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Effect of enteral feeding on lipid subfractions in children with chronic renal failure

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Abstract. The anorexia of chronic renal failure (CRF) is frequently managed with enteral feeds using combinations of commercial preparations, glucose polymers and fat emulsions. Such feeds might predispose to atherogenic blood lipid profiles. Our aim, therefore, was to compare the blood lipid profiles of enterally fed and non-enterally fed children. Plasma lipid subfractions were measured in 37 children with CRF managed conservatively and 10 managed with peritoneal dialysis (PD); 10 of the children were tube fed, 5 of whom were on PD. Results were compared between these groups. Overall, triglycerides (TGs, mean ± SD) were high (2.3 ± 1.4 mmol/l) and total cholesterol (TC) was at the upper limit of normal (5.2 ± 1.5 mmol/l). Low-density lipoprotein (LDL), high-density lipoprotein (HDL), apoprotein A1 (apo A1), A2 (apo A2) and B (apo B), and lipoprotein (a) [Lp(a)] were within the normal range. There was an inverse correlation between TGs and glomerular filtration rate (P = 0.0001). There were no differences in the levels of TC, TG, LDL, HDL, apo A1, apo A2 or Lp(a) between tube-fed and non-tube-fed children. We conclude that enteral feeding does not enhance hyperlipidaemia.

Key words: Chronic renal failure – Lipids – Lipoproteins – Enteral feeding

Introduction

Hyperlipidaemia is one of the factors believed to be responsible for the high incidence of atherosclerosis in chronic renal failure (CRF) [1]. Abnormalities of lipids and lipoproteins reported in CRF include: increased triglycerides (TGs), total cholesterol (TC), low-density lipoprotein (LDL), apoprotein B (apo B) and lipoprotein(a) [Lp(a)], and reduced high-density lipoprotein (HDL), apo A1 and apo A2 [2], all of which are believed to predispose to atherosclerosis. Studies in children have demonstrated similar findings, but with a higher incidence of hypercholesterolaemia [3].

As well as the metabolic effects of CRF, the blood lipid profiles of patients may be influenced by their diet. High intakes of saturated fatty acids (FAs) increase serum LDL and TGs. Polyunsaturated FAs reduce LDL, but at the same time also reduce HDL [4], which is protective against coronary heart disease [5]. Monounsaturated FAs lower both LDL and TGs, and are associated with higher levels of HDL. High intakes of refined carbohydrate (CHO) increase TGs and reduce HDL [4].

It is our policy to institute early enteral feeding in children with CRF with a declining growth velocity. Such feeds are based on whole-protein (and occasionally protein hydrolysate) complete feeds and are supplemented with glucose polymers and/or peanut oil emulsions as additional energy sources. The children eat little or no complex CHO or non-starch polysaccharides (fibre), so most of their intake of CHO is refined. We were concerned, therefore, that while providing adequate nutrition for growth, tube feeding regimens might have an adverse effect on the blood lipid profiles of the children.

Our purpose was to study the lipid profiles of children attending our CRF clinic who were eating a high-energy, low-phosphate, but otherwise unrestricted diet and to compare the results with those of a group of children who were receiving at least 50% of their energy as an enteral feed.

Patients and methods

Patients. Forty-seven children (32 boys) aged 1–17 years [mean 9.3 ± 5.2 (SD)] with CRF [defined for the purposes of this study as a plasma creatinine concentration >150 μmol/l (1.7 mg/dl)] were studied. Thirty-seven were managed medically, 5 of whom were enterally fed. The other 10 were receiving peritoneal dialysis (PD), 5 of

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Table 1. Serum lipid subfractions[a]

