PAPERS AND ORIGINALS

Metabolic acidosis and infant feeding

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Summary

Most cows' milk based formulae for infant feeding present a greater acid load to the infant than breast milk. To determine the effect of this difference the acid base state of 180 healthy term infants was measured on the sixth day of life and related to the type of feed. Those infants fed on cows' milk formula (SMA) had a mean pH of 7·34±0·05 and a base deficit of 8·8±3·1, while those fed on breast milk had a mean pH of 7·38±0·05 and a base deficit of 5·6±3·1. The difference between the two groups of infants was significant for both these measurements.

Metabolic acidosis was defined as a base deficit greater than 10 mmol/l. Seventy-four per cent of the 34 infants who were acidotic at six days were bottle-fed, whereas only 34% of the total population were bottle-fed. There was a significant correlation between the pH of the feed and the degree of acidosis in the infant as measured by the base deficit.

The findings suggest that when breast milk is not available a pH-adjusted milk formula would be desirable for preventing and treating neonatal metabolic acidosis.

Introduction

Metabolic acidosis in premature infants is well recognised,[1 2] resulting from an imbalance between the infant's limited ability to excrete hydrogen ions and the total intake and metabolic production of acid.[3 4] In most cases it resolves spontaneously in four to six weeks, but therapeutic correction with alkali is sometimes necessary.[2]

Early this century acidified milk was recommended for feeding sick infants[5] to facilitate the digestion of cows' milk protein. The acid produced finer milk curds and was thought to reduce bacterial infection of the gut. More recently it has been suggested that a more alkaline milk may have a bacteriostatic effect on specific *Escherichia coli* in vitro.[6] The modifications to the protein in the newer baby milk formulae make acidification unnecessary for digestion. Acidified milks fell into disfavour when it was realised that some of the infants became severely acidotic.[7] Nevertheless, most of the manufactured baby milks on the market still present a greater acid load to the infant than breast milk.

The acid load of any milk formula depends on the titratable acidity, the production of non-volatile acids from protein catabolism, and the net base concentration of the formula.[2] This study was designed to determine whether the difference in acid load between breast milk and a modified cows' milk formula (SMA) had any effect on the acid-base balance of healthy full-term neonates.

Method

Arterialised capillary blood was collected from a heel stab on the sixth day of life in 180 healthy term neonates at the same time as the routine Guthrie test was performed. The mother's informed consent was obtained. The samples were all taken at the same time of day into sealed heparinised capillary tubes, immediately placed on ice, and analysed on a Corning 165 pH/blood gas analyser within four hours of collection. In most cases the analysis was done in duplicate and the mean value was used. The titratable acidity of pooled breast milk and SMA (Wyeth Laboratories) was measured by titrating 30 ml of milk with 0·1-M NaOH to pH 7·40.

One hundred and three infants were given breast milk alone (mean pH 7·1, range 6·7-7·4), and 61 were fed with SMA (mean pH 6·67, range 6·63-6·73). A third group of 16 infants, who were mainly breast fed but were also given complements of SMA, was too small to compare with the first two groups, but these infants were included to determine the overall incidence of metabolic acidosis in the population.

All infants were healthy at the time of sampling, but the 29 infants with a history of perinatal complications, such as difficult delivery or caesarean section, fetal distress, or birth asphyxia, were considered separately.

By the sixth day the infants were offered 90 ml SMA formula or breast fed every three to four hours on demand. Infants were considered to be acidotic if the base deficit exceeded 10 mmol (mEq)/l, confirmed in most by a repeat estimation 24-48 hours later.

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Results

The titratable acidity of pooled breast milk (pH 7·1) was 1·35 mmol (mEq)/l and that of SMA formula (pH 6·67) 3·11 mmol (mEq)/l.

The mean values for both pH and base excess were significantly lower in the SMA-fed group than in the breast-fed group ($P < 0·001$). There was no significant difference between the two groups in birth weight, sex, race, or gestational age (table I). In the 29 infants with perinatal complications the base deficit in the SMA group was not significantly lower than that in the breast-fed group (table II).

TABLE I—*Acid base state of 6-day-old normal infants*

	No of infants	Birth weight (g)	pH*	P_{CO_2} (kPa)	HCO_3^-* (mmol/l)	Base excess* (mmol/l)
Breast-fed	84	3290 ± 500	7·38 ± 0·05	3·97 ± 0·85	17·4 ± 3·18	−5·6 ± 3·1
SMA-fed	51	3250 ± 400	7·34 ± 0·05	3·72 ± 0·78	14·9 ± 3·0	−8·8 ± 3·1

*The difference between values in the two groups was highly significant ($P < 0·001$).
Conversion: SI to traditional units—P_{CO_2}: 1 kPa ≈ 7·5 mm Hg. HCO_3^- and base excess: 1 mmol/l = 1 mEq/l.

