

Special issues in nutritional therapy of inflammatory bowel disease

CN WILLIAMS, FRCPC, FACP

CN WILLIAMS. Special issues in nutritional therapy of inflammatory bowel disease. Can J Gastroenterol 1993;7(2):196-199. There are many issues and controversies concerning nutrition in inflammatory bowel disease (IBD). Most authorities now accept that total parenteral nutrition (TPN) is useful, both as primary and adjunct therapy in the management of patients with Crohn's disease, but only useful as adjunct therapy in patients with acute flare-ups of ulcerative colitis. In both, there is a role for TPN in preparing patients for imminent surgery. In comparison with TPN, defined formula (elemental diet) therapy has less complications, is easier to monitor, is less costly, and gives equivalent results. Several controlled trials have shown that elemental diet therapy is as useful as prednisone in inducing remission in patients with active Crohn's disease. Elemental diets have been compared with polymeric diets in patients with Crohn's disease, and have been shown to be effective; recently a semi-elemental diet has also been shown to be as effective as elemental diet, but with a conferred benefit of maintaining essential fatty acid levels. Elemental diets do not appear to be effective in closing fistulas. If the problems of palatability and, in some patients, nausea, vomiting, abdominal cramps and diarrhea persist, these can be overcome to some extent by flavour changes, chilling, gradual introduction and counselling or nasogastric tube feeding. Recently, fish oils have been used in patients with IBD. There is suggestive evidence that they are of benefit in patients with ulcerative colitis but not in Crohn's disease. There is a suggestion that fish oils have a steroid-sparing effect which, if confirmed, will be of great potential benefit to patients with ulcerative colitis. (*Pour résumé, voir page 197*)

Key Words: Crohn's disease, Enteral nutrition, Inflammatory bowel disease, Nutrition, Polymeric diet, Total elemental diet

Division of Gastroenterology, Department of Medicine, Dalhousie University, Halifax, Nova Scotia

Correspondence and reprints: Dr CN Williams, Room C-12, CRC, Dalhousie University, 5849 University Avenue, Halifax, Nova Scotia, B3H 4H7. Telephone (902) 494-2333, Fax (902) 494-1624

THE INTRODUCTION OF TOTAL parenteral nutrition (TPN) has had a major influence in reducing morbidity and mortality, particularly in patients with Crohn's disease (1). These patients are often malnourished; because of pain and chronic illness they have reduced intakes, and because of the nature of the disease, they undergo maldigestion and malabsorption, or lose nutrients through inflammatory secretions. Total parenteral nutrition has been used as primary therapy for Crohn's disease and has an established role (2,3). It is accepted as adjunctive therapy in nutritionally compromised patients with inflammatory bowel disease (IBD), and has a role for nutritional support in both Crohn's disease (4) and ulcerative colitis when surgery is imminent. There is no accepted primary role for TPN in patients with ulcerative colitis (5,6).

Uncontrolled data in Crohn's disease show initial remission rates between 60 and 70%, and at three months between 40 and 50%. An open trial of TPN was performed in a surgical unit over a 12-week period (2). Operations were avoided in 25 of 30 patients ad-

Particularités du traitement nutritionnel dans la maladie inflammatoire de l'intestin

RÉSUMÉ: Il y a plusieurs questions et controverses au sujet de la nutrition dans la maladie intestinale inflammatoire. La plupart des autorités acceptent maintenant l'utilité de la nutrition parentérale totale, tant en traitement primaire qu'en traitement d'appoint chez les patients atteints de maladie de Crohn, mais en traitement d'appoint seulement chez les patients qui présentent des exacerbations aiguës de colite ulcéreuse. Dans les deux cas, la nutrition parentérale totale a un rôle à jouer dans la préparation des patients à une chirurgie imminente. En comparaison avec la nutrition parentérale totale, le traitement, avec une formule définie (régime élémentaire) s'accompagne de moins de complications et est plus facile à surveiller, moins coûteuse et donne des résultats équivalents. Plusieurs essais contrôlés ont révélé que le traitement par diète élémentaire est aussi utile que la prednisone pour induire la rémission chez les patients atteints de maladie de Crohn active. Les diètes élémentaires ont été comparées aux diètes polymériques chez les patients atteints de maladie de Crohn et se sont révélées aussi efficaces. Récemment, une diète semi-élémentaire s'est révélée aussi efficace que la diète élémentaire, mais avec l'avantage d'un maintien des taux d'acide gras essentiels. Les diètes élémentaires ne semblent pas efficaces pour la fermeture de fistule. Si les problèmes de goût et chez certains patients, la nausée, les vomissements, les crampes abdominales et la diarrhée persistent, ils peuvent être surmontés jusqu'à un certain point par une modification de l'arôme, le refroidissement, l'introduction graduelle et le counselling, ou encore l'installation d'une sonde naso-gastrique. Récemment, des huiles de poisson ont été utilisées chez les patients atteints de maladie intestinale inflammatoire. Les résultats indiquent que les patients atteints de colite ulcéreuse pourraient en bénéficier, contrairement à ceux qui souffrent de maladie de Crohn. Les huiles de poisson exerceraient un effet d'épargne stéroïdienne qui, si elle est confirmée, pourrait offrir un avantage considérable aux patients atteints de colite ulcéreuse.

mitted for surgery. Subsequent follow-up showed a relapse rate in this group of 60% at two years and 85% at four years. When compared with historical controls requiring surgery in this unit, a four-fold higher relapse rate was seen.

