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Short-term effects of parenteral nutrition of cholestatic infants with lipid emulsions based on medium-chain and long-chain triacylglycerols

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Abstract

Objective: Infants with chronic cholestasis may require parenteral nutrition with lipid emulsions to provide energy and essential fatty acids but the optimal strategy is controversial.

Methods: We studied the effects of parenteral lipid emulsions with long-chain triacylglycerols (LCTs) or a mixture of LCTs and medium-chain triacylglycerols (MCTs/LCTs) on serum bilirubin and lipid metabolism in cholestatic infants who received these 20% emulsions in alternating order for 3 d each, together with a glucose and amino acid infusion.

Results: Of 11 recruited infants, two dropped out because enteral feeding could be established. In nine infants (2–8 mo of age, mean age 4.2 mo) who completed the study, serum bilirubin decreased from baseline to 6 h after the end of LCT infusion (from 8.5 ± 2.0 to 7.8 ± 1.8 mg/dL, mean ± SEM, $P < 0.05$) and MCT/LCT infusion (7.9 ± 6.5 to 7.1 ± 6.5 mg/dL, $P < 0.05$). Cholesterol, triacylglycerol, and phospholipid concentrations in plasma and in chylomicrons, very low-density lipoprotein, low-density lipoprotein, and high-density lipoprotein were not changed by either emulsion. Total polyunsaturated fatty acid contents in high-density lipoprotein phospholipids increased during LCT infusion (from 29.8 ± 0.9 to 35.9 ± 1.4% wt/wt, $P < 0.05$) and MCT/LCT infusion (from 30.4 ± 1.0 to 33.0 ± 0.7%, $P < 0.05$). The long-chain polyunsaturated fatty acid docosahexaenoic acid increased only with the LCT infusion. Because docosahexaenoic acid availability during infancy is important for early visual and cognitive development, the use of soybean oil–based lipid emulsions may be preferable for infants with severe progressive cholestasis.

Conclusion: The MCT/LCT and LCT emulsions showed a good metabolic tolerance in infants with chronic cholestasis but had a differential effect on high-density lipoprotein phospholipid contents of arachidonic and docosahexaenoic acids.

Keywords: Essential fatty acids; Long-chain polyunsaturated fatty acids; Lipid metabolism; Liver; Lipoproteins; Apolipoproteins

Abbreviations: AA, arachidonic acid; DHA, docosahexaenoic acid; LCP, long chain polyunsaturated fatty acids; PL, phospholipids; PUFA, polyunsaturated fatty acids; TBARS, thiobarbiturate reactive substance; TG, triacylglycerols

Introduction

Lipid metabolism is often disturbed in cholestatic patients as manifested by hypertriglyceridemia, hypercholesterolemia, or even hypocholesterolemia in cases with malnutrition or acute liver failure [1,2]. Advanced cholestasis is associated with markedly reduced plasma levels of the biologically important long-chain polyunsaturated fatty acids (LCPs), arachidonic acid and docosahexaenoic acid, which are essential constituents of cell membranes and particularly

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of neural tissues [3]. Many infants and children with chronic cholestasis present with malnutrition and may require courses of parenteral nutrition with lipid emulsions to provide energy and essential fatty acids. For pediatric parenteral nutrition usually lipid emulsions based on soybean oil are used, which are rich in ω-6 fatty acids (about 54% linoleic acid) and ω-3 fatty acids (about 6–8% α-linolenic acid). A potential alternative is a mixture of soybean oil and medium-chain triacylglycerols (MCTs), which might present a more readily available source of energy in stressed patients [4]. MCTs are rapidly removed from the plasma and oxidized, and they are hardly incorporated into tissue lipids [5]. MCT/long-chain triacylglycerol (LCT) emulsions contain less polyunsaturated fatty acids (PUFA) [6,7]. The liver plays a crucial role in lipid and lipoprotein metabolism, including conversion of PUFAs to LCPs but it is not clear to which extent chronic liver disease in children alters tolerance and metabolism of different lipid infusions [1,8].

