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ORIGINAL CONTRIBUTION

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Food mineral composition and acid–base balance in preterm infants

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Abstract *Background* Due to a transient age-related low renal capacity for net acid excretion, preterm infants fed formula are at a considerable risk of spontaneously developing incipient late metabolic acidosis, clinically characterized by e.g., disturbed bone mineralization and impaired growth. *Aim of the study* From acid–base data in blood and urine under different diets of modified human milk or preterm formulas is attempted to explore the impact of food mineral (and protein) composition on renal regulation and systemic acid–base balance in preterm infants. *Patients and methods* Data were collected from 48 infants fed their own mother's milk (28 native human milk, 20 enriched with fortifier) and 34 patients on formula (23 on a standard batch, 11 on a modified batch with reduced acid load). Intake of food was measured and acid–base data were determined in blood and timed-urine (8–12 h) samples. *Results* Differences in mineral composition of the diets led to considerable differences of daily "alkali-intake", without significant effects on non-respiratory (base excess, BE) and respiratory (PCO_2) acid–base data in the blood. In contrast, a highly significant proportionality between individual dietary alkali intake and daily renal base ($Na^+ + K^+ - Cl^-$) excretion was observed ($y = 0.32x - 0.70$, $n = 80$, $r = 0.77$, $P < 0.0001$), irrespective of the type of the diet. *Conclusion* Renal base saving mechanisms are normally effective in preterm infants to compensate for differences in dietary acid–base load. Generally, nutritional acid–base challenges can be judged much earlier and more safely by urinary than by blood acid–base analysis. Taking into account the age specific low capacity for renal NAE, the relatively high nutritional acid load of preterm standard formula should be reduced.

Key words nutrition – preterm infants – acid–base intake – acid–base balance – renal acid–base excretion – latent acidosis

Introduction

Preterm infants are especially vulnerable for disturbances of acid–base metabolism with a predisposition to metabolic acidosis due to a transient age-related low renal capacity for net acid excretion (NAE) [23]. On alimentation with common preterm formulas they show a high renal NAE, thus further decreasing their low age-specific functional reserve capacity of acid

Table 1 Composition and energy content of different diets for preterm infants

	Human milk (native) *HM*	Human milk (enriched) *HMF*	Formula (high acid) *FH*	Formula (low acid) *FL*
Sodium (Na^+) (mEq/dl)	0.72	1.84	1.35	1.74
Potassium (K^+) (mEq/dl)	1.38	1.57	2.05	2.63
Magnesium (Mg^{++}) (mEq/dl)	0.30	0.47	0.49	0.39
Calcium (Ca^{++}) (mEq/dl)	1.29	3.49	4.34[a]	4.24[a]
Total fixed cations (mEq/dl)	*3.69*	*7.37*	*8.23*	*9.00*
Phosphorus (P_i) (mEq/dl)	0.90	2.61	2.50[a]	2.44[a]
Chloride (Cl^-) (mEq/dl)	1.14	1.55	1.49	1.41
Total fixed anions (mEq/dl)	*2.04*	*4.16*	*3.99*	*3.85*
Cations–Anions (mEq/dl)	1.65	3.21	4.24	5.15
(Na^++ K^+–Cl^-) (mEq/dl)	0.96	1.86	1.91	2.96
Energy (kcal/dl)	67[b]	85	75	75
Protein (g/dl)	1.2 [b]	2.0	1.8	1.8
Fat (g/dl)	3.8 [b]	3.8	4.0	4.0
Carbohydrates (g/dl)	7.0 [b]	10.6	8.0	8.0

Average data for the composition of native low-protein human milk (*HM*) and high-protein human milk (*HMF*) enriched with fortifier Nestlé FM 85 (5 g per 100 ml), compared to the standard formula for preterm infants (Prematil®) with higher acid load (*FH*) and a modified batch formula with reduced acid load (*FL*). Mineral content is based on own analysis (Research Institute of Child Nutrition Dortmund)

1 mmol represents 1 mEq for Na^+, K^+, Cl^-; 2 mEq for Ca^{++}, Mg^{++}, and 1.8 mEq for Phophorus.

