Nutritional Considerations and Management of the Child with Inflammatory Bowel Disease

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ABSTRACT

Crohn's disease and ulcerative colitis are chronic inflammatory diseases of the bowel often associated with significant malnutrition, particularly in children because of increased nutrient demands due to growth. We discuss the increasingly prominent role of nutritional support in inflammatory bowel disease (IBD). Issues that are addressed include the etiology of malnutrition in IBD, assessment and monitoring of patient nutritional status and the use of nutrition in the management of growth failure and as primary medical therapy. Nutrition 1996;12:151–158

Key words: Crohn's disease, growth failure, inflammatory bowel disease, malnutrition, ulcerative colitis
INTRODUCTION

Crohn's disease and ulcerative colitis are chronic inflammatory diseases of the bowel with childhood onset in approximately 25% of cases. Both can be debilitating processes characterized by unpredictable remissions and exacerbations. Although malnutrition is considered a significant problem for patients of all ages with inflammatory bowel disease (IBD), children are especially affected because of increased nutrient demands due to growth. Over the last two decades, nutritional support in active IBD has played an increasingly prominent role. This report presents an overview of nutritional management pertaining to the pediatric patient with IBD, including recognition of the nutritional consequences of chronic IBD, the nutritional management of growth failure in children with IBD, and the role of nutrition as the primary therapy of IBD.

MALNUTRITION AND GROWTH FAILURE IN INFLAMMATORY BOWEL DISEASE

Malnutrition

As shown in Fig. 1, the factors involved in the malnutrition associated with IBD are numerous and include those affecting nutrient intake, digestion, absorption, and metabolic demands. Caloric insufficiency, however, is generally recognized as the major cause of undernutrition and growth failure in the pediatric IBD patient. In particular, Crohn's disease, with its propensity to involve the small intestine, can create significant nutritional problems.

Most children with IBD do not eat well, usually consuming 40–80% of their estimated growth needs. Food often precipitates abdominal pain, and children try, either consciously or subconsciously, to prevent symptoms by decreasing their oral intake. Even when the child is eating a favorite meal, the complaint of early satiety is not uncommon. The unsubstantiated recommendation of low fiber, low sugar or lactose-free foods also contribute, iatrogenically, to the decreased intake because children find these diets unpalatable and socially unacceptable. In addition to caloric insufficiency, malnutrition can result from increased losses or malabsorption due to inflammation, surgical resection, fistulas or bacterial overgrowth—all of which can functionally decrease intestinal absorptive area. Pharmacological agents used in the treatment of IBD may contribute to a net loss of nutrients. For example, sulfasalazine competes with folic acid absorption, steroids increase calcium loss and cholestyramine may increase the malabsorption of fat and fat soluble vitamins.

Altered metabolism is another factor that should be considered, but whether malnourished IBD patients have increased energy requirements is debatable. According to Chan et al., the resting energy expenditure, as measured by indirect calorimetry, of adults with active Crohn's disease was equivalent to the predicted energy expenditure for healthy subjects as estimated from the Harris-Benedict equation. A study reporting that patients weighing less than 90% of their ideal body weight had a modestly higher energy expenditure per kilogram of body weight when compared with those weighing greater than 90% suggested that metabolic rate might be affected by the degree of malnutrition rather than the degree of inflammation. Overall, except in fever and sepsis, increased energy requirements have not been found in most studies of IBD patients.

Deficiencies of macro- and micronutrients are frequently seen in IBD. Decreased protein stores and low serum albumin can be seen in up to 80% of patients with Crohn's disease, partly from increased intestinal and transcapillary losses and partly from inadequate oral intake. Yet, despite the potential for protein-losing enteropathy, most children with IBD have more than adequate protein intakes and normal nitrogen balance.

Although lactose malabsorption can occur whenever there is small intestinal villus blunting, its prevalence in children with IBD is very similar to that seen in the normal population. The diagnosis of lactose, or any carbohydrate malabsorption, should be confirmed with a breath hydrogen test. If a positive test indicates the need for dietary alterations, such as the removal of dairy products, supplementation with protein, calcium and phosphorous, should be considered and the family counseled on alternate food sources.

