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Nutrition of newborns small for gestational age with human milk lyophilisate enriched human milk during the first week of life

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In 24 very low birth weight infants appropriate or small for gestational age, the metabolic response to nutrition with human milk lyophilisate enriched human milk was estimated during the first week of life.

In contrast to newborns appropriate for gestational age, in newborns small for gestational age signs of metabolic overloading could be observed: increased urinary amino acid excretion and neonatal cholestasis. Both depended on the degree of fetal growth retardation.

It was concluded that nutrition with human milk lyophilisate enriched human milk cannot be recommended for very low birth weight infants during the first week of life. In newborns small for gestational age the metabolic situation has to be estimated before starting a high protein diet. If the level of total bile acids amounts to more than 30 μmol/l, protein intake should be increased carefully during the first week of life.

In the first days of life pooled human milk (HM) is sufficient for the enteral nutrition of newborns weighing at birth less than 1500 g. This is due to the low concentration of protein and energy substrates of pooled HM on the one hand and the limited capacity of the gastrointestinal tract on the other hand [4]. As parenteral nutrition is affected by metabolic imbalance, nosocomial infections and some other factors [5, 14], concentrated formulae [1, 9, 10, 18] or enriched HM [13, 17, 19] are desired for the nutrition of these newborns. Most of these recommendations have been given for very low birthweight infants independent of their intrauterine development [9, 10, 17, 18, 19].

In a previous study it has been shown that in newborns with a birthweight lower than 1500 g and severe fetal growth retardation the metabolic capacity is decreased during the first days of life [7]. In these newborns feeding with native HM led to increased cholestasis while in newborns weighing more than 1500 g with only mild fetal growth retardation the metabolic response to enteral feeding with native HM showed no difference as compared to newborns appropriate for gestational age (AGA) [6].

The present study had the aim to clarify whether very low birthweight infants with mild fetal growth retardation could be nourished with enriched HM without any risk during the first week of life.

Patients

Eleven premature AGA newborns fed human milk lyophilisate (HML) enriched HM (Group 1), five premature SGA newborns between the 5th and 10th percentile according to Lubchenco et al [16] fed HML enriched HM (Group 2), and eight premature SGA newborns with the same degree of fetal growth retardation (FGR) as in Group 2, fed native HM were studied. All of them were without signs of evident illness, especially without idiopathic respiratory distress syndrome, persistent fetal circulation, and bacterial infectious disease.

In Table I details of the infants studied are given.

Table I

Details of the infants studied

Group	1	2	3
Weight at birth, g	1396.4 (1270—1460)	1310.6 (1160—1420)	1385.0 (1250—1410)
Length at birth, cm	40.9 (36.5—43.0)	43.4 (37.5—45.0)	44.2 (39.5—45.5)
Gestational age, weeks	29.9 (29—31)	32.2 (31—33)	32.6 (32—33)
Intrauterine development	appropriate for GA	small for GA	small for GA
Nutrition	HM[1] + HML[2]	HM + HML	native HM
Number	11	5	8

[1] Human milk [2] Human milk lyophilisate

Methods

During the first week of life the following parameters were estimated daily: nitrogen intake (Kjeldahl method), urinary nitrogen losses (Kjeldahl method), alpha amino nitrogen excretion (ninhydrin method) and body weight. On the 2nd, 4th, 6th and 8th days, serum alpha nitrogen concentration and the acid base balance (Astrup method) were measured. On the 8th day of life the serum bile acid concentration (according to Senger et al [22]), and the amount of stools were also estimated.

To have comparable nitrogen intakes within the different groups, only milk from mothers delivering preterm babies was used for nutrition as well as for lyophilisation. In Table II the composition of native HM, and HM enriched with HML are given, and Table III shows the mean daily nitrogen intake in the different groups during the first week of life.