[a] Formulas *FH* and *FL* were supplemented with calcium-L-lactate and calcium-glycero-phosphate (Ca–P)

[b] In case of human milk, contents of fat, carbohydrates, protein and energy is given according to Renner [29], in case of milk formulas according to the analytical data of the manufacturer

excretion. Therefore, preterm infants fed formula are at a considerable risk of spontaneously developing a positive acid balance [15]. Although this diet-induced incipient metabolic acidosis does not produce major changes in the blood pH, it is associated with ongoing consumption of endogenous buffer reserves, clinically characterized by e.g., impaired bone mineralization and impaired growth [12].

Feeding human milk results in a low renal NAE in preterm infants. Moreover, human milk is generally well tolerated by preterm infants and provides immunologic and antimicrobial components, hormones, and enzymes that may contribute positively to the infant's health and development [33]. However, the nutritional needs of the preterm infant exceed the content of human milk for e.g., protein and minerals like sodium, calcium, and phosphorus [2, 3, 32]. To correct these nutritional inadequacies of human milk for preterm infants human milk, fortifiers are available that provide additional factors like e.g., minerals and protein [5, 7, 11, 20, 30].

In an earlier study we demonstrated that modification solely of the mineral content of a standard preterm formula, mainly by increased alkali (potassium) content, decreased renal NAE, and effectively prevented the spontaneous development of incipient metabolic acidosis in preterm infants fed this modified formula [6].

The aim of the present study is to obtain fundamental acid–base data in blood and urine of preterm infants under four different diets of modified human milk or preterm formulas to delineate the impact of food mineral composition and renal regulation on systemic acid–base disorders.

Patients and methods

Data were collected from 82 preterm infants with body weight <2.0 kg treated in the neonatal ward of the paediatric clinic in Dortmund from 1993 to 1994. All patients were fed according to the standard regimen of the ward, additionally a supplement of vitamin D (25 μg/day) was started on day 10. Forty-eight infants were fed their own mother's milk, in 20 of these human milk was supplemented with fortifier (Nestlé FM 85, at that time 5 g per 100 ml: 0.8 g protein, 3.6 g carbohydrates, 1.2 mmol sodium, 0.3 mmol potassium, 1.3 mmol calcium, 1.1 mmol phosphorus, 0.5 mmol chloride, 0.1 mmol magnesium). From 34 preterm infants on formula, 23 patients were fed a standard batch (Prematil, Milupa, Friedrichsdorf, Germany), and 11 patients a modified batch of this formula with reduced acid load [16]; all patients on formula received a calcium-phophorus supplement by increasing Ca concentration in the applied two standard preterm milk formulas to a total Ca content of 4.2–4.3 mEq/ and P concentration to a total P content of 2.4–2.5 mEq/dl (see Table 1).

As composition of human milk varies over a broad range, electrolyte composition of formulas and of human milk was determined by own analysis of the ashes (Research Institute of Child Nutrition Dort-

Table 2 Age, weight and daily nutritional characteristics in preterm infants

	Human milk (native) *HM*	Human milk (enriched) *HMF*	Formula (high acid) *FH*	Formula (low acid) *FL*
Number of cases (*N*)	(28)	(20)	(23)	(11)
Gestational age (weeks)	32.8 ± 2.7	32.9 ± 2.9	30.9 ± 3.0[a, b]	31.5 ± 2.4
Birth weight (kg)	1.48 ± 0.30	1.45 ± 0.35	1.27 ± 0.32[a]	1.42 ± 0.27
Actual age (days)	27 ± 16	34 ± 17	39 ± 16[a]	34 ± 20
Body weight (kg)	1.73 ± 0.26	2.02 ± 0.38[a]	1.91 ± 0.10[a]	1.96 ± 0.11[a]
Food intake (ml kg^{-1} d^{-1})	185 ± 18	186 ± 15	175 ± 12[a, b]	168 ± 15[a, b]
Energy intake (kcal kg^{-1} d^{-1})	124 ± 12	158 ± 13[a]	131 ± 9[a, b]	126 ± 11[b]
Alkali intake (Na^++K^+–Cl^-) (mEq kg^{-1} d^-)	1.79 ± 0.54	3.46 ± 0.64[a]	3.34 ± 0.23[a]	4.96 ± 0.44[a–c]
(Cations–anions) (mEq kg^{-1} d^-)	3.05 ± 0.66	5.96 ± 1.26[a]	7.42 ± 0.51[a, b]	8.64 ± 0.76[a–c]

