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Plasma and tissue levels of lipids, fatty acids and plasma carnitine in neonates receiving a new fat emulsion

G Magnusson[1], M Boberg[2], G Cederblad[3] and S Meurling[1]

Department of Paediatric Surgery[1], University Hospital, Uppsala; Department of Geriatrics[2], Uppsala University, Uppsala; Department of Medical Laboratory Sciences and Technology[3], Huddinge Hospital, Huddinge, Sweden

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This study was undertaken to compare Intralipid® with a new fat emulsion containing gamma-linolenic acid and carnitine, named Pediatric Fat Emulsion 4501, in neonates with regard to lipid and carnitine metabolism over a short period of total parenteral nutrition. There were 10 neonates in each group and they tolerated the total parenteral nutrition well. In spite of the gamma-linolenic acid supplementation in the new emulsion, arachidonic acid decreased significantly in plasma lipid esters and adipose tissue in both groups after 5 d of treatment. Also, there was a decrease in plasma docosahexaenoic acid which was more pronounced in the treatment group. The relative percentage values of linoleic and linolenic acids in adipose tissue were increased, indicating that newborns have a rapid accretion of fatty acids. Plasma triglycerides were effectively cleared during the periods without fat infusion. In the group that received Pediatric Fat Emulsion 4501 the means of both free and total plasma carnitine concentrations increased significantly, whereas they tended to decrease in the Intralipid® group. □ *Carnitine, fatty acid metabolism, neonates, parenteral nutrition*

G Magnusson, Department of Paediatric Surgery, University Hospital, S-751 85 Uppsala, Sweden

Fat plays an important role in total parenteral nutrition (TPN) as a source of energy and in supporting the structure of cell membranes. The polyunsaturated fatty acids linoleic acid (LA, 18:2 n-6) and alpha-linolenic acid (18:3 n-3) are used for cell growth and function (1), and the metabolites of these fatty acids, arachidonic acid (AA, 20:4 n-6) and docosahexaenoic acid (DHA, 22:6 n-3), respectively, are also important. DHA is an eicosanoid precursor (2) which is essential for the development and function of the retina and the brain (3, 4). In neonates requiring TPN for a long period, the relative amounts of different essential fatty acids in the fat emulsion are of great importance (1). In neonates, especially those born preterm, a high fat intake is essential because of their limited fat reserves. All neonates grow rapidly if the energy supply is adequate and the amount of essential fatty acids sufficient. However, they can only tolerate a certain amount of fluid given intravenously (i.v.) and the energy content per millilitre in the TPN therefore has to be high.

Carnitine (3-hydroxy-4-trimethyl-aminobutyric acid) acts as a carrier substance, facilitating the transport of long-chain fatty acids into the mitochondria, where they are β-oxidized. Carnitine also functions as a buffer for acetyl groups that have been regenerated intramitochondrially, whether by pyruvate or by fatty acid oxidation. Excess acetyl groups are transferred from acetyl-coenzyme A (CoA) to carnitine, thereby regenerating free reduced coenzyme A (CoASH), which is necessary for the metabolic flux through the citrate cycle. Both preterm and full-term infants are able to maintain the plasma concentration of carnitine at a relatively constant level when fed breast milk. The carnitine intake from breast milk has been reported to be 5–7 μmol (0.8–1.2 mg) kg^{-1} d^{-1} in preterm and full-term infants (5, 6). The bioavailability of carnitine from breast milk is not known, but there are several indications that it is considerably higher than that of carnitine in formulae (6).

During recent decades the most widely used fat emulsion for neonates and adults has been Intralipid®, which contains no carnitine. The predominant fatty acid in this emulsion is LA (53%). The enzyme delta-6-desaturase is essential in the conversion from LA to gamma-linolenic acid (GLA, 18:3 n-6) and is considered to be the rate-limiting step in the metabolism from LA to AA (1). Not only long-chain n-3 fatty acids but also the long-chain n-6 fatty acid AA are essential for growth and development. In newborns there are indications of impaired metabolism of LA, probably due to a poorly developed enzyme system as a result of their immature liver (7–9).

A new fat emulsion supplemented with GLA and carnitine has now been developed (Table 1). This emulsion, Pediatric Fat Emulsion (PFE) 4501 (Pharmacia and Upjohn, Stockholm, Sweden), is intended for administration to both preterm and full-term neonates.

