Review Article

Nutritional support of the hospitalized patient

Part II. Clinical indications

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Summary

The first part of this review dealt with the background, methodology and techniques of nutritional support. As a significant proportion of hospitalized patients suffer from various forms of unrecognized and untreated malnutrition, nutritional support is essential for the maintenance of body mass and function until specific treatment is able to influence the course of disease. The following review highlights various medical and surgical conditions in which nutritional support, in particular total parenteral nutrition, has been advocated in adult patients. Nutritional repletion as a therapeutic modality is still in its infancy, and consequently its true role in patient management is still undergoing evaluation.

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Pre- and postoperative nutritional support

The combination of starvation, injury and major sepsis results in excessive catabolism of the body cell mass.[1] The provision of adequate nutrients in such a situation, particularly in undernourished patients, remains difficult as the metabolic demands in terms of energy are considerable. A significant proportion of hospitalized patients suffer from various forms of unrecognized and untreated malnutrition,[2-4] and nutritional support is therefore essential for the maintenance of body mass and function until specific treatment is able to influence the course of the disease. Supplemental intravenous feeding should be given to undernourished patients, particularly those with cancer of the upper gastro-intestinal tract, before surgery is undertaken. In this group of patients malignant cachexia and immunoparesis increases the postoperative morbidity and mortality. Improvement in the nutritional status of cancer patients by oral feeding may be difficult because of anorexia, mechanical obstruction and malabsorption, or take so long that adequate antineoplastic therapy is delayed. Total parenteral nutrition may then be necessary.

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Muller *et al.*[5] have shown a reduction in postoperative mortality from 18% to 5% in malnourished cancer patients receiving preoperative intravenous alimentation.

The total number of patients requiring intravenous nutrition for more than a few days is less than 5% of all hospital admissions.[6] The objectives of nutritional repletion are enhanced wound healing, a reduction in postoperative complications and more rapid convalescence. In non-depleted postoperative patients who are unable to eat or absorb food adequately 1 week after operation, parenteral nutrition providing 0,8 - 1 g of amino acids per kilogram of body weight per day and a total number of kilojoules 20% above the basal energy expenditure should be instituted.[7] In depleted patients this increases to 1,5 - 1,8 g/kg amino acids and a total kilojoule intake 50% above estimated basal energy expenditure. Several well-controlled trials[5,8-10] have already shown that postoperative parenteral feeding with amino acid and hypertonic glucose solutions is more effective in preventing postoperative catabolism, promoting tissue protein synthesis and reducing complication rates than is infusion of 5% dextrose with electrolytes.

High-output fistulas of the alimentary tract

The treatment of gastro-intestinal fistulas has been associated with significant morbidity, and mortality rates as high as 65%.[11] The prognostic importance of nutritional status in the management of fistulas was first emphasized by Chapman *et al.*,[12] who dramatically reduced mortality by correcting malnutrition before the surgical closure of fistulas. More recently, Voitk *et al.*,[13] using a chemically formulated diet, reported a mortality rate of 28%, and MacFadyen *et al.*,[14] by treating gastro-intestinal fistulas with total parenteral nutrition, achieved a mortality rate of 6,4%. Treatment without nutritional support will result in a high mortality rate, particularly in association with early, aggressive surgery.[15] Moreover, if the patient survives recurrence of the fistula is common. Definitive surgical closure of the fistula should only be performed when the patient is apyrexial and has good nutritional status, and if the fistula effluent shows no sign of decreasing in volume after 6 weeks of nutritional support.

Most postoperative fistulas can be prevented. Of particular importance is the avoidance of enterotomy as a method of decompressing obstructed bowel, and careful suture repair of the extensive serosal tears which may follow the lysis of adhesions. Pre-operative nutritional repletion will also help to decrease the incidence of postoperative fistulas. Our experience in the management of 63 patients with high-output alimentary tract fistulas treated over a 3-year period, using 3 different regimens of nutritional support, showed a spontaneous closure rate of 73%, while another 11% were cured by direct surgical closure.[16] The combination of nutritional support, skin protection and timed surgical intervention can reduce the mortality rate in this group of patients to below 10%. Sepsis must be treated aggressively as this is the major factor in mortality and morbidity.