Absorption of water-soluble vitamins such as folic acid can be affected by inflammation, bowel resection or sulfasalazine use. Vitamin B12 deficiency can arise from decreased oral intake, ileal inflammation or resection and bacterial overgrowth. Other rarely reported deficiencies in the water-soluble vitamins include thiamine (B1), riboflavin (B2), pantothenic acid, vitamin C, niacin and biotin. Low serum levels of the fat-soluble vitamins (A, D, E, and K) resulting from fat malabsorption and bile acid loss can be seen in patients with more severe malnutrition.

Iron deficiency, by far the most common micronutrient deficiency, also results from multiple factors such as inadequate intake, malabsorption and blood loss. Along with B12 and folate deficiency, it contributes to the nutritional anemia.

The contribution of zinc deficiency to growth retardation in IBD has received a good deal of attention but has not been
clearly defined. Although low serum zinc levels may be due to malabsorption, excessive colonic and urinary losses or decreased intake, they often reflect hypalbuminemia, and zinc status is actually normal in most patients. Calcium and magnesium malabsorption may occur secondary to steroids, steatorrhea or loss of intestinal absorptive area. Hypocalcemia can have deleterious effects on skeletal growth and maturation and also places IBD patients, particularly those taking corticosteroids, at high risk for developing calcium phosphate renal stones. Similar to what is seen with zinc, hypocalcemia is also often associated with low serum albumin, instead of reflecting a true deficit. Hypomagnesemia may cause symptoms including muscle cramps and bone pain. Other rarely described deficiencies, mostly reported in IBD patients on long-term total parenteral nutrition (TPN), include copper, chromium, iodine and selenium.

The consequences of global nutrient deficiency include alterations in cellular immunity with increased risk of infection, prolonged cellular renewal of inflamed tissues, delayed wound healing, diminished skeletal muscle function and growth retardation in children. Growth Failure

The potential complication for growth impairment in IBD is unique to pediatric patients. As shown in Fig. 1, the multiple factors involved in IBD-associated malnutrition make children with this disease at risk for the slowing or cessation of linear growth. Such growth failure can be manifested as an unexpected decrease in height velocity (height increment in cm/yr) or a progressive deviation downward from a child's established growth curve. Growth failure has been noted in about 30% of children with Crohn's disease and in 5–10% with ulcerative colitis. Actually, some degree of linear growth impairment has been reported in as many as 88% of children with Crohn's disease; it may even precede clinical evidence of bowel disease and progress despite minimal symptoms.

An endocrine basis for the IBD-associated growth failure has been sought but not routinely found despite frequently observed delays in bone maturation and secondary sexual characteristics. Thyroid, adrenal and pituitary hormones, whose deficiencies can lead to growth failure, are usually normal. The hormonal abnormalities that have been reported do not appear to be specific in that they are also associated with protein-energy malnutrition.

Once IBD is diagnosed, relapses of disease activity and the severity of gastrointestinal symptoms can contribute to the growth failure already present. The detrimental effects of the inflammatory process on growth must be weighed against the necessity for a complete medical history and physical examination and bone age may all potentially contribute to negative effects upon patient self-esteem, school performance and social interactions.

Although the association between IBD and impairment of linear growth is widely accepted, there are few studies delimiting the frequency of permanent growth failure. The abnormalities in growth may be prolonged or permanent and not reversible with surgical interventions regardless of stage of pubertal development. Castile et al. reported that the adult heights of 142 patients with childhood onset Crohn's disease, regardless of therapeutic management, were shorter than the normal population (37–42 percentiles). Likewise, Markowitz et al. using three different methods as predictors of adult height, reported permanent growth failure in 19–35% of subjects. Hildebrand et al. found subnormal adult heights in children with Crohn's disease but not ulcerative colitis. These authors remarked that the delayed epiphyseal plate fusion compensated for the period of poor growth in earlier life and reduced the negative effects on permanent adult height.