Data are means ± SD in preterm infants on nutrition with native low-protein human milk (*HM*) and high-protein human milk (*HMF*) enriched with fortifier Nestlé FM 85 (5 g per 100 ml), compared to the standard formula for preterm infants (Prematil®) with higher acid load (*FH*) and a modified batch formula with reduced acid load (*FL*)

Significance of group mean differences at levels of $P < 0.05$ (independent samples *t*-test) is indicated by superscripts,when compared to native human milk [a], to fortified human milk [b], and to standard preterm milk formula [c]

Table 3 Capillary acid–base and serum values in preterm infants on different diets

	Human milk (native) *HM*	Human milk (enriched) *HMF*	Formula (high acid) *FH*	Formula (low acid) *FL*
Number of cases (*N*)	(28)	(20)	(23)	(11)
Capillary blood				
pHc	7.397 ± 0.047	7.412 ± 0.033	7.415 ± 0.033	7.402 ± 0.043
$PcCO_2$ (mmHg)	37.8 ± 5.5	40.1 ± 4.3	36.5 ± 3.5[b]	39.3 ± 4.8
HCO_3^- (mmol/l)	23.0 ± 2.5	25.7 ± 2.4[a]	23.5 ± 2.4[b]	24.6 ± 2.5
Base excess (BE) (mmol/l)	−0.8 ± 2.2	1.6 ± 2.4[a]	0.0 ± 2.3[b]	0.6 ± 2.2
Blood serum				
Sodium (Na^+) (mmol/l)	136.9 ± 2.6	138.8 ± 2.2[a]	138.3 ± 3.1	138.5 ± 2.1
Potassium (K^+) (mmol/l)	4.56 ± 0.63	4.34 ± 0.49	4.77 ± 0.48[b]	4.87 ± 0.43[b]
Calcium (Ca^{++}) (mmol/l)	2.46 ± 0.10	2.40 ± 0.09[a]	2.39 ± 0.10[a]	2.40 ± 0.07
Chloride (Cl^-) (mmol/l)			102.6 ± 4.2	103.1 ± 2.5
Phosphorus (mEq/l)	3.33 ± 0.59	3.71 ± 0.58[a]	3.83 ± 0.30[a]	4.29 ± 0.28[a–c]

Data are means ± SD in preterm infants on nutrition with native low-protein human milk (*HM*) and high-protein human milk (*HMF*) enriched with fortifier Nestlé FM 85 (5 g per 100 ml), compared to the standard formula for preterm infants (Prematil®) with higher acid load (*FH*) and a modified batch formula with reduced acid load (*FL*)

Significance of group mean differences at levels of $P < 0.05$ (independent samples *t*-test) is indicated by superscripts, when compared to native human milk [a], to fortified human milk [b], and to standard preterm milk formula [c]

mund). In case of human milk, values for contents of fat, carbohydrates, protein and energy were taken according to [29], in case of formula according to the analytical data of the manufacturer. Milk samples were digested according to [31].

Based on a standard regimen every intake of food was measured, body weight was determined daily. In all patients, timed urine samples were collected for 8–12 h, regularly between 6 and 8 a.m., using a specially designed freezer (−20°C) with a sensor and a printer to register the time of micturition. The electrolyte content of the blood as well as urinary concentrations of creatinine, Na, K, Ca, Mg, chloride, and phosphate were assayed by standard methods [e.g., 6] in the laboratory of the Paediatric Clinic, Dortmund. Urinary concentrations of titratable acidity, ammonium, and bicarbonate were determined as described by [21], the organic acids were measured by titration [36] with a Memotitrator DL, 40 RC (Mettler-Toledo, Gießen, Germany), and sulfate was determined with a Dionex 10 Ion Chromatograph (DionexGmbH, Weiterstadt, Germany). For phosphate, conversion of mmol in mEq is based on measured pH-values in capillary blood samples or urine, thus considering, respectively, the ratio of primary and secondary phosphate (Tables 3 and 4). Renal net acid excretion (NAE) corresponds to the sum of titratable acidity and ammonium minus bicarbonate. Daily renal base excretion was assessed as sodium plus potassium minus chloride in collected urine.

