. It may be necessary to observe the effect of a trial of iron therapy or to evaluate bone marrow iron. Patients with ileal resection commonly require parenteral vitamin B_{12}, because the vitamin B_{12}–intrinsic factor complex is absorbed only in the terminal ileum. Folate supplementation is also frequently required, because patients have poor dietary intake.

Metabolic bone disease also commonly occurs in patients with Crohn's disease and is usually the result of dietary calcium and vitamin D deficiencies or malabsorption. Serum calcium is typically normal, being maintained in the normal range by secondary hyperparathyroidism, at the cost of loss of calcium from the skeleton. Serum phosphate levels are depressed. Metabolic bone disease is assessed by a bone density scan with dual energy x-ray absorptiometry. Overt vitamin D deficiency disease may occur; patients often present with bone pain and mild myopathy.

Table 1: Nutritional problems of patients with Crohn's disease

Deficiency	Assessment
Protein–energy	Subjective global assessment, serum albumin and total protein (reduced)
Vitamin	Erythrocyte folate, vitamin B_{12}, INR (will often be high because of reduced vitamin K–dependent coagulation factors), vitamin D, parathyroid hormone (increased secondary to low serum calcium levels)
Minerals and electrolytes	Calcium, magnesium, phosphorus, sodium, potassium, chloride, phosphate, ferritin, iron, serum electrolytes

Note: INR = international normalized ratio.

Management of nutritional problems

Protein–energy malnutrition

Decisions about the dietary rehabilitation of malnourished patients with Crohn's disease require a review of the patient's gastrointestinal investigations: What is the extent of the disease? Is there intestinal obstruction? Is there a significantly short bowel? From this information, a decision should be made to determine whether the patient can eat a normal or modified oral diet. If so, a dietitian should be consulted to prescribe suitable protein and energy intakes and to modify the diet to account for food intolerances or allergies and adjust vegetable and fruit intake for bowel obstruction. It is generally believed that fruit and vegetables may not pass through strictures and may cause a bolus obstruction behind a stricture. Hence, patients with symptoms suggestive of mild or partial bowel obstruction, consisting of severe abdominal pain associated with vomiting and the in-

Table 2: Factors responsible for malnutrition in patients with Crohn's disease

Factor	Cause	Consequence
Anorexia	TNF-α and other cytokines	Reduced dietary intake
Bowel obstruction	Stricture, abscess	Reduced dietary intake
Abdominal pain	Inflammation, obstruction	Reduced variety and amount of food
Malabsorption	Reduced absorptive surface area, absence of terminal ileum (vitamin B_{12} not absorbed)	Vitamin and mineral deficiencies
Losses from the gut	Inflammation	Protein and mineral losses

Note: TNF-α = tumour necrosis factor–α.

ability to pass stools or flatus, should avoid the intake of raw fruit and vegetables. In general, intestinal obstruction due to vegetable matter often occurs in patients who have had gastric surgery,[6] but this has also been seen in patients with an intact bowel,[7] including those with Crohn's disease.[8] On the other hand, in controlled trials fibre made of fine particles, such as bran in unrefined cereal, is tolerated quite well.[9]

The target protein–energy intake should be 126–146 kJ/kg per day, with 1.5–1.7 g/kg of protein per day. However, patients with a short bowel (such as those who have had a previous bowel resection for obstructions) and malabsorption should increase both their protein and energy intake to compensate for the reduced absorption.

Fluid and electrolyte deficiencies

These usually occur in patients with a short bowel. This is best treated by using an oral rehydration solution (ORS), which was first described by Harrison as a treatment for infantile diarrhea.[10] Since then the composition has evolved so that the composition for adults should approximate the following: glucose 90 mmol/L, sodium chloride 45 mmol/L, sodium citrate 45 mmol/L and potassium chloride 20 mmol/L. The sodium concentration must be at least 90 mmol/L.[11] Sports drinks designed to replace losses due to sweating, such as Gatorade, are often prescribed as a substitute for ORS. This is inappropriate, because these drinks contain a very low concentration of sodium, are rich in soluble carbohydrates and have high osmolality, characteristics that may even increase the volume and frequency of diarrhea.

