Fat as an energy supplement for preterm infants

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SUMMARY   The absorption and utilisation of dietary fat as an energy supplement was studied in 15 healthy preterm infants. They were given two formulae for periods of one week. The standard low solute feed supplied 6 g fat and 476 kJ (114 cal) per kg. The high energy feed supplied 10 g of the same fat and 623 kJ (149 cal) per kg. Fat supplementation resulted in increased absorption (significantly higher chylomicron levels) without steatorrhoea or metabolic disturbance, apparently unchanged differential absorption of fatty acids, and a significantly higher rate of weight gain (mean 25·9 ± 4·6 compared with 20·3 ± 4·4 g/24 h). A high energy formula prepared with supplements of complex dietary fat is therefore of potential value in ensuring the adequate nutrition and growth of preterm infants.

The gastrointestinal energy losses of preterm infants are high[1] and increase the already considerable energy requirements for growth which, if not met, may place infants at risk from malnutrition. In order to meet such energy requirements an alternative to the standard milk feed has been proposed. As large feed volumes are poorly tolerated high energy formulae have been used in attempts to improve energy balance. Although hyperosmolality is avoided by the use of fat as an energy supplement, immaturity of digestive and absorptive processes may limit the usefulness of fat in clinical practice. We have therefore studied the absorption and utilisation by preterm infants of dietary fat when the proportion in a standard feed is increased.

Patients and methods

With parental consent we studied 15 preterm infants of similar gestations and birthweights but of varying postnatal ages; clinical details are given in Table 1. All were well and already gaining weight steadily. Nearly all had regained their birthweights. None was breast fed and all had received a full strength low solute cows' milk formula supplying 2720 kJ/l (650 cal/l) for at least a week.

The two milk feeds differed in fat and energy content. The standard feed, Premium*, was a low solute modified cows' milk formula containing butterfat and vegetable oils. The high energy feed was prepared by Cow and Gate at our request using an energy supplement of the same fat. No change

was made to the protein, lactose, mineral, or vitamin content, although the percentage of protein energy was reduced by the addition of fat. The composition of both milk feeds is shown in Table 2. A volume of 175 ml/kg a day was chosen. This supplied infants on the standard feed with 6 g fat and 476 kJ (114 cal) per kg, and those on the high energy feed with 10 g fat and 623 kJ (149 cal) per kg.

Infants were randomly allocated to two groups. Eight infants received the standard feed first and 7 infants the high energy feed first. All received each feed for one week. Feeds were given at 2- or 3-hourly intervals either by nasogastric tube or bottle. The

Table 1   *Clinical details of 15 preterm infants*

Case	Sex	Gestation (weeks)	Birthweight (g)	Age at start of study (days)	Weight at start of study (g)
1	F	31	1530	22	1710
2	M	28	870	70	1700
3	F	31	1540	13	1510
4	F	31	1320	39	1550
5	M	32	1480	11	1560
6	F	28	1030	30	1350
7	M	31	1550	16	1610
8	F	30	1120	62	2060
9	M	27	1100	36	1590
10	F	28	1090	17	1180
11	F	32	1680	11	1670
12	F	29	1310	27	1520
13	M	30	1420	21	1690
14	F	31	1600	12	1640
15*	M	32	1050	15	1190
Mean		30	1310	27	1570
SD		1·7	250	18	220

*Small for gestational age.

Table 2   *Approximate composition of standard and high energy formulae (per 1 prepared feed)*

Formula	Fat (g)	Protein (g)	Casein (g)	Whey (g)	Protein energy %	Lactose (g)	Minerals (g)	Energy kJ (Cal)	
Standard	34·5	18·0	5·7	12·3	11·0	69·0	3·5	2720	(650)
High energy	57·2	18·0	5·7	12·3	8·9	69·0	3·5	3550	(850)

Energy 1 Cal ≈ 4·18 kJ.

high energy feed was not introduced in graduated strengths and was well tolerated. Daily weighing to the nearest 10 g ensured that feed volumes were increased as necessary.

After 6 days, stools were collected over a 24-hour period, during which cream was not applied to the napkin area, and urine was collected in an adhesive bag and drained intermittently. Fresh stool specimens were collected on polyethylene and frozen immediately in a sealed container. On completion each stool collection was weighed and homogenised. Aliquots were taken for analysis : water content by drying to constant weight, total lipid content by a spectrophotometric micromethod based on the sulfophosphovanillin reaction,[2] fatty acids by gas chromatography,[3] and sugars by thin layer chromatography.[4] After each 7-day period a prefeed sample of plasma was obtained for standard biochemical analysis, estimation of lipoproteins by nephelometry, and cholesterol by a specific enzyme method.