The difference between "fixed cations" and "fixed anions" from the ash analysis provides a measure of different nutritional acidity and/or "potential renal acid–base load" [25, 27]. For inter-individual corre-

Table 4 Acid–base status in 8–12 h urine from premature infants on different diets

	Human milk (native) *HM*	Human milk (enriched) *HMF*	Formula (high acid) *FH*	Formula (low acid) *FL*
Number of cases (*N*)	(28)	(20)	(23)	(11)
Excreted Volume (ml kg^{-1} d^{-1})	98.0 ± 28.7	82.9 ± 29.2	95.1 ± 20.4	78.8 ± 12.6[a, c]
Creatinine (mg kg^{-1} d^{-1})	8.19 ± 2.30	8.26 ± 2.69	9.20 ± 1.53	10.30 ± 1.60[a, b]
pHu	5.76 ± 0.53	6.20 ± 0.46[a]	5.95 ± 0.57	6.77 ± 0.21[a–c]
TA (mEq kg^{-1} d^{-1})	0.31 ± 0.14	0.40 ± 0.37	0.64 ± 0.30[a, b]	0.30 ± 0.14[c]
NH_4^+ (mEq kg^{-1} d^{-1})	0.78 ± 0.26	0.90 ± 0.31	1.22 ± 0.44[a, b]	0.80 ± 0.11[c]
NAE (mEq kg^{-1} d^{-1})	0.94 ± 0.52	1.02 ± 0.59	1.73 ± 0.67[a, b]	0.71 ± 0.41[c]
Cations				
Sodium (mEq kg^{-1} d^{-1})	0.54 ± 0.43	1.34 ± 0.87[a]	0.86 ± 0.58[a, b]	1.21 ± 0.31[a]
Potassium (mEq kg^{-1} d^{-1})	0.81 ± 0.56	1.11 ± 0.52	1.97 ± 0.60[a, b]	2.40 ± 0.29[a–c]
Calcium (mEq kg^{-1} d^{-1})	0.21 ± 0.19	0.21 ± 0.16	0.11 ± 0.09[a, b]	0.13 ± 0.10
Magnesium (mEq kg^{-1} d^{-1})	0.05 ± 0.04	0.04 ± 0.04	0.06 ± 0.05	0.03 ± 0.03
Anions				
Chloride (mEq kg^{-1} d^{-1})	1.15 ± 0.61	1.38 ± 0.84	1.35 ± 0.73	0.96 ± 0.20
Phosphorus (mEq kg^{-1} d^{-1})	0.15 ± 0.16	0.48 ± 0.33[a]	0.79 ± 0.26[a, b]	1.05 ± 0.84[a, b]
Organic acids (mEq kg^{-1} d^{-1})	1.27 ± 0.32	1.55 ± 0.59	1.70 ± 0.27[a]	1.88 ± 0.22[a]
Bicarbonate (mEq kg^{-1} d^{-1})	0.14 ± 0.34	0.28 ± 0.55	0.13 ± 0.20	0.39 ± 0.25[c]

Data are means ± SD in preterm infants on nutrition with native low-protein human milk (*HM*) and high-protein human milk (*HMF*) enriched with fortifier Nestlé FM 85 (5 g per 100 ml), compared to the standard formula for preterm infants (Prematil®) with higher acid load (*FH*) and a modified batch formula with reduced acid load (*FL*)

Significance of group mean differences at levels of $P < 0.05$ (independent samples *t*-test) is indicated by superscripts, when compared to native human milk [a], to fortified human milk [b] and to standard preterm milk formula [c]; Titratable acid, TA; net acid excretion, NAE = TA + NH_4^+–HCO_3^-

