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Brief Communications

Comparison of a New 10% and 20% Safflower Oil Fat Emulsion in Pediatric Parenteral Nutrition

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ABSTRACT. A new 20% safflower oil fat emulsion was compared with its 10% counterpart in a small series of pediatric patients. Five infants and children, studied for a 2-week period, received either the 10% or 20% emulsion for 1 week and the other emulsion the 2nd week. No serious toxicity or side effects were noted in any of the patients following the infusion of either emulsion. In addition, significant weight gain was noted in the children, and clinical improvement was apparent in all cases. This preliminary study suggests that the 20% Liposyn is as safe and effective as its 10% counterpart.

Intravenously administered fat emulsions are an important component of any program of total parenteral nutrition (TPN). In addition to providing essential fatty acids, they offer a concentrated source of energy substrate in an isotonic solution. These characteristics make them particularly useful in the infant in whom glucose intolerance and renal function limitations may contraindicate the sole use of large volume glucose and amino acid (AA) solutions for intravenous nutrition.[1]

Peripherally-administered TPN regimens consisting solely of glucose and AA supply insufficient calories for growth unless massive volumes of fluid are given.[2] The addition of a fat emulsion which will provide 30–50% of the total caloric requirements makes peripherally-administered TPN far more practical and attractive.[3,4]

Having safely tested a new safflower oil emulsion (Liposyn-10%, Abbott Laboratories, Chicago, IL) in a small group of pediatric patients, we proceeded to compare this 10% safflower oil emulsion with one which is twice as concentrated (Lipsoyn-20%).[5] The obvious advantage of the 20% emulsion over the 10% preparation is the provision of the same number of calories in half the volume. In infants, in whom fluid tolerance is critical, Liposyn 20% would allow significant reductions in total fluid volume without compromising caloric input.

This study was undertaken to compare the toxicity and efficacy of the 20% with 10% Liposyn over a 2-wk period. The results document the improved nutritional status and weight gain of the patients studied with no adverse side effects or toxicity attributable to either lipid emulsion.

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MATERIALS AND METHODS

This study was conducted at the Mott Children's Hospital, Unversity of Michigan Medical Center, from November 1979 through March 1980, in infants and children from 1 day to 12 yr of age who required TPN for at least 14 days. Patients receiving any enteral nutrition and those demonstrating disturbances in normal fat metabolism such as pathological hyperlipemia, lipoid necrosis or acute pancreatitis accompanied by hyperlipemia were excluded from the study. Five pediatric patients completed the study. Their summary histories follow and their nutritional status is presented in Table I.

Patient #1, a 4-day-old, 2.6 kg, white female who underwent an esophagostomy and gastrostomy for esophageal atresia without tracheoesophageal fistula. Patient #2, a 1-day-old, 1.7 kg, white female underwent a primary repair of an esophageal atresia with tracheoesophageal fistula. Patient #3, a 12-yr-old, 56.8 kg, white female with ulcerative colitis and severe rectal bleeding, underwent a subtotal colectomy and ileostomy. Patient #4, a 2-wk-old, 1.9 kg, white female underwent a colectomy for perforated necrotizing enterocolitis. Patient #5, a newborn, 2.3 kg, white male with a gastroschisis, was treated with a staged procedure.

After parental informed consent was obtained, the following preinfusion tests were performed: urinalysis, complete blood count with differential white blood cell count, platelet count, blood urea nitrogen, serum uric acid, albumin, total protein, cholesterol, triglycerides, total bilirubin, alkaline phosphatase, LDH, and SGOT. Subclavian vein catherization was performed on patient #3, while peripheral venous access was established in the