Malnutrition and cancer

Cachexia is the commonest cause of death in cancer patients.[17] The reduction in body cell protein leads to respiratory inefficiency and terminal respiratory infection. Cancer cachexia is a multifactorial entity and is clearly affected by anorexia, gastro-intestinal malfunction and abnormalities of taste.[18] Tumour metabolism, necrosis and infection, together with surgery, radiotherapy and chemotherapy, can all contribute, singly or in combination, to the weight loss that often attends treatment.[19,20] The response to chemotherapy is poorer in the cachectic than in the well-nourished patient.[21] The cellular immune response may be depressed in the presence of cancer,[22] but published reports are conflicting, possibly as a result of a failure to analyse homogeneous tumour groups or to take into account such factors as the effects of treatment or malnutrition. We have shown that protein-calorie malnutrition contributes significantly to the immunoparesis evident in patients with oesophageal carcinoma, and this may also be an important factor in tumour prognosis, immunotherapy and the immunoparesis of other solid tumours.[23]

Parenteral or enteral alimentation can be used to improve nutritional status before commencing surgery or chemotherapy.[24-26] Enteral nutrition is cheap and has the advantage of simplicity, ease of administration and fewer complications. It should be considered the most appropriate method of nutritional support unless contraindicated.[27] The best method of enteral feeding in the severely anorectic patient is via the nasogastric fine-bore tube.[28] Lim *et al.*[29] have shown that although gastrostomy feeding is inferior to total parenteral nutrition in achieving positive nitrogen balance and weight gain in patients with oesophageal cancer, it is still a simple and safe method of nutritional support in these patients. Intravenous alimentation is an important treatment modality in cancer patients,[30-33] but the suggestion that feeding the host may also stimulate tumour growth is cause for concern.[34] However, Copeland *et al.*[25] could find no evidence of increase in tumour growth in over 1 000 patients treated with total parenteral nutrition. Similar conclusions have been reached by other authors.[35,36] At present, total parenteral nutrition allows specific tumoricidal therapy to be administered to malnourished cancer patients who might otherwise be excluded from intensive treatment. In this group nutritional support has been efficacious, safe, and possibly life-saving.[37]

Short-bowel syndrome

Extensive intestinal resection for inflammatory bowel disease or mesenteric vascular occlusion can result in the development of short-bowel syndrome. Adequate nutritional support is essential for the survival and rehabilitation of these patients.[38,39] Total parenteral nutrition should be maintained for approximately 21 days in order to allow compensatory adaptation in the residual healthy intestine. During the postoperative period chemically formulated diets have a distinct advantage over normal foods.[40] These diets are almost totally absorbed in the upper small intestine with minimal digestive requirements. A high-carbohydrate, high-protein, low-fat diet should be the final goal in nutritional therapy. Intestinal absorption is also more complete with frequent feedings of equally divided portions of nutrients. Gastric hypersecretion may complicate the short-bowel syndrome, but this is usually an acute and temporary phenomenon.[41]

Ambulatory home care using total parenteral nutrition is a novel and optimistic approach for patients with inadequate residual bowel; these patients are now able to live under conditions of almost total social rehabilitation.[42,43]

Inflammatory bowel disease

The activity of inflammatory bowel disease can be reduced by bowel rest, especially when the site of involvement is the small intestine.[44] The concept of bowel rest is supported by experimental observations of a reduction in gastro-intestinal secretions during total parenteral nutrition or with the use of chemically defined diets.[45] Although evidence exists that intravenous amino acids may stimulate gastric and pancreatic secretions,[46] this need not adversely affect patient response to parenteral nutrition. Nutritional support in patients with small-bowel Crohn's disease will increase total plasma proteins, reduce protein loss into the gastro-intestinal tract and increase peripheral blood lymphocyte counts.[47]