In view of the influence of maturity and postnatal age on gastrointestinal function each infant was used as his own control. Statistical comparisons of paired values for each infant and values for all infants on each milk feed were then made using the *t* test.

Results

The results of stool analyses are given in Table 3. Stool collection from one infant was abandoned because of irritation by the urine bag and in 4 infants one stool collection was discarded after contamination with urine. As a result there were 10 pairs and groups of 11 and 14 infants. No significant difference in stool water or pH was found, but the stool lipid content while on the high energy feed was significantly higher (pairs $P<0·005$, groups $P<0·01$).

Table 4 shows how the faecal fatty acid profile after each milk differed from the milk fatty acid profile. Medium chain fatty acids appeared to be well absorbed but with increasing chain length and saturation the proportion absorbed decreased. Faecal fatty acids profiles after the two milk feeds were not significantly different from each other.

The semi-quantitative stool sugar analysis showed glucose (∼25–50 mg/100 ml), galactose (∼50/150 mg/100 ml), and lactose (occasional trace) irrespective of feed. Chromatography of the stool fluids after hydrolysis in 1 mol/l hydrochloric acid showed a 2- to 5-fold increase in glucose and galactose and the appearance of fucose.

Standard plasma biochemical analysis did not show abnormalities or significant differences between pairs and groups. The plasma calcium level of infants on the high energy feed (2·33 ± 0·13 mmol/l; 9·32 ± 0·52 mg/100 ml) was similar to that of infants on the standard feed (2·29 ± 0·17 mmol/l; 9·16 ± 0·68 mg/100 ml).

Table 4   *Fatty acid composition of milk and stool fat from preterm infants on standard and high energy formulae (%)*

Principal fatty acids	Milk fat	Stool fat			
		Standard (11)		High energy (15)	
		Mean	SD	Mean	SD
Total saturated	47·5	61·6	6·6	58·1	7·2
$C_{10}:0$	2·0	—	—	—	—
$C_{12}:0$	8·5	2·0	0·4	1·9	0·6
$C_{14}:0$	7·5	5·0	0·5	4·9	0·9
$C_{16}:0$	18·0	29·5	3·8	27·7	4·2
$C_{18}:0$	7·0	25·1	3·4	23·6	3·6
Others	4·5	—	—	—	—
Total unsaturated	52·5	38·4	6·6	41·9	7·2
$C_{16}:1$	3·0	1·0	0·6	1·1	0·5
$C_{18}:1$	33·5	28·4	2·7	31·5	5·4
$C_{18}:2$	14·5	9·0	4·4	9·3	2·6
$C_{18}:3$	0·5	—	—	—	—
Others	1·0				

Table 3   *Analysis of stool from preterm infants on standard and high energy formulae*

Formula	Infants	Fat (g/100 g)		Water (g/100 g)		pH	
		Mean	SD	Mean	SD	Mean	SD
Standard	11	7·1	3·9	75	11	6·3	0·6
High energy	14	12·3*	4·9	72	8	6·2	0·3

*Grouped data: *t* 2·87 $P<0·01$, paired data (not shown but similar): *t* 3·73 $P<0·005$, from 10 infants.

Table 5 *Prefeed plasma lipoprotein profile at one week in 15 preterm infants on standard and high energy formulae*

	Chylomicrons (g/l)		Pre β-lipoproteins (g/l)		β-lipoproteins (g/l)		Cholesterol (mmol/l)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Standard	0·45	0·22	1·69	0·89	2·32	1·27	3·1	0·8
High energy	1·18*	0·35	1·82	1·06	1·92	0·56	2·9	0·7

*Grouped data: *t* 6·84 P<0·001, paired data: *t* 7·06 P<0·001.
Conversion SI to traditional units—cholesterol: 1 mmol/l ≈ 38·7 mg/100 ml.

The high energy feed resulted in chylomicron levels which were higher in 14 infants and lower in one. There was a significant difference between the pairs (P<0·001) and between the groups of infants on each milk (P<0·001). Levels of pre-β-lipoprotein which reflect triglyceride clearance, cholesterol, and β-lipoprotein, did not change significantly. These results are shown in Table 5.