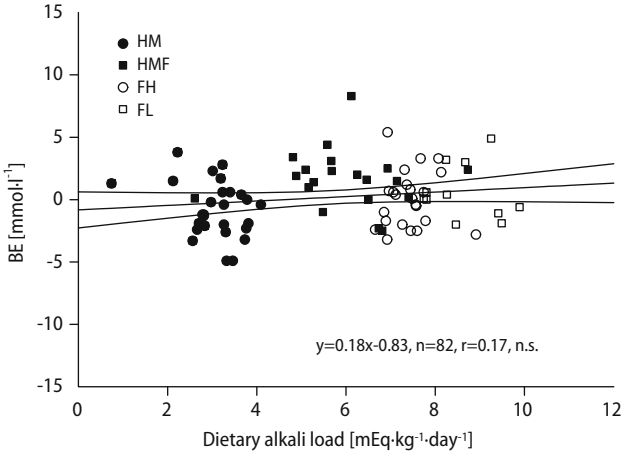

Fig. 1 Effect of dietary alkali load on arterial base excess. Ordinate: Arterial base excess (BE) determined in 82 preterm infants on different diets: native human milk (*HM*), enriched human milk (*HMF*), standard milk formula for preterm infants (*FH*) and on a modified acid-reduced formula (*FL*). Abscissa: Dietary alkali load calculated from diets' ash cation–anion difference and daily milk intake. Linear regression analysis includes the 95% mean confidence interval. Note that arterial base excess is maintained over a wide range of dietary alkali load

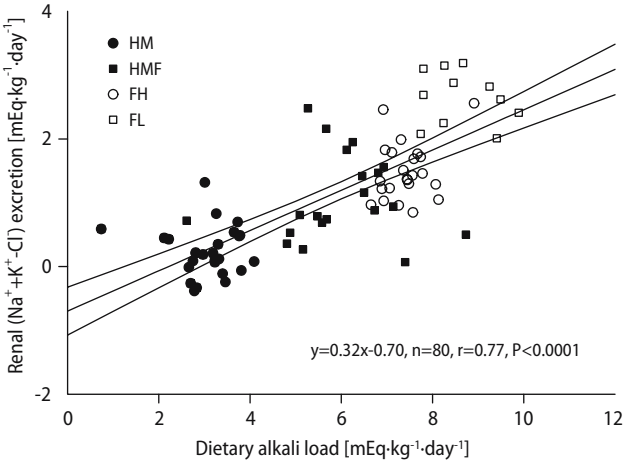

Fig. 2 Effect of dietary alkali load on renal (Na^++K^+–Cl^-) excretion. Ordinate: Daily renal sodium plus potassium minus chloride excretion determined in urine sampled from 80 preterm infants on different diets: native human milk (*HM*) enriched human milk (*HMF*), standard milk formula for preterm infants (*FH*) and on a modified acid-reduced formula (*FL*). Abscissa: Dietary alkali load calculated from diets' ash cation-anion difference. Linear regression analysis includes the 95% mean confidence interval. Note the highly significant proportionality between dietary alkali load and renal (Na^++K^+–Cl^-) excretion

lation analysis (Figs. 1, 2), dietary alkali excess was calculated from diet's ash cation–anion difference and individual data of daily food intake for each patient. To assess the acid–base status of the blood, base excess (BE) can be read from the Siggaard-Andersen Nomogram [34, 35] for any given pair of blood pH and PCO_2 (Blutgassystem Corning 278, Ciba-Corning, Gießen).

Data were analyzed by SPSS statistical software, first calculating group mean values and standard deviations (SD). Variables were tested for normal distribution by the one sample Kolmogorov–Smirnov