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Table 1. Contents of the two fat emulsions per 1000 ml and the relative concentrations of fatty acids.

	Intralipid®	PFE 4501
Fractionated soybean oil	200 g	–
Purified mixture of soybean oil (85%) and borage oil (15%)[a]	–	200 g
Fractionated egg phospholipids	12 g	12 g
Glycerol	22.5 g	22.5 g
Sodium hydroxide for adjustment to pH	8	8
Water added for injection	1000 ml	1000 ml
C 16:0	10.8	11.2
C 18:0	4.2	4.1
C18:1 n-9	22.2	20.9
C 18:2 n-6	52.9	50.8
C 18:3 n-6	–	3.2
C18:3 n-3	6.8	5.9

[a]With a content of 23% GLA.

The aim of this study was to compare Intralipid® with PFE 4501 in neonates with special reference to changes in fatty acid composition in plasma and adipose tissue and plasma carnitine concentrations as well as tolerance during a short period of TPN.

Patients and methods

Patients

Neonates undergoing surgery for various oesophago-gastrointestinal malformations were assigned the day after surgery to either Intralipid® (control group) or PFE 4501 (treatment group) in a double-blind, randomized manner. The primary diagnoses and numbers of patients (n) in the control group were: oesophageal atresia, $n=2$; gastrochisis, $n=3$; omphalocele, $n=1$; small bowel atresia, $n=2$ (1 excluded); and small bowel obstruction, $n=2$. In the treatment group they were: oesophageal atresia, $n=4$; gastrochisis, $n=1$; omphalocele, $n=1$; small bowel atresia, $n=2$ (1 excluded); and small bowel obstruction, $n=2$. TPN with fat (Intralipid® or PFE 4501), amino acids (Vaminolac®), vitamins (Soluvit®, Vitalipid®Infant) trace elements (Ped-el®) and electrolytes (Addex®–Natriumklorid and Addex®–Kaliumklorid) was given daily for a total of 18 h. Glucose (Glucose® Pharmacia) was infused continuously, 24 h a day. The total amount of fat infused was 2 g kg^{-1} on the first day, and this amount was increased at a daily rate of 1 g kg^{-1} until an infusion rate of 4 g kg^{-1} d^{-1} was reached (Table 2).

A total of 20 neonates initially entered the study, 10 in each group. The inclusion criteria were: neonates of both sexes needing surgical treatment, age up to and including 7 d, and requiring TPN for a minimum of 5 d. The exclusion criteria were: metabolic disease, renal disease, inflammatory disease, septic syndrome or a haematological disorder. The neonates should not be receiving treatment with catecholamines, or have any known malignancy. Further, they could not be participating in any other study. Parents received verbal and written information about the study before it began, and gave their consent. They were able to discontinue their participation at any time. The study was approved by the Ethics Committee, Faculty of Medicine, Uppsala University.

Methods

The heart rate, body temperature, body weight and any clinical symptoms were recorded daily, as was the platelet count. Haematological (haemoglobin, leucocytes) and biochemical (aspartate aminotransferase, alanine aminotransferase, sodium, potassium, creatinine, alkaline phosphatase, albumin, bilirubin and gamma-glutamyl transferase) parameters were measured on d 0 just before the first TPN started and after termination of the study. These parameters were measured by routine methods in the hospital laboratory.

Triglycerides, cholesterol and glucose in plasma were determined twice a day, just before the fat infusion started and after 7 h of TPN. On each occasion, 30 μl of capillary blood (heparin plasma) was taken and analysed on a Reflotron® (Boehringer-Mannheim Diagnostics Scandinavia AB, Stockholm, Sweden).

Table 2. TPN schedule.

Study day	Total non-protein energy kcal kg^{-1} bw	Fat g kg^{-1} bw (ml)	Amino acids g kg^{-1} bw (ml)	Glucose 10% g kg^{-1} bw (ml)
1	56	2.0 (10)	0.95–1.3 (15–20)	9 (90)
2	66	3.0 (15)	1.3–1.62 (20–25)	9–10 (90–100)
3–6	80	4.0 (20)	1.95–2.27 (30–35)	10–11 (100–110)

TPN schedule for vitamins and trace elements in ml and electrolytes in mmol given per kg body weight (bw)

Soluvit® N	Vitalipid® Infant	Ped-el®	Sodium	Potassium
1	1	4	2–3	2–3

Table 3. Mean concentrations of free, acyl and total carnitine in plasma in the control and treatment groups before and after 5 d of treatment, and the differences between the two occasions. The ratio of acyl to free carnitine concentration is also given.