The high energy feed was associated with rates of weight gain which were higher in 11 infants, unchanged in one, and lower in 3 infants when comparisons with the standard feed were made (mean daily weight gain on high energy feed 25·9 ± 4·6; on standard feed 20·3 g ± 4·4). There were significant differences between the 15 pairs (P<0·01) and between the two groups (P<0·005).

Discussion

In the neonatal period the mechanisms of fat absorption are immature.[5-8] It has been estimated that at birth term infants absorb between 85 and 90% of their dietary fat, and preterm infants between only 65 and 75%.[1] Energy retention increases with maturity and postnatal age [9 10] and by 4–6 months the proportion approaches adult values of 95%.[11] Nevertheless, it is well known that increased fat intake results in greater net fat absorption in preterm infants.[12]

The pronounced variation in fat absorption by neonates reflects the rapidly changing functional maturity of the various processes of digestion and absorption. In this study the use of each infant as his own control has reduced the influence of physiological variation as far as possible.

The higher chylomicron levels are evidence of the increased absorption of dietary fat from the high energy formula. Despite this greater absorption the proportion of faecal fat increased. It is known that as fat intake increases less is absorbed, and a point of maximal absorption is reached; any additional increase then results in an almost identical rise in faecal fat.[13] We have not calculated coefficients of absorption for the dietary fat in this study in view of the limitations which a 24-hour collection

period imposes. Macroscopically, all stools appeared normal. Daily fat excretion was considerably less than 2 g/kg so by definition steatorrhoea did not occur.

The relationship between fat excretion and calcium absorption is controversial; [13 14] in our study no change in dietary calcium was made and no significant effect on plasma calcium was demonstrated during the study period.

In all stools, reducing sugars were found in only small quantities and are unlikely to have interfered with fat absorption. The appearance of fucose and increased quantities of glucose and galactose after stool fluid hydrolysis probably indicates the presence of oligosaccharide material—such as fucosyllactose.

The absorption of a fatty acid is influenced by its position within the triglyceride molecule,[15 16] competition from other fatty acids,[17] the composition of dietary fat[17] and, as we have confirmed, by chain length[17 18] and saturation.[19] The mechanism by which fatty acids are absorbed remains unknown. Specific receptors have not been identified. The extracellular concentration, pH, specificity of lipase, and adequacy of micelle formation are all important influences but the passive absorption and cellular transport of long chain fatty acids is also facilitated by an intracellular soluble fatty acid binding protein. Found predominantly in villi from the proximal and middle intestine its concentration varies in response to changes in dietary fat.[20] We would expect the activity of this protein to vary with maturity and further limit the absorption of long chain fatty acids by preterm infants.

The faecal fatty acid profile is influenced not only by dietary composition and differential absorption in the small-bowel but also by bacterial hydrogenation in the large-bowel and endogenous lipid from sources such as bile and intestinal debris. By minimising these influences and avoiding qualitative change we were able to study the effect of an increase in dietary fat on differential absorption. The hydrogenation of unsaturated fatty acids by bacteria[21] can be prevented by analysis within 24 hours of specimens stored at room temperature.[18] We chose to freeze stool samples during the collection period

and did the analysis as soon as this was completed. Branched chain and odd numbered fatty acids are also produced by bacteria[18] and as significant amounts were not found we can assume that the influence of bacteria was negligible. The small proportion of faecal linoleic acid suggests that endogenous biliary lipid was also of minimal influence.[18] Our results therefore indicate that the differential absorption of fatty acids is unchanged by a quantitative increase in dietary fat.

A high energy formula will only be of value if it promotes increased energy retention and growth. Although the study was brief, we found that the rate of weight gain of infants on the high energy feed was significantly greater than that on the standard formula. However, the 4 infants who failed to gain weight at an increased rate all showed evidence of increased fat absorption. That this could be due to the decrease in percentage of protein energy that follows the addition of dietary fat is unlikely. The proportion of protein energy in the fat supplements feed remained higher than that in breast milk and a protein:energy ratio conducive to normal growth was preserved.[10] However, the use of a high energy formula[10] or failure to ensure a neutral thermal environment can increase energy expenditure. Such variations in energy utilisation might explain why not all the 15 infants gained weight at an increased velocity on the high energy formula.

In this study the fatty acid content of the standard feed was similar to that of breast milk. We have shown that the use of a high energy feed, prepared with supplements of this fat, results in increased fat absorption and in increased nutrition and growth of preterm infants, particularly those unable to tolerate large feed volumes.

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