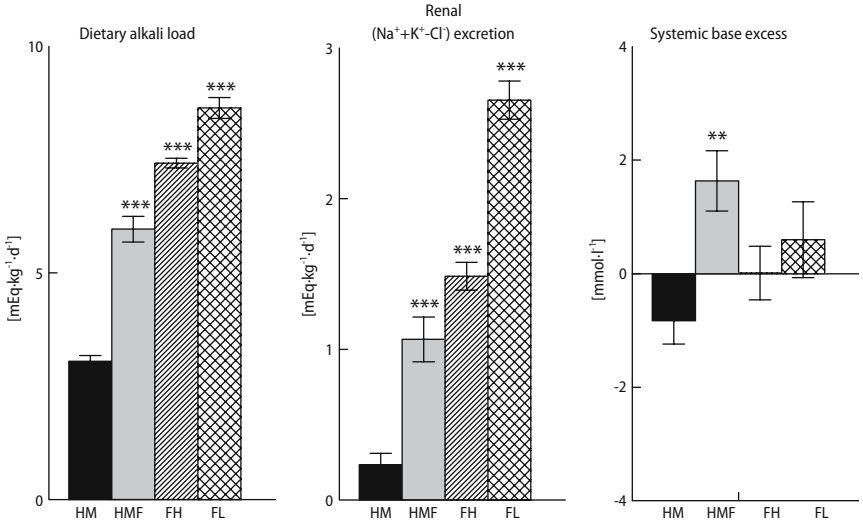

Fig. 3 Comparison of the relationship between dietary alkali load, renal (Na^++K^+–Cl^-) excretion and systemic base excess in preterm infants on different types of nutrition, native human milk (*HM*), enriched human milk (*HMF*), standard milk formula for preterm infants (*FH*) and on a modified acid-reduced formula (*FL*). Bars are means ± SEM. Significant differences compared to the group on native human milk are indicated as ** $P < 0.01$ and *** $P < 0.001$ (independent samples *t*-test). Renal (Na^++K^+–Cl^-) excretion is adapted to dietary alkali intake and effectively maintains systemic base excess within the normal range, but low alkali intake may increase the risk for metabolic acidosis

test. For the groups on different types of nutrition, with native human milk (*HM*), with fortified human milk (*HMF*), with a standard preterm milk formula (*FH*) and with a modified low-acidogenic formula (*FL*), differences of mean values were tested for significance by independent samples *t*-tests. *P* values ≤ 0.05 were accepted as significant. The degree of correlation between pooled variables of all groups was determined by linear regression analysis, regression lines being characterized by slopes, intercepts and 95% mean confidence intervals.

Results

Diet composition and alimentary intake

The energy content and the composition of the different diets fed in this study are shown in Table 1. The usable energy of fortified human milk (*HMF*) was highest, followed by that of formula (*FH* and *FL*), with lowest values in native human milk (*HM*). Considering fixed cation–anion difference of intake, preterm formulas provided higher values than human milk, mainly due to the higher contents of potassium and calcium. Alkali-excess (Na^+ + K^+–Cl^-) values [28] as well as the difference of cations and anions, representing one important determinant of "potential bicarbonate of a diet" [10], were increased by fortification of human milk, reaching the range found in formula. As intended, fortification of human milk increased phosphorus, calcium and protein concentrations to levels seen in formula preparations.

There were no significant differences in gestational age and birth weight between the two groups on either human milk or on formula. Body weight was higher in all groups compared to nutrition with native human milk. Intake of energy was quite similar, except for fortified human milk. Several small differences of electrolyte concentrations, however, added up to a considerable difference in daily "alkali-intake" (Table 2).

Metabolic and respiratory acid–base status

The acid–base status in capillary blood samples is shown in Table 3. Base excess values were balanced around zero; only preterm infants on fortified human milk showing small but significantly higher bicarbonate and base excess values than those on native human milk or on standard formula. However, considering the individual scatter of data (base excess values ranged between −4.9 and +8.3 mmol l^{-1}), linear regression analysis (Fig. 1) did not show any significant correlation between capillary base excess and dietary alkali load. Mean capillary PCO_2, although higher on fortified human milk than on standard formula, did not leave the normal range.

Renal acid–base excretion

Urinary acid–base values are shown by Table 4. Preterm infants on standard formula presented highest renal net acid excretion of all groups (~1.7 mEq kg^{-1} d^{-1}), whereas preterm infants on the modified formula with reduced acid load showed lowest renal net acid excretion (~0.7 mEq kg^{-1} d^{-1}). Compared to standard formula, net acid excretion was significantly lower on alimentation with either native or fortified human milk. Individual values of

urine-pH ranged between 4.76 and 7.24. On formula, mean urine pH-values mirrored the significant reduction of acid load achieved by modification (*FL*) of the standard formula (*FH*). In human milk, fortification had no significant impact on net acid excretion, but nevertheless resulted in a small, but significant increase of urine-pH values.

