Simplified intravenous nutrition using Intralipid-based mixtures in patients with serious gastrointestinal disease

W. R. BURNHAM*
M.D., M.R.C.P.

J. A. COOK
B.Sc., M.P.S.

C. E. KNOTT
B.Pharm., M.P.S.

M. J. S. LANGMAN
M.D., F.R.C.P.

University Department of Therapeutics and Department of Pharmacy, City Hospital, Nottingham, England

Summary

An Intralipid-based intravenous feeding mixture has been given to 20 patients with serious gastrointestinal disease who required parenteral nutritional support (mean duration 13.75 days). In half of the patients, only peripheral veins were used for infusion (mean duration 12 days), the infusion site being changed every 24-48 hr. Positive nitrogen balance was maintained in all but one individual and other parameters of nutrition improved. No serious complications due to intravenous feeding were encountered, although some patients did develop abnormal liver function tests and mild phlebitis at the peripheral vein infusion site. No abnormalities of pulmonary gas exchange attributable to the infusion were noted.

We conclude that this mixture is safe, relatively simple to use and effective. Consequently, it may be especially appropriate for patients in general medical and surgical wards as well as those in specialist units.

KEY WORDS: intravenous nutrition, Intralipid mixtures.

Introduction

Intravenous feeding is recognised as valuable in patients unable to take nourishment by mouth or nasogastric tube. The feeds are usually administered via a subclavian catheter which requires skilful placement. The risks of insertion and infection of the catheter are well recognised, so some hospitals employ a peripatetic team of experts to manage their patients (Powell-Tuck *et al.*, 1978; Fischer, 1977).

Peripheral veins may be used for intravenous nutrition if lipid emulsions such as Intralipid (Kabi Vitrum Ltd) rather than dextrose are used as the major calorie source. This also reduces the risk of hyperglycaemia during infusion, but it has been

assumed that the fat emulsion must be kept separate from other infusates. The infusion of more than one bottle simultaneously or sequentially complicates nursing procedures, makes errors more likely and makes it difficult to ensure the administration of a balanced regime.

In this paper, we describe the use of an Intralipid-based intravenous feed made up in a single 3 litre bag and infused over 24 hr. The stability of the mixture as measured by physical tests has been reported elsewhere (Burnham *et al.*, 1983). This feed can be given through peripheral veins, and appears safe and effective in achieving positive nitrogen balance.

Materials and methods

Intravenous feeding mixture

Intralipid (20%) was mixed with dextrose (10%), electrolytes and amino acid glucose solution (Vamin glucose) under laminar flow conditions in the Sterile Product Unit of Nottingham City Hospital Pharmacy. The composition of a typical feed is given in Table 1; the feed was designed to meet the needs of patients with diarrhoea or fistula losses. Patients with other conditions might need less potassium. The calcium and phosphate ion concentrations were well below the point at which precipitation would be likely (Nedich, 1977). Further unpublished work confirms that this does not occur (Davis, personal communication, 1982).

Less nitrogen or electrolyte was given if clinically appropriate and all ingredients were mixed in a three litre bag (Travenol Laboratories Ltd.). In some instances 2000 i.u. heparin was added because it was thought possible that it might reduce the frequency of deep vein thrombosis and pulmonary embolism (Negus *et al.*, 1980) and increase the survival of peripheral veins (Stradling, 1978). It might also

*Present address: Oldchurch Hospital, Romford, Essex RM7 0BE.

slightly improve the stability of the emulsion mixture (Kawilarang, Georgiou and Groves, 1980).

Patients studied (Table 2)

These were patients with severe alimentary disease in need of intravenous nutritional support. Infusions were made through peripheral veins whenever possible. Nitrogen balance was calculated from daily blood and urinary area measurements (Lee and Hartley, 1975) using standard techniques. Stool losses were not measured, but only two of the patients with active inflammatory bowel disease likely to cause such significant losses (as opposed to structural disease such as obstruction) were studied before surgical treatment. Even in these two patients (2 and 7, Table 2) stool nitrogen losses were unlikely to exceed 4 g/day (Buckell *et al.*, 1977). Patients were usually weighed daily and blood was taken for regular biochemical and haematological measurements; this included an anti-Factor X assay (Sigma Ltd.) in those given heparin, this being the best method available for measuring small amounts of the anticoagulant. Arm muscle bulk was measured in 10 patients by comparing triceps fat fold (estimated with calipers) and arm circumference (Gurney and Jelliffe, 1973).

