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Blood biochemical profile of very preterm infants before and after trophic feeding with exclusive human milk or with formula milk

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ABSTRACT

Objectives: To determine whether feeding type of trophic feeds affect haematological and biochemical markers in the very preterm infant.

Design and methods: Fifty-six very preterm infants were enrolled in this retrospective study (30 infants were included in the only human milk-fed group and 26 in the formula-fed group). Routine haematological and biochemical variables were collected in both groups on days 1 and 4 of life and fourteen serum markers were measured.

Results: There were no significant differences between the two groups before starting trophic feeds. After starting trophic feeds, sodium and lactate levels were significantly higher in the human milk-fed group compared with those measured in the formula-fed group.

Conclusion: The study demonstrates that supplementation of minimal enteral feeding with human milk does affect biochemical profiles in very preterm infants. Small amounts of enteral feedings of formula and/or human milk may result in different metabolic responses; these differences are reflected by different serum biochemistries.

Introduction

In the first postnatal days disturbances in the fluid and electrolyte balance occur frequently in very preterm infants. This imbalance can lead to neurological impairment, amongst others [1,2]. Previous studies have been designed to compare the biochemical status of newborn infants fed human milk (HM) with that of similar infants fed formula.

No differences have been found in mean serum concentrations of potassium, chloride, calcium, urea nitrogen, blood glucose, lactate or pyruvate concentrations between feeding groups [3,4]. However, the values for serum total proteins, albumin, gamma-globulins, serum cholesterol, triglyceride, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyltransferase, total bilirubin, direct bilirubin, methionine, threonine, ketone body and sodium levels were significantly higher in the breast-fed group compared with those measured in the formula-fed group [4–8].

The milk amount required for this metabolic effect is not known. These studies were carried out on full term neonates at or beyond day 5 of life, involving infants on nutritive milk feeds [9]. To date, no study has been carried out to determine specifically the effect on very preterm neonates of nutritionally insignificant volumes designed to stimulate the developing gastrointestinal system (gut priming or trophic feeding). We hypothesise that a very small amount of human milk in the first days of life is enough to change the metabolic response of very preterm infants.

In our neonatal intensive care unit (NICU), we recently implemented the strategy to use pasteurized human donor breast milk (DM) on preterm infants whose mothers suffered from breastmilk shortage. Motivated by the scarce data available in the literature, we decided to analyse our data in order to verify that our shift to exclusive human milk trophic feeding during the first four days of life was associated with changes of biochemical and haematological markers in the premature baby.

Method

DM has been available in our NICU since April 2009. Thereafter, trophic feeds consisted of non-fortified DM when there was an insufficient mother's breastmilk supply. Until April 1, 2009, the nutrition regimen consisted of preterm formula when there was an insufficient mother's breastmilk supply.

This is a preliminary report that compares laboratory results of infants who received only-HM with a historical cohort that received any

Abbreviations: DM, pasteurized human donor breast milk; HM, human milk; NICU, neonatal intensive care unit.

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amount of formula. We performed a retrospective search for laboratory results for the first four days of postnatal life from eligible infants (<30 weeks of gestational age admitted to our NICU between 1st January 2007 and 31st December 2012). Day 1 sample was taken before starting feeds from every infant's first available blood test result on day 1 of life. Day 4 sample was taken after starting feeds from every infant's last available blood test result on day 4 of life. The following exclusion criteria were the same for both groups: death on day 1 of life, admission to the NICU after day 1 of life and fasting until day 5 of life. There was one additional exclusion criterion for the historical cohort: exclusively breastfed infants. Finally, 30 infants made up the experimental group and 26 infants, the historical group.

Clinical features and laboratory parameters were collected from the hospital charts. Infant growth was classified as small for gestational age using the Fenton chart. Table 1 presents the variables considered to assess the comparability of the two groups. The study was approved by the Institutional Review Boards of our Hospital and informed consent was obtained from parents of all infants.

Standard care

Enteral feeding was usually initiated on the second day of life. Every infant received 1 mL every 3 h, with daily increments <10 mL/kg/day according to clinical condition. Whenever possible, parenteral nutrition was initiated on the second day of life. All infants received standard management in the NICU. None of these practices changed over the course of the study periods.

Evaluation of biochemical and haematological parameters

Electrolyte levels were measured by indirect Ion Selective Electrode on the Abbott Architect CI16000 laboratory analyser. Conventional laboratory analyses of pH and blood gases were performed with bench-top analysers (GEM 3500 Premier).