Evaluation of the growth response to disease control and nutritional or pharmacological intervention must be performed over extended intervals by repeated measurements of height. However, this reflects growth over many months and may not provide a correct indication of current growth activity. Given that it may take long periods of time for decreases in linear growth to become measureably obvious, recent interest has focused on using short-term serological markers of nutrition and growth. Levels of somatomedin-C, which is known to exert anabolic effects on peripheral tissues, are depressed in chronic undernutrition. Therapeutic intervention that increases caloric intake results in improved levels and growth velocity. Kirschner and Sutton reported that somatomedin-C in growth-impaired children with IBD could be a useful marker of nutritional sufficiency and reversibility of growth retardation. Hyams et al. suggested that other serum markers, the carboxy-terminal propeptide of type I procollagen and the amino-terminal propeptide of type III procollagen, could be used to accurately predict early growth responses to therapy in patients. Their serum levels displayed significant correlations to growth velocity. The use of daily steroids has been associated with significantly lower concentrations in both propeptides than alternate day or no corticosteroid therapy. Thus, routine measurement of collagen propeptides may have clinical value in monitoring normal and abnormal growth.

NUTRITIONAL ASSESSMENT AND MONITORING

Assessment of nutritional status should be regarded as an integral part of the routine management of pediatric patients with IBD. Early recognition and nutritional support can help avert the long-term sequelae of malnutrition, including growth failure, and complications of specific nutrient deficiencies. Consultation or supervision from a dietician or nutritionist experienced in the care of children with IBD can be invaluable.

Initial nutritional assessment should focus on identifying evidence of growth failure and nutritional deficiencies. Assessed in Table I, most children presenting with IBD will require a fairly thorough evaluation. Rigid recommendations for screening of nutritional deficiencies, however, would not be practical because the variables affecting patient nutritional status, such as disease type, location, severity, medications and surgical therapies, all need to be taken into consideration. The necessity for a complete medical history and physical examination should be obvious. Sequential measurements of height and weight, with calculation of the respective velocities, can serve as indicators of growth. Height-for-age, weight-for-age and weight-for-height measurements provide further information about the nutritional status of the child. It should be kept in mind that short stature alone does not imply impaired growth and may be of constitutional origin. One should also remember that alterations in weight may be influenced not only by disease but by factors including hydration status and corticosteroids and should therefore not be the sole index of growth. Radiological studies to determine bone age may not detect early growth failure in children with chronic disease but may differentiate those children with constitutional short stature. Anthropometrical including midarm circumference and triceps skinfold thickness, which can be used as estimates of protein and fat stores, can be easily obtained in the clinical setting and compared with readily available standards for age. Estimates of lean body
mass can also be obtained with measurements of serum proteins, including albumin, transferrin, prealbumin and retino binding protein. Lean body mass has been reported reduced by 33% despite patients consuming two times their recommended daily allowance (RDA), but fat stores are usually well preserved. Other methods for analyzing body composition, such as underwater weighing, bioimpedance analysis and stable isotope dilution, are usually available only in the research setting. Basal energy requirements can be measured by indirect calorimetry or estimated by the Harris-Benedict equation.

Although not necessary in every patient, an assessment of gastrointestinal digestion and absorptive ability may be required to explain specific nutritional deficiencies. As previously mentioned, the hydrogen breath test is useful in assessing the absorption of lactose and other carbohydrates. Fat absorption can be evaluated with a 72-hour fecal fat balance study or serum fat-soluble vitamin levels. Protein loss can be evaluated with a 72-hour fecal fat collection or estimated by the Harris-Benedict equation.*

NUTRITIONAL CORRECTION OF MAJOR NUTRITION AND GROWTH FAILURE

Multiple studies have been undertaken to evaluate the role of nutrition in the prevention or reversal of IBD-associated growth failure. Dietary manipulations have ranged from the use of high-caloric foods, to supplementation with specialized formulas, to the use of parenteral nutrition.

In the 1970s, TPN was shown to achieve weight gain and reverse growth arrest in children with Crohn's disease. It was not long before other researchers reported that parenteral nutrition alone, or in combination with oral feedings, led to significant increases in weight gain and growth velocity whether administered in a hospital or home setting.* These studies emphasized the importance of nutritional intervention, along with medical treatment, in the management of children with growth failure.