The issue of whether the bowel should be placed at rest when TPN is given was investigated in 20 patients. There was no advantage of TPN with and without bowel rest, as shown by clinical scores or nutritional indices (7).

In another study, TPN given over three weeks as the only treatment to patients with Crohn's disease was compared with a defined formula diet, given via a nasogastric tube, and with partial parenteral nutrition and supplemental oral food. There were no differences in the remission rates of the TPN alone group (71%) compared with the defined formula group (58%) and the partial parenteral nutrition group (60%). By 12 months, the remission figures were 42, 55 and 56%, respectively. The conclusion of the group

was that TPN was a useful adjunct, but was no better than the others (8).

There have been two studies (5,6) comparing TPN with oral diet in patients with ulcerative colitis treated with corticosteroids; both showed no difference in the time required for remission or necessity for colectomy when TPN was used.

One of the first direct comparisons between TPN and elemental diet in patients with Crohn's disease was performed by Jones and co-workers (3). In this 14-day, controlled trial, a similar number of patients entered remission on the two treatments. The Crohn's disease activity index (CDAI) in those completing the trial compared with those pretrial showed significant drops in each group into the normal range (267 ± 94 to 115 ± 85 in the TPN group and 248 ± 49 to 119 ± 83 in the elemental diet group). Although there was improvement in the albumin and orosomucoid levels in both groups, these did not reach significance. These authors then excluded from the diets of

these patients foods considered to exacerbate the disease activity, with subsequent follow-up reporting ongoing benefit from this approach. The foods that were most commonly recorded included wheat, dairy products, brassicas, corn, yeast, tomatoes, citrus fruit and eggs (3). The findings in this study have not yet been convincingly confirmed by others (9).

Elemental diet has been used as primary treatment in acute Crohn's disease (10,11), and is reported to be as effective as corticosteroids in inducing remission (12,13). In a controlled trial, patients were randomized to an elemental diet consisting only of Vivonex (Norwich Eaton, Montreal), compared with a control group receiving prednisolone (0.75 mg/kg/day) reducing the dose as the clinical condition improved (12). At four weeks, eight of 10 patients in the prednisolone group and nine of 11 in the Vivonex group were in remission. At 12 weeks, one patient had dropped out from each group. The beneficial effect of this controlled trial was confirmed by others (8,13,14), but not with universal agreement (15,16). Savarymattu studied 37 patients, also randomized to elemental diet or to a control group consisting of prednisolone (0.5 mg/kg/day) plus oral, nonabsorbable antibiotics (13). Likewise, Greenburg, using a control group of partial TPN versus elemental diet, found similar remission rates in the two groups (8).

In a larger, randomized, multicentre trial of defined formula diet and prednisolone plus sulphasalazine in Crohn's disease, similar six-week improvements were reported in those who completed the trial (14). However, 29 of 51 withdrew from the trial, 20 of these owing to unpalatability of the defined formula diet. The CDAI in the diet group fell from 281 to 152, and in the drug group, from 264 to 129.

The therapeutic effect of an elemental diet (Pepti 2000; Nutricia, Zoetermeer) was randomly compared with a blended normal diet (as placebo) in 43 out-patients with IBD (24 ulcerative colitis, 19 Crohn's disease). A reduction in frequent bowel movements was seen in both diet groups, particularly in

TABLE 1

Comparison of defined formula (elemental) diets

	Peptamen™	Vital HN™	Criticare HN™	Vivonex Ten™
Protein %	16	16.7	14	15.3
Amino acids %	12	17	3	100
Peptides %	88 Whey Pr H	83	97 (Casein hydrolysate)	0
Carbohydrate %	51	74	81	82.2
Maltodextrin	M 88 Starch 12	M Corn syrups	M 92 Corn starch	M
Fat %	33 70 MCT 30 LCT	9.3 45 MCT 55 Safflower oil	5 Safflower oil	2.5 Safflower oil
Osmolarity	270	460	650	630

Pr H Protein hydrolysate; MCT Medium chain triglyceride; LCT Long chain triglyceride; ™Peptamen: Clinitec Nutrition; ™Vital HN: Ross Laboratories; ™Criticare HN: Mead Johnson; ™Vivonex Ten: Norwich Eaton

the ulcerative colitis graph. No effect on inflammatory indices was seen. The authors point out that reduced bowel movements and pain reduced clinical indices, eg, the CDAI, without affecting inflammation (16).

The effects of elemental diets have been compared with polymeric (full protein) diets (9,17). In 16 patients who were randomized to receive Vivonex, 12 achieved remission and showed a significant drop in CDAI from 300 to 150 ($P < 0.01$). In the 14 patients receiving Fortisan (Clinitec Nutrition, Mississauga), only five entered remission, with no significant change in the CDAI (17).