There are few if any controlled studies defining the role of pre- or postoperative nutritional therapy in promoting the recovery of patients undergoing surgery for gastro-intestinal disorders. It is generally conceded that the role of parenteral nutrition in the treatment of patients with inflammatory bowel disease is adjunctive to surgical or medical management. The best results are found in those patients with regional enteritis confined to the small bowel — a remission rate of 75% has been reported.[44] Less favourable results in patients with active, non-fistulous Crohn's disease treated with parenteral nutrition have been reported in prospective trials by Driscoll and Rosenberg[48] and Dickinson *et al.*[49] Steroid dosage may be reduced to 5 - 10 mg/d in patients receiving nutritional support. Granulomatous disease involving the colon is associated with a lower remission rate, and regardless of the severity of disease the response to parenteral nutrition in patients with ulcerative colitis is poorer than in those with Crohn's disease.[45] Enterocutaneous fistulas complicating Crohn's disease may heal but frequently re-open once oral feeding is resumed. Resection is indicated in such circumstances. Mullen *et al.*[50] claimed that 70% of fistulas due to Crohn's disease healed spontaneously on parenteral feeding. The response to nutritional support of growth retardation in adolescents with inflammatory bowel disease may be striking. Weight gain, a positive nitrogen balance, linear growth and significant increases in growth velocity have been observed with total parenteral nutrition.[51]

Burns

Major thermal injury is characterized by a hypermetabolic response,[52] the magnitude of which parallels the extent of the thermal injury and may be 150-200% of the normal resting metabolic expenditure (see Part I, *SAMJ* 1983; **63:** 610-615). Such hypermetabolism is associated with markedly increased energy requirements. Indeed, weight loss may not be totally prevented even when an intake of 37 800 - 42 000 kJ per day is achieved by combined enteral and parenteral feeding.[53] The abnormal red blood cell sodium concentration gradients seen in patients with burns can be corrected with adequate nutrition.[54] Patients with major burns treated with aggressive nutritional support have a higher survival rate,[55] but catheter-related sepsis tends to be more common in this group. Since in severely burned patients sites of access may be limited, central catheters are used for the administration of all fluids as well as for parenteral nutrition, but are changed more frequently. It is preferable to insert central venous catheters through unburned skin, but this may be impossible in the severely burned patient. Late deaths occur 3 - 6 weeks after burn injuries, commonly as a result of complications involving sepsis. Contributing factors include abnormalities in the humoral and cellular immune mechanisms during the acute burn phase.[56]

Severe trauma or infection

Severely traumatized, ventilator-dependent patients have increased metabolic demands (20-60% above basal requirements) (see Part I, *SAMJ* 1983; **63:** 610-615). A recent review of the nutri-

tional status of patients supported by ventilation showed an almost universal iatrogenic malnourished state.[57] This group of patients should be considered for nutritional support after an initial 48-hour period which allows for adequate resuscitation, oxygenation, correction of fluid, electrolyte and acid base imbalance, initiation of appropriate antibiotics and surgery. Where glucose is the sole energy source the respiratory quotient is increased as a result of increased carbon dioxide output.[58] Metabolic acidosis develops and this may further compromise pulmonary function in severely ill patients. As a method of determining energy requirements, indirect calorimetry may be helpful in the clinical management and eventual 'weaning' of these ventilator-dependent patients.[59] Woolfson *et al.*[60] have shown that in these catabolic patients insulin has a specific protein-sparing effect which is independent of the nature of the energy source used.