TABLE II—*Acid base state of 6-day-old infants with perinatal complications*

	No of infants	Birth weight (g)	pH	P_{CO_2} (kPa)	HCO_3^- (mmol/l)	Base excess (mmol/l)
Breast-fed	19	3250 ± 320	7·36 ± 0·04	4·07 ± 0·04	16·98 ± 2·18	−6·9 ± 2·0
SMA-fed	10	3490 ± 460	7·34 ± 0·05	3·52 ± 0·65	16·96 ± 5·6	−8·7 ± 3·6

Only five (4·9%) of the breast-fed infants became acidotic compared with 25 (41%) of the SMA-fed infants, and this difference was highly significant ($P < 0·001$) (table III). The overall incidence of acidosis at six days in the group with perinatal complications (21·1%) was not significantly higher than in the normal group (18·6%). Seventy-four per cent of the infants who became acidotic were bottle-fed, whereas only 34% of the whole population were bottle-fed.

TABLE III—*Incidence of metabolic acidosis in healthy 6-day-old neonates*

	Breast-fed	Fed with SMA and breast milk	SMA-fed	Total
No of infants	103	16	61	180
No (%) of acidotic infants (base deficit >10 mmol/l)	5 (4·9)*	4 (25)	25 (41)	34 (18·9)

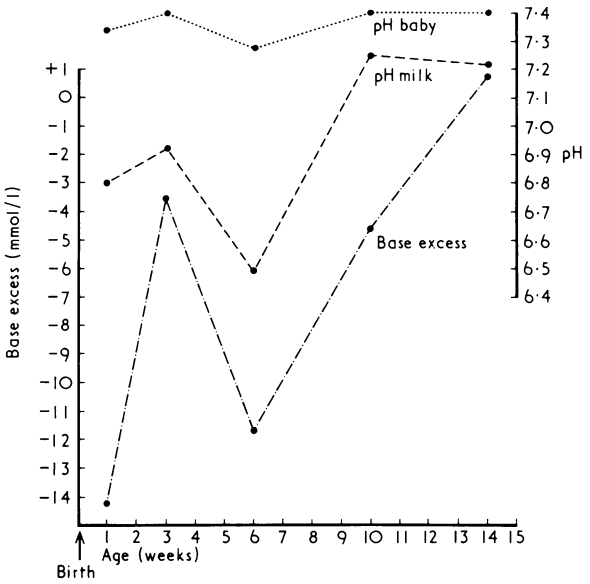
*Difference in incidence between breast-fed and SMA-fed groups was highly significant ($P < 0·001$).

The pH of the ingested milk was measured in 75 infants and related to the degree of metabolic aciodisis as measured by the base deficit. The correlation, although not close ($r = 0·38$), was significant ($P < 0·001$). In one infant the correlation was found to be much closer ($r = 0·9$; $P < 0·01$) (see figure).

All the infants in this study weighed over 2500 g at birth. No correlation was found between birth weight and acidosis, nor between the weight curve in the first six days and acidosis. By 4 weeks of age the acidosis had spontaneously resolved in all but four of the acidotic infants, in whom the acidosis persisted for three and a half to four months. Three of these were Negroes and three weighed under 3000 g at birth. Most of these infants were completely asymptomatic but a few had minor feeding problems.

Discussion

Infants fed with cows' milk formula (SMA) had a greater tendency to develop metabolic acidosis than those who were breast-fed, and as the two groups were comparable in other



Variations in pH of breast milk reflected by variations in pH and base excess of one infant over three months.

respects the differences can be ascribed to the difference in the diet. This is supported by the correlation found between the pH of the milk and the degree of acidosis. The pH of breast milk fluctuates widely in the first 10 days.[8] In the case of the infant illustrated in the figure the breast milk at six days had a pH of 6·8, which is well below the normal mean pH 7·1 for early breast milk. Although the maternal acid base state was not determined at the time, this relatively acid milk may have been related to maternal ketoacidosis, which in turn may have been related to a self-imposed ketogenic diet in place of the food served on the ward.

The high incidence of metabolic acidosis among healthy term neonates in this study is surprising. In Sweden in 1973 Svenningsen and Lindquist[9] found that 5% of normal term infants were acidotic after the fifth day compared with 20% of preterm infants, but the incidence of breast feeding in this population was not stated. These workers also found no significant difference in the weight curve in the first five days but a significantly lower rate of weight gain among acidotic infants between the fifth and fifteenth days.

There have been reports of severe metabolic acidosis in infants fed Nutramigen,[10 11] which is a milk substitute with a pH of 6·4, a high titratable acidity, and a low potential net base concentration. These infants failed to thrive until the acidosis was corrected by adding sodium bicarbonate to the diet. The importance of the dietary acid load to the net acid balance has been emphasised by Kildeberg,[12] who showed that the main variables in the net acid balance of healthy premature infants were the dietary intake and the faecal excretion of anions. Moreover, he suggested an actively regulated mechanism for the faecal excretion of base. In growing infants the deposition of base in the skeleton releases more acid into the circulation, and in premature or malnourished infants the buffering capacity of the blood may be reduced by a low haemoglobin concentration.