TABLE I
Baseline nutritional status

	Patient #				
	1	2	3	4	5
Height percentile	10th		95th	5th	5th
Initial weight (kg)	2.6	1.7	56.8	1.9	2.3
Weight percentile	5th	5th	90th	5th	5th
Serum albumin g%	2.8	2.0	3.2	3.0	2.6
Total lymphocyte count	2756	3390		1470	3706

remaining patients. All 5 patients were started on a program of glucose, AA, and a safflower oil emulsion (Liposyn) at a concentration of either 10 or 20%. The study was divided into 2 periods of 7 days each. During the 1st wk, one of the fat emulsions (10 or 20%) provided one-third to one-half of the patient's total daily caloric requirements (TDCR). During the second 7-day period, the alternate fat emulsion was substituted in the feeding regimen, supplying the same number of calories as the first fat emulsion. Thus, patients #1, #4, and #5 received Liposyn 20% during the 1st wk while patients #2 and #3 received Liposyn 10% during the 1st wk. The emulsion was infused through a Y-connector into the line containing the glucose-AA solution and the infusion was administered continuously over the 24-hr period.

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

Each 100 ml of Liposyn-10% contains 10 g safflower oil, 1.2 g emulsifying agent, an egg phosphatide, and 1.2 g glycerine to make the solution isotonic (340 mOsm/liter). Liposyn-20% differs only in that it contains 20 g safflower oil/100 cc solution. Sodium hydroxide is used to adjust the pH of both solutions between 5.0 and 9.0. Liposyn-10% provides 1.1 kcal/ml; Liposyn-20% provides 2.0 kcal/ml. The fatty acid composition of this emulsion is listed in Table III.

Table IV summarizes the TPN treatment of these patients and includes calculations of the amount of the various nutrients provided during each weekly period. Daily observations included vital signs, weight, and a report of adverse symptoms or side effects. Estimated caloric requirements were computed daily and were compared to calories actually received. 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.

TABLE II
Guidelines for TPN additives

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

[a] MVI concentrate (US 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; and vitamin E, 5 IU.

[b] Trace element solution (manufactured by University of Michigan Pharmacy Department)—each ml contains: zinc, 2 mg (0.060 mEq); copper, 0.4 mg (0.030 mEq); manganese, 0.2 mg (0.015 mEq); and iodide, 0.056 mg (0.00044 mEq).

TABLE III
Fatty acid composition of different 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.

RESULTS

All patients gained weight (Tables I and IV) during the course of the study. The per cent change during the 20% lipid sequence was 5.0 ± 3.1 compared with 9.2 ± 1.8 during the 10% sequence, a highly significant difference. The total weight gain from baseline of the end of the study period was 14.6 ± 3.4%, a significant increase from initial levels.

All patients started the study with abnormally low serum albumin levels (Table V). The only one to achieve normal levels during either lipid regimen was patient #3 (sequence 10-20). The remaining patients finished both sequences with serum albumin levels below the normal range.

Baseline triglyceride levels (Table V) were normal in all patients; no initial value was obtained for patient #1. Patients #1, #4, and #5 (sequence 20-10) had triglyceride levels which were 1.0, 1.9, and 1.0 times normal, respectively, at the end of the 20% sequence, and triglyceride levels which were 1.1, 1.1, and 2.2 times normal, respectively, at the conclusion of the 10% sequence. Patients #2 and #3 (sequence 10-20) completed the 10% regimen with triglyceride levels which were 1.2 and 1.0 times normal; both patients finished the 20% period with normal triglyceride values.

Blood urea nitrogen remained within the normal range in patients #1, #5 (sequence 20-10) and #2 (sequence 10-20) throughout both courses of therapy (Table V). Patient #4 had a baseline value of 1.2 times normal which returned to the normal range during the study period. Patient #3 (sequence 10-20) had abnormally low blood urea nitrogen values, 35 and 30% below normal, at the conclusion of the 10 and 20% sequences, respectively.

