Early Enteral Fat Supplement and Fish Oil Increases Fat Absorption in the Premature Infant with an Enterostomy

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Objective To test the hypothesis that in the premature infant with an enterostomy, early enteral supplementation with Microlipid (fat supplement) and fish oil increases enteral fat absorption and decreases the requirement for Intralipid (intravenous fat emulsion).

Study design Premature infants (<2 months old) with an enterostomy after surgical treatment for necrotizing enterocolitis or spontaneous intestinal perforation and tolerating enteral feeding at 20 mL/kg/day were randomized to usual care (control 18 infants) or early supplementing enteral fat and fish oil (treatment 18 infants). Intravenous fat emulsion was decreased as enteral fat intake was increased. Daily weight, ostomy output, and nutrition data were recorded. Weekly 24-hour ostomy effluent was collected until bowel reanastomosis, and fecal fat, fecal liquid, and dry feces were measured. Fat absorption (g/kg/d) was calculated by subtracting fecal fat from dietary fat. The fecal liquid and dry feces were reported as mg/g wet stool. Date were analyzed by using ANOVA and mixed-effects model.

Results The interval from initial postoperative feeding to bowel reanastomosis varied from 2 to 10 weeks. The treatment group received more dietary fat and less intravenous fat emulsion and had higher enteral fat absorption, less fecal liquid, and drier feces than the control group. These effects were greater among infants with a high ostomy compared with those with a low ostomy. Enteral fat intake was significantly correlated with fat absorption.

Conclusion Early enteral fat supplement and fish oil increases fat absorption and decreases the requirement for intravenous fat emulsion. This approach could be used to promote bowel adaptation and reduce the use of intravenous fat emulsion in the premature infant with an enterostomy. *(J Pediatr 2013;163:429-34)*.

Intestinal perforation, due to necrotizing enterocolitis or spontaneous intestinal perforation, is typically treated with resection of necrotic bowel and creation of an enterostomy (hereafter referred to as an ostomy).[1] In the weeks to several months between this surgical procedure and bowel reanastomosis, infants with an ostomy often malabsorb enteral feeding as indicated by increased stool output and poor growth. Parenteral nutrition, including intravenous fat emulsion, improves growth but is associated with cholestasis.[2,3] Thus, infants with an ostomy might benefit from an intervention that promotes bowel adaptation and reduces exposure to parenteral nutrition, especially to the intravenous fat emulsion.[3,4]

After bowel resection in animal studies, a low-fat diet impairs and a high-fat diet,[5] especially one with long-chain polyunsaturated fatty acids (LCPUFAs),[6-8] promotes intestinal adaptation and increases dietary fat absorption.[9] However, there is scant information regarding the translation of these research findings into clinical practice. The objective of this study was to test the hypothesis that in the premature infant with an ostomy, early enteral fat supplement and fish oil increases enteral fat absorption and decreases the requirement for intravenous fat infusion. To evaluate this hypothesis, we performed a randomized trial of enteral polyunsaturated fatty acid (PUFA) supplementation to the premature infant after bowel resection and placement of an ostomy. The primary results of that trial will be described in a separate report.

Methods

The study protocol was approved by Wake Forest University Health Science Institutional Review Board and implemented in the Neonate Intensive Care Unit at Wake Forest Baptist Medical Center, Brenner Children's Hospital. Eligibility criteria were the presence of a jejunostomy or ileostomy and age <2 months. We excluded the infants who had a colostomy, congenital anomaly, or metabolic disease and those who had received enteral feedings for >4 days or were unable to initiate enteral feeding within 28 days after ostomy placement. Written

LCPUFA	Long-chain polyunsaturated fatty acid
n-3	Omega-3
n-6	Omega-6
PUFA	Polyunsaturated fatty acid

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informed consent was obtained from the parent. We used blocked randomization, with a block size of 8. Sealed envelopes were used to conceal the randomization assignments.

Infants in the control group received usual nutritional care, and infants in the treatment group received usual nutritional care plus supplementation with Microlipid (fat supplement, Nestle Nutrition, Florham Park, New Jersey) and fish oil once they tolerated the enteral feeding at 20 mL/kg/day. Fat supplement was started at 1 g/kg/d and then increased by 0.5 g/kg/d up to 2.5 g/kg/d, and Intralipid (intravenous fat emulsion, Baxter Healthcare, Deerfield, Illinois) was decreased by 0.5 g/kg/d and discontinued when the dose <1 g/kg/d. Fish oil was started at 0.2 g every 12 hours for infant weight <1000 g or at 0.25 g every 12 hours for infant weight >1000 g, and then weight adjusted up to 0.5 g every 6 hours. Fat supplement was mixed with human milk or infant formula and administered with continuous feeding, and fish oil was given as a scheduled bolus via a nasogastric or orogastric feeding tube.

