Occasional Review

Total parenteral nutrition: value of a standard feeding regimen

OXFORD PARENTERAL NUTRITION TEAM

Abstract
In 1978 an unofficial total parenteral nutrition service was established in a regional hospital. For simplicity, safety, and economy patients needing this form of treatment were supplied, whenever possible, with a standard feeding regimen containing 14 g of nitrogen and equicaloric amounts (4.2 MJ) of non-nitrogen calories as fat and glucose. From May 1978 to April 1982 179 patients received 190 courses of total parenteral nutrition, and 134 (70.5%) of these courses were the standard regimen throughout. A positive nitrogen balance was maintained, and complications were mostly minor. One hundred and forty patients left hospital alive. One death was related to the total parenteral nutrition.

Parenteral nutrition is an effective method of nourishing selected patients and a simple standard regimen can safely provide the total nutritional requirements for the majority. The value of a nutrition team and close supervision of the feeding is emphasised.

Introduction
In the past decade the use of total parenteral nutrition for treating malnourished and seriously ill patients has increased dramatically. The indications for this treatment, however, are not clear, and its clinical value is in some cases debatable. The choice of regimen in particular is difficult because the precise nutritional requirements of patients are not known. Most patients with gastrointestinal disease require less than 10.5 MJ/24 h (2500 kcal/24 h), and there is no merit in exceeding 16.8 MJ/24 h (4000 kcal/24 h); even in patients with major burns.

An unofficial parenteral nutrition service was established in Oxford in 1978 as such groups can reduce the morbidity and mortality of parenteral nutrition. For simplicity, safety, and economy we used a standard prescription in adult patients whenever possible. The regimen was formulated to mimic a normal oral diet and contained equicaloric amounts of glucose and fat with amino acids, electrolytes, vitamins, and minerals. We describe our experience and results and in particular those of a standard feeding regimen.

Nutrition service
The total parenteral nutrition service is provided by clinicians, pharmacists, a biochemist, a full time specialist nursing sister, and a dietitian. The clinical members of the team were recruited from among the surgical registrars and lecturers. Patients referred for parenteral nutrition were seen by a clinical member of the team, who confirmed their suitability for total parenteral nutrition and prescribed the standard or an individual regimen. A central venous catheter was then inserted and feeding began after the position of the catheter had been confirmed by x-ray examination. Daily ward rounds were performed to detect clinical and metabolic complications, and all members of the service met once a week to review patients receiving total parenteral nutrition.
INDICATIONS

Patients were accepted for total parenteral nutrition if they had had a prolonged period of starvation, there was evidence of malnutrition or hypercatabolism, and there was no other suitable means of nutrition. Most patients had several of these indications. Malnourished patients with adequate gastrointestinal function were fed enterally whenever possible, often with a fine bore nasoenteric tube.

Prescriptions

STANDARD REGIMEN

The standard regimen supplied 4.2 MJ/24 h (1000 kcal/24 h) of both fat (500 ml 20% Intralipid, Kabivitrum) and glucose (250 g). The amino acid source (Synthamin, Travenol Ltd) provided 14 g of nitrogen every 24 hours. The glucose-amino acid solution was made up in sterile conditions under a laminar flow hood to 2.5 l in a three litre bag (Viafix, Travenol Ltd). Water soluble vitamins (Parenterovite, Bencard) were added. Table I shows the energy, nitrogen, and electrolyte content. Alterations of the fluid volume and electrolyte content were made when required as a normal part of patient management. The bag was connected by a giving set (Intrafix B, Braun Ltd) and extension set (Vygon) to the central venous catheter (Nutricath, Vygon). A 500 ml bottle of 20% lipid emulsion (Intralipid, Kabivitrum Ltd) was connected to a side port of the infusion apparatus. The fat was infused over 9-12 hours, and the glucose-amino acid mixture over 24 hours.

| TABLE I—Standard adult total parenteral nutrition regimen (1982) |
|---------------------------|---------------------------|
|                          | Energy (MJ) | Volume (l) |
| Glucose                  | 250 g       | 4.18       |
| Nitrogen                 | 14 g        | 1.43       |
| Sodium                   | 100 mmol    | 1.43       |
| Phosphorus               | 30 mmol     | 0.25       |
| Calcium                  | 14 mmol     | 0.10       |
| Potassium                | 20 mmol     | 0.25       |
| Magnesium                | 19 mmol     | 0.10       |
| Folic acid               | 15 mg       | 0.01       |
| Parenterovite (water soluble vitamins) | 4.18 | 0.5 |
| Intralipid 20% | | |
| Total                    | 9.823       | 3          |

Conversion: SI to traditional units—Energy: 1 MJ = 239 kcal.