Patients #1, #4 and #5 (sequence 20-10) started the study with baseline SGOT levels (Table V) which were 2.2, 3.9, and 5.0 times normal, respectively, and concluded the 20% sequence with values which were 1.1, 1.0, and 2.8 times normal. They completed the 10% regimen with levels of 1.0, 1.9, and 1.7 times normal. Patients #2 and #3 (sequence 10-20), with baseline measurements of 2.0 and 1.0 times normal, finished the 10% sequence with

TABLE IV
Average daily nutritional components

Patient #	1		2		3		4		5	
Week #	1	2	1	2	1	2	1	2	1	2
Lipid emulsion	20%	10%	10%	20%	10%	20%	20%	10%	20%	10%
Type of access	Peripheral		Peripheral		Central		Peripheral		Peripheral	
Caloric requirements/kg (estimated)	110	100	120	120	75	75	110	110	110	100
Calories/kg received	119	116	99	110	40	42	105	119	128	89
Total caloric requirement (estimated)	275	278	204	212	4275	4425	209	214	251	277
Calories received	297	304	174	201	2325	2526	202	240	280	239
Total volume (cc/kg)	138	146	150	127	41	40	141	160	181	139
Volume fat emulsion (cc)	47	79	39	34	452	345	26	74	38	91
Calories provided as fat	84	79	35	62	407	621	48	67	68	32
% Total caloric requirement given as fat	30%	26%	17%	29%	10%	14%	23%	31%	27%	30%
% Nonprotein caloric requirement given as fat	34%	31%	21%	33%	12%	16%	25%	38%	30%	36%
g Fat/kg	3.7	3.0	2.3	3.8	0.8	0.6	2.8	3.7	3.5	3.4
g Protein/kg	2.6	2.9	2.1	2.9	1.1	1.1	2.7	3.0	2.7	2.4
Nonprotein calorie/protein calorie ratio	11.4/1	9.7/1	11.8/1	9.5/1	9.2/1	9.6/1	9.7/1	9.9/1	11.9/1	9.3/1
Weight gain (kg) at end of each week	−0.1	+0.2	+0.1	+0.2	+2.1	+1.1	+0.1	+0.2	−0.1	+0.3

TABLE V
Levels achieved with the two regimen

Patient #	Lipid sequence	Baseline	Post-10% sequence	Post-20% sequence	Post study
Serum albumin (mg%)—normal range 3.5–4.9					
1	20–10	2.8	2.7	2.8	2.7
4	20–10			3.0	
5	20–10	2.6	2.3	2.3	2.3
2	10–20	3.0	2.9	2.8	2.8
3	10–20	3.2	3.4	3.6	3.6
Triglyceride (mg%)					
1	20–10		163	107	163
4	20–10	58	164	94	164
5	20–10	104	334	278	334
2	10–20	110	174	132	132
3	10–20	142	104	68	68
Blood urea nitrogen (mg%)					
1	20–10	9	15	18	15
4	20–10	23	13		13
5	20–10	13	11	18	11
2	10–20	15	15	12	12
3	10–20	8	7	6	6
SGOT (IU/liter)					
1	20–10	5	24	25	24
4	20–10	90	44	24	44
5	20–10	114	38	64	38
2	10–20	46	27	46	46
3	10–20	10	28	26	26
LDH (IU/liter)					
1	20–10	356	277	235	277
4	20–10	650	520	415	520
5	20–10	1080	350	365	350
2	10–20	499	397	575	575
3	10–20	81	117	115	115
Alkaline phosphatase (IU/liter)					
1	20–10	152	259	184	259
4	20–10	142	294	212	294
5	20–10	154	206	252	206
2	10–20	199	339	492	492
3	10–20	89	111	92	92
Total bilirubin (mg%)					
1	20–10	9.5	0.9	2.0	0.9
4	20–10	2.4	2.1	0.9	2.1
5	20–10	4.7	8.2	3.8	8.2
2	10–20	9.0	0.7	0.4	0.4
3	10–20	0.2	0.5	0.3	0.3

SGOT levels 1.8 and 1.2 times normal and completed the 20% sequence with SGOT values of 1.1 and 1.2 times normal, respectively.

