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Case Report

Pediatric TPN: Efficacy and Toxicity of a New Fat Emulsion

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ABSTRACT. Fat emulsions are particularly valuable in pediatric total parenteral nutrition (TPN) because they provide an isotonic solution rich in calories. Little is known about the ideal composition of fatty acid emulsions, however, and very few formulations are commercially available. A new fat emulsion using a safflower oil base has recently been approved. We have used this new emulsion to provide a significant percentage of the nonprotein caloric requirements (24 to 42%) in 4 patients requiring TPN. These patients ranged in age from 1 to 15 years and received no enteral nutrition during the 3-week course of the study. Nutritional improvement without major toxic effects was documented in each patient.

Intravenously administered fat emulsions are now widely used in programs of total parenteral nutrition (TPN). In addition to providing essential fatty acids, they offer a concentrated energy source in an isotonic solution. These properties make them particularly useful in the pediatric population in whom glucose intolerance and renal function limitations may contraindicate the sole use of large volume glucose and amino acid (AA) solutions for intravenous (IV) nutrition.[1] In concentrations that can be tolerated by peripheral veins, glucose and AA solutions alone cannot provide adequate calories for growth without the use of prohibitively large volumes. However, the addition of a fat emulsion which provides up to 20 to 50% of the caloric requirements makes peripherally administered TPN more widely applicable.[2,3]

Fat emulsions using soybean or cottonseed oil as the major lipid source have been used clinically. The most widely used product in this country has been a 10% soybean oil emulsion (Intralipid). The cottonseed preparation has been used in Europe. We have recently tested a new 10% safflower oil emulsion (Liposyn, Abbott Laboratories) in a small group of pediatric patients. Using this new emulsion as a major caloric source in TPN, this study has evaluated weight changes, routine laboratory findings, changes in nutritional status, and side effects during 21 days of treatment in 4 children ranging in age from 1 to 15 years.

MATERIALS AND METHODS

The study was conducted in Mott Children's Hospital, University of Michigan Medical Center, Ann Arbor, Michigan, during February, March, and April 1979. Children under age 16 requiring TPN for at least 21 days were candidates for the study. Patients receiving any enteral nutrition, and those with liver damage, renal failure, or massive systemic infection were excluded. Four patients completed the study. Their histories are summarized below and their nutritional assessments are summarized in Table I.

Patient 1 is a 7-year-old white female with ulcerative colitis who was admitted for weight loss and diarrhea. Seven months previously she had undergone a subtotal colectomy, endorectal pull-through and loop ileostomy. Five months before admission her ileostomy was closed.

Patient 2 is a 1-year-old white male born with a tracheoesophageal fistula. Primary repair was attempted at another hospital, but was complicated by an anastomotic disruption which was treated with a feeding gastrostomy and a cervical esophagostomy. He underwent esophageal replacement with a colon interposition 3 days prior to initiation of TPN therapy.

Patient 3 is a 15-year-old white male with Crohn's disease who was admitted for hypoproteinemia and marked edema. He had done well on medical management for 3½ years until shortly before this admission.

Patient 4 is a 15-year-old white male who is presumed cured of his stage 1A Hodgkins disease treated 7 years before admission. An episode of *Hemophilus influenzae* meningitis 2 years before admission left him with a neurogenic bladder. He was admitted for vomiting and weight loss of unknown origin.

Parental informed consent was obtained and additional subject consent was received from children over 7 years old. The following preinfusion tests were performed: urinalysis, complete blood count with differential white blood cell count, platelet count, serum electrolytes, urea nitrogen, creatinine, glucose, calcium, phosphorus, uric acid, albumin, total protein, cholesterol, triglycerides, total bilirubin, alkaline phosphatase, LDH, and SGOT. Subclavian vein catheterization was carried out in pa-

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tients 1, 3, and 4. In patient 2, peripheral venous access was established. All 4 patients were begun on a TPN program of glucose, AA and the new safflower oil emulsion. The emulsion was infused through a Y-connector into the line containing the glucose-AA solution and the infusion was continuously administered during each 24-hr period for 21 days.

A typical solution used for centrally administered TPN consisted of 25% glucose and 3.5% AA (Aminosyn, Abbott Laboratories). The peripheral regimen consisted of 12.5% glucose and 2.5% AA. The TPN solution also contained routine vitamin and mineral additives which are summarized in Table II.

Each 100 ml of the new fat emulsion contains 10 g safflower oil, 1.2 g emulsifying agent egg phosphatide, 1.2 g glycerin to make the emulsion isotonic (340 mOsm/L), and is adjusted to a pH between 5.0 and 9.0. The solution provides 1.11 kcal/ml. The fatty acid composition of this oil is compared to that of soybean and cottonseed oils in Table III.[4]

Table IV summarizes the TPN treatment of these 4 children, and includes calculations of the amount of various nutrients provided. Daily observations included vital signs, weight, and a report of adverse symptoms or side effects. Estimated caloric requirements were computed daily and compared to calories actually given. At weekly intervals, the initial battery of blood and urine tests were repeated and an assessment was made of any changes in the patient's nutritional status.