INDIVIDUAL REGIMEN

Hypermetabolic patients with urinary nitrogen losses greater than 14 g/24 h had an individually prescribed regimen. The energy content was increased by adding glucose, and extra nitrogen was added to maintain a positive nitrogen balance. Patients who were seriously ill with major electrolyte imbalance or shock were not fed parenterally until their clinical condition was stable. Fat was withheld in cases of hyperlipidaemia, known hypersensitivity to Intralipid, severe liver or pulmonary failure, coagulopathy, or fat embolus.

ADDITIVES

All patients received vitamin K (10 mg) intramuscularly twice a week. Fat soluble vitamins (Vitilipid Adult, Kabivitrum Ltd) and other trace elements (table II) were given to patients fed for more than one week. Steroids and cimetidine were added to the three litre bag in the pharmacy when clinically indicated. The central venous catheter was preserved entirely for parenteral nutrition except in rare cases with difficult vascular access. A peripheral venous infusion was used to administer antibiotics, insulin, blood products, and additional electrolytes when necessary. Parenteral nutrition was withdrawn gradually as normal nutrition was reintroduced.

Measurements

Accurate fluid balance and temperature charts were kept, and the urine was analysed every six hours for glucose (Labstix, Boehringer). Patients were weighed twice weekly. Haemoglobin concentration; white cell count, blood electrolytes, urea, glucose, and creatinine concentrations, were measured and liver function tested daily for the first week and twice weekly thereafter so long as they remained stable. Twenty four urine collections were analysed for urea excretion, from which the daily nitrogen balance was estimated. Major losses of fluid from surgical drains and fistulae were also measured. Blood withdrawn from the catheter and skin swabs taken from the catheter entry site were sent for bacterial and fungal culture three times a week when the catheter was re-touched. All data were recorded on the patients' total parenteral nutrition charts kept by the nutrition sister.

Results

In the three years from May 1979 to April 1982 179 patients (104 men and 75 women) received a total of 190 courses of total parenteral nutrition. The mean age of the patients was 48.6 years (range 15-87). The average duration of parenteral feeding was 15.4 days (median nine, range 1-137) (fig 1). Two hundred and six central venous lines were required—an average of 1-1 lines for each course. Although 136 patients came from the Oxford health district, 43 were from the region or further afield and receiving treatment in specialist or regional units within the Oxford hospitals. Most patients were referred from surgical specialties (table III), and most suffered from gastrointestinal disease (table IV).

The standard regimen was used exclusively in 134 (70.5%) courses, one of which was a course lasting 83 days undertaken at home. An individual prescription was necessary for all or part of 56 courses: 34 had an altered nitrogen content, usually accompanied by an increase in energy to a maximum of 12.6 MJ/24 h (3000 kcal/24 h). In the other 22 courses the nitrogen content was standard but the total energy content was altered. Fat was withheld in 17 patients.

![Fig 1—Duration of courses of total parenteral nutrition, including duration of courses in patients who died. The final week includes courses of nine or more weeks.](http://www.bmj.com/)

| TABLE III—Specialties that referred patients for total parenteral nutrition |
|---------------------------|---------------------------|
| Surgery                   | 155                      |
| Medicine                  | 21                       |
| Accident and emergency    | 7                        |
| Nephrological             | 4                        |
| Neurosurgical             | 2                        |
| Radiotherapy              | 1                        |
| Other                     | 208                      |
The initial weight of the patients was maintained during the early days of nutrition, and the mean weights gradually increased as feeding became established (fig 3).

**COMPLICATIONS**

**Mechanical**

A total of 190 central venous catheters were inserted without incident, but one or more complications occurred on 16 occasions (table VI). In 13 cases the operator was unable to enter one subclavian vein but could enter the contralateral subclavian vein. Three immediate pneumothoraces were produced (1·5%). In six patients the chest x-ray film showed the catheter tip in the internal jugular vein. The catheter was withdrawn into the superior vena cava or reinserted. Table VI also shows the mechanical complications that occurred during the course. One hundred and forty six (77·2%) lines were free of mechanical problems. Infection proved by positive blood cultures and culture of infected catheter tips after removal occurred in 13 (6·5%) central catheters. We have reported elsewhere that 37 lines inserted early in the review period were polyvinyl chloride catheters (Intramedic) and seven of these became infected. The remaining 169 catheters were silicone rubber (Nutricath, Vygon) and only three (1·8%) of these used for total parenteral nutrition alone became infected. Three others used for nutrition and vascular access also became infected. One late pneumothorax detected five days after insertion of the catheter, despite a normal chest x-ray film after insertion has been reported, and another has also occurred. Accidental disconnection of the giving set from the catheter hub occurred seven times, but there were no disconnections of the detachable hub from the catheter itself. No patient suffered air embolism. Line blockage, which occurred on 22 occasions, was usually due to uninfomned medical and nursing staff stopping the infusion without consultation.
Metabolic