Carnitine (μmol l^{-1})	n	Free	n	Acyl	n	Total	Acyl:free
Control group							
Before	9	15.3 ± 10.0	8	7.3 ± 3.0	8	21.1 ± 12.0	0.6 ± 0.2
After	9	9.6 ± 2.6	8	4.7 ± 2.0	8	13.6 ± 2.8	0.6 ± 0.3
Difference	9	−5.7 ± 8.3	8	−2.6 ± 2.4**	8	−7.5 ± 9.8	
Treatment group							
Before	9	17.5 ± 6.7	8	9.0 ± 3.7	8	25.6 ± 10.1	0.6 ± 0.2
After	9	35.3 ± 3.9	8	14.2 ± 2.9	8	50.0 ± 4.5	0.4 ± 0.1
Difference	9	17.8 ± 8.3***	7	5.5 ± 2.8*** ###	7	26.3 ± 6.8*** ###	

**$p < 0.01$, ***$p < 0.001$: statistically significant changes in free, acyl and total carnitine within the control and treatment groups.
###$p < 0.001$: statistically significant differences between the two groups.

Before TPN was started, after 5 d of TPN and 5 h after the fat infusion ended, a blood sample (2 ml) was taken for measurement of both the plasma carnitine concentration (free and total) and the fatty acid composition of the plasma lipid esters (cholesterol esters, triglycerides and phospholipids). No oral feeding was provided. The samples were drawn from a peripheral vein into a vacutainer tube containing heparin. They were centrifuged at +4°C and the plasma was frozen at −72°C.

A piece of adipose tissue weighing approximately 15 mg was taken when the patients were only receiving glucose infusion during surgery, and after 5 d of TPN under local anaesthesia, both times as an open biopsy with a scalpel, put into a mixture of alcohol and dry ice and kept at −72°C.

The adipose tissue biopsies were dissolved in 1 ml of hexane and homogenized in a tissue grinder. The hexane was pipetted off and the solvent was evaporated to dryness. Lipids were extracted into chloroform–methanol with 0.005% butylated hydroxytoluene added as an antioxidant. The plasma lipid esters were separated by thin-layer chromatography. After transmethylation, the fatty acid methyl esters in the plasma lipid fractions and in adipose tissue were determined by capillary gas–liquid chromatography as described previously (10, 11).

The total and free plasma carnitine concentrations were determined by enzymatically converting carnitine to acetylcarnitine using [1-^{14}C]acetyl-CoA as substrate (12, 13). Total carnitine was assayed after alkaline hydrolysis, and free carnitine without such hydrolysis. The radioactivity was measured in a liquid scintillation counter. The acyl-carnitine concentration was calculated as the difference between the total and the free carnitine values.

Statistics

Data are presented as means ±SD except for fatty acids. The hypothesis of equal pretreatment and posttreatment means was tested with a paired Student's t-test within each treatment group. Differences between the effects of the two treatments were tested with an unpaired two-sample Student's t-test. Fatty acid values below the detection limit were considered to be zero in tables and statistical analyses. The analyses for changes in fatty acids between d 0 and d 5 within each treatment group were made with Wilcoxon's matched-pairs signed rank test. Comparisons between groups were analysed with a Mann–Whitney U-test. For all analyses, the statistical analysis package SAS for Windows, version 6.08, was used.

Results

The study initially comprised 20 neonates, 0–4 d old. There were 10 neonates in the control group, with a mean gestational age of 36 ± 2 weeks and a mean birth weight of 2631 ± 643 g, and 10 in the treatment group, with a mean gestational age of 38 ± 2 weeks and a mean birth weight of 2837 ± 391 g. No significant differences in these variables were found between the two groups. In the control group the mean postnatal age at the start of the study was 1.33 ± 1.00 d and in the treatment group 1.11 ± 1.00 d. Two patients, one in each group, were later excluded, as they had received breast milk. All neonates in both groups tolerated TPN well and thus the TPN schedule was followed. The haematological and biochemical values were all within normal ranges. Two patients in the treatment group with physiological icterus needed treatment with UV radiation.