Iron deficiency

Iron deficiency is treated with iron supplements, such as ferrous sulfate or gluconate starting with doses of 300 mg once a day and increasing to 300 mg 3 times a day, but patients with inflammatory bowel disease often do not tolerate oral iron. In addition, there is some evidence that iron in the colon increases oxidative stress and may exacerbate inflammation.[12] For these reasons, it is sometimes necessary to administer iron by intravenous infusion or intramuscular injection.[12] Even if oral iron is tolerated, the degree of deficiency may be such that ferritin levels do not rise and the hemoglobin level remains low. Under these circumstances, after suitable observation for about a month showing no change in hemoglobin, parenteral iron should be given.

Other mineral deficiencies

Magnesium deficiency is common in Crohn's disease, especially in patients who have had an intestinal resection. The best treatment consists of oral supplements with magnesium heptogluconate (Magnesium-Rougier) or magnesium pyroglutamate (Mag 2). The other salts of magnesium will cause more diarrhea. The total dose of elemental magnesium required to ensure normal serum magnesium varies between 5 and 20 mmol/day. To avoid causing diarrhea with magnesium supplements, I recommend that the total dose be mixed in the ORS and sipped throughout the day, ice cold and flavoured with non–sugar-containing agents.

Although difficult to diagnose biochemically, zinc deficiency occurs in patients with inflammatory diarrhea owing to considerable losses in the stools.[13] All patients with Crohn's disease who have significant diarrhea, passing more than 300 g of stool per day, should receive zinc supplements for as long as their diarrhea continues. Zinc deficiency can be treated by the administration of zinc gluconate, 20–40 mg/day.

Calcium supplements usually consist of calcium carbonate, providing 1000–1500 mg of elemental calcium per day in divided doses.

Vitamin deficiencies

Adequate folic acid nutrition is important in light of recent data indicating that folate supplementation may provide protection against colon cancer.[14] Patients with Crohn's disease should routinely take folic acid, 1 mg/day. Owing to the high prevalence of biochemical vitamin deficiency even in patients with inactive disease, supplementation with thiamine, riboflavin, pyridoxine, niacin and ascorbate should be recommended using a standard decavitamin preparation. The treatment of vitamin D deficiency depends on the cause. If it is the result of malabsorption, large doses (2000–4000 IU/day), or even calcitriol (0.25–0.5 μ/day), may be necessary.

Management of nutritional problems associated with high-dose glucocorticoid therapy

Crohn's disease is frequently treated with prednisone. The adverse nutritional effects of prednisone therapy are osteopenia or osteoporosis, muscle wasting and the development of diabetes. Therefore, during prednisone treatment the patient should be monitored for the development of osteopenia or osteoporosis, and prophylactic treatment with calcium and vitamin D supplementation should be instituted. There is evidence that prednisone induces a state of vitamin D resistance, which in turn results in increased levels of parathyroid hormone and increased calcium loss. By giving larger doses of vitamin D, this process can be inhibited. Typical doses of vitamin D_2 are 50 000 IU, or one capsule (Ostoforte), at intervals of 2–4 weeks. Although vitamin D_2 is less effective than vitamin D_3,[15] this level of intake will raise circulating 25-hydroxyvitamin D (25-OH-D) levels significantly without causing toxicity.[15,16] In addition, parenteral bisphosphonates such as clodronate, 600 mg, or pamidronate, 30 mg, at intervals of 3 months can be prescribed. Although risedronate, 5 mg/day, and alendronate, 10 mg/day, have been given orally, they are poorly absorbed and are unlikely to be absorbed by patients with an intesti-

nal resection or those with diarrhea. It is advisable to measure bone density with DEXA, and patients on steroids with normal bone density or mild osteopenia may be treated with vitamin D and calcium. If there is osteoporosis, then the bisphosphonates should be prescribed. The patient should also be advised to start resistive exercise to increase bone mass.

The prednisone-associated diabetes and muscle wasting are best treated by stopping prednisone and using an alternative drug. If it is not possible to stop the steroids, then insulin has to be given for the diabetes and resistive exercise to strengthen muscles for patients with muscle wasting.

Nutritional alternatives to high-dose glucocorticoid therapy

Not infrequently, when confronting continuing symptoms of Crohn's disease, the physician and patient must balance the beneficial and harmful effects of high-dose glucocorticoid therapy. Thus, it is useful to consider whether there may be alternative nutritional options available.