Another study compared Vivonex (an elemental diet) to Peptamen (manufacturer, city?) (a semi-elemental diet) in patients with active Crohn's disease; 26.3% were intolerant of the Vivonex diet and 14.3% were intolerant of the Peptamen diet (18). Three-week remission rates were 84 and 75%, respectively. There was a significant drop in the CDAI in both groups into the normal range. In addition, there was a significant fall in indicators of inflammation (C-reactive protein and acid alpha-glycoprotein) in those taking the semi-elemental diet. In this group, plasma phospholipids increased significantly, while in the elemental diet group the percentage of linoleic acid fell significantly. It was

concluded that semi-elemental diets were as effective as elemental diets in achieving remission in Crohn's disease, but, in addition, maintained essential fatty acid stores. Elemental diet has been used to heal fistulas in patients with Crohn's disease, but with very poor results (10,11,19).

One of the unsolved questions is the role of elemental diet in treating patients with chronic active, steroid-resistant Crohn's disease. Only anecdotal reports are available (10); there are no controlled trials addressing this specific question.

QUESTIONS ABOUT ELEMENTAL DIETS

How do elemental diets work? Elemental diets may work by diminishing intraluminal antigen stimulation or perhaps by improving immune host function. Other theories include altered gut bacteria and provision of epithelial cell specific nutrients, such as glutamine (12).

Which enteral diet should be used?

Commonly available, defined formula (elemental) diets used in Canada are shown in Table 1. There is a big variation as to whether these come prepackaged for immediate use or whether they are available in powder form, requiring reconstitution and, thus, increasing pharmacy costs. There appears to be a minimal cost per day of \$40.00, with

costs often exceeding this depending on the amount of nutrient used. The defined formula diets vary in composition (as shown in Table 1); the proportion of protein is much the same, but the sources vary from pure amino acids (as in Vivonex) to predominant peptides, such as whey protein or casein hydrolysate. The percentage carbohydrate varies from 51 to 82.2%, usually a high proportion of maltodextrin. There is a large variation in the amount of calories from fat, varying from 2.5% in Vivonex to 33% in Peptamen. Safflower oil is used in three of the preparations, with Peptamen using 70% medium-chain triglyceride. Only Peptamen is dispensed in an iso-osmolar preparation.

Problems of compliance arise in 10 to 30% of patients. Commonly these problems include taste intolerance and upper gastrointestinal symptoms of nausea, bloating and cramps, together with diarrhea in the occasional patient. There is a potential problem for essential fatty acid deficiency in a low-fat, defined formula diet. Problems to some extent can be reduced by the use of different flavours, by diluting the hyperosmolar preparations, by chilling before use and by using a nasogastric or nasoduodenal tube (compliance with this is increased if the tubes remain soft and pliable, and if they are capped). In selected patients, feeding can be readily provided through a percutaneous, endoscopic gastrostomy tube. Essential fatty acids can be added to a formula diet without essential fatty acids, and requirements can be monitored. There is a need for continuous support and encouragement from nurses, physicians and dietitians. There is also a role perhaps, for national patient groups, such as the Canadian Foundation for Ileitis and Colitis, and national professional groups, such as the Canadian Association of Gastroenterology, which may unite and bring pressure to reduce the costs of these preparations.

Not all patients have problems taking high osmolarity preparations. In one study (20), 12 patients (seven with Crohn's disease, five with ulcerative colitis and two with short-bowel syndrome) were given full-strength

Vivonex Ten via a nasogastric tube with success. Although five patients experienced nausea, bloating and pain, this did not necessitate reduced intake and the symptoms abated with continued use (20).

Leukotriene B₄ is the metabolite produced from arachidonic acid by 5-lipoxygenase. Fish oil contains eicosapentaenoic acid, which is metabolized preferentially by neutrophils to leukotriene B₅, which is 30-fold less active as an inflammatory mediator than leukotriene B₄.

Should fish oil supplements be used in patients with IBD and thereby limit production of leukotriene B₄ – a powerful inflammatory mediator? Fish oil

supplements have been used in patients with both ulcerative colitis and Crohn's disease, with variable success (21,22). Stenson (21) reported a placebo-controlled trial of four months' duration in 24 patients with ulcerative colitis using 18 capsules of maxeicosopentanoric acid. In six patients, leukotriene B₄ levels were reduced, histological improvement and weight gain were observed, and patients could reduce their dose of prednisone.

In a study of 39 patients with IBD (10 with ulcerative colitis, 29 with Crohn's disease)(22), Lorenz and co-workers performed a placebo-controlled trial over a seven-month period using a lesser dose of max EPA. Eleven

reported no clinical improvement.

Salomon (23) reported an open trial of 15 capsules of max EPA in 10 patients over a two-month period, where seven were improved and steroids were reduced in four of five.

There is a suspicion that steroid-sparing occurs in patients with ulcerative colitis when fish oil supplements are used (21). If confirmed, eating more fish, perhaps, may be more attractive than swallowing fish oil capsules.

Further controlled trials to document significant benefit from fish oils are required before they can be recommended for patients with ulcerative colitis.

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