Despite the success seen with TPN, its metabolic and infectious complications and cost considerations make it impractical for use in most patients. TPN is now recommended primarily to provide nutritional repletion in severely malnourished patients, in pre- and postoperative nutritional rehabilitation and in patients with complications such as strictures, short-bowel syndrome or high-volume fistulas that limit enteric function.

The search for alternatives to TPN led to elemental formulas composed of simple easily assimilable nutrients, such as amino acids, glucose polymers and short-chain triglycerides. These formulas have been effective in reversing growth failure when used alone for short periods of time such as 3—6 weeks. In a longer 2-year controlled study, Belli et al. compared the use of an intermittent elemental diet given 1 out of every 4 months plus standard therapy to standard therapy alone and found that the pediatric patients on the elemental diet showed significant increases in weight gain and growth velocity compared to the controls. Although the response of growth to elemental diets has been quite favorable, the drawback of these diets is that they are unpalatable, hyperosmolar and expensive. As a result, other researchers have turned to the use of more standard formulas for supplementing a patient's regular oral intake and achieved similar results with regard to improvements in growth.

Even though oral, enteral and parenteral supplementation has been widely used in the nutritional rehabilitation of patients, there is no panacea to the treatment of growth-retarded children with IBD. Oral supplementation, although usually viewed as the most acceptable option for a child with growth failure, places a great deal of stress on both the patients and their families. These children may be highly motivated and initially compliant, but it is difficult for them to consume the necessary volumes. Most eventually give up the supplements or just eat less of their regular meals. Therefore, serious consideration should be given to the administration of calories via a nasogastric (NG) tube. Such an infusion could be given overnight, not because it is more effective than oral or NG boluses but to avoid interfering with school or daily routines. Patient acceptance of NG feedings is highly dependent on the way in which it is presented—positive and sustained encouragement is the key to maintaining a high degree of compliance. A randomized prospective multicenter study is currently evaluating...
the effect of intermittent elemental diet administration versus alternate day prednisone on the long-term clinical course and growth of children with Crohn’s disease.46

In our institution, NG feedings are usually initiated during a 3- to 5-day hospitalization. Trained nurses educate the parents and child on the techniques of NG tube insertion and the monitoring of feeds. After an assessment by pediatric nutritionists, patients are usually given about one third of their estimated growth of children with Crohn’s disease.41

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require long-term infusion. Although the risk of fistula formation, infection and adhesions needs to be kept in mind in children with Crohn’s disease, we and others have successfully percutaneously placed, and subsequently removed, gastrostomy tubes in children with nongastric Crohn’s disease who required supplemental tube feedings generally for 6 months or more.

Over the past decade, the role of supplemental feeding has become an accepted treatment in the pediatric IBD patient, particularly in the patient with growth failure. Because accelerated growth has been reported with multiple forms of nutritional support, it appears that the form or route of administration is not as important as ensuring that the energy intake is sustained. It must be emphasized that the opportunity for a child with established growth failure to catch-up is limited in time by the advancement of bone age. Thus, it is critical to intervene before epiphyseal fusion to maximize the prepubertal growth potential genetically determined for that patient.

USE OF NUTRITION AS PRIMARY THERAPY

The corticosteroids used as the mainstay of therapy for patients with IBD are known to cause significant side effects, especially if administered long term.4 Historically, nutrition was considered valuable adjunctive therapy in the management of malnourished patients, but there has been recent increasing interest in the use of diet as primary therapy.