RESULTS

Each patient survived the observation period and showed clinical improvement. Daily weight information is summarized in Figure 1. Patient 1 showed a weight gain of 3.1 kg over the 3 week period and her strength improved markedly. Her initially low serum albumin and total lymphocyte counts showed no significant change, however. Patient 2 showed stable weight maintenance despite increased demands secondary to pneumonia which required assisted endotracheal ventilation. He did not, however, receive sufficient calories for growth, due to the limitations on total calorie infusion with a peripheral line. His serum albumin, which was initially low, did not change significantly. Patient 3 gained 5 kg during the study. His edema resolved as his serum albumin increased from 1.8 to 3.0 g% and his very low total lymphocyte count improved only slightly from 115 to 133. Patient 4 gained 6.8 kg and his initially normal laboratory finding remained unchanged.

The patients were closely monitored for any signs of toxicity. Each episode of nausea, vomiting, chills, or headache was noted. No such symptoms were attributed to the fat emulsion infusion. Patient 3 had fever secondary to his pneumonia. Patient 4 complained of nausea, vomiting, chills, and headache prior to and throughout the course of the study. These symptoms decreased in frequency and severity during therapy. He developed a significant fever on the 16th day of infusion which was thought to be related to his central venous catheter. Though no culture evidence of infection was found, the fever resolved following discontinuance of his old CVP and insertion of a new central line.

No significant toxicity was noted by laboratory examinations. Hypertriglyceridemia in the range of 1.5 to 2 times normal values was seen in all the patients. Patient 3 and 4 had only transient elevations which returned to normal by the end of the study. The younger patients (1

TABLE I
Initial nutritional assessments

	Patient			
	1	2	3	4
Height percentile	35th	<5th	5th	65th
Weight percentile	5th	<<5th	5th	25th
Serum albumin (g%)	3.8	2.7	1.8	3.7
Total lymphocyte count	1360	4032	115	2278

TABLE II
Guidelines for TPN additives

Constituent	Amt kg/24 hr	Maximum/24 hr
Heparin	100 IU[a]	500 IU/liter
Sodium	2–4 mEq	150 mEq
Potassium	2–3 mEq	240 mEq
Chloride	2–4 mEq	120 mEq
Magnesium	0.6 mEq	24 mEq
Calcium	1.0 mEq	11 mEq
Phosphate	3.5 mm	50 mm
MVI[b]	0.5 ml	2.5 ml
Folic acid		0.5 mg
Trace elements[c]	0.3 ml	0.3 ml
Iron, vitamin B_{12}, vitamin K	As needed parenterally	

[a] International units.

[b] MVI concentrate (U.S. Pharmaceutical Corporation): Each 5 ml contains: ascorbic acid, 500 mg; vitamin A, 10,000 IU; vitamin D, 1,000 IU; thiamine, 50 mg; riboflavin, 10 mg; pyridoxine, 15 mg; niacin, 100 mg; Dexpanthenol, 25 mg; vitamin E, 5 IU.

[c] Trace element solution (Manufactured at University of Michigan Pharmacy Dept.) Each ml contains: zinc, 2 mg (0.060 mEq); copper, 0.4 mg (0.030 mEq); manganese, 0.2 mg (0.015 mEq); iodide, 0.056 mg (0.00044 mEq).

TABLE III
Fatty acid composition of the oils in fat emulsions

	Cottonseed	Soybean	Safflower
Linoleic acid[a]	45%	54%	79%
Oleic acid	30	26	12
Palmitic acid	22	9	7
Linolenic acid		8	
Other fatty acids	3	3	2

[a] Essential fatty acid.

TABLE IV
Average daily nutritional components

	Patient			
	1	2	3	4
Route of administration	Central	Peripheral	Central	Central
Initial weight (kg)	17.8	6.5	47.4	51
Caloric requirement/kg (estimated)	80	100	45	45
Calories/kg received	100.4	88	54.2	55.4
Total volume (cc/kg)	108	151	54	73
Volume of fat emulsion (cc)	504	183	503	454
% nonprotein caloric requirements given as fat	42%	37%	29%	24%
g fat/kg	2.82	2.85	1.1	0.9
g protein/kg	2.7	2.3	1.5	1.6
Nonprrotein calorie/protein calorie ratio	8.4/1	8.4/1	8.1/1	8/1