Patients #1, #4 and #5 (sequence 20-10), with baseline LDH measurements of 2.5, 4.5, and 7.5 times normal, respectively, concluded the 20% period with values of 1.6, 2.9, and 2.5 times normal and the 10% sequence at 1.9, 3.6, and 2.4 times normal (Table V). Patient #3 (sequence 10-20) remained in the normal range during the entire study period. Patient #2 (sequence 10-20), who had a baseline LDH measurement of 3.4 times normal, finished the 20% sequence at 4.0 times normal and the 10% sequence at 2.7 times normal.

All patients except #3 exhibited abnormal alkaline phosphatase levels (Table V) during the course of the study. Patients #1, #4, and #5 (lipid sequence 20-10), who had baseline alkaline phosphatase levels of 1.3, 1.2, and 1.3 times normal, concluded the 20% regimen at 1.6, 1.8, and 2.2 times normal and the 10% sequence with levels 2.3, 2.6, and 1.8 times normal, respectively. Patient #2 ended the 10% sequence at 3.0 times normal and the 20% period at 4.3 times normal.

All patients except number # 3 had abnormal bilirubin values during the study (Table V). Patients #1, #4, and #5 (sequence 20-10), who had baseline measurements of 10.6, 2.3, and 5.2 times normal, respectively, ended the 20% sequence at 2.2, 1.0, and 4.2 times normal and the 10% regiment at 1.0, 2.3, and 9.1 times normal. Patient #2 (sequence 10-20) who had a baseline value of 1.7 times normal, completed the 10% sequence at 3.0 times normal and the 20% period at 4.3 times normal.

DISCUSSION

Although the use of the fat emulsions as a component of a parenteral nutrition program is well accepted, the varied biological activity of different fat emulsions makes it difficult to generalize about their toxicity and efficacy.[6] Fat emulsions have different combinations of fatty acids and the effect of such combinations on the nutritional efficacy of the solution are not known. Both the 10 and 20% offer a theoretical advantage of having a higher percentage of essential fatty acids (linoleic acidS) than any other commercially available fat emulsions. Studies thus far, including the present one, have not provided data indicating any advantage from this high concentra-

tion of linoleic acid. A previous report from this institution verified that no serious side effects or toxicity occurred in a small group of children who received 10% Liposyn as part of their nonprotein caloric requirements.[5] The present study was designed to compare the same fat emulsion in a 10 and 20% form with regard to toxicity and therapeutic effectiveness.

In none of the patients could any difference be detected clinically following the infusion of the 10 or 20% emulsion. However, there was a significantly greater weight gain following the 10% emulsion in this small series of children. This difference was statistically significant even in this small group of patients. No other significant differences in the nutritional effects of the emulsion were noted. The only other difference noted between the 10 and 20% emulsion was a lower triglyceride level following the 20% sequence, but this was not statistically significant. Except for a mild elevation in alkaline phosphatase, no significant abnormalities in the liver function tests were noted during this 2-wk period. The alkaline phosphatase elevation has been noted in other series of patients treated both with and without fat emulsions.[7]

Changes in serum cholesterol and triglycerides with different fat emulsions have been variable, and the small, transient elevations in serum triglycerides noted in this study are consistent with previous findings for other preparations.[8,9] No instance of the "overloading syndrome" was observed even though this has been reported with other preparations, especially cottonseed emulsions.[10] Although the period of study was probably too short, no evidence of fatty acid deficiency was observed in any of the 5 children.

Except for the slightly greater weight gain noted with the 10% emulsion, no significant difference between the 10 and 20% preparation was noted in this small group of children with regard to toxicity or efficacy. Furthermore, no serious side effects or toxicity occurred in any of the patients, and all gained weight and improved clinically during the 2-wk study. These data support the conclusion that both the 10 and 20% safflower oil emulsions are safe and effective in a parenteral nutrition program for children.

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