The heart rate, body temperature and respiratory rate were measured daily and there were no significant changes in either group or any significant differences between the two groups.

The body weight was measured daily and showed a decrease in the first 3 d and then an increase during the rest of the study period in both groups. These changes were not statistically significant. There was no significant difference between the two groups on each day or between the changes in the two groups from d 1 to d 5.

Carnitine

In the control group, the mean concentrations of total

Table 4. Fatty acid composition of plasma cholesterol esters before and after 5 d of TPN with the two fat emulsions.

	Control group, Intralipid®				Treatment group, PFE 4501			
	Median	Range min–max	Median	Range min–max	Median	Range min–max	Median	Range min–max
Fatty acid	Day 0		Day 5		Day 0		Day 5	
16:0	21.7	15.9–24.0	11.9**	10.8–13.3	20.7	18.9–24.0	12.8**	12.0-13.5
18:0	2.9	1.2–4.1	1.7**	1.0–2.0	3.3	2.1–5.4	2.2**	1.0–3.0
18:1 n9	29.3	22.9–37.3	28.3	23.8–30.5	28.7	23.1–33.7	30.0	21.5–34.4
18:2 n6	18.7	10.6–24.7	44.1**	40.7–45.7	20.0	12.3–26.3	41.6**	37.3–46.1
18:3 n6	0.6	0.0–1.5	1.1*	0.5–1.5	0.4	0.0–0.7	1.6**	1.2–2.7
18:3 n3	0.0	0.0–3.7	1.8**	1.2–6.2	0.0	0.0–0.3	1.2**	0.8–1.7
20:3 n6	0.9	0.0–1.4	0.5	0.4–0.6	1.0	0.0–1.1	0.7	0.0–0.9
20:4 n6	11.6	6.4–17.0	6.1**	3.0–8.1	11.4	6.7–12.6	6.1**	4.1–8.2
20:5 n3	0.0	0.0–0.8	0.5*	0.0–1.3	0.3	0.0–1.1	0.3	0.0–0.6
22:6 n3	0.5	0.0–1.6	0.8	0.0–1.0	0.9	0.0–1.7	0.7	0.0–1.0
X	15.7	11.1–21.0	3.9**	3.0–4.5	12.9	10.6–18.6	4.1**	3.0–5.0

Results are given as relative per cent of fatty acids presented (median and range).
*$p < 0.05$, **$p < 0.01$: significant change during treatment.
X (14:0, 16:1 n7, 18:1 n7, 22:0, 22:4 n6 and 22:5 n3) = sum of the remaining FA analysed.

and free plasma carnitine showed only a tendency to a decrease ($p < 0.07$), but the mean acyl carnitine concentration decreased significantly ($p < 0.02$; Table 3). In the treatment group the mean concentrations of both total and free plasma carnitine increased twofold ($p < 0.001$) and the mean acyl carnitine concentration in plasma increased to a lesser extent but also significantly ($p < 0.002$; Table 3).

Fatty acids

There was a significant increase in the relative percentage of values of LA and alpha-linolenic acid in all plasma lipid esters, in both the control and treatment groups, with a concomitant decrease in saturated fatty acids. In the treatment group a pronounced increase in GLA in all plasma lipid fractions was found. However, a slight increase was also seen in cholesterol esters and in the triglycerides in the control group. In both groups there was a similar decrease in the long-chain n-6 metabolites dihomo-gamma-linolenic acid (DHLA, 20:3 n-6) and AA in phospholipids as well as in AA in cholesterol esters.

In the treatment group there was a significant decrease in DHA in phospholipids and triglycerides. A decrease in phospholipid DHA was also seen in the control group (Tables 4–6).

In adipose tissue a similar increase in both groups was found in the relative concentrations of LA, alpha-linolenic acid and GLA. There was an increase in DHLA in the treatment group, whereas AA decreased in both groups. The long-chain n-3 fatty acids remained unchanged (Table 7).

Table 5. Fatty acid composition of plasma phospholipids before and after 5 d of TPN with the two fat emulsions.