Within the first 8 hours of life it was decided whether or not a predominant enteral nutrition should be started. The volume of enteral feeding was 45 ml/kg BW as a maximum on the first day of life, and this was increased to 200 ml/kg BW by the 8th day of life. Depending on the clinical course, supplementary parenteral nutrition with nitrogen free solutions was given during the first two days of life.

Enteral nutrition was realized by nasogastric tube two hourly.

For statistical analysis, Student's t test was applied.

TABLE II

Composition of native pooled human milk (HM) and human milk lyophilisate enriched human milk (HM + 6 g HML/dl) used in this study (M ± SD)

	GM	HM + 6 g HML/100 ml
Protein (g/l)	11.8±1.2	15.8±2.1
Fat (g/l)	41.4±4.9	55.4±6.1
Lactose (mmol/l)	174.2±16.2	242.6±20.8
Osmolality (mosmol/l)	291.6±11.2	384.9±19.6

TABLE III

Daily (M ± SD) nitrogen intake (mmol/kg BW/24 h) in the different groups during the first week of life

Day	Group 1	Group 2	Group 3
1	6.3±0.5	6.5±0.7	6.0±0.2
2	13.9±0.9	14.7±1.0	11.1±0.3
3	18.4±0.8	18.7±0.9	13.9±0.3
4	21.5±0.8	21.5±0.8	16.7±0.3
5	25.3±0.9	25.1±0.8	19.8±0.4
6	28.9±0.9	29.1±0.9	22.1±0.4
7	32.4±1.1	32.5±1.0	24.9±0.5
8	35.4±1.1	35.7±1.1	27.6±0.6

RESULTS

During the balance periods there were no signs of an enteral volume overloading. During the study three patients had to be excluded owing to disturbances in which predominant enteral nutrition was impossible. These patients were, one with persistent ductus arteriosus observed on the 3rd day of life, one with intracranial haemorrhage on the 2nd day of life, and one patient affected by *E. coli* infection on the 6th day of life. Disturbances of acid base balance were not observed in any infant during the study.

The renal nitrogen losses were not significantly different. Even if there was an increasing nitrogen excretion in SGA newborns fed HML enriched HM from the 6th day of life, the differences were not significant (Fig. 1). The slightly higher nitrogen excretion in this group was caused by a significantly higher urinary alpha amino nitrogen excretion from the 2nd day of life (Fig. 2). There were no significant differences between Group 1 and Group 3.

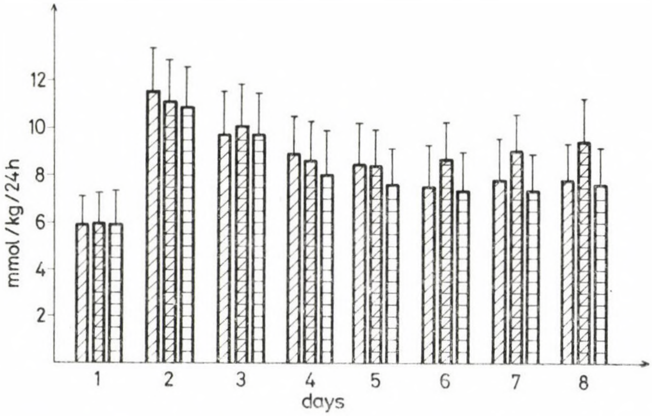

FIG. 1. AGA (//////) and SGA (//////) infants fed HM enriched with HML and SGA infants (| | | |) fed native pooled HM

The amount of stools in SGA newborns fed HML enriched HM was twice more than in AGA newborns fed HML enriched HM; they amounted to 28.9 ± 6.2 g/kg BW/24 h, and 13.2 ± 4.9 g/kg BW/24 h, respectively.

The significantly higher stool losses and the slightly increased renal nitrogen excretion in SGA newborns fed HML enriched HM led to a steadily increasing difference in the nitrogen balance in Group 1 (Fig. 3). From the 6th day of life this difference has become significant. In the same period, the differences between SGA newborns fed HML enriched HM and those fed native HM has become smaller day by day (Fig. 3).