We compared the effects of a soybean oil–based lipid emulsion and a lipid emulsion based on soybean oil and MCTs on metabolic tolerance and essential fatty acid status in cholestatic infants.

Materials and methods

Eligible for participation in the study were infants with chronic cholestasis admitted as inpatients with malnutrition and poor tolerance of an energy-rich diet and, hence, requiring parenteral nutrition. An exclusion criterion was administration of lipid emulsions in the preceding 3 wk. The study protocol was approved by the local ethical committee, and parental informed consent was obtained. The weight-for-age percentile was estimated in all children before entering the study.

Each child received two 3-d courses of parenteral nutrition with 20% lipid emulsions, in addition to amino acid and glucose solutions, separated by a 3-d period without lipid infusions. Lipid emulsions were infused at a dose of 1 g of triacylglycerol (TG) per kilogram of body weight on day 1 and 2 g/kg on days 2 and 3. The two emulsions used in random order were Intralipid 20% (Fresenius Kabi, Warsaw, Poland) and Lipofundin MCT 20% (B. Braun, Melsungen, Germany). In addition, the infants were offered small amounts of a therapeutic enteral infant diet based on hydrolyzed protein with MCTs (Pregestimil, Mead Johnson Nutritionals, Dietzenbach, Germany), provided the enteral intake did not exceed about 30% of total energy intake.

Blood samples were collected during the two study periods, before the start of the lipid infusion (baseline sample), at the end of lipid infusion on the third day while the lipid infusion was still running, and exactly 6 h after the end of the lipid infusion, while glucose and amino acid solutions were administered. Serum bilirubin, activities of alanine aminotransferase, γ-glutamyltransferase, prothrombin time, and albumin concentration were measured with standard methods. Plasma cholesterol, TG, and phospholipid (PL) concentrations were determined by enzymatic colorimetric tests. Retinol and α-tocopherol serum concentrations were determined by high performance liquid chromatography [9].

The separation of different lipoprotein fractions (low-density lipoprotein, high-density lipoprotein [HDL], very low-density lipoprotein, chylomicron fraction) was obtained by sequential ultracentrifugation of 2 mL of fresh plasma [10]. After cholesterol concentrations were measured in each fraction, they were dialyzed against phosphate buffered saline buffer to enable measurement of TG and PL concentrations. Dialysis was found necessary because the ultracentrifugation medium affected the lipid determinations (Stajniak, Bednarska-Makaruk, unpublished observation, 2000). Cholesterol, PL, and TG concentrations in lipoproteins were measured as described for plasma and corrected for volume changes by dialysis if applicable.

Apolipoprotein (Apo) concentrations (Apo-AI, Apo-AII, Apo-B) were determined in plasma by an electroimmunodiffusion technique in agarose gel (Hydragel ApoAIB and Hydragel ApoAII, Sebia, France).

Plasma lipid peroxides were determined with the spectrofluorometric method described by Yagi [11,12] and expressed as thiobarbiturate acid-reactive substance (TBARS; nanomoles per milliliter) in cholestatic patients and in 12 age-matched controls.

The fatty acid composition of plasma PL was determined in the liver before and after LCT and MCT/LCT infusions and in a reference group of 12 infants in good general health who attended the same hospital (diagnosed with mild bronchitis, cardiac murmur, and urinary tract infection, with normal weight and length, age range 1–11 mo, median age 5 mo). Measurements were made from venous plasma obtained with sodium ethylene diaminetetra acetate (1 mg/mL) as the anticoagulant and stored at −20°C until analysis. In addition, we analyzed the PL fatty acid composition of HDL in patients before and after lipid infusion. Lipids were extracted from 0.5 mL of plasma or from isolated HDLs with chloroform/methanol and lipid classes were separated by thin layer chromatography as previously described [13]. Fatty acids were transesterified with methanol and hydrochloric acid and analyzed by high-resolution capillary gas liquid chromatography using a Hewlett-Packard Series II 5890 gas chromatograph (Hewlett-Packard, Cupertino, CA, USA) with column injection and flame ionization detection (SGE column 50QC2/BPX70, column diameter 0.22 mm, column head pressure 1.5 bar; oven temperature initially 150°C, temperature rise by 3°C/min up to 180°C, then temperature rise by 4°C/min up to 200°C, then rise by 1°C/min up to 210°C, isothermic period 20 min). Peak identification was verified by comparison with authentic standards (Nu Check Prep Inc., Elysian, MN, USA). Results are expressed as percentage (% wt/wt) of all fatty acids detected with a chain length of 12 to 22 carbon atoms [14].