	Control group, Intralipid®				Treatment group, PFE 4501			
	Median	Range min–max	Median	Range min–max	Median	Range min–max	Median	Range min–max
Fatty acid	Day 0		Day 5		Day 0		Day 5	
16:0	33.0	29.3–35.7	29.4**	28.2–31.7	33.3	28.6–33.7	28.9**	27.3–30.4
18:0	12.8	11.1–14.8	15.1**	14.0–15.8	13.3	12.1–15.3	14.8**	14.3–15.8
18:1 n9	11.9	9.5–15.2	15.1**	13.9–18.0	11.7	0.3–14.3	13.8**	10.2–14.9
18:2 n6	8.6	6.0–10.4	19.0**	17.0–22.9	8.7	5.4–12.6	18.7**	17.0–20.0
18:3 n6	0.0	0.0–0.1	0.1	0.0–0.2	0.0	0.0–0.2	0.2**	0.1–0.3
18:3 n3	0.0	0.0–0.0	0.2*	0.0–0.3	0.0	0.0–0.0	0.2**	0.2–1.9
20:3 n6	2.8	1.6–3.4	1.3**	1.0–1.8	3.2	1.7–3.8	2.3**	2.0–3.1
20:4 n6	14.9	9.3–16.1	7.5**	4.6–9.1	13.7	11.6–15.5	7.5**	6.7–8.6
20:5 n3	0.7	0.0–1.1	0.4	0.4–1.0	0.7	0.0–1.0	0.4*	0.3–0.5
22:6 n3	5.7	3.7–6.5	4.2*	3.6–5.0	6.1	4.0–7.6	4.4**	3.5–5.5
X	11.7	10.2–13.6	7.1**	6.4–7.9	11.2	9.7–14.5	8.3**	7.4–9.3

Results are given as relative per cent of fatty acids presented (median and range).
*$p < 0.05$, **$p < 0.01$: significant change during treatment.
X (14:0, 16:1 n7, 18:1 n7, 22:4 n6 and 22:5 n3) = sum of the remaining FA analysed.

Table 6. Fatty acid composition of plasma triglycerides before and after 5 d of TPN with the two fat emulsions.

	Control group, Intralipid®				Treatment group, PFE 4501			
	Median	Range min–max	Median	Range min–max	Median	Range min–max	Median	Range min–max
Fatty acid	Day 0		Day 5		Day 0		Day 5	
16:0	32.4	26.7–42.3	20.0**	15.8–22.9	31.2	26.2–46.8	21.8**	20.3–25.8
18:0	6.0	3.0–8.5	4.6	2.8–6.5	6.2	5.0–9.4	4.4**	3.5–5.4
18:1 n9	35.0	33.1–39.9	26.3**	23.9–30.2	33.9	28.2–37.8	26.9**	22.7–30.6
18:2 n6	6.1	3.8–8.0	37.4**	30.5–40.6	8.0	2.7-10.0	34.8**	29.3–37.3
18:3 n6	0.2	0.0–0.3	1.1*	0.0–1.9	0.0	0.0–0.5	1.7**	1.0–2.6
18:3 n3	0.0	0.0–0.2	2.8**	2.0–4.6	0.0	0.0–0.5	2.0**	1.6–2.2
20:3 n6	0.3	0.0–0.7	0.3	0.0–0.5	0.5	0.0–0.9	0.7	0.0–0.8
20:4 n6	2.3	1.6–3.1	2.7	1.2–4.0	2.8	0.5–3.8	2.3	0.4–3.5
20:5 n3	0.0	0.0–0.3	0.0	0.0–0.8	0.0	0.0–0.5	0.0	0.0–0.4
22:6 n3	3.1	0.0–4.5	1.7	0.0–3.1	3.3	0.8–6.8	2.1**	0.9–2.5
X	15.1	7.0–20.6	2.8**	2.1–7.8	14.2	7.8–17.6	5.2**	2.1–8.6

Results are given as relative per cent of fatty acids presented (median and range).
*$p < 0.05$, **$p < 0.01$: significant change during treatment.
X (14:0, 16:1 n7, 18:1 n7, 22:0, 22:4 n6 and 22:5 n3) = sum of the remaining FA analysed.

Glucose and lipids in plasma

In both groups the plasma glucose concentration remained within the normal range during the study period. Triglycerides in plasma returned to baseline in both groups after the 6-h period without fat infusion. Cholesterol in plasma tended to increase during the study period (Fig. 1).