In contrast to the very different urinary alpha amino nitrogen excretion (Fig. 2), the serum concentrations were not so different (Table IV). In both groups fed on HML enriched

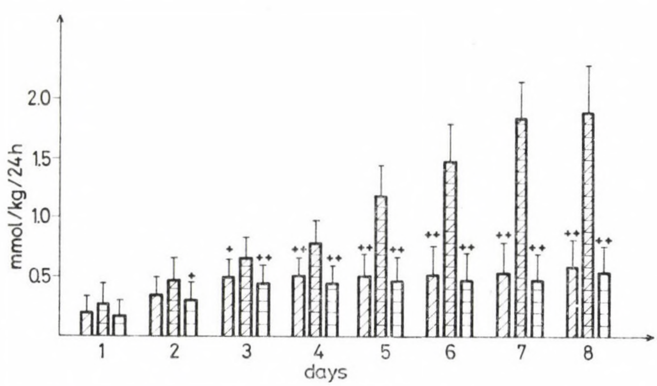

FIG. 2. Mean (M ± SD) daily renal amino acid elimination (mmol/kg BW) 24h in AGA (//////) and SGA (//////) infants fed HM enriched with HML and in SGA infants (| | | |) fed native pooled HM

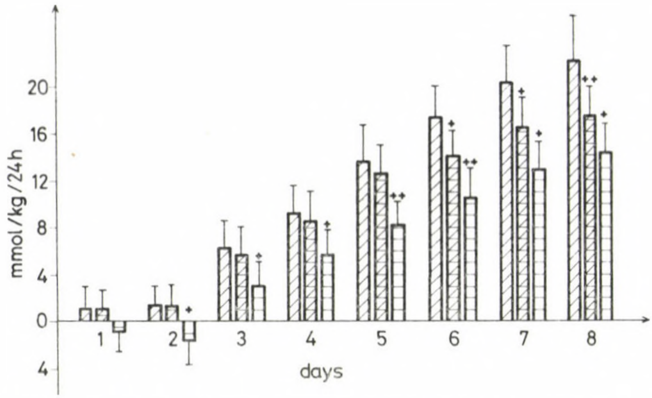

FIG. 3. Mean (M ± SD) daily nitrogen balance (mmolkg BW) (24h) in AGA (////////) and SGA (////////) infants fed HM enriched with HML, and SGA infants (| | | |) fed native pooled HM

HM the serum alpha amino nitrogen concentrations were higher than in Group 3 in the second part of the observation period, while in SGA newborns fed native HM were the lowest con.entrations observed. The differences between Group 1 and Group 2 were significant only on the 8th day of life ($p < 0.01$), and between Group 2 and Group 3 on the 6th and 8th days of life ($p < 0.05$ and <0.01, respectively).

The serum concentrations of total bile acids were remarkably high in SGA newborns fed HML enriched HM, on the 8th day of life (Fig. 4); there was a significant difference between the AGA and SGA newborns fed native HM ($p < 0.01$). In SGA newborns the higher protein intake led to a significant increase in serum total bile acid concentration ($p < 0.01$) and the values reached were unambignously pathological.

The highest postnatal weight loss was observed in Group 1 (Table V). The difference between Group 1 and Group 2 as well as between Group 2

TABLE IV

Serum alpha amino concentration (mmol/l) during the first week of life in the different groups (M ± SD)

Day	Group 1	Group 2	Group 3
2	3.39±0.51	3.49±0.57	3.47±0.65
4	3.38±0.63	3.71±0.71	3.11±0.59
6	3.26±0.59	3.92±0.81	2.97±0.60
8	3.22±0.62	4.36±0.78	2.62±0.64