Table 1
Premature newborn characteristics and postnatal outcome in the first six days of life according to type of feeding.

Baseline characteristics	Formula[a] N = 26	Human milk[a] N = 30	P
Demographics			
Gender (M/F), n	11/15	13/17	1.000
Primiparous, n (%)	10 (42%)	19 (63%)	0.11
Gestational age (wk), mean ± SD	27.36 ± 1.52	26.88 ± 1.54	0.67
Multiple births, n (%)	8 (32%)	8 (27%)	0.66
NI from another hospital, n (%)	4 (16%)	2 (7%)	0.27
Birth weight (g), mean ± SD	1000 ± 221	899 ± 237	0.55
Small for gestational age, n (%)	3 (12%)	5 (17%)	0.62
Perinatal care			
Prenatal steroids, n (%)	20 (83%)	29 (97%)	0.093
Mode of delivery (V/CS), n	11/13	18/12	0.30
Apgar 5th minute, mean ± SD	8.13 ± 1.55	8.48 ± 1.05	0.10
Respiratory interventions			
Exogenous surfactant, n (%)	18 (72%)	20 (67%)	0.67
Other interventions			
Age at onset of enteral feeds (days), mean ± SD	2.24 ± 0.83	1.97 ± 0.32	0.002*
Postnatal outcomes			
Early onset sepsis, n (%)	6 (24%)	3 (10%)	0.16
IVH grades 3–4, n (%)	2 (8%)	2 (7%)	0.42

Abbreviations: CPAP — continuous positive airway pressure; CS — Caesarean section; F — female; g — grams; IPPV — intermittent positive pressure ventilation; IVH — intraventricular haemorrhage; M — male; n — number; NI — newborn infant; SD — standard deviation; V — vaginal delivery; wk — weeks.

[a] Given as a supplement to mother's own breast milk.

* Significant at the 0.05 level.

Biochemical parameters were also measured by the Abbott Architect CI16000 laboratory analyser. Complete blood count and the differential leukocyte count were carried out on blood samples by a cell counter (Sysmex XE-500, USA).

Statistical analysis

The data were analysed using the SPSS statistical package. Categorical variables were compared by means of the χ^2 test or, when appropriate, Fisher's exact test. Continuous variables were compared by means of the *t*-test. Multivariate analysis was not performed because it is not recommended for small samples.

Results

As shown in Table 1, only-HM and formula groups were comparable in terms of maternal and infant characteristics, except in the case of age at the onset of enteral feeds. Table 2 shows that there were no statistically significant differences in laboratory results between the two groups before starting the feeds.

After starting trophic feeds

Serum sodium levels (mean 141 versus 142 mmol/L; $p = 0.026$) and serum lactate levels (mean 1.4 versus 1.6 mmol/L; $p = 0.049$) were significantly decreased in the formula group compared to the only-HM group.

Glycaemia levels were close to significantly decreased in the formula group compared to the only-HM group (mean 5.8 versus 7.6 mmol/L; $p = 0.065$).

There were no statistical differences in any other biochemical or haematological markers between groups.

Multiple births: surfactant therapy

There were considerable numbers of multiple births and of infants requiring an exogenous surfactant. Hence, we have analysed if there are any significant differences in baseline biochemical parameters between these groups and if they respond similarly to trophic feeds.

Single births compared to multiple births. Baseline levels of sodium (136 versus 134; $p = 0.019$), haemoglobin (14.6 versus 15.5; $p = 0.03$) and leukocyte count (13,320 versus 8260; $p = 0.008$) were significantly different. On day 4, levels of sodium (142 versus 137; $p = 0.035$), haemoglobin (13 versus 13.8; $p = 0.005$) and potassium (4.3 versus 5.5; $p = 0.033$) were significantly different.

Effect of exogenous surfactant. Baseline aspartate aminotransferase levels were significantly decreased in the 'without exogenous surfactant' group (25.5 vs 35.5; $p = 0.017$). On day 4, platelet count was significantly increased in the 'without exogenous surfactant' group (272,500 vs 161,000; $p = 0.016$).

There were no statistical differences in any other biochemical or haematological markers between these groups.

Discussion

Comparison with other studies.

A recent international survey observed that most of the units with access to DM start enteral feeding on the first day of life and advance more rapidly than units without access to DM [10]. These data are in line with our findings, where DM recipients exhibit an earlier onset of enteral feeds.

Slight differences in sodium intake do not change sodium levels in adults and supplemented diets (4–5 mmol sodium/day versus 1–1.5