It has been claimed that if a patient with Crohn's disease takes nothing by mouth, this will induce remission by "resting the bowel." However, resting the bowel in this way will cause malnutrition unless parenteral nutrition is given concurrently. In several small series, total parenteral nutrition (TPN) and bowel rest induced remission in about 59% of patients with Crohn's disease.[17] In a series of 100 patients whose condition was resistant to prednisone therapy, TPN and bowel rest induced remission in 75%.[18] In another study, long-term TPN induced remission in patients with steroid-resistant Crohn's disease,[19] and endoscopic evidence of improvement was seen.[20] The question remained, however, as to whether TPN and absolute bowel rest were required to induce remission. In none of these studies could the mechanism of clinical improvement be identified. Was it caused by bowel rest or by the administration of nutrition (TPN)? Two studies[21,22] showed that enteral nutrition, in which the bowel was not at complete rest (because it was receiving liquid nutrients), was as effective as TPN in inducing remission. Greenberg and colleagues[23] found that bowel rest per se had no effect on the disease, but even patients whose condition was resistant to prednisone improved when given nutritional support. The possibility that feeding the patient may aid remission is supported by studies showing that diet counselling, with a view to encouraging increased energy and protein intake, and better oral nutrition improved outcome by maintaining remission and reducing disease activity.[24,25]

The next question is whether nutritional therapy with an enteral diet (Fig. 1) is as effective as the most effective phar-

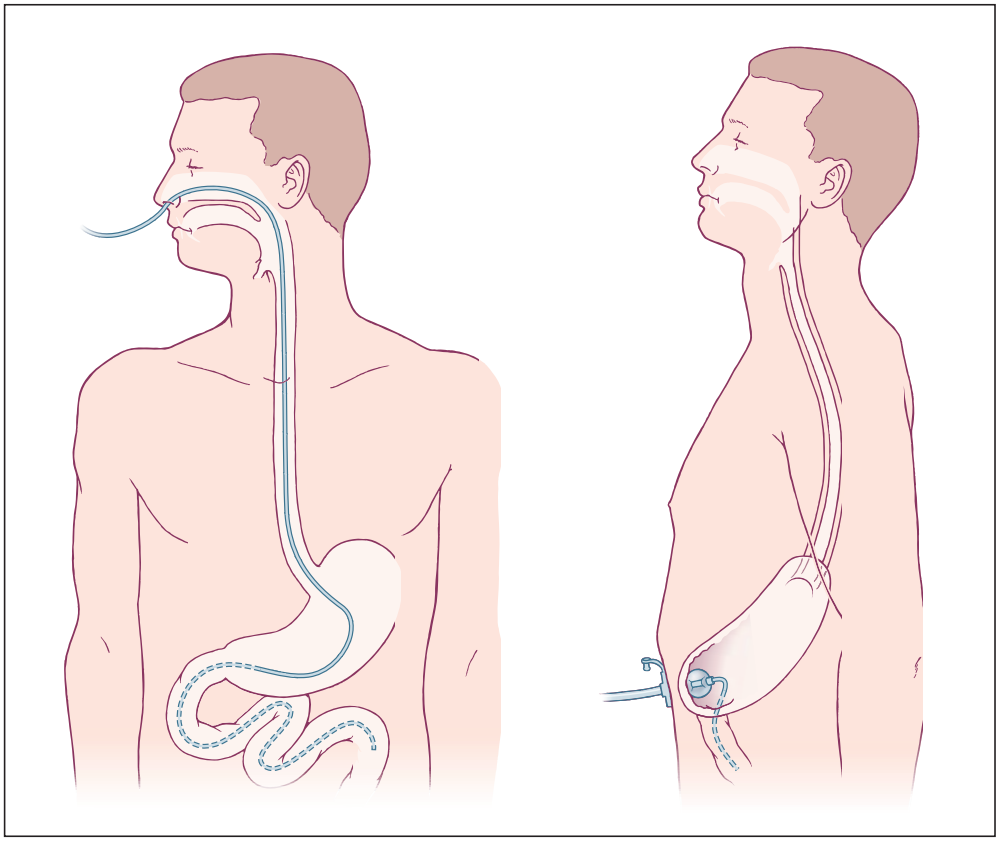

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Fig. 1: Enteral feeding of patients with Crohn's disease using a nasogastric tube (solid line) and nasojejunal tube (solid plus dashed line) (left). For long-term feeding, a percutaneous endoscopic gastrostomy (PEG) tube is extended to the duodenum (dashed line) (right).