Intralipid-induced hyperlipidaemia has been reported to cause abnormalities of pulmonary diffusion in adults (Greene, Haslett and Demaree, 1976) and lung damage in premature babies (Levine, Wigglesworth and Desai, 1980). Other workers have not found this (Wilmore, Moyland and Helmkamp, 1973), but as large or aggregated fat particles in the emulsion mixture might, in theory, block pulmonary capillaries, single breath carbon monoxide transfer factor analyses were made. Blockage of pulmonary capillaries would lead to decrease in alveolar capillary blood volume and thus pulmonary diffusing capacity. Transfer factor is a measure of pulmonary diffusion capacity. The single breath technique requires little patient compliance and seemed most appropriate for these patients. The measurements were performed during and before or after treatment, whenever patients were well enough to travel to the lung function laboratory. A Transfer Test Model B instrument with valve box (Morgan Ltd.) was used and a correction was made for changes in haemoglobin concentration (Cotes, 1975).

The project was approved by the North Nottingham District Hospitals Ethical Committee.

Results

Twenty patients (12 of whom had inflammatory bowel disease with complications requiring surgery) (Table 2) received infusates of mixed nutrients for an average of 13.75 days each (range 8–23 days); in 10 of

TABLE 1. Typical intravenous feed used in this study

Intralipid 20%*	1 litre
Vamin glucose*	1.5 litres
Dextrose 10	0.5 litres
Potassium chloride	54 mmol
Potassium dihydrogen phosphate	30 mmol
Sodium chloride (as 30% solution)	51.3 mmol
Addamel*	10 ml
Vitlipid*†	1 vial
Solvivito*†	1 vial
Provides:	
2800 non-protein kcal	14.1 g nitrogen
126.3 mmol sodium	114 mmol potassium
30 mmol phosphate	8.75 mmol calcium
3.75 mmol magnesium	Trace elements
Vitamins	

*Kabi Vitrum Ltd.; †Vitamins were omitted from feeds prepared on Fridays for use on Saturday and Sunday.

Feeds containing vitamins were stored at 4°C for no longer than 12 hr before commencement of infusion. Weekend feeds (without vitamins) were stored for no longer than 48 hr at 4°C. These procedures were based on the results of physicochemical studies reported elsewhere (Burnham *et al.*, 1983).

these patients only peripheral veins were used (mean duration 12 days, range 8–18 days), the infusion site being changed every 24–48 hr. Positive nitrogen balance as measured in this study was maintained in all but one individual (M.H.) (Fig. 1), although many were very ill (Table 2). Even assuming the most severe stool nitrogen loss of 4 g/day, of those with acute inflammation studied before surgery only one other patient (D.P.) would have been in deficit. This in itself is unlikely, as he gained 4 kg in weight and increased his serum albumin from 14 g/litre to 21 g/litre during intravenous feeding. The mean arm muscle area (in the 10 patients measured), mean weight and mean serum albumin tended to increase during the period of intravenous feeding. The differences were not statistically significant; the study period was probably too short to show this (Table 3). The weight and serum albumin measurements were subject to some distortion because initially oedematous patients lost weight during intravenous feeding and dehydrated patients showed a fall in serum albumin when this was corrected by infusion.

No patient showed clinical evidence of adverse effects, hyperglycaemia did not occur and serum triglyceride levels never rose above 2 mmol/litre. Transfer factor did not deteriorate as a consequence of the infusion in the 12 patients studied (Fig. 2). Abnormal liver function tests developed in 9 patients during feeding, changes consisting of an elevated alkaline phosphatase (5 patients), and glutamyl transpeptidase (8 patients), serum glutamate pyruvate transferase (3 patients) and serum bilirubin (2 patients). In no case was it necessary to discontinue intravenous feeding, and all tests returned to normal after intravenous feeding had ceased.

FIG. 1. Nitrogen balances in 20 patients during the period of intravenous feeding (mean $\pm$ standard deviation). Where no standard deviation is shown, the intake/output was constant.

TABLE 2. Details of patients fed intravenously with Intralipid emulsion mixtures

Patient	Age (years)	Sex	Diagnosis	Before surgery	After surgery
1	25	F	Toxic dilatation of colon	—	+
2	29	M	Severe Crohn's colitis with bilateral psoas abscesses	+	—
3	21	F	Extensive small bowel Crohn's disease	—	+
4	57	F	Toxic dilatation of colon and perforation	—	+
5	36	F	Ulcerative colitis and obstructing colonic carcinoma	+	+
6	22	M	Extensive small bowel Crohn's disease	+	+
7	28	M	Severe Crohn's colitis	+	+
8	36	F	Ileo-caecal Crohn's disease	+	+
9	54	F	Crohn's disease	—	+
10	38	M	Crohn's disease	—	+
11	67	F	Severe colonic Crohn's disease + malnutrition	—	+
12	42	F	Crohn's disease	—	+
13	62	F	Post-colonic carcinoma resection + malnutrition	—	+
14	47	M	Carcinoma of the stomach	—	+
15	42	M	Pancreatitis and intestinal obstruction	—	+
16	85	F	Traumatic oesophageal tear, mediastinal abscess	—	+
17	53	M	Carcinoma of rectum, wound dehiscence	+	+
18	66	F	Intestinal obstruction. Diverticular disease + paracolic abscess	+	+
19	34	M	Post-gastrectomy + pelvic abscess	—	+
20	80	F	Pyloric obstruction	+	+