Discussion

The aim of this study was to compare the two fat emulsions Intralipid® and PFE 4501. Their basic compositions are essentially similar, with LA as the main component, but PFE 4501 also contains GLA and carnitine. The two emulsions have the same phospholipid : TG ratio (Table 1). The plasma triglycerides were effectively cleared during the periods without fat infusion, although the fat content in the TPN gradually increased to a maximum of 4 g kg^{-1} d^{-1}, which did not seem to cause accumulation of plasma triglycerides for full-term neonates (Fig. 1). The relative percentages of values of LA in plasma lipid esters increased in both groups, but there was a significant decrease in the long-chain n-6 fatty acid AA in both TPN groups in spite of the GLA supplementation in the new emulsion. In adipose tissue a similar decrease in AA was found, although there was an increase in DHLA in the treatment group. This might indicate a mechanism to maintain AA within certain limits. Previous studies have shown a similar decrease or an unchanged AA content in adipose tissue with LA-enriched diets even when supplemented with GLA (14, 15). Another possibility could

Table 7. Fatty acid composition of adipose tissue before and after 5 d of TPN with the two fat emulsions.

	Control group, Intralipid®				Treatment group, PFE 4501			
	Median	Range min–max	Median	Range min–max	Median	Range min–max	Median	Range min–max
Fatty acid	Day 0		Day 5		Day 0		Day 5	
16:0	44.2	41.1–46.9	40.1**	37.2–42.0	43.3	38.7–55.6	40.0*	37.7–44.1
18:0	3.4	3.2–4.4	3.0**	2.6–3.6	3.7	2.5–5.0	2.9**	2.3–3.6
18:1 n9	27.8	22.7–31.3	26.5*	23.7–28.0	26.9	17.4–31.2	24.8	20.7–27.0
18:2 n6	2.7	1.3–3.9	9.3**	5.0–13.0	2.5	1.8–4.0	8.6**	5.6–10.5
18:3 n6	0.1	0.1–0.2	0.2**	0.1–0.2	0.1	0.1–0.3	0.4**	0.2–0.5
18:3 n3	0.1	0.0–0.1	1.1**	0.6–1.6	0.1	0.1–0.2	0.9**	0.5–1.1
20:3 n6	0.1	0.1–0.2	0.2	0.1–0.2	0.2	0.1–0.2	0.3**	0.2–0.4
20:4 n6	0.8	0.6–1.3	0.7**	0.5–1.0	0.9	0.7–1.5	0.8*	0.6–1.0
20:5 n3	0.3	0.0–0.4	0.3	0.2–0.4	0.3	0.0–0.4	0.3	0.0–0.4
22:6 n3	0.8	0.3–1.4	0.5	0.3–0.9	0.8	0.5–1.1	0.7	0.4–0.8
X	19.6	17.5–22.6	18.5	16.7–23.2	21.5	18.0–25.1	21.0	16.7–23.1

Results are given as relative per cent of fatty acids presented (median and range).
*$p < 0.05$, **$p < 0.01$: significant changes during treatment.
X (14:0, 16:1 n7, 18:1 n7, 22:0, 22:4 n6 and 22:5 n3) = sum of the remaining FA analysed.