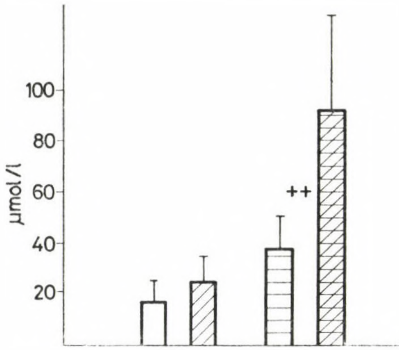

FIG. 4. Mean (M ± SD) serum concentration of bile acids in AGA infants fed native pooled HM (□) as well as HM enriched with HML (▨) and SGA in infants also fed native pooled HM (▤) as well as HM enriched with HML (▨), on the 8th day of life

TABLE V

Body weight (M ± SD) in the different groups during the first week of life

Group	1	2	3
Maximum postnatal weight loss, per cent	−1.5 ±1.10	+0.6 ±0.69	−1.0 ±0.87
BW on the 8th day of life, in per cent of birth weight	+0.99 ±0.49	+1.21 ±0.63	+0.4 ±0.43

and Group 3 was significant ($p < < 0.01$), whereas there was no difference in relative body weight between Group 1 and Group 2 on the 8th day of life, but relative body weight was significantly lower in SGA newborns fed native HM ($p < 0.05$).

Discussion

The metabolic situation of SGA newborns was characterized, depending on the fetal growth retardation, by a reduced cellular mass caused by the reduced number of cells as well as the reduced cell volume, lower intracellular concentration of enzymes, and low insulin levels [2, 8, 15, 20]. All these result in a diminished functional capacity of the liver of such infants, leading to particular problems of nutrition during the first days of life. There is a discrepancy between the substrate deficiency caused by fetal malnutrition and a limited capacity for substrate utilization. As it has been shown in SGA newborns with severe fetal growth retardation, feeding native HM in the same amount as in the present study caused metabolic overloading [6, 7].

The present results demonstrate that in SGA newborns with mild to moderate fetal growth retardation, feeding of HML enriched HM may overcharge the metabolic capacity during the first week of life.

Two facts seem to be important: the insufficient utilization of reabsorbed amino acids and the increased cholestasis.

Because only HM was used in the present study, an inadequate amino acid supply could not be the cause of the high amino acid excretion in SGA newborns fed HML enriched HM [4, 20, 21]. The high serum concentration of bile acids points to an overcharged liver function [12, 22, 25]. The insufficient amino acid utilization shown by the urinary amino acid elimination increases with increasing protein intake.

On basis of the present results the question cannot be answered when the postnatally developing liver function permits a higher nitrogen intake. Most investigators started nitrogen balance studies when enteral feeding had reached a constant level, e.g. during the 2nd or 3rd week of life [11, 13, 19, 23]. This, together with the different degree of fetal growth retardation of the investigated newborns may be the most important reason for the fact that the limited metabolic capacity of SGA newborns has been described by only few investigators [7, 15, 20], while a high protein intake was recommended for all low birth weight infants [1, 9, 10, 13, 17, 18, 19].

The higher amount of stools of SGA newborns fed HML enriched HM than that of AGA newborns on the same diet must have also been due to the inadequate liver function and especially to the limited fat absorption [9, 12].

The higher osmolality of HML enriched HM (Table II) did not cause any clinical problem during the observation period, but in agreement with some other authors [3] we decided that 400 mosmol/l should be the upper limit from this point of view.

In SGA newborns as well as in AGA newborns, nitrogen retention can be improved by increasing the protein intake. The signs of a metabolic overloading in SGA newborns, especially the high serum concentration of bile acids, are, however, reasons to increase the protein intake very carefully in these infants during the first week of life. The serum concentration of bile acids seems to be a good marker to recognize this metabolic situation. In each case with a serum bile acid concentration of more than 30 μmol/l one hour after a meal, concentrated nutrients are certainly unfavourable. Thus, in SGA newborns concentrated HM or formulae cannot be recommended for very low birthweight infants. The influence of fetal growth retardation on metabolic capacity has to be estimated before starting a high protein diet.

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