Parenteral nutrition in inflammatory bowel disease

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SUMMARY Nutritional support, administered via the enteral or parenteral routes, has been widely introduced in the treatment of inflammatory bowel disease over the past decade. The precise place of total parenteral nutrition, however, as a sole or adjunct treatment of inflammatory bowel disease, has yet to be defined.

Expected theoretical effects of total parenteral nutrition

There are three theoretical benefits of total parenteral nutrition in bowel disease: nutritional effect; bowel rest; and prolonged substitution of intestinal function in short bowel syndrome and chronic Crohn’s disease extended to the entire small bowel. The nutritional effects of total parenteral nutrition include: stimulation of protein synthesis, at the systemic – that is, muscle and bone level, but also at the local (intestinal) level, resulting in stimulation of cell renewal and healing processes, together with correction of vitamin and trace element deficiencies; stimulation of systemic, mainly cellular, immunity; contribution to intestinal adaptation of which nutritional state is, in addition to intraluminal stimulation of gastrointestinal (GI) hormones, a clinically important factor.1 Bowel rest is due to the main expected effects despite the fact that there is no statistically confirmed benefit. Bowel rest implies interference with digestive secretions and motility; antigenic (chemical, dietary, and bacterial) stimulation of mucus from the lumen; mucosal permeability and vascular supply; as well as interference with the trophic effect of gastrointestinal hormones. The expected consequences of these interactions include a decrease in local inflammatory and infectious processes, healing of ulcerated mucosa, decreased output from fistulae, relief of partial inflammatory obstruction and, particularly in Crohn’s disease, a possible temporary break in pathogenetic interactions between external agents, host genetic receptivity, and intestinal cellular immunity.

Total parenteral nutrition in Crohn’s disease: a critical analysis of indications and results

TRANIENT TOTAL PARENTERAL NUTRITION

Of 18 published papers (1973–84) discussing trans-
results of five main series of published reports, as well as relevant clinical experiences. Optimal duration of total parenteral nutrition to induce remission is four to six weeks; after this time there is little hope of a remission using total parenteral nutrition alone. In steroid resistant cases a clinical or anatomical remission, or both, may be obtained with total parenteral nutrition in 40 to 80% of cases,68 and in steroid dependent cases in almost 100% of cases.9 Adjunctive steroids do not improve the result obtained with three to eight weeks of total parenteral nutrition in Crohn's ileo-colitis.10 No prospective controlled study of total parenteral nutrition v steroids on the activity of disease and incidence of subsequent acute stenoses is, to our knowledge, available.

The site of Crohn's disease does not influence the incidence of remission induced by total parenteral nutrition, but small intestinal lesions are the most reliable indication. Acute Crohn's colitis, when requiring nutritional support, should primarily be treated by enteral nutrition. Total parenteral nutrition may6 11 or may not2 be useful. The use of short (five to 10 days) preoperative total parenteral nutrition in acute Crohn's disease has been suggested on the basis of a reduced postoperative incidence of complication.7 12 Further controlled prospective studies in this area are clearly needed.

Natural history of Crohn's disease
Current data suggest that transient total parenteral nutrition, of 4–12 weeks' duration, does not influence the natural course of the disease, which is judged in terms of either clinical or anatomical relapse, or reoperation rate or mortality. Whether or not total parenteral nutrition influences dependence on steroids has not been ascertained.

Relapse and reoperation rates
After two years the rate of relapse and reoperation following total parenteral nutrition is 40 to 62% and 30%, respectively.7 In the study by Müller et al6 on patients with severe Crohn's disease treated by total parenteral nutrition alone the actuarial relapse rate was 32% after one year but 85% after four years. In our own experience the rate of overt clinical relapse after three years in patients with non-surgical Crohn's ileo-colitis was 26% in a series of 21 patients treated with total parenteral nutrition and 29% in a series of 29 comparable patients who received drug treatment without nutritional support.

Steroid dependence
Data are scarce, but two findings may be cited: Messing et al13 showed that total parenteral nutrition was followed by reduction (from an average of 1·2 to 0·5) in the rate of annual relapses in steroid resistant cases; we observed that the percentage of steroid dependency (defined by a minimal necessary daily dose of 10 mg of prednisone) in patients with Crohn's disease of all localisations was 20% and 27% after three years in groups treated or untreated by total parenteral nutrition, respectively; these figures were 18% and 37·5% respectively, when the ileo-colonic site alone was considered. Given the potential consequences of prolonged treatment with steroids on survival of young patients, these preliminary data require further confirmation.

Enterocutaneous Fistulæ
The Table shows the negative influence of fistulæ on the one year remission rate in active Crohn's disease (89% ν 50%, in the absence or presence of fistulæ, respectively). The mean rate of healing of chronic fistulæ is 40%, the figure being greater for small bowel (75%) than for colonic fistulæ (33%). The main effect of total parenteral nutrition on the healing of Crohn's fistula apparently resides in the induced nutritional repletion rather than in bowel rest. As long as there is no distal obstruction, however, closure of fistulæ seems to be achieved quicker with parenteral, rather than enteral, nutrition.16 In association with total parenteral nutrition no other treatment, either steroids or azathioprine, has proved as clinically efficient in fistula healing.