Currently, many laboratories are investigating immunodepression following injury and its relationship to septic complications. However, the available tests will not accurately identify the patient at increased risk of infection after surgery. Skin test anergy to recall antigens may correlate with age, magnitude of injury and survival,[61] but it is still unclear whether nutritional support can reverse this stage of relative immuno-incompetence and influence patient prognosis. Factors other than malnutrition, including the presence of circulating immunosuppressive peptides, may contribute to infection in the postoperative period.[62]

Miscellaneous conditions

Liver failure

Nutritional requirements are different in patients with liver failure, particularly as regards protein and vitamins.[63] Protein intolerance is a consequence of both increased endogenous protein catabolism and reduced aromatic amino acid clearance by the liver.[64] Consequently, diets low in aromatic amino acid content and high in glucose (anticatabolic effect) are commonly advocated. More recently branched-chain amino acid supplements (BCAAs) have been added, for the reason that tolerance is normal because they are oxidized extrahepatically. In addition, a number of trials have demonstrated a beneficial effect on encephalopathy.[65,66] Preliminary evidence suggests that the ornithine salts of the α-keto analogues of BCAAs may be even more efficacious.[67] However, in practical terms these solutions are unavailable in South Africa, and 'hepatic support' should be based on the constant infusion of hypertonic glucose and dilute amino acid solutions.[63] The role of glucose is twofold: to prevent hypoglycaemia and to reduce protein catabolism. Given at a rate of 3 g/h amino acids are within tolerance levels, and will prevent the otherwise inevitable protein depletion associated with zero-protein diets.[68] Generally, increased requirements of both water- and fat-soluble vitamins result from increased urinary losses, reduced hepatic stores and reduced dietary intakes.[63]

Renal failure

Whether nutritional support alters overall survival and hastens recovery of renal function in patients with acute renal failure has not been elucidated. In one prospective trial of randomized, relatively homogeneous surgical patients with acute tubular necrosis no decrease in dialysis requirements was observed, but there was a tendency to increased survival.[69] Once the need for dialysis is established most clinicians would use a combination of essential and non-essential amino acids, because both types of amino acids are lost during dialysis. The effects of the increased nitrogen load can be ameliorated by dialysis. However, the precise role of essential amino acids alone versus mixtures of essential and non-essential amino acids in treating patients with acute renal failure remains controversial.[70,71] Histidine and perhaps arginine may be regarded as being essential in adults with renal failure;[71] α-keto acids have been tried in chronic renal failure patients with beneficial effects.[72] The use of hypertonic glucose as an energy source is associated with a lower incidence of uraemic encephalopathy.[73]

Cardiac failure

Malnutrition can lead to cardiac dysfunction and, conversely, cardiac impairment can lead to malnutrition, commonly referred to as cardiac cachexia. Sudden death due to ventricular fibrillation has been documented in otherwise healthy individuals consuming inadequate amounts of protein.[74] Intracellular electrolyte and trace element deficiency not detected by routine clinical testing may have contributed to the arrhythmia. Double or triple heart valve replacement in cachectic patients has a mortality rate of 50-75%; in these patients pre-operative nutritional support may be of benefit.[75]

Pancreatitis

Total parenteral nutrition may be used in patients with severe pancreatitis (regardless of aetiology) with minimal technical or metabolic morbidity, and has contributed in part to a reduction in overall mortality.[76] Approximately 10% of patients will require parenteral nutritional support.[77] Initial glucose intolerance is common but is easily controlled by decreasing the infusion rate or by the addition of soluble insulin (10-20 U) to the parenteral mixture. Malnutrition and specific amino acid deficiencies, e.g. of methionine, can exacerbate pancreatic inflammatory disease,[78] but no definite conclusions can be drawn regarding the effect of nutritional support on complications such as respiratory and renal failure. In the absence of main duct obstruction pancreatic fistulas will respond satisfactorily to parenteral alimentation, obviating the need for surgical intervention.[16] Patients must be carefully monitored for elevations of serum calcium and amylase levels during total parenteral nutrition. Parenteral nutrition in pancreatitis fulfils a supportive role, but when patients are referred for laparotomy, jejunostomy should be performed as a means of long-term nutritional support.

Conclusion

Nutritional support is playing an increasing role in total patient care, and will undoubtedly expand into every medical discipline. Research in this area is still proceeding, and patient populations likely to benefit most by nutritional repletion are being more clearly defined. Current techniques of total parenteral nutrition are relatively safe and effective, and will undoubtedly improve as newer methods and materials become available. The multidisciplinary approach to nutritional support of the hospitalized patient cannot be overemphasized.

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