In preterm infants on nutrition with human milk urinary excretion of calcium was not increased by fortification and serum Ca^{++} rather decreased, in spite of the remarkable increase of Ca content (Table 1). Fortification resulted in a significant increase of urinary excretion of the sum of cations (2.71 ± 0.31 vs 1.61 ± 0.16 mEq kg^{-1} d^{-1}, $P < 0.001$). This increase of urinary cation excretion was nearly counterbalanced by a comparable increase in the sum of urinary anion excretion (3.30 ± 0.36 vs 2.56 ± 0.23 mEq kg^{-1} d^{-1}, $P = 0.09$), mainly due to the higher phosphorus excretion together with the tendencies to simultaneously increase urinary excretion of organic acids, bicarbonate and chloride. Consequently, the resulting difference in urinary excretion of cations minus anions (~1.1 mEq kg^{-1} d^{-1}) was not significantly changed by fortification of human milk.

In preterm infants, modification of the standard formula in a way to reduce the nutritional acid load did not significantly change the urinary excretion of calcium, phosphorus, and organic acids, whereas the urinary cation excretion was significantly increased (from 2.99 ± 0.23 to 3.78 ± 0.16 mEq kg^{-1} d^{-1}, $P < 0.05$), reflecting the rise in (sodium and) potassium excretion (Table 4) corresponding to the change of electrolyte content (Table 1). Considering urinary anions in preterm infants on formula, the excretion of chloride and organic acids was comparable to the range observed in preterm infants fed fortified human milk.

The effect of dietary alkali load on renal base ($Na^+ + K^+ – Cl^-$) excretion is shown by Fig. 2. In striking difference to the lacking correlation between alimentary alkali load and capillary acid–base variables (Fig. 1), linear regression analysis showed a highly significant proportionality between individual dietary alkali load and daily renal base excretion over the whole investigated range, irrespective of the type of diet.

Figure 3 shows the distribution and interrelation of dietary alkali load, renal base excretion and systemic base excess values in the four groups of preterm infants on different diets. Renal base excretion shows an excellent adaptation to dietary alkali intake thus effectively maintaining systemic base excess (BE) within the normal range. However, the group on fortified human milk shows significantly higher BE values than the other groups, possibly bearing a lower risk for developing metabolic acidosis upon additional acid load than the group on native human milk.

Discussion

The effect of diet on acid–base homeostasis has been a subject of controversy in the past. New findings have helped to furnish causal evidence on the positive effects of a well-balanced acid–base equilibrium. Although diet-induced latent (or incipient) metabolic acidosis does not produce major changes in blood (systemic) pH, compensation mechanisms of the kidney are accompanied by the consumption of endogenous buffer reserves [8], leading predominantly to a loss of bone substance, if the increased acid content of a diet persists [22]. Preterm infants with (physiologically) impaired renal function are at a special risk spontaneously to develop latent metabolic acidosis [12].

Systemic metabolic acid–base conditions

Pronounced differences in dietary alkali load corresponding to the four types of investigated diet for preterm infants were responded to by proportional rates of renal base excretion, but were only weakly reflected by the metabolic acid–base status of blood, without clinical diagnostic value in the individual infant.

Generally, systemic metabolic acid–base values were maintained within the normal control range by an effective renal adaptation. The neonate, as the adult, must excrete acid equivalents generated from metabolism in the form of ammonia and titratable acid. When net acid excretion is unable to match the non-volatile acids produced daily, metabolic acidosis develops [17]. Due to their intensive growth, preterm infants and neonates need to excrete daily up to ~2 mEq kg^{-1} acids on nutrition with standard formula [12, 24], compared to ~1 mEq kg^{-1} excreted daily by the adult on normal western diet [26]. In the present study, the group on lowest nutritional alkali intake showed also lowest levels of daily net acid excretion of less than 1 mEq kg^{-1}. As the capacity of renal acid excretion is limited in preterm infants [23], low alimentary ($Na^+ + K^+ – Cl^-$) intake may increase the risk to develop incipient late metabolic acidosis (ILMA), characterized by activation of compensating pathophysiological mechanisms disposing a pool of transiently disposable net base to lift the renal bicarbonate threshold to a higher plasma bicarbonate level [12, 23]. Extracellular volume, disposing net base by volume contraction and the bone releasing so-

dium, potassium, calcium and carbonate (by e.g., impaired mineralization) might be such pools [1, 14].