Daily weight and nutrition data were recorded from nursing flow sheets. The 24-hour ostomy effluent was quantitatively collected weekly after starting enteral feeding until bowel reanastomosis. For each 24-hour stool collection, a sample was immediately stored at −80°C until analysis.

All 36 enrolled infants had 2-10 stool samples. A total of 219 stool samples (101 from the control infants and 118 from the treatment infants) were analyzed to determine the fecal fat content, fecal liquid, and dry feces. One milliliter of stool sample was weighed in a glass tube and then dried overnight in a 60°C vacuumed oven. Total fecal fat was extracted from the dry stool using methanol and chloroform.[10] The dry stool was ground as finely as possible, and 2 mL of methanol and chloroform was added followed by 1 mL of normal saline. After vigorous shaking, the chloroform phase containing the lipid extract was carefully transferred into a new weighed glass tube and dried at 60°C under N_2 flow. The glass tube was weighed again after the lipid extraction was dried, and the fecal fat was expressed as grams of lipid per milliliter of stool. The 24-hour total fecal fat was calculated and expressed as g/kg/d. Fecal liquid and dry fecal weight were calculated as follows:

$$\text{Fecal liquid (mg/g wet stool)} = (\text{g of wet stool} - \text{g of dry stool}) \times 1000/\text{g of wet stool}$$

$$\text{Dry feces (mg/g wet stool)} = (\text{g of dry stool} - \text{g of fecal fat}) \times 1000/\text{g of wet stool}$$

Daily dietary fat intake included the fat from human milk or formula plus the fat from fat supplement and fish oil. Because the fat content in human milk varies with maternal diet, we used an average of 4 g of fat/100 mL of human milk for the calculation. Dietary fat absorption was calculated and expressed as follows:

$$\text{Dietary fat absorption (g/kg/d)} = \text{dietary fat (g/kg/d)} - \text{fecal fat (g/kg/d)}$$

$$\text{Dietary fat absorption (\% of dietary fat)} = [\text{dietary fat (g/kg/d)} - \text{fecal fat (g/kg/d)}/\text{dietary fat (g/kg/d)}] \times 100\%$$

Statistical Analysis

All results are reported as mean ± SD. Group means were compared using the Student *t* test. In addition to comparisons of the 2 randomization groups, we analyzed the effect of enteral fat supplementation within 2 strata: infants with a high ostomy (defined as jejuno- to proximal ileostomy) and with a low ostomy (defined as mid- to distal ileostomy). Group means for dietary fat, fecal fat and fat absorption, fecal liquid, and dry feces were compared using ANOVA followed by Bonferroni post-test. The mixed-effects model was used to evaluate the correlation between dietary fat and fat absorption in all infants. A *P* value <.05 was considered statistically significant.

Results

The control and treatment groups were similar with regard to infant characteristics and reasons for bowel surgery (Table I).

No adverse gastrointestinal reactions such as increasing gastric residual, abdominal distention, and/or ostomy output were noted among the infants who received the early supplementation of fat supplement and fish oil. In the treatment group, the fat intake, fat excretion, and fat absorption were increased almost 2-fold (Table II). In addition, this group received fewer days of intravenous fat infusion and had a higher enteral feeding volume and calorie intake, a lower fecal liquid, and a higher dry fecal weight than the control group but similar weight gain and ostomy output. Fat absorption (g/kg/d) was highly correlated with dietary fat intake (g/kg/d) ($P < .0001$) in both control and treatment groups.

Table I. Patient demographics

	Control group (n = 18)	Treatment group* (n = 18)
Median GA, wk (range)	$27^{5/7}$ ($23^{1/7}$-$35^{3/7}$)	$26^{2/7}$ ($22^{6/7}$-34)
Median BW, g (range)	810 (530-1981)	764 (601-2179)
Sex, No. male (%)	14 (78)	9 (50)
Cause of ostomy, No. (%)		
Necrotizing enterocolitis	9 (50)	7 (39)
Small intestine perforation	8 (44)	10 (56)
Small bowel atresia	1 (6)	1 (6)
Site of ostomy, No. (%)		
High†	6 (33)	8 (44)
Low†	12 (67)	10 (56)

GA, gestational age; *BW*, birth weight.
*Treatment group received enteral fat supplement and fish oil.
†High ostomy is defined as jejuno- to proximal ileostomy, and low ostomy as mid- to distal ileostomy.