Nutritional management of Crohn's disease in childhood

R M Beattie MRCP

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Crohn's disease can affect any part of the gastrointestinal tract from the mouth to the anus. The disease is mostly seen in adults but 10%–15% of cases present in childhood, usually during adolescence. There is some suggestion that the incidence is increasing[1]. The clinical manifestations are varied and diagnosis is often delayed. Classical symptoms include abdominal pain, diarrhoea, weight loss and lethargy. Growth failure is present in up to 50% at presentation and up to 90% are underweight[2,3]. Diagnosis is by barium radiography or white cell scanning and by colonoscopy with biopsy[4–6]. The most common disease site is the terminal ileum. Therapeutic options include enteral nutrition, corticosteroid therapy and surgery. The surgical option is often necessary for local disease complications. Corticosteroid therapy induces a clinical remission and is as effective as enteral nutrition; however, side-effects including growth failure are common and enteral nutrition has been used increasingly as primary therapy.

NUTRITIONAL THERAPY: BACKGROUND

Many studies have shown children with Crohn's disease to have a low energy intake which improves after treatment[7,8]. Kirschener[7] reported 7 children with moderately active Crohn's disease all with growth retardation, who responded to nutritional supplementation with improved wellbeing and an increase in height velocity. O'Morain[9] reported 15 children treated with the elemental diet Vivonex (Eaton Laboratories) for 4 weeks after which food was reintroduced over another 4 weeks; the effects in terms of clinical remission and growth outcome were good, even though no other therapy was given. Sanderson *et al.*[10] compared the peptide-based semi-elemental formula Flexical (Mead Johnson) with corticosteroid therapy and showed the two to be equally effective in inducing remission. The diet was given for 6 weeks by nasogastric tube. New foods were introduced every two days for two months thereafter. Linear growth, as assessed by height velocity over six months, was significantly greater in the group treated with elemental diet.

There have been several other paediatric studies. Thomas *et al.*[8] compared the elemental formula EO28 (Scientific Hospital Supplies) with steroids and again reported similar efficacy in the two groups. Height velocity was better in the diet group even though energy intake was higher in the steroid group. In this study elemental diet was well tolerated by mouth. Papadopoulou[11] in a retrospective analysis found EO28 superior to steroids for treatment of proximal disease. Lately, interest has switched to cheaper and more palatable formulae. We reported 7 children, all new patients with small-bowel Crohn's disease, treated with the polymeric formula feed AL110 (Nestlé-Clintec); all entered full clinical remission by 8 weeks, the C-reactive proteins becoming normal by 2 weeks[12]. Ruuska *et al.*[13] reported a randomized controlled trial comparing the polymeric feed Nutrison Standard (Nutricia) with corticosteroid therapy. 8 weeks of nutritional treatment was followed by food reintroduction over 3 weeks. Response to therapy was equal in the two groups, whether disease was in the small or large bowel or both. The relapse rate was lower in the group treated with diet. Although these results indicate that enteral nutrition is effective therapy for Crohn's disease, many issues are unresolved. Should we use polymeric or elemental feeds? Is dietary therapy effective at all disease sites? For how long should it be given?

In adult disease the emphasis has moved away from enteral nutrition. Fernandez-Banares *et al.*[14] reported a meta-analysis of studies comparing enteral nutrition (polymeric, oligopeptide and elemental) with steroids which suggested that steroids were more efficacious in the induction of disease remission. Toxicity was not considered and many of the studies included in the analysis were marred by poor compliance. A second meta-analysis, by Griffiths[15], reached similar conclusions. These results, however, cannot be extrapolated to children, whose compliance is much higher and who are subject to more side-effects from steroids, particularly on growth. In addition the studies did not distinguish between newly diagnosed patients and those with established disease.

NUTRITIONAL THERAPY: PRACTICAL ASPECTS

Before starting enteral nutrition the patient must be fully assessed with regard to nutritional status and disease extent and severity. The options include elemental, semi-elemental (oligopeptide) and polymeric formulae, the differences reflecting the degree of protein hydrolysis. The most commonly prescribed diet in the UK is probably EO28, an elemental feed. This comes in 'user friendly' 250 mL packs, and the energy content is 0.86 kcal/mL.

Peterborough District Hospital, Thorpe Road, Peterborough PE3 6DA, UK

Palatability is helped by various flavourings including grapefruit, summer fruits and orange and pineapple. Polymeric feeds are more palatable. Examples include Nutrison (Nutricia) and AL110. Feeds such as Flexical and Peptamen (Nestlé) are semi-elemental or oligopeptide based. Whether these different feeds are equally efficacious in children has not been resolved by a large trial. Variables such as calorie density and glutamine, fat and carbohydrate content may be relevant[16,17]. Cost is certainly a factor, since elemental feeds are very much more expensive than polymeric formulae.