With their limited renal function[3 4] newborn infants depend on the presence of adequate urinary buffers, especially phosphate to excrete acid load.[13] Breast milk contains only 5 mmol/l (15·5 mg/100 ml) of phosphorus, compared with 33 mmol/l (102 mg/100 ml) in whole cows' milk. Widdowson *et al*[14] found that the urinary phosphate excretion in 6 to 8-day-old breast-fed infants was only 0·016 mmol/kg body weight/24 hours (0·5 mg/kg/24 hours) compared with 1·1 mmol/kg/24 hours (33 mg/kg/24 hours) in those fed on cows' milk. Furthermore, Fomon *et al*[15] have shown that infants fed with a high-protein cows' milk formula could excrete more of a given acid load than

breast-fed infants because their urine contained more ammonia and phosphate to act as buffers.

The calcium: phosphorus ratio of cows' milk based formulae has been adjusted to improve calcium metabolism. As a result the phosphorus content has been reduced in SMA to 14·5 mmol/l (44·9 mg/100 ml), with a consequent decrease in the amount of urinary phosphate excreted. This limits the infant's capacity to excrete hydrogen ions buffered by phosphate and may be a disadvantage if the formula still contains a considerable acid load.

The high incidence of metabolic acidosis among bottle-fed infants in this study leads us to speculate on its possible role in the sudden infant death syndrome, which is commoner among bottle-fed infants.[16] The syndrome's peak incidence at two to four months coincides with the time when the haemoglobin concentration is at its lowest.[17] Infants who are already acidotic, although asymptomatic, would be less able to withstand the additional respiratory acidosis incurred by an upper respiratory infection or by hypoventilation during sleep,[13] and it is possible to imagine that irreversible acidosis might lead to sudden death.

The evidence suggests that the dietary acid load has an appreciable effect on the acid-base balance of normal term infants, and when breast milk is not available a pH-adjusted milk formula might be a desirable modification for preventing and treating neonatal metabolic acidosis. With the recent observations of hyponatraemia in infants of very low birth weight fed with low-sodium milk formulae[19] there is a possibility that the addition of base in the form of sodium salt might lead to improved electrolyte and acid-base homoeostasis in bottle-fed infants.

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Tetracycline resistance in pneumococci and group A streptococci

Report of an ad-hoc study group on antibiotic resistance*

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Summary

In a nationwide survey in the spring of 1975 into the prevalence of tetracycline resistance among pneumoccoci and group A streptococci isolates, 21 laboratories reported the sensitivity of isolates and details of the patients. Altogether 13% of the 1528 pneumococci isolated were resistant to tetracycline, but there were wide geographical variations.

Thirty-six per cent of the 1515 streptococci isolated were resistant, and again there was considerable geographical variation. A high level of resistance in one organism did not correlate with a high level in the other. For both organisms resistance was commoner among inpatients and those aged 50 or over.

Tetracycline should probably not be the drug of choice in penicillin-sensitive patients with group A streptococcal infections, but geographical variations were so wide that decisions on treatment are best made on the basis of local survey data.

*The study group comprised: Dr A B White, Inverness; Dr I A Porter, Aberdeen; Dr J A N Emslie, Ayr; Dr R J Fallon, Glasgow; Dr J C Gould, Edinburgh; Dr J B Selkon, Newcastle; Dr R N Peel, York; Dr A Percival, Liverpool; Dr P J Cavanagh, Stafford; Dr R Wise, Birmingham; Dr M J Lewis, Nottingham; Dr T Brogan, Cardiff; Dr M H Robertson, Epping; Dr D A Leigh, High Wycombe; Professor I Phillips, London; Dr N A Simmons, London; Professor J D Williams, London; Dr E J Stokes, London; Dr D S Reeves, Bristol; Dr O Okubadejo, Portsmouth; Dr G M Churcher, Plymouth.

The report was prepared by the following staff of London Hospital Medical College: J Kensit, lecturer; W Farrell, senior technician; S Evans, lecturer; J D Williams, professor.

Introduction

Tetracycline-resistant pneumococci were first reported in Australia[1] and later in the USA and West Germany.[2 3] Percival *et al*[4] observed tetracycline resistance in up to 23% of pneumococci isolated from patients at Liverpool Royal Infirmary during 1968, while Gopalakrishna and Lerner[5] reported a 6% resistance rate in Cleveland, Ohio. Resistant organisms were isolated mainly from patients with chronic lung disease in Ohio.

Tetracycline resistance in group A streptococci was first reported in 1954,[6] and resistance rates rose during the 1960s.[7]