TPN was the first mode of nutritional intervention recognized to be effective in inducing remission and treating specific complications of Crohn’s disease.42 The trend seen in published retrospective, and more recent prospective, studies suggest that TPN given for a short period of weeks achieves a clinical response rate of greater than 60% when follow-up is less than 3 months, regardless of concurrent steroid use. The clinical response of a flare is more significant with small bowel disease alone or in combination with large bowel involvement.19 In patients with primarily colitic involvement, coadministration of steroids has been necessary for the achievement of similar remission rates; thus, there appears to be a limited role for TPN in patients with Crohn’s colitis.43

Elemental diets were introduced as primary therapy for Crohn’s disease for two main reasons. First, with an amino acid-based source of nitrogen, they were considered hypoallergenic and less prone to initiate the antigenic response that whole proteins were hypothesized to elicit in IBD. Second, these diets are almost totally absorbed in the duodenum and proximal jejunum, thus decreasing the fecal stream coming in contact with inflamed mucosa.

Since the first randomized trial comparing the efficacy of an elemental diet versus prednisolone was reported by O’Morain et al.,44 multiple prospective randomized studies have evaluated the efficacy of elemental diets in Crohn’s disease. These diets have been demonstrated to decrease gastrointestinal protein loss,10 reduce fecal leukocyte excretion and improve intestinal permeability45 in acute Crohn’s disease. In patients with Crohn’s disease, remission rates of 60–90% have been reported with elemental diets.44–46 Elemental diets appear to be as effective as steroids44,46–48 and TPN49,50 in achieving short-term remission, particularly for patients with small-bowel Crohn’s disease. Although the studies with elemental diets have primarily used adult patients, the findings have been confirmed in pediatric trials47,48. It should be kept in mind that in some of these studies, patient withdrawal rates of up to 21% have been noted because of poor compliance due to diet unpalatability. Because this could have an affect on the results, analyzing this factor as an independent variable could increase the overall response rates of patients receiving the elemental diets.

Taken as a whole, the reported trials suggest that elemental diets can induce remission in Crohn’s disease with an efficacy and rapidity that is comparable with standard medical management. The diets have been beneficial in patients with long-standing disease, as well as those newly diagnosed. Patients in good and poor nutritional states have responded equally well, but relapse rates have been higher with elemental diets than with steroids in both adult and pediatric studies. Even higher relapse rates have been reported in colonic disease.23,47 Overall, as with TPN, the remissions achieved with an elemental diet depend on the continuation of the diet, with relapse usually occurring shortly after resumption of a normal oral diet.

As previously mentioned, the unpalatability, hyperosmolarity and expense of elemental diets have led to the evaluation of other formulas without these drawbacks. In fact, whether or not the absence of whole protein is necessary to achieve clinical remission in active Crohn’s disease has yet to be fully assessed. A small pediatric study57 showed equal efficacy of a hydrolysate diet to steroids, whereas two large adult trials have not.58,59 Although in one of these prospective adult randomized trials, a large number of patients were excluded due to noncompliance.58 Of several prospective randomized trials that have investigated the role of polymeric formulas in Crohn’s disease,51–53,56,59 most, including a recent meta-analysis, have shown this diet to be as effective as elemental diets in achieving remission.51,52,59,60 A study that showed very poor response (75% versus 36%) to a polymeric casein-based diet had a patient population that was quite heterogeneous for disease location.51 Additionally, the polymeric formula used in that study had 15 times more fat than the elemental formula and 36% of the fat was linoleic acid, a precursor of arachidonic acid. The contribution of fat to the success of these formulas is discussed in further detail in a following section.

Two large trials have compared polymeric enteral formulas with standard pharmacotherapy, and both found that diminishing doses of methylprednisolone and a level dose of sulfasalazine was superior to the enteral feeds.50,58 However, in a recent controlled randomized trial by Gonzalez-Huix et al.,61 the efficacy and safety of a polymeric diet was compared with steroid therapy in achieving and maintaining clinical remission in Crohn’s disease. Both forms of management were as effective in gaining remission within 4 weeks. In this study, the improvement noted with the polymeric diet did not seem to be secondary to nutritional enhancement alone because biological indices of inflammation (erythrocyte sedimentation rate and C reactive protein) improved similarly in both groups. No statistical differences were noted in relapse rates, but the rate tended to be lower in the polymeric group. Although the authors concluded that polymeric diets are as safe and effective as steroids in nutritional management of the child with IBD.155
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inducing short-term remission, more studies with larger patient populations are still needed to confirm these findings.