macological treatment, namely, prednisone, for inducing remission. Initial controlled trials[26,27] showed that feeding patients an elemental diet (one that is very low in fat and containing amino acids) is as effective as prednisone in inducing remission. This conclusion was supported by other controlled studies.[28,29,30,31] Subsequently, as a result of 2 other multicentre studies,[32,33] it was concluded that remission was more likely to occur with prednisone therapy than with enteral feeding. Analysis of treatment failures associated with enteral feeding indicated that intolerance to these diets and consequently a high dropout rate was responsible for the less favourable outcome. In their meta-analysis, Griffiths and colleagues[34] concluded that enteral nutrition was inferior to corticosteroids in inducing remission. On the other hand, following their meta-analysis, Middleton and associates[35] concluded that the remission rate of a given enteral diet was inversely proportional to the content of long-chain triglycerides (LCTs) in the diet. Although there are no studies comparing enteral diets with placebo, the mean remission rate observed with enteral diets is about 60%,[36] which is twice the remission rate observed in other studies with placebo. Taken as a whole, the data suggest that nutritional support is probably more effective than placebo in inducing remission. Diets low in LCTs may be as effective as prednisone, thus, enteral nutrition with a low-LCT diet is an alternative form of therapy for patients who are averse to taking steroids. Belli and colleagues[29] found that intermittent elemental diet feeding not only encouraged growth but reduced disease activity. Similar results were obtained by Polk and coworkers.[37] Therefore, despite uncertainty about the role of enteral therapy in adults with Crohn's disease, it should be strongly encouraged in growing children.[38]

Do food elimination diets or specific nutrients have a role in the management of Crohn's disease?

Although food intolerance has been shown to occur in small series of patients with Crohn's disease,[22,39,40] it is not a reproducible problem and the role of elimination diets in the management of this condition has yet to be defined. Short-chain fatty acids, namely, organic fatty acids with 1–6 carbon atoms, are produced by the fermentation of dietary polysaccharides in the colon; they are an energy source for the colonocyte. For patients with ulcerative colitis, butyrate (a fatty acid with 4 carbon atoms) has been shown to induce remission.[41] Omega-3 fatty acids, namely, eicosapentaenoic and docosahexaenoic acids have anti-inflammatory properties.[42] They have also been shown to induce improvement in patients with ulcerative colitis.[43]

It is clear that Crohn's disease can lead to nutritional deficiency, which, if associated with a short bowel or chronic obstruction, is severe. Nutritional support with enteral feeding can be used to treat nutritional deficiency successfully and improve function, promote restitution of body mass and prevent septic complications, and hence plays an essential role in the management of this disease. A more contentious issue is whether nutrition can control active inflammatory bowel disease in the same way as medication. The data on this issue are far from clear, but it is possible to arrive at a few practical (but not necessarily proven) conclusions:

- Nutritional treatment is not likely to induce remission in patients with colitis.
- Enteral feeding can induce disease remission in adults and children and can promote growth in children. Current evidence showing that disease activity is perhaps the most important cause of growth retardation supports the belief that enteral nutrition reduces disease activity.
- The efficacy of enteral diets seems to depend upon patient acceptance and the ability to consume such diets for prolonged periods.
- The data suggesting that TPN can induce disease remission are indirect, and its use should be reserved to give nutrional support to patients for whom enteral feeding is impossible.
- It remains to be determined whether the elemental nature, nutrient content or the pharmacological effect of nutritional therapy is important for its success.
- The use of elimination diets, short-chain fatty acids and fish oils remains experimental.

The case revisited

Because Ms. C had a restricted food intake and moderate recent weight loss, but no physical signs of wasting, her condition was classified as SGA class B. Colonoscopy and small bowel barium follow-through revealed active Crohn's disease without evidence of bowel obstruction from stricture or abscess formation. Medical management was intensified by introducing immunosuppression using azathioprine, 100 mg/day. The dietitian assessed the patient's protein–energy requirements and questioned the patient about her food intolerances and preferences. Using this information, suggestions were made about food choices and liquid supplements to allow the patient to have a balanced diet that met her energy and protein needs. As suggested by the diet history and confirmed by hematologic and biochemical tests, the patient was moderately deficient in iron and folate, and folic acid, 1 mg/day, and ferrous gluconate, 300 mg twice a day, were prescribed. She was prescribed a vitamin preparation. Her symptoms improved, and with this improvement she regained some of the weight that she had lost, and her vitamin and mineral status became normal.

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