Results were evaluated with the Statistica 5.0 for Windows (Statsoft, Inc., Tulsa, OK, USA). We present the data

Table 1
Plasma triacylglycerol, cholesterol, phospholipid, and apolipoprotein concentrations at baseline, at the end of LCT or MCT/LCT infusion, and 6 h thereafter in nine cholestatic children studied twice under each of the two alternating emulsions*

Infusion	Plasma concentration	Baseline	End of infusion	6 h thereafter
LCT	Triacylglycerols (mg/dL)	122 ± 33	117 ± 24	94 ± 26
	Cholesterol (mg/dL)	243 ± 70	239 ± 51	212 ± 46
	Phospholipids (mg/dL)	353 ± 115	392 ± 103	336 ± 100
	Apo-I (mg/dL)	54.8 ± 12.5	54.4 ± 10.3	51.6 ± 10.2
	Apo-II (mg/dL)	7.5 ± 0.8	6.7 ± 0.7	6.5 ± 0.7
	Apo-B (mg/dL)	77.1 ± 7.9	82.2 ± 7.6	79.0 ± 7.9
MCT/LCT	Triacylglycerols (mg/dL)	103 ± 12	145 ± 41	144 ± 26
	Cholesterol (mg/dL)	230 ± 65	233 ± 44	228 ± 47
	Phospholipids (mg/dL)	355 ± 117	366 ± 87	340 ± 84
	Apo-I (mg/dL)	44.7 ± 9.1	47.0 ± 8.4	60.1 ± 12.6†
	Apo-II (mg/dL)	6.3 ± 0.7	7.6 ± 1.1	7.1 ± 1.0
	Apo-B (mg/dL)	81.7 ± 5.1	91.1 ± 5.6	93.6 ± 8.4

Apo, apolipoprotein; LCT, long-chain triacylglycerols; MCT/LCT, medium-chain/long-chain triacylglycerols
* Data are presented as mean ± SEM.
† $P < 0.05$ versus baseline.

as mean ± SEM. For comparison of the results obtained in the same subjects at different time points the Wilcoxon matched pairs test was used. Fatty acid profiles and TBARS results in cholestatic children and in the reference groups were compared with the Mann-Whitney two-sided rank test. Differences were regarded statistically significant at $P < 0.05$.

Results

Two infants dropped out after inclusion into the study because enteral feeding could be introduced as a major source of energy supply, exceeding 30% of total intake. Nine infants with chronic cholestasis (two with progressive familial cholestasis, two with biliary atresia, one with α-1-antitrypsin deficiency, and four with intrahepatic cholestasis with unknown origin), 2 to 8 mo of age (mean age 4.2 mo), with low weight for age (weight below the third percentile in six infants, at the 10th percentile in one infant, and between the 3rd and 10th percentiles in two infants) completed the study.

The patients studied received parenteral nutrition with glucose and amino acids but no lipids for 3–6 d before the study. During both study periods with the two lipid emulsions, infants received similar parenteral energy and nutrient intakes.