Groups	(1) Medically managed	(2) Enterally fed	(3) Peritoneal dialysis (PD)	(4) Enterally fed and on PD	Normal values	*P* value (ANOVA)
Number	32	5	5	5		
Age (years)	11.1 (0.8)	2.3 (0.6)	12.3 (2.0)	3.9 (0.8)		<0.0001
Creatinine (μmol/l)	344 (25)	415 (98)	777 (130)	516 (40)		<0.0001
Height SDS	–1.1 (0.2)	–2.7 (1.3)	–2.5 (0.4)	–2.1 (0.2)		0.025
Body mass index	18.9 (0.5)	17.1 (1.4)	20.3 (0.9)	20.5 (2.6)		0.33
TG (mmol/l)	1.8 (0.2)	2.4 (0.5)	3.9 (0.4)	2.7 (0.8)	<1.7	0.002*
TC (mmol/l)	5.1 (0.3)	4.2 (0.6)	6.1 (0.6)	5.1 (0.4)	<5.2	0.25
LDL (mmol/l)	3.0 (0.3)	2.4 (0.2)	3.6 (0.7)	2.8 (0.3)	<3.3	0.55
HDL (mmol/l)	1.3 (0.1)	1.3 (0.5)	1.1 (0.1)	1.0 (0.1)	1.0–2.0	0.59
apo A1 (g/l)	1.7 (0.1)	1.8 (0.5)	1.5 (0.1)	1.5 (0.2)	0.7–1.7	0.75
apo A2 (g/l)	0.6 (0.02)	0.7 (0.04)	0.8 (0.07)	0.7 (0.04)	0.3–0.8	0.0002*
Apo B (g/l)	1.1 (0.07)	0.9 (0.17)	1.5 (0.18)	0.9 (0.20)	0.6–1.4	0.03
Lp(a) (g/l)	0.18 (0.03)	0.14 (0.06)	0.3 (0.04)	0.23 (0.03)	<0.3	0.47

ANOVA, Analysis of variance; SDS, standard deviation score; TG, triglyceride; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; apo A1, apoprotein A1; Lp(a), lipoprotein (a)

* Insignificant when adjusted for age and creatinine by analysis of covariance

[a]Values expressed as mean (SEM)

Table 2. Enteral feed composition[a]

Source	Total energy intake (%)		
	Enteral feeds	Dietary reference values[b]	Dietary and nutritional survey (OPCS)[c]
Feed	86.5 (5.0)		
Protein	8.1 (1.2)	15	15
Carbohydrate	58.3 (3.8)	50	42
Total fat	32 (3.7)	35	38
Saturated FAs	10.1 (1.6)	11 (+2% *trans*)	16
Monounsaturated FAs	13.3 (2.4)	13	12
Polyunsaturated FAs	6.6 (0.8)	6.5[d]	6

FA, Fatty acid; *trans*, transpolyunsaturated FA

[a] Values expressed as mean (SEM)

[b] Dietary reference values for food energy and nutrients for the United Kingdom [17]

[c] The Dietary and Nutritional Survey of British Adults [18]

[d] Maximum recommended 10% of total energy intake

whom were enterally fed (Table 1). The mean (range) glomerular filtration rate (GFR) of the medically managed children was 15 (5–35) ml/min per 1.73 m^2. Children with nephrotic syndrome were excluded because of its effect on lipid metabolism [5].

The mean (range) length of time on enteral feeds was 18.2 (6–32) months. The feeds were prepared from whey-based infant formulae or cows' milk protein-based adult enteral feeds, and were delivered by pump overnight. One child received a soya-based feed because of parental suspicion of cows' milk protein intolerance. One received a whey hydrolysate to enhance stomach emptying. All feeds included a comprehensive range of vitamins and minerals. The aim was to offer adequate nutrition for growth, while maintaining blood chemistry within acceptable parameters by the provision of at least the estimated average requirement for energy for chronological age using additional glucose polymers and peanut oil emulsions, and reference nutrient intake for protein for height age (dietary reference values, Table 2).

Table 2 shows the tube feed composition for protein, CHO and FAs, and the corresponding United Kingdom recommended dietary intakes for a healthy population. Also shown are the observed dietary intakes of British adults (comparable figures are not available for children). The dietary intake of the non-tube-fed children was not assessed formally: they were recommended to eat the family diet but with an emphasis on high-energy, low-phosphate foods.

Older children were fasted overnight prior to blood sampling, but younger children were fasted for at least 4 h (although they were allowed water). This length of time has been used in other large studies [6]. Serum TC, TG, LDL, HDL, apo A1, apo A2, apo B and Lp(a) and plasma creatinine were measured.

Lipid subfractions were compared between the four patient groups (Table 2) using analysis of variance. Analysis of covariance (ANCOVA) was used to adjust for age and creatinine when a significant difference was found between groups. A significant *P* value was defined as <0.05. Each subject and/or their parents gave informed consent to the study, which was approved by the local committee on ethical practice.