Remarkably few metabolic problems or complications arose and those that did were due mostly to disturbed glucose homeostasis. Twelve (9%) patients receiving the standard feeding regimen required insulin. One of these was an insulin dependent diabetic, another had severe pancreatitis, and two others were being treated with large doses of corticosteroids for active inflammatory bowel disease. Seven of the 56 patients receiving the individual regimen required insulin, and one of these was also an insulin dependent diabetic. In five patients fat was replaced with equicaloric additional glucose. A further patient had fat and increased glucose. Insulin was administered by subcutaneous injection on a sliding scale early in the series, but more recently it has been given intravenously using a syringe pump.

All patients in this review who were fed with a standard regimen received 165 mmol of chloride a day. This produced a persistent hyperchloraemia in eight, all of whom had some renal impairment. On another occasion already mentioned the hyperchloraemic acidosis was fatal.

Most patients had hypoalbuminaemia (fig 4) when the course was started, but the mean serum albumin concentration rose to within the normal range after one week and was usually maintained without additional plasma derivatives. Serum bilirubin, alkaline phosphatase, and serum aspartate transferase concentrations rose in all patients (fig 4). Some of these increases were dramatic. The changes of liver enzyme concentrations were similar in regimens with and without fat. The changes in liver function did not seem to affect the clinical progress of the patients, but on two occasions when the rises were particularly great the lipid emulsion was withdrawn. A rapid but incomplete improvement of liver function followed, but fat provocation tests were not subsequently performed.

Cost

The overall cost of total parenteral nutrition for three years in these 179 patients fed for a total of 2926 days was about £200 000 at 1985 prices. Nutrients, infusion apparatus, and central venous catheters accounted for most of this sum. Individual regimens are more expensive because they take longer to prepare and entail expensive small purchases and obligatory wastage. The salary of the nutrition nurse whom we paid the cost of the pharmacist's time in preparing the prescriptions makes up the remainder. The time spent on the service by the doctors has not been costed but consumed about 14 man hours each week.

Discussion

Total parenteral nutrition is now the accepted treatment for patients with malnutrition and intestinal failure. Nevertheless, it is difficult to justify its more widespread use. There are few controlled studies to prove its value because of the difficulties of mounting such a trial and the ethical problems posed by sick malnourished patients. There is substantial circumstantial evidence, however, that malnutrition and starvation compromise health and healing, and there is a priori reasoning that food is beneficial. There is also considerable evidence that parenteral nutrition can reverse some of the measurable consequences of malnutrition—for example, immune deficiency—but the clinical success or failure of total parenteral nutrition must be judged by other criteria, such as mortality, morbidity, changes in nutritional indices, and cost.

One hundred and forty of our patients left hospital alive and well, while 39 died. Such rates of mortality inevitably depend on the initial assessment and selection of patients to be fed. The service was available on request and was provided if the patients seemed to require parenteral nutrition. Early in this series several patients died of their disease within hours or days of starting the course, and this represents a failure of selection (fig 1). Selection is difficult, however, and this is illustrated by the number of deaths that occurred after relatively long courses of parenteral nutrition. An unanswerable question remains; did total parenteral nutrition merely delay death in these particular patients?

There are few satisfactory comparisons of survival, but before good total parenteral nutrition was available about 60% of patients with entero-cutaneous fistulae died.

The majority are now expected to survive, and 15 of the 20 patients with high output entero-cutaneous fistulae in our series recovered and left hospital. In contrast, five of the seven patients with multiple injuries died. Parenteral nutrition was started seven, 15, and 22 days after injury in three patients, and this delay may have contributed to their deaths.

Most of our patients were seriously ill with the complication of surgery or of their disease, and it is unlikely that any would have survived a prolonged period of starvation. One third of the patients were fed for more than two weeks, and therefore it seems likely that without total parenteral nutrition more than 39 would have died. One death could be attributed to parenteral nutrition, which emphasises the close supervision required in these patients.

