To feed or not to feed? Are nutritional supplements worthwhile in active Crohn's disease?

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Partial enteral nutrition is unlikely to suppress inflammation and so treat active Crohn's disease

Enteral nutrition is an effective therapy for active Crohn's disease (CD) although less effective than steroids. This has been shown in a number of original studies and meta-analyses.^{1,2} Enteral nutrition leads to remission in approximately 60% of patients within 4–6 weeks. Unfortunately, enteral nutrition has never been compared with placebo or other medical therapies such as mesalamine or topical steroids. With the lack of such studies demonstrating that enteral nutrition is superior to placebo, the question has been raised if enteral nutrition has any therapeutic effect at all. However, remission rates with enteral nutrition range from 53% to 80%, which is higher than remission rates of placebo groups in most studies, which range from 18% to 40%. Therefore, a direct anti-inflammatory effect of enteral nutrition in active CD is generally accepted. The therapeutic efficacy of enteral nutrition in active CD is also suggested by results of recent studies demonstrating mucosal healing as well as a reduction in proinflammatory cytokines^{3,4} by enteral nutrition. The effect of enteral nutrition appears to be similar if the diet is drunk or applied via a tube and is also comparable with the effect of parenteral nutrition. Specific compositions of enteral diets—elemental diets or diets containing specific components—have no advantage over standard polymeric diets.^{1,5–7}

In adults, enteral nutrition is rarely used as the sole therapy for active CD in clinical practice. This is partly due to its inferiority compared with steroids and partly to the inconvenience of enteral nutrition, resulting in low patient compliance—specifically if the mostly unpalatable diets are drunk. This appears to be different in children, who accept enteral nutrition much better, with compliance rates of up to 100%. Furthermore, malnutrition with growth retardation is a leading symptom in adolescents suffering from CD, and enteral nutrition does effectively improve the nutritional status

of CD patients and increase growth velocity.^{8,9} Therefore, enteral nutrition is considered the treatment of choice for active CD in children, as also reflected by recent guidelines.

The mode of action of enteral nutrition is still unclear although several mechanisms have been discussed: (a) bowel rest with alteration of the intestinal flora and elimination or reduction of dietary antigens and (b) improvement in nutritional status by increase in nutritional intake and/or increase in substrate absorption as well as reduction in intestinal protein loss.

A study by Johnson and colleagues¹⁰ in this issue of *Gut* raises new questions about both the efficacy and possible mechanism of action of enteral nutrition in active CD (see page 356). They randomised children with active CD to either receive 100% of their nutrition as elemental diet (total enteral nutrition) or only 50% (partial enteral nutrition), thereby replacing 50% of standard food by an elemental diet. Total nutritional intake was similar in both groups. They found a remission rate of 42% with total enteral nutrition and a significantly lower rate of 15% with partial enteral nutrition. However, this low remission rate, especially in the partial enteral nutrition group, does not exceed the range reported in placebo groups, arguing against a significant role for enteral nutrition in the treatment of CD. Two specific questions need to be discussed to explain these results and put them into perspective.

(1) IS BOWEL REST IMPORTANT AFTER ALL?

In Johnson's study,¹⁰ the total enteral nutrition group was put on "bowel rest" as they were not allowed to eat anything apart from the elemental diet, while the other group was not on bowel rest.

To date, the importance of bowel rest has only been investigated in two studies^{11,12} which showed no advantage of total parenteral nutrition (TPN) or total enteral nutrition compared with

partial parenteral nutrition (PN) in addition to standard food. No difference in the time point or number of patients achieving remission with TPN or PN plus oral nutrition or enteral nutrition was found. Therefore, it was concluded that bowel rest is not necessary, enteral nutrition should be preferred, and patients might eat ad libitum in addition to enteral nutrition. However, both studies differ in design from the study of Johnson and colleagues.¹⁰ In our own study, all patients received the same PN, which covered estimated energy needs.¹¹ One group was allowed to drink fluids and enteral diet in addition to PN, while the other group was put on nil per os. In the Greenberg study, patients in the "oral group" received only about 50% of their energy and substrate needs via PN and ate fully.¹² In neither study was a group on partial enteral nutrition included, as in the Johnson's study. We therefore lacked information of the effect of partial enteral nutrition in active CD.

Several studies offering oral nutritional supplements to patients with chronic active CD^{13,14} cannot be compared with this situation as, in contrast with Johnson's study,¹⁰ in these investigations an increase in total nutrient intake was attempted and achieved, and mostly enteral nutrition was given in addition to medical therapy.

(2) IS IMPROVEMENT IN NUTRITIONAL STATUS THE KEY?

Malnutrition and nutritional deficiencies are frequent in active CD and may contribute to the low quality of life and increase clinical disease activity in these patients. Some studies indicate, for example, that effective treatment of iron deficiency and anaemia might be crucial to improve the quality of life and decrease disease activity in patients with inflammatory bowel disease.¹⁵ Most studies on enteral nutrition as sole therapy for active CD also show nutritional improvements in patients, apart from a decrease in disease activity. On the other hand, treatment of malnutrition by total or partial enteral nutrition is usually followed by a decrease in disease activity. This has been shown in children as well as in adults.^{8,13} Improvement in nutritional status appears to be important not only in achieving but also in maintaining remission, as has been shown in a study by Royall and colleagues.¹⁶ Consequently, improvement in nutritional status and correction of micronutrient deficiencies are considered key factors for the effect of enteral nutrition and may be associated with effect on disease activity.

Such an improvement in nutritional status might not have been achieved in

the group with partial enteral nutrition in Johnson's study.¹⁰ While these patients gained some weight, they had a significant decrease in haemoglobin and no change in albumin, in contrast with the group with total enteral nutrition despite similar total intakes. This might however be explained by higher intestinal losses in the partial enteral nutrition group. This shows the limitations of giving partial enteral nutrition in active CD when replacing part of the normal diet rather than being given in addition to normal food intake. While enteral nutrition overnight in addition to normal food increases nutrient intake in CD patients and reduces disease activity, this appears not to be the case if 50% of food intake is replaced by an enteral diet.

WHAT IS THE CONCLUSION FOR CLINICAL PRACTICE?

Despite the fact that the hypothesis of bowel rest as the main mechanism of enteral nutrition in active CD was dismissed many years ago, all later studies put patients on "bowel rest" while on enteral nutrition. They usually allowed them to drink only clear liquids apart from enteral nutrition. Apparently investigators considered bowel rest important despite opposing results in some studies. This view is supported by Johnson and colleagues.¹⁰

In contrast, correction of nutritional status appears to be crucial for the anti-inflammatory effect of enteral nutrition. This can only be achieved if either total enteral nutrition is given or substrate and energy intake is increased by enteral nutrition over the amount eaten normally. Replacement of part of the standard food by an elemental diet does not appear to be sufficient. If such an

increase in intake is achieved, it is unclear if addition of normal food would reduce the effect of enteral nutrition.

In the view of these uncertainties it appears important to further investigate the effect of partial enteral nutrition and to carefully check the effect of this therapy on the nutritional status of these patients. Until the results of such studies are available, clinical practice does not need to be changed. It seems advisable to restrict oral intake to clear liquids in patients with active CD while on enteral nutrition as sole therapy, and to ensure adequate nutritional intake via enteral nutrition, until we have more information on the effect of normal food in this situation. Furthermore, if patients are not treated with enteral nutrition as sole therapy, they may take oral nutritional supplements in addition to medical therapy to improve their nutritional status. Such a therapy would be more acceptable for these patients than tube feeding.

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