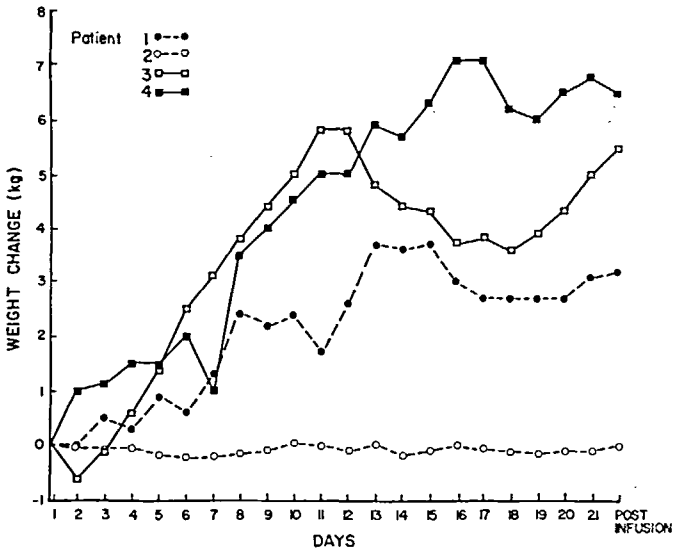

FIG. 1. Daily weights.

and 2) showed significant elevations initially, followed by gradually declining values. Serum cholesterol levels were all normal at the completion of the study and showed only mild early elevations of 15% above normal in patients 1 and 2. Serum urea nitrogen remained normal in all the subjects. Serum GOT levels showed an initial elevation to approximately twice normal followed by a return toward normal. Three of four subjects showed an actual decline of LDH and alkaline phosphatase levels during the study. Patient 1 showed a small increase in LDH and patient 2 had a small increase in alkaline phosphatase. Serum bilirubin remained normal in all the patients.

DISCUSSION

The practice of using fat as a component of TPN is well accepted. However, a wide variation in the biological activity of various fat emulsions makes it difficult to generalize about safety or effectiveness.[5] The effects of different fatty acid combinations are not fully known. The new safflower oil emulsion may offer a theoretical advantage since it contains a higher percentage of the essential fatty acid linoleic acid than previously available oil emulsions. It does not contain the linolenic acid found in small amounts in soybean oil emulsions. Structures related to linolenic acid are found in some human tissues, but there is no conclusive evidence that linolenic acid is essential to man's diet.[6] This area needs further investigation.

This study does not show isolated effects of the new safflower oil emulsion, since it was given in a multiple-nutrient program of TPN. Changes in liver function tests similar to those observed in our patients have been frequently noted during TPN with or without a fat emulsion.[7] Changes in serum cholesterol with different oils have been variable, and the small, transient elevations noted in this study are consistent with previous findings for other preparations.[8,9] The mild serum triglyceride elevations seen as the body processes this exogenous oil are expected. None of the patients exhibited signs of the "overloading syndrome" seen with some other preparations, especially cottonseed oil products.[10] None exhibited any clinical signs of essential fatty acid deficiency.

It can be concluded that no serious side effects or toxicity occurred in this small group of children who received a significant percentage (24 to 42%) of their nonprotein caloric requirements from a new safflower oil emulsion. They all maintained or gained weight, and improved clinically during the 3-week study period. These early results suggest that this safflower oil emulsion is safe and effective, and deserves further use and evaluation.

REFERENCES

1. Borresen HC, Coran AG, Knutrud O: Metabolic results of parenteral feeding in neonatal surgery: a balanced parenteral feeding program based on a synthetic L-amino acid solution and a commercial fat emulsion. Ann Surg 172:291–301, 1970
2. Coran AG: The long-term intravenous feeding of infants using peripheral veins. J Ped Surg 8:801–805, 1973
3. Coran A G: Total intravenous feeding of infants and children without the use of a central venous catherter. Ann Surg 179:445, 1974
4. Wretlind A: The pharmacological basis for the use of fat emulsions in intravenous nutrition. Acta Chir Scand Suppl 325:31–42, 1964
5. Grotte G, Jacobson S, Wretlind A: Possibilities and limitations of intravenous fat emulsions. IN Total Parenteral Alimentation, Manni C, Magalini S, Scrascia E (eds), New York, American Elsevier Publishing Co, Inc, 1976, p 51
6. Olson R (ed): Linolenic acid: is it essential? Nutr Rev 37:396, 1979
7. Hallberg D: Experimental and clinical studies of fat emulsions for intravenous nutrition. IN Parenteral Nutrition, Meng H C (ed), Springfield, Ill, Thomas Publishing Co, 1970, p 376
8. Coran AG, Edwards B, Zaleska R: The value of heparin in the hyperalimentation of infants and children with a fat emulsion. J Ped Surg 9:725–732, 1974
9. Thompson SW: The Pathology of Parenteral Nutrition with Lipids. Springfield, Ill, Thomas Publishing Co, 1974, p 935
10. Grotte G, Jacobson S, Wretlind A: Possibilities and limitations of intravenous fat emulsions. IN Total Parenteral Alimentation, Manni C, Magalini S, Scrascia E (eds), New York, American Elsevier Publishing Co, Inc, 1976, p 65