The calculated energy intakes were 72.4 ± 4.7 kcal/kg of body weight with LCT infusion and 72.7 ± 4.6 kcal/kg with MCT/LCT infusion, respectively (not significant). Intakes of glucose were 10.9 ± 0.7 and 10.9 ± 0.7 g/kg, lipid to total parenteral energy ratios were 0.274 ± 0.004 and 0.277 ± 0.003, and energy to nitrogen ratios were 179.2 ± 3.2 and 178.7 ± 3.2, respectively (all not significant). All infusions were delivered by the parenteral route for 20 h (lipids in a separate bottle, all other nutrients mixed in one bag). Enteral nutrition with Pregestimil provided 28.2 ± 1.0 kcal/kg of body weight during LCT infusion and 29.7 ± 1.0 kcal/kg during MCT/LCT infusion (not significant).

Before entering the study all children presented with hyperbilirubinemia and increased concentrations of serum bile acids (153.3 ± 16.6 μmol/L) and increased activities of ALAT (133 ± 35 U/L). The patients had relatively low vitamin E concentrations (2.9 ± 0.6 mg/L).

Plasma lipid concentrations at the end of both lipid infusions and 6 h thereafter did not differ from baseline values (Table 1). Similarly cholesterol, TG, and PL concentrations at the end of MCT/LCT infusion and 6 h thereafter did not differ from baseline (Table 1). There were no changes of plasma apolipoproteins Apo-AI, Apo-AII, and Apo-B with either lipid infusion (Table 1). Lipid infusions did not result in significant changes in lipoprotein cholesterol, PL, and TG concentrations but the LCT infusion led to significant decreases in very low-density lipoprotein cholesterol and very low-density lipoprotein PLs and chylomicron TGs (Table 2).

Total bilirubin concentrations were significantly below baseline values 6 h after both lipid infusions (Fig. 1). This was accompanied by a significant decrease in direct bilirubin with the LCT infusion from 7.9 ± 1.7 to 6.6 ± 1.6 mg/100 mL ($P < 0.05$) at the start and end of the lipid infusion, respectively, and 6.7 ± 1.7 mg/100 mL 6 h later ($P < 0.05$ versus baseline). In contrast, no significant changes in direct bilirubin concentration occurred during MCT/LCT infusion (8.0 ± 1.9, 8.0 ± 2.0, and 8.0 ± 2.1 mg/100 mL at baseline, infusion, and 6 h thereafter, respectively).

At baseline TBARS were increased, reflecting enhanced lipid peroxidation (2.8 ± 0.3 nmol/mL in patients versus 0.9 ± 0.9 nmol/mL in healthy controls, $P < 0.001$). TBARS were not altered by lipid infusions and were measured as 2.8 ± 0.3, 2.7 ± 0.2, and 2.6 ± 0.2 nmol/mL at baseline, at the end, and 6 h after LCT infusion, respectively, and 2.8 ± 0.2, 2.8 ± 0.3, and 2.7 ± 0.2 nmol/mL with the MCT/LCT infusion, respectively.

Table 2
Mean lipoprotein triacylglycerol, cholesterol, and phospholipid concentrations at baseline, at the end of LCT or MCT/LCT infusion, and 6 h thereafter in nine cholestatic children studied twice under each of the two alternating emulsions

LP	Infusion	TG (mg/dL)			Ch (mg/dL)			PL (mg/dL)		
		Basal	End	6 h	Basal	End	6 h	Basal	End	6 h
Chylomicron	LCT	18.66	18.8	12.3*	17.6	17.8	14.9	28.9	31.1	22.3
	M/L	16.7	36.3	24.6	18.0	22.5	19.4	25.3	37.0	29.4
VLDL	LCT	35.8	31.3	27.6	15.5	11.4*	9.3*	15.3	12.6	10.3*
	M/L	33.2	33.8	29.6	11.0	11.0	8.6	9.8	11.8	9.6
LDL	LCT	25.7	26.4	26.6	105.1	88.6	90.8	125.0	103.0	101.7
	M/L	21.1	24.9	24.7	72.9	72.7	79.7	94.1	98.2	101.1
HDL	LCT	54.6	50.3	49.5	15.4	14.8	14.8	49.6	49.3	36.3
	M/L	42.6	59.6	54.6	13.5	15.2	15.3	45.2	39.5	35.6

Ch, cholesterol; HDL, high-density lipoproteins; LCT, long-chain triacylglycerol infusion; LDL, low-density lipoproteins; LP, lipoprotein fraction; M/L, medium-chain/long-chain triacylglycerol infusion; PL, phospholipid; TG, triacylglycerol; VLDL, very low-density lipoproteins
* $P < 0.05$ versus baseline.