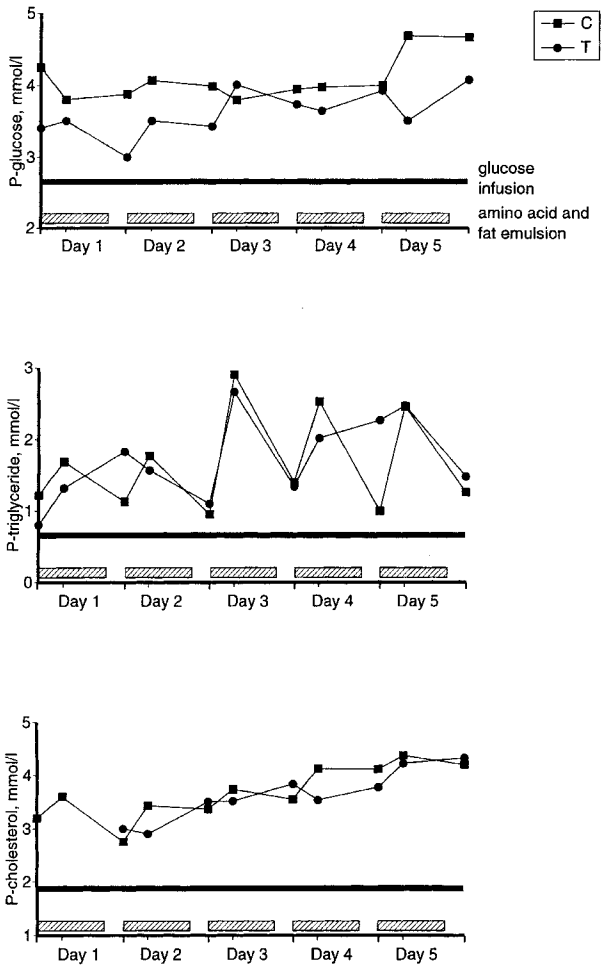

Fig. 1. Plasma glucose, triglyceride and cholesterol concentrations (mean values) from d 1 to d 5 in the Intralipid® control group (C) and the group that received PFE 4501 (treatment group, T). No significant differences were observed either between the two groups on each day or between the changes from d 1 to d 5 in each group.

be that the enzymes delta-6 and delta-5 desaturase are inhibited by excess substrate (16).

Although the desaturase enzymes are known to show a preference for n-3 over n-6 fatty acids, high plasma concentrations of LA have been shown to inhibit the metabolism of alpha-linolenic acid to eicosapentaenoic acid (EPA, 20:5 n-3) and DHA (16). This might explain the reduction of long-chain n-3 fatty acids in spite of the relatively high concentrations of alpha-linolenic acid in both emulsions. Long-chain fatty acids are incorporated in the structural phospholipids of cell membranes. The composition of the membrane lipids will determine the membrane functions, such as receptor activity, transmembrane transport and enzyme activity. DHA in particular is important for brain and retinal development. Deficiency of DHA and also of AA in early life is known to result in learning difficulties and visual dysfunction which may be irreversible (17, 18).

In adults the composition of fatty acids in adipose tissue is a reliable marker of the dietary fat composition over a long period (up to 1 y), indicating a slow turnover in the adult's fat depot (19). In the present study the relative percentage of values of LA and linolenic acid in adipose tissue increased in both groups after 5 d of TPN, an indication that the fatty acids in adipose tissue of newborns are rapidly accreted.

It has been shown that the plasma carnitine concentration decreases during carnitine-free parenteral feeding (20–22), and when this feeding lasted more than 10 d the tissue carnitine levels were also lowered (23). In the present study the plasma carnitine concentration tended to decrease after only 5 d in the control group receiving the carnitine-free Intralipid®.

The clinical consequences of the decrease in plasma and eventually tissue carnitine concentrations are not fully known. Several investigations have been conducted concerning the effect of carnitine supplementation on fatty acid oxidation in term and preterm infants. With carnitine dosages in the range of 8–16 mg kg^{-1} d^{-1}, no or only subtle effects were found, such as an increase in 3-hydroxybutyrate and/or a decrease in the free fatty acid (FFA) concentration or FFA : 3-hydroxybutyrate ratio (22, 24–27). In one study improved nitrogen retention was also observed (27). Several adverse effects were noted when carnitine supplementation was given in a high dosage (48 mg kg^{-1} d^{-1}) to low-birth-weight infants during their first postnatal week (2). The treated group showed higher fat and protein oxidation and also took a longer time to regain their birth weight compared with the control group.

The final carnitine dosage used in the present study, approximately 8 mg (50 μmol) kg^{-1} d^{-1}, resulted in a two-fold increase in the mean plasma carnitine concentration, which was still in the range of the highest values that can be seen physiologically (28). No beneficial or adverse effects were observed in routine and biochemical tests reflecting lipid and carbohydrate metabolism.

In conclusion, supplementation of the new fat emulsion with GLA did not increase the relative concentration of AA in plasma and adipose tissue as expected. In spite of the relatively high concentration of alpha-linolenic acid in both emulsions, a reduction of the important long-chain n-3 fatty acid DHA was observed in both groups. This reduction during long-term parenteral nutrition may have a negative impact on the development of the neonate.

The possible benefit of the use of prophylactic carnitine supplementation is an issue that is not yet resolved, especially in the perinatal period. In spite of low tissue carnitine levels, the individual infant may be asymptomatic (29). However, such low levels may be potentially harmful in situations where the organism has to depend on fatty acids as an energy source, such as prolonged starvation and metabolic stress.

Further long-term studies are needed to elucidate the potential benefit of carnitine supplementation and to ascertain the optimal fatty acid composition of a lipid emulsion for neonates.

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