Growth retardation
This important complication of Crohn's disease in children and adolescents is observed, with or without associated delay in sexual maturation, in about 20% of cases (13 to 58%).17 Its principal mechanism is prolonged protein-energy malnutrition, primarily dependent on intestinal losses and, above all, on a prolonged reduction of nutritional intake (by 38 to 55%) compared with that in normal children. Total parenteral nutrition is indicated only after treatment with steroids associated with enteral nutrition has failed. In 60% of cases it may result in resumption of growth.17

Prolonged home total parenteral nutrition
Crohn's disease accounts for 25 to 59% of the indications for home total parenteral nutrition.16 18 In these patients the main indications are postoperative short bowel syndromes, prolonged active or chronically relapsing Crohn's disease affecting the entire small bowel, multiple chronic small bowel stenoses or fistulæ, or both. The duration of prolonged total parenteral nutrition for Crohn's disease extends from two months to several years.
Particular technical and metabolic aspects of total parenteral nutrition

CYCLIC TOTAL PARENTERAL NUTRITION
Due to the fact that almost all patients with Crohn’s disease remain mobile, cyclic (nocturnal) total parenteral nutrition (in hospital as well as at home) is an optimal technique of parenteral nutrition. In conjunction with the psychological improvement of the quality of personal life and tolerance to treatment, cyclic total parenteral nutrition has, at least in non-severely hypermetabolic patients, been shown to have a beneficial effect on protein-energy metabolism, as well as on fat and water deposits.

ENERGY SUPPLY
Contrary to initial belief, most patients with Crohn’s disease are not hypermetabolic. Energy expenditure is, on the whole, closely correlated with the degree of recent weight loss: energy supply should be increased above 35–40 kcal/kg ideal body weight in the event of treatment with steroids, abscesses, severe sepsis or fistulae; in all other cases energy supply may be calculated on the basis of the product of basal energy expenditure by a coefficient of 1.25 to 1.50.

VITAMIN AND TRACE ELEMENT DEFICIENCIES
Vitamin B₁₂ and magnesium deficiencies favoured by ileal disease may easily be prevented by adequate supplementation. This also holds true for folate deficiency, which may be severe in malnourished patients and which aggravates malabsorption. Although only partially reflected by serum concentrations, zinc deficiency is often severe and aggravated by losses in diarrhoea and fistula effluent. Daily supply may be calculated from the formula proposed by Wolman et al., which integrates urine, faeces, fistula and stoma losses. Selenium deficiency may be observed after massive intestinal resection. Carnitine deficiency has been reported in patients with Crohn’s disease and cholestasis or hepatic steatosis, or a combination of all three. All may be prevented by adequate daily or twice weekly supply.

CHOLESTASIS
The incidence of cholestasis (20 to 50% of patients treated with total parenteral nutrition, seems to be increased in patients with Crohn’s disease, especially in the event of continuous (24 hour) delivery. Cholestasis associated with total parenteral nutrition may indicate a latent hepatic dysfunction directly linked to Crohn’s disease (pericholangitis, chronic hepatitis, amyloidosis). The possible beneficial effect of metronidazole on cholestasis suggests that intestinal bacterial flora have a pathogenetic role.

GALLSTONES
The incidence of biliary “sludge” and gallstones, which is high during prolonged total parenteral nutrition, is further increased in adult patients with Crohn’s disease with ileal resection or disease (7% vs 29%); it may reach 60% in children. The possible importance of biliary stasis occurring as a consequence of bowel rest has been emphasised.

Comparison of total parenteral nutrition with enteral nutrition
The cost and the risks of total parenteral nutrition, compared with those of enteral nutrition, should result in the preferential use of enteral nutrition in patients with Crohn’s disease; this is especially so in the case of colonic or distal ileal Crohn’s disease associated with normal jejunal and proximal ileal function. The results of a few prospective controlled studies are presently available. According to a recent paper published in abstract form, total parenteral nutrition would more favourably influence Crohn’s activity index, whereas enteral nutrition would have more effect on nutritional variables. In a randomised trial in 51 patients with active Crohn’s disease unresponsive to conventional medical management total parenteral nutrition proved, in terms of clinical remission, slightly but not significantly better (71%) than partial parenteral nutrition and oral food (60%), or enteral nutrition with a defined formula diet (58%).

Total parenteral nutrition in idiopathic ulcerative colitis
The limited role of total parenteral nutrition – compared with that of enteral nutrition – may be summarised as follows: (i) prolonged total parenteral nutrition is not, or rarely, useful in acute forms of ulcerative colitis; (ii) by postponing the decision in favour of total colectomy it may be dangerous; (iii) total parenteral nutrition is ineffective in active ulcerative colitis treated by steroids; (iv) short term total parenteral nutrition (two to seven days) may be useful as a preparation for total colectomy in the event of failure of enteral nutrition.

Conclusion
To conclude: (i) total parenteral nutrition should be used in Crohn’s disease only in the event of failure or impossibility of use of enteral nutrition – that is, in extensive active jejuno-ileal or ileal disease resistant to medical treatment, chronic forms with multiple small bowel stenoses or enterocutaneous fistulae, short bowel syndromes, or where there is
severe growth retardation; (ii) total parenteral nutrition is much less useful in Crohn’s colitis and is not indicated in most cases of ulcerative colitis; (iii) as with home total parenteral nutrition, hospital total parenteral nutrition should be, as early as possible, cyclic; (iv) the question of whether or not total parenteral nutrition reduces steroid dependency in patients with severe Crohn’s disease warrants further controlled studies. As enteral nutrition has proved effective in distal forms of inflammatory bowel disease total parenteral nutrition should be used as a last resort therapeutic tool.

References