Cholestatic children had significantly lower total PUFA levels in plasma, whereas LCP with 20 and 22 carbon atoms were within the normal range (Table 3). The depletion of PUFA was attributed mainly to low levels of linoleic acid, although there were clearly elevated levels of the non-essential fatty acids mead acid (20:3ω-9) and palmitoleic acid (16:1ω-7), indicative of essential fatty acid deficiency (Table 3). Baseline total and individual ω-6 fatty acids were not significantly different, but total ω-3 fatty acids were slightly higher before infusion with the MCT/LCT infusion compared with baseline before LCT infusion ($P < 0.05$), whereas there were no significant differences for individual ω-3 fatty acids (18:3ω-3, 20:5ω-3, 22:6ω-3; Table 3).

Long-chain PUFA infusion increased total PUFA content in HDL PLs due to increases in linoleic and α-linolenic acid values. The respective LCP arachidonic acid did not increase with LCT infusion, but there was a small but statistically significant increase with the MCT/LCT infusion (Fig. 2). Docosahexaenoic acid increased only after the LCT infusion but not after the MCT/LCT infusion (Fig. 2).

Discussion

The children with severe liver disease in the present study had evidence of PUFA deficiency with particularly low values for ω-6 fatty acids and for docosahexaenoic acid, which agrees with previously reported findings in cholestatic children [3]. Moreover, levels of lipid soluble vitamins A and E were abnormally low. Cholestasis-associated lipid malabsorption and a low energy supply relative to the high energy requirements of children with chronic liver disease [15] may have contributed to an enhanced PUFA oxidation and to PUFA depletion. Therefore, these children may benefit from a parenteral supply of lipid emulsions.

Comparative studies performed in adult patients with liver disease who received LCT or MCT/LCT emulsions showed that the plasma clearance and hydrolysis of both emulsions were not different in patients and in healthy controls [16]. In our study LCT and MCT/LCT infusions did not lead to significant changes in plasma lipids and lipoproteins, which indicates an effective clearance of infused lipids in our patients.

Druml et al. [16] reported profoundly low HDL cholesterol levels in adult patients with chronic hepatic failure, whereas fat elimination was normal. Similarly, the cholestatic infants in this study presented with only about one-third of the HDL cholesterol concentrations (Table 2) of 39.6 ± 10.8 mg/dL found in healthy infants aged 7 mo [17], and Apo-AI levels in the cholestatic infants studied (Table 1) reached only about half the concentrations found in healthy infants at 7 mo (107 ± 26 mg/dL [18]), which might reflect accelerated HDL catabolism in liver disease [18].

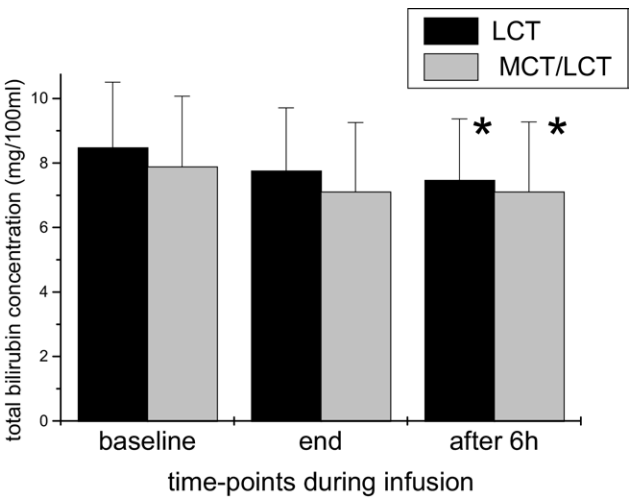

Fig. 1. Total serum bilirubin concentrations at baseline, at the end of LCT or MCT/LCT infusion, and 6 h thereafter in nine cholestatic children studied twice under each of the two alternating emulsions (mean ± SEM, *$P < 0.05$ versus baseline). LCT, long-chain triacylglycerol infusion; MCT/LCT, medium-chain/long-chain triacylglycerol.