Methods. TC was measured using the cholesterol C system high-performance cholesterol oxidase 4-aminophenazone method and TG by glyceryl phosphate oxidase 4-aminophenazone high-performance enzymatic colorimetric test (both Boehringer Mannheim Diagnostica) [7]. HDL was measured following precipitation of apo B-containing lipoproteins and LDL was calculated using the Friedewald formula [8]. apo A1 and apo B were measured using immunoturbidimetry (Immuno, Sevenoaks, Kent, UK) [9], and Lp(a) by enzyme-linked immunosorbent assay (Immuno) [10]. GFR was estimated from the clearance of ^{51}chromium EDTA [11] or by the Schwartz formula [12].

Results

Children who were managed medically and on PD without enteral feeds (groups 1 and 2) were older than the enterally fed children. Medically managed children were taller, but there was no difference in body mass index among the four groups.

The results of the lipid subfractions are shown in Table 1. TGs were elevated in all groups. Figure 1 illustrates the relationship between serum TGs and method of feeding, plasma creatinine and treatment modality. There was an overall positive correlation between TGs and creatinine ($r = 0.63$, $P < 0.0001$). However, there was no difference among the patient groups when the results were corrected for age and creatinine (ANCOVA $P = 0.07$). There was also a negative correlation between TGs and GFR in children in

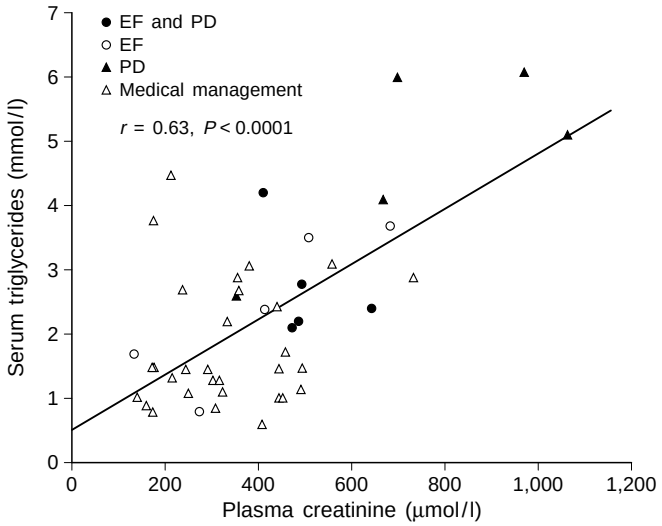

Fig. 1. Effect of method of feeding, plasma creatinine and treatment modality on serum triglycerides. *EF*, Enteral feeding; *PD*, peritoneal dialysis

group 1 ($P = 0.0001$), even when age was taken into consideration.

Children managed by PD (group 3) were the only group with levels of the atherogenic lipids TC, LDL and apo B that were above the normal range, although TC levels were at the upper limit of normal in the other groups. However, only apo B was significantly higher in children on PD when adjusted for age and creatinine (ANCOVA $P = 0.01$). No other lipid subfractions were abnormal in any other group. There was no correlation between GFR and any lipid subfraction other than TGs.

Discussion

In this study we have confirmed previous reports that hypertriglyceridaemia correlates inversely with GFR in CRF, and that TC is at the upper limit of the normal range [2, 3]. Our patients did not, however, have abnormalities of apo A1, apo A2, apo B and Lp(a), which have been found in some, although not all, previous studies [2, 3]. Angiographic studies have shown that low apo A and high apo B (or their ratio) may be better indicators of future coronary heart disease than HDL levels [5]. HDL, high levels of which protect against vascular disease, was reduced in previous studies [2, 3], but was also normal in our patients.

We were concerned that the enteral feeds we give to our patients might have an adverse effect on their blood lipids and lipoproteins. The value of tube feeding in the promotion of catch-up growth is well established [13, 14]. However, such feeds contain added glucose polymerase and fat emulsions which may be atherogenic. Ingestion of a bolus of refined CHO causes an increase in TGs and reduces HDL, and a high intake of saturated fat raises TGs and LDL [4]. Furthermore, an imbalance of mono- and polyunsaturated fat can also promote atherogenesis by reducing HDL [4].

However, we achieved a balanced energy intake with our enteral formula composition, which did not differ significantly from published recommendations for dietary intake for a normal population. Indeed, the total fat intake, and particularly the saturated fat intake, was less in the tube-fed children than in a normal adult population eating an unrestricted diet (Table 2). Despite a CHO intake comprised mainly of refined sugars rather than a mixture of sugars, starch and fibre, there was no adverse effect on serum TGs and HDL.