TABLE 3. Changes in measurements of nutritional status before and after intravenous feeding

	Before	After	s.e.d.
Mean arm muscle area (cm ²)	32.60	34.75	2.17
Mean serum albumin (g/litre)	23.45	25.60	1.70
Mean weight (kg)	51.55	52.60	2.49

s.e.d. = standard error of difference.

Some 'creaming' of the emulsion (Burnham *et al.*, 1983) in the 3 litre bag was seen after the infusion had

been running for 16–18 hr, but was easily reversed by gentle squeezing of the bag and did not recur in the remaining 6–8 hr. Heparin activity in plasma never exceeded 0.03 U/ml in those who received this agent. No patient developed deep vein thrombosis, pulmonary embolism or bleeding problems during surgery while feeds containing heparin were being infused. Five patients did develop mild phlebitis at the drip site, but this was rarely a difficulty provided the cannula was resited regularly in a large arm vein, and drugs likely to cause phlebitis were not given by the same route.

FIG. 2. Single breath carbon monoxide transfer factor on and off intravenous feeding in 12 patients. The mean in days refers to (a) average time from commencement of feeding to measurement or (b) average time from cessation of feeding to measurement.

Discussion

Our results show that certain mixtures of Intralipid can be safely mixed in a 3 litre bag and infused via peripheral veins. The advantages of such a system over infusions into a central line or multiple bottle infusions are considerable. It requires less nursing time, can be easily managed in a busy general ward, ensures administration of a balanced regime and avoids the problems associated with central vein catheter insertion and maintenance. There was an increase in the pharmacy work load during the week, but no increase in weekend working, as bags were made up in advance on Fridays. Thus any increase in work was managed in normal working hours and the nursing problems which may previously have occurred at night are greatly reduced. Most Districts now have Laminar air flow units and the remainder are likely to obtain them in the future.

The problem of hyperglycaemia seen with dextrose based solutions is also avoided, even in those patients whose poor peripheral veins mean a central line must be used for long-term feeding.

Despite the simplicity of the method, adequate nutritional support can be provided for ill patients. Within the limits of the mixtures tested, the intake of energy, nitrogen and electrolytes can be adjusted to the needs of each patient. Clearly, further studies are required to define other mixtures which may be safely used. However, our results agree with clinical studies performed in France (Solassol and Joyeux, 1974), where an Intralipid-based feeding mixture has been used successfully for some years. There is evidence that a combination of fat and carbohydrate

calories is to be preferred as an energy source in intravenous nutrition (Lee, 1977; Askanazi *et al.*, 1980; Macfie, Smith and Hill, 1981; Kirkpatrick, Dahn and Lewis, 1981).

Creaming of the emulsion during infusion, presumably due to the presence of aggregated particles, was easily reversed by gentle shaking. This did not recur during the infusion and did not pose a clinical or pharmaceutical problem.

Abnormal liver function tests were noted in 9 of the patients. However, this is a recognised complication of intravenous and nasogastric tube feeding (Tweedle *et al.*, 1979), and did not occur more frequently than would be expected; in no case did it necessitate a cessation of the treatment, and no other adverse effects were noted. It was reassuring that no patient developed symptoms of fat embolism in the lungs and that no significant deterioration was detected in measurements of transfer factor during infusion. No patient developed clinical evidence of deep vein thrombosis or pulmonary embolism and no bleeding problems were encountered in 2 patients who underwent surgery during infusion of heparin-containing feeds. Minor phlebitis occurred at the drip sites in some patients, especially if certain antibiotics were administered also, but careful placement and regular changing of the cannula avoided serious problems.

We conclude that this relatively simple method of intravenous feeding is both safe and effective in clinical practice. However, until further pharmaceutical and clinical studies have been performed, only those Intralipid mixtures which have been tested can

be recommended for use. Particular care is required in those with higher concentrations of divalent cations (Burnham *et al.*, 1983). Further experience with this method of intravenous feeding confirms the clinical benefit reported in this paper. We are now examining other amino acid solutions to assess their suitability for mixing with Intralipid.

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