Thus, the question as to whether elemental or polymeric diets are better for Crohn’s disease remains open. Although early data favored elemental diets as long as they were tolerated by patients, recent evidence suggests that polymeric diets can be as effective. Taken in total, the composite data on enteral feeds indicates that nutritional therapy can induce remission in Crohn’s disease with an efficacy comparable with TPN and standard medical management. The mechanisms by which nutritional therapies improve Crohn’s disease remain unknown. Initially, much emphasis was placed on the concept of “bowel rest.” In fact, one argument favoring the use of elemental diets is that the absorption of these diets is virtually complete in the proximal small intestine. This leads to decreased stool output, stimulation of motility and secretion and therefore less fecal residue to irritate disease-involved segments. But, evidence to date tends to favor the concept of nutritional support rather than bowel rest as a main factor contributing to disease prevention. Research has shown that there is little “rest” when the bowel is deprived of nutrients. In experimental animals, the absence of intraluminal nutrition during TPN has been associated with subtotal villous atrophy of the intestines and breakdown of the mucosal barrier, which promotes translocation of bacteria normally confined to the gastrointestinal tract. Bowel rest is now not considered a major factor or prerequisite contributing to clinical remission. Yet nutrition alone cannot be solely responsible, because many patients improve before any significant changes occur in their nutritional parameters.

Dietary proteins have been argued to contribute to IBD because of the ability of protein to induce intestinal inflammation, the numerous reports of circulating antibody to dietary antigens in IBD and “hypoantigenic” oral elemental diets are of therapeutic value. The potential role of allergy in the etiology of Crohn’s disease and breakdown of the mucosal barrier, resulting in a shift from production of LTβ to production of leukotriene B4, which has only 3-10% of the potency of LTβ. Fish oil therapy has subsequently been demonstrated to be efficacious in the management of mild to moderate ulcerative colitis. Recent studies in humans have also emphasized the possible role of fatty acids and their derivatives in mediating inflammation, with alterations in the plasma pattern of PUFAs being described in IBD. In contrast, essential fatty acid deficiency exerts an anti-inflammatory effect in several models of inflammation by inhibiting eicosanoid generation and levels of resident macrophages and diminishing the influx of elicited leukocytes in acute inflammation.

Other factors mentioned in the positive response of IBD patients to nutrition include increased T-lymphocyte counts and improved T cell responses to mitogens that occur after enteral nutrition and may contribute to decreasing intestinal disease activity.

UCERATIVE COLITIS

When acute ulcerative colitis is severe enough to require hospitalization, the mainstays of therapy include high-dose steroids, fluids and electrolyte replacement. Two prospective controlled trials have evaluated the role of TPN in ulcerative colitis and showed no improvement in clinical response or requirement for surgery. Although retrospective studies have reported clinical remission rates of approximately 30%, there is a lack of prospective studies addressing the role of enteral diet in the management of ulcerative colitis. The decision to perform a curative colectomy in a deteriorating patient should not be delayed for modest gains in nutritional status. Actually, increased morbidity may be caused by protracted time before colectomy to achieve nutritional repletion.

SUMMARY

Growth failure is a significant feature of pediatric IBD patients, particularly those with Crohn’s disease. Although the etiology is multifactorial, the most accepted cause of the growth failure appears to be insufficiency of nutrient intake. Nutritional support in the form of diet supplementation, defined liquid formulas or parenteral nutrition can restore normal body composition and reverse the growth failure, but only if administered before completion of skeletal growth.

In addition to reversing growth failure, parenteral and enteral nutrition has been shown to control inflammation and is able, in some patients with small-bowel Crohn’s disease, to replace standard medications to induce remission. Nutritional therapy, however, is less satisfactory for patients with Crohn’s colitis. Nutritional support, either parenteral or enteral, is of little value in the primary management of patients with active ulcerative colitis.

The mechanisms by which such nutritional therapies improve disease activity are unclear but may involve the intestinal adaptive response to bowel rest, immunologic effects and nutritional factors. More research is needed to increase our understanding of these mechanisms.

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