The amount of feed required will depend on disease severity, patient tolerance and the degree of nutritional impairment at the onset of therapy. 100–120% of the recommended daily allowance should be used. The calorie density of most feeds is between 0.7 and 1.0 kcal/mL, so the volume administered must often be large. The feed can be administered either wholly or partly by nasogastric tube. Of the children who prefer to drink the formulae, most prefer them chilled.

In our practice, courses of enteral nutrition last for 8 weeks, during which no other foodstuffs are taken; water is allowed. The amount of feed should be increased gradually in quantity and strength over several days to ensure it is well tolerated.

The child usually feels better within days of starting treatment and the improved wellbeing provides an incentive to continue. At each review general progress should be assessed. Substantial weight gain is to be expected, particularly in children who are underweight at onset. If inflammatory indices such as the C-reactive protein do not improve, this indicates that remission is not being induced. In resolving individual difficulties the community nurse and paediatric dietician can be very helpful.

Lack of response may be a consequence of poor compliance, inadequate energy intake or intolerance of the feed. Alternatively the disease may be resistant to enteral nutrition. Risk factors for this include severe colonic disease, longstanding disease and surgical complications such as stricture. In most series 20–30% of patients are unresponsive, though some selection improves on this.

How should normal food be reintroduced? We do this over 4–8 weeks as follows, each new food being added two days after the previous one: potatoes, lamb, chicken, yeast, wheat (spaghetti), bread, cabbage, rice, apple, carrot, beef, milk, butter, cheese, eggs. Once these foods have been reintroduced, a free diet is allowed. Difficulties with food reintroduction may be a consequence of disease relapse or food intolerance. Intolerance is usually general rather than specific. In adults, Pearson *et al.*[18] reported food intolerance on food reintroduction in 20 of 28 patients treated with 4 weeks of enteral nutrition. Many different foodstuffs were incriminated, the commonest offenders being milk (5 cases) and peanuts (5). Interestingly, only 3 were confirmed on double-blind challenge. Riordan *et al.*[19] reported a high incidence of intolerance after 2 weeks of enteral nutrition, offending foodstuffs in order of frequency being corn, milk, yeast, egg, potatoes, rye, tea, coffee, apples, mushrooms, oats and chocolate. Double-blind challenge was not used. In children, there is very little evidence of specific food intolerances.

MAINTENANCE THERAPY

Crohn's disease has a high frequency of relapse and, once disease remission has been induced, maintenance therapy needs to be considered. 5-acetylsalicylic acid derivatives are the most widely used therapy, and they should be continued for at least two years after the last relapse. Continued nutritional supplementation is often required. Belli *et al.*[21] reported 8 children aged between 10 and 14 years all of whom had Crohn's disease associated with severe growth failure. They were given an elemental diet (Vivonex) for one out of each four months. All achieved catch-up growth during the subsequent 12 months. Corticosteroid requirements fell and disease activity improved during the same period. Lately the same group[23] showed, in a multicentre randomized controlled study, that a cyclical elemental diet (Vital HN, Ross Products, Abbott Laboratories) was superior to low-dose alternate-day steroids in prolonging the time to relapse and in sustaining height velocity. The maintenance therapy does not need to be cyclical. Wilschanski *et al.*[23] reported, in a retrospective series, a longer time to first relapse and better long-term growth in children who elected to continue on nutritional support after the induction of remission with enteral therapy[23]. Long-term nutritional supplementation can be given by nasogastric tube or via percutaneous endoscopic gastrostomy[24].

OTHER THERAPIES

The efficacy of corticosteroids in the induction of remission in Crohn's disease is well established. For many patients, corticosteroid therapy is more acceptable than nutritional therapy and compliance is better. In disease which is resistant to enteral nutrition corticosteroid therapy is clearly appropriate. Courses should be for a limited period, maintenance doses being avoided where possible. Prednisolone is the most widely used, in a dose starting at 2 mg/kg (maximum 40 mg) to induce remission. The dose should then be tapered slowly over the subsequent weeks. Some children become steroid dependent (unwell unless on steroid therapy) and azathioprine can be helpful; however, in such cases surgical resection is often the best option, particularly if there is associated growth retardation. Other therapies including cyclosporin,

methotrexate and monoclonal antibodies have been used in refractory disease[25].

Surgery, which is required in up to 50% within 5 years of diagnosis[26], should be regarded as part of the overall therapeutic strategy. The timing is crucial and paediatricians should liaise closely with surgical colleagues from an early stage. The indications for surgery are acute complications such as abscesses or stricture, disease dependent upon steroid therapy with growth failure, and steroid-resistant disease. The outcome of surgical resection is usually good, with accelerated growth in many cases[27], but the disease commonly relapses either at the site of surgery or at a distant site.

CONCLUSION

Crohn's disease requires a thorough assessment of extent and severity before treatment is started. Management should be multidisciplinary. Growth and nutritional status are key issues. Enteral nutrition is appropriate initial therapy in most cases, with steroids as the second line. Surgical resection should be considered for refractory disease. Which enteral diets are best and for how long they should be given are questions still to be resolved.

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