In adults under steady state conditions, the impact of a given diet on systemic acid–base balance can be estimated, e.g., using a physiologically based calculation model to predict renal net acid excretion by analyzing intake, intestinal absorption and metabolism of several nutrients [26, 27]. In animals, variations of dietary electrolyte balance have been shown to result in small but significant changes in arterial acid–base status [9], in the presence of considerable variations of urinary pH, strong-ion difference and net acid excretion in urine [37]. Only recently, a systematic analysis of food mineral composition and acid–base balance in rabbits demonstrated that dietary base variations were more accurately reflected in the urine than by the blood acid–base status [18].

Respiratory acid–base conditions

Excretion of CO_2 by lung ventilation is known to be an important process in regulation of the systemic pH in body fluids of air-breathers [4]. We observed small changes in capillary PCO_2-values proportional to the inter-individual variations of base excess, pointing to only a negligible role for respiratory control functions, when alimentary acid–base load is varied in the investigated range.

Urinary acid–base conditions

Preterm infants present an age specific small renal reserve capacity of acid excretion [23]. Nevertheless, nutrition with commercially available preterm formula results in a rather high renal net acid excretion, so that preterm infants fed standard formula may be at the upper limit of renal compensation and at a considerable risk of spontaneously developing incipient, and occasionally manifest, metabolic acidosis [15]. Modification of the mineral content of a standard preterm formula increasing the alimentary ($Na^+ + K^+ – Cl^-$) load decreased renal NAE (Table 4) and effectively prevented the spontaneous development of incipient metabolic acidosis in preterms fed this modified formula [16]. Recently our group proposed a physiologically based and empirically adjusted algorithm to estimate renal NAE from the analytical data of a formula (electrolyte and protein content) [13].

Three groups of nutrients seem to be primary determinants of the estimated average renal acid load in preterm newborns [23]. First, Na, K, and Cl intake and their intestinal absorption or retention determine urinary ($Na^+ + K^+ – Cl^-$). Second, Ca and P intake and metabolism influence phosphaturia. Third, protein intake and quality determine generation of organic acids and SO_4. Preterm infants need supplementation of native human milk to avoid nutritional deficiencies (for literature see [19]).

Renal control functions

In our preterm infants dietary acid–base variations were more accurately reflected in the urine than by the blood acid–base status. This underlines the priority of maintaining homeostasis of systemic acid–base status, which is achieved by effective adaptation of renal control functions to nutritional acid–base challenges.

Preterm infants have specific nutritional needs, e.g., for intensive mineralization processes. However, to minimize risks like incipient metabolic acidosis, nephrocalcinosis or phosphaturia, mineral composition of formula should not only reflect the mineral composition of bone and tissues in growing preterm infants [38], but the age-specific characteristics of intestinal absorption as well (for a review of literature data see [13]). Moreover, our observation of a nearly unchanged net acid excretion despite a higher urine-pH induced by fortification of human milk may support the hypothesis, that the elevated protein and phosphate content may imply an increased renal acid load and thus an impact on acid excretion capacity in preterm infants as well.

Conclusion

Preterm infants on different types of diet presented considerable variations in dietary alkali surplus in our study. Due to effective renal compensation, no notable acid–base disturbances were detected in blood samples. However, possible risks by nutritional acid–base challenges in preterm infants can be judged much earlier and more safely by urinary than by blood acid–base analysis. As the low ($Na^+ + K^+ – Cl^-$) content of a standard preterm formula turned out to have a strong impact on the age-specific low capacity of renal acid–base compensation, the high nutritional acid load of preterm formula should be further reduced.

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