The acceptability of total parenteral nutrition depends on a low rate of morbidity from insertion and maintenance of the central venous catheter and from the infusion of the solutions. Ninety two percent of catheter insertions were free from complications, and 76% of the courses were free from any mechanical problems. The catheter infection rate was low except when catheters were used for vascular access as well as feeding. We attribute this low morbidity rate to our policy of restricting the insertion and care of central venous catheters to members of the nutrition service, and to the introduction of the tunnelled silicone rubber catheter.

Metabolic complications, with the exception of the death already discussed, were mostly minor. Hyperglycaemia and glycosuria were easily identified and corrected with insulin infusions. Minor fluctuations in plasma electrolyte concentrations were common, and these were corrected by alterations to the regimen or additions given via a peripheral vein. During this study we used a high chloride regimen (165 mmol/l) which contributed to a mild hyperchloraemic acidosis, particularly in patients with impaired renal function. The chloride...
content has therefore been reduced to 124 mmol/l/24 h and the consequent anion deficit made up with acetate. Abnormalities of liver function are common, and in our patients there were progressive rises of plasma aspartate transaminase and alkaline phosphatase activities (fig 4). Sepsis may also cause these changes, but this was unlikely in these patients because blood cultures were seldom positive and most patients improved clinically as intravenous feeding progressed. Rises were occasionally dramatic, but the precise cause of the enzyme changes remains uncertain. Nevertheless, they do not seem to have been detrimental, and liver synthesis of albumin and prothrombin was maintained.

Many other indices such as immune competence, dynamometry, and anthropometry have been used to assess the state of nutrition, but their value is controversial. We have used the clinical states of the patients as our main assessment, and most patients recovered to leave hospital. Most patients also gained weight, were in positive nitrogen balance, and albumin concentrations returned to normal ranges but interpretation of these results is difficult, and they are clearly not ends in themselves. For example, Hill et al have shown that the weight gain in the first two weeks of total parenteral nutrition is mostly fluid.12 The standard regimen restored nitrogen balance, maintained plasma albumin concentrations, and promoted weight gain in 70%, of patients referred for parenteral nutrition. The remainder received an individual regimen for at least part of their course for various reasons. Most, however, were converted to a standard regimen as their condition improved and nitrogen requirements decreased. The weight gain and nitrogen balance of both groups were almost identical. A high mortality among the patients on individual regimens is due to selection of ill patients for such regimens. A standard regimen may be criticised on the grounds that its use is empirical and may not be best suited to most patients.14 Nevertheless, 70% of our patients were satisfactorily maintained on such a regimen, and the nutrition service was organised to recognise the seriously ill patients and to ensure flexibility.

A standard regimen in a three litre delivery system greatly facilitates nursing and may also reduce both infection and metabolic complications. It reduces the cost of prescription by enabling bulk purchase of nutrients and reduction of wastage. Extra bags may be stored ready prepared at 4°C to provide a reservoir to cover busy periods, and some pharmaceutical companies now supply ready mixed solutions in big bags (Travenol). In contrast, individually prescribed regimens are less flexible and cost more for nutrients and preparation. A 20%, reduction in cost could be achieved by replacing the lipid with glucose, but lipid has the advantages of reducing osmolality, minimising hyperglycaemia, providing essential fatty acids, and is non-thrombogenic. Although the annual cost of the service is about £67 000, this is only 0.15% of the central Oxford hospitals' budget, and we believe it has contributed greatly to the survival of 140 patients.

References

(Accepted 2 February 1983)

A 60 year old patient who has had long term lithium treatment for depression was recently found to have diabetes. He has also been having difficulty micturating, with diminished bladder sensation. Is the neuropenic bladder symptom due to lithium or to diabetes, and how might the diagnosis be made?

Lithium has many side effects; in the present context disturbances of the nervous system resulting in a lack of coordination and impairment of renal function usually with thirst and polyuria might be relevant. As a first step the plasma concentration of lithium should be checked and the dose of lithium adjusted to achieve concentrations of 0.6-1.2 mmol/l, the lower end of the range being desirable in the elderly, who are particularly sensitive to toxic effects. Neurogenic bladder features in diabetes result in difficulty in emptying the bladder, hesitancy, a poor stream, and sometimes incontinence. Other features of diabetics should be sought: these include pain and paraesthesiae in the limbs, absent tendon reflexes, and evidence of autonomic disease, such as diarrhoea, postural hypotension, and impaired cardiac reflexes. If the cause of the symptoms cannot be established referral to a urological surgeon for urodynamic investigation of bladder function might be considered. Presumably prostatic enlargement has been excluded.—ALEX PATON, postgraduate dean, NE Thames region.