Table 3
Fatty acid composition (% wt/wt) of plasma phospholipids in nine cholestatic infants at baseline before LCT and MCT/LCT infusions, respectively, and in 12 age-matched controls*

Fatty acid	Before LCT	*P* versus controls	Before MCT/LCT	*P* versus controls	Controls
Saturated fatty acids					
C16:0	32.7 ± 0.9	<0.001	33.4 ± 1.3	<0.001	27.9 ± 0.5
C18:0	15.0 ± 0.6	NS	14.0 ± 0.9	NS	14.5 ± 0.4
C16:1ω-7	1.8 ± 0.2	<0.001	1.9 ± 0.4	<0.01	0.5 ± 0.05
C18:1ω-9	13.3 ± 0.7	<0.05	10.9 ± 1.6	NS	11.3 ± 0.5
C20:3ω-9	1.3 ± 0.3	<0.001	0.9 ± 0.2	<0.001	0.2 ± 0.03
Total ω-6 fatty acids	25.4 ± 0.8	<0.001	27.1 ± 1.0	<0.001	33.7 ± 0.8
ω-6 LCP	11.5 ± 0.7	NS	11.6 ± 0.8	NS	12.7 ± 0.6
C18:2ω-6	13.7 ± 0.7	<0.001	15.1 ± 0.7	<0.001	20.9 ± 0.9
C20:4ω-6	6.5 ± 0.5	NS	6.4 ± 0.4	<0.05	8.5 ± 0.6
Total ω-3 fatty acids	2.3 ± 0.4	<0.05	3.2 ± 0.7	NS	3.5 ± 0.2
ω-3 LCP	2.2 ± 0.4	<0.05	3.0 ± 0.7	NS	3.2 ± 0.2
C18:3ω-3	0.12 ± 0.02	NS	0.14 ± 0.03	NS	0.16 ± 0.03
C20:5ω-3	0.26 ± 0.04	NS	0.55 ± 0.21	NS	0.36 ± 0.05
C22:6ω-3	1.6 ± 0.3	NS	1.7 ± 0.3	NS	2.1 ± 0.3
Total PUFA	27.6 ± 1.1	<0.001	30.3 ± 0.9	<0.001	37.2 ± 0.7
Total LCP	13.6 ± 1.0	NS	14.7 ± 0.7	NS	15.9 ± 0.7

LCP, long-chain polyunsaturated fatty acid; LCT, long-chain triacylglycerol infusion; MCT/LCT, medium-chain/long-chain triacylglycerol infusion; PUFA, polyunsaturated fatty acid

* Data are presented as mean ± SEM.

Plasma lipid concentrations were not changed by either of the lipid emulsions used. Hydrolysis of both emulsions appears to be mediated primarily by peripheral lipoprotein lipase, which is not affected in liver disease [16,19], and not by hepatic lipase. In adults with liver disease only a negligible fraction of infused lipid particles is degraded in the liver, whereas the majority is hydrolyzed in the peripheral microvasculature [16,20]. In studies investigating an excessive administration of artificial lipid particles, alternative pathways of elimination such as sequestration into the reticuloendothelial system could be demonstrated [21,22], but this is not observed during low infusion rates [23].

Excretory liver cell function seems not to be disturbed by lipid infusion because bilirubin levels decreased. Although Rubin et al. [24] also reported decreasing bilirubin levels in premature infants with indirect hyperbilirubinemia, the underlying mechanisms remain unclear. It is conceivable that the supply of PLs acting as an emulsifier in lipid emulsions might enhance the solubility of other bile components and thus augment bile flow because bilirubin and PL are excreted together in bile [25]. PLs administered to patients with liver diseases were reported to improve hepatocyte function [26].