Although the children were under regular dietary review, we were not able to fully analyse the intakes of those who were not tube fed because there are only a few foods that have been analysed for their FA composition. As these children were eating a relatively free diet rather than receiving a precisely prescribed enteral feed, it is possible that their diet was less balanced than that of the tube-fed children.

It might be expected that the glucose load during PD would have an adverse effect on plasma lipids, resulting in hypertriglyceridaemia and decreased HDL [15]. Although the patients on PD were the only group to have levels of atherogenic lipids above the normal range, those on PD who were enterally fed did not. One possible explanation is that the enteral feed was beneficial to the plasma lipids, but the numbers are too small to draw any conclusions.

All the children had high TG levels. The importance of TGs in atherogenesis is controversial, but recently it has been found that hypertriglyceridaemia is associated with a high proportion of small, dense LDL, which is now recognised to be particularly atherogenic. Although overall the lipid fractions that we measured were at acceptable levels, we did not study those subfractions that are now recognised as important [16].

In conclusion, this small study would suggest that an enteral feeding regimen providing an appropriate energy intake with a balanced profile of fat and CHO can be administered to children with CRF who are both conservatively managed and on PD, without detrimentally affecting their serum lipids.

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Literature abstracts

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Pharmacokinetics of tacrolimus (FK 506) in children and adolescents with renal transplants

G. Filler, R. Grygas, I. Mai, H. J. Stolpe, C. Greiner, S. Bauer, and J. H. H. Ehrich

Background. Only few data exist on pharmacokinetics of tacrolimus in children.
Patients. In 1995 and 1996, 14 children (mean age 13 years, range 5–23 years) received tacrolimus after renal transplantation; 10 of these after biopsy-proven steroid-resistant rejection (2 with vascular rejection), two for cyclosporin A (CsA)-induced severe nephrotoxicity, one for untreatable gingival hyperplasia on CsA, and one child was treated primarily after transplantation because of severe liver involvement in nephronophthisis. Pharmacokinetic investigations were performed after establishing a stable maintenance dose with trough levels in the desired window of 5–12 ng/ml.
Results. Mean follow-up time was 6 months (range 3–25 months). Eleven patients are still on tacrolimus. Two were discontinued because of severe aggravation of chronic persistent hepatitis C (one of them also developed diabetes mellitus), and one patient was subsequently switched to conventional immunosuppression because of tacrolimus-associated nephrotoxicity. All tacrolimus levels were measured by a modified assay (MEIA, Tacrolimus, Abbott) with improved sensitivity. At the time of switch, median serum creatinine was 234 ± 82 µmol/l and 6 months after switch 201 ± 99 µmol/l. All grafts are still functioning. Mean FK-506 dose was 0.16 mg/kg body weight/day (range 0.036–0.30 mg/kg). Mean trough level was 7.1 ± 2.6 ng/ml in the morning and 6.5 ± 2.0 ng/ml in the evening. Median time of maximum concentration (t_{max}) was 120 min after application, and the mean maximum concentration (C_{max}) was 15.2 ± 6.7 ng/ml. Mean area under the curve (AUC) was 104 ± 33 ng * h/ml, with a range from 65 to 169 ng * h/ml. No patient had unsatisfactorily low trough levels during the study. There was only a weak but significant ($P < 0.05$) correlation between dose per kg body weight and AUC and, as expected, an excellent correlation ($r = 0.73$, $P < 0.001$) between AUC and trough level.
Conclusion. Because of interindividual variation between patients, therapeutic drug monitoring of tacrolimus is mandatory. In this study, a daily dose of 0.15 mg/kg was sufficient in most patients. We recommend the performance of at least one pharmacokinetic study after establishing stable FK 506 trough levels to ascertain a safe profile.

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Immunity of diphtheria and tetanus in a young population on a dialysis regimen or with a renal transplant

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In 54 transplant recipients diphtheria and tetanus immunity after primary vaccination was significantly lower than in 57 control subject and 35 patients on a dialysis regimen. After a booster, tetanus antibodies developed in the transplant recipients and dialysis patients but no diphtheria antibodies developed in two transplant recipients. No adverse reactions, including acute graft rejection episodes, occurred.