We used HDL PLs to determine the effect of lipid infusions on fatty acid status because plasma total PLs might not be a good indicator of tissue fatty acid status during parenteral feeding because PLs supplied with the emulsions may accumulate in plasma. Because HDLs are synthesized by the liver, they may better reflect intrahepatic fatty acid status and metabolism than total plasma lipids, even though to a certain degree HDL PL may be exchanged in the circulation.

Our results support the hypothesis that using a mixed MCT/LCT emulsion, with a lesser supply of precursor PUFAs, may enhance the hepatic synthesis of arachidonic acid and, hence, increase the arachidonic acid content of HDL PLs [27]. However, it is more difficult to understand why the LCT emulsion resulted not only in a rapid increase of the essential fatty acids linoleic and α-linolenic acids but also in a significant increase in the LCP docosahexaenoic acid. Although endogenous arachidonic acid synthesis from linoleic acid requires only two desaturation and one chain elongation steps, docosahexaenoic acid synthesis from

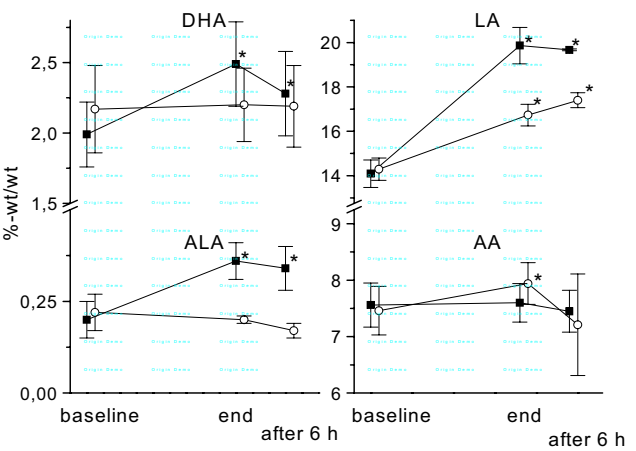

Fig. 2. Percentages (mean ± SEM) of 18:3ω-3, 22:6ω-3, 18:2ω-6, and 20:4ω-6 in high-density lipoprotein phospholipids of children receiving long-chain triacylglycerol (squares) or medium-chain/long-chain triacylglycerol (circles) lipid infusions. Percentages were measured before (basal), at the end (end), and 6 h after (after) lipid infusion. Nine cholestatic children were studied under each of the two alternating emulsions. *$P <$ 0.05, difference versus baseline values. AA, arachidonic acid; ALA, α-linolenic acid; DHA, docosahexaenoic acid; LA, linoleic acid.

α-linolenic is far more complex and rather ineffective [27]. The balance of endogenous formation and plasma disappearance might show a particularly marked disturbance in patients with severe liver disease who are often depleted in LCPs, whereas the activity of their fatty acid desaturation and chain elongation pathway seems low [3]. The greater availability of α-linolenic in the plasma pool (Fig. 2) may also have increased docosahexaenoic acid incorporation into PLs.

Peroxidation of unsaturated fatty acids may be an additional risk factor for PUFA depletion. In this study high TBARS concentrations were found at baseline without further change by short-term lipid infusion. Low vitamin E levels in cholestatic children may contribute to high lipid peroxide concentrations [28], whereas the PL administration with both lipid emulsions may protect against further lipid peroxidation [29].

We conclude from our results that short-term infusion of MCT/LCT and LCT emulsions in infants with cholestasis shows good metabolic tolerance. The HDL PL contents of the biologically important docosahexaenoic acid shows a greater increase with the LCT emulsion. Docosahexaenoic acid deficiency may occur with progressing severity of cholestasis [3]. Because the availability of docosahexaenoic acid during infancy is of major importance for visual and cognitive development [27,30], the use of soybean oil–based lipid emulsions may be preferable to the use of MCT/LCT emulsions for infants with severe progressive cholestasis.

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