CHLORIDE INTAKE AND METABOLIC ACIDOSIS IN PRETERM INFANTS AT THE NATIONAL HOSPITAL OF PEDIATRICS

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ABSTRACT

Background: *Optimal chlorine intake in premature infants has been very little studied, while high chlorine intake has been shown to be associated with hyperchloremic metabolic acidosis.*

Objective: *To describe the first 10 days after birth chlorine intake in premature infants less than 32 weeks and to investigate the association between high chlorine intake and metabolic acidosis.*

Subjects and methods: *Prospective Descriptive Study on 95 premature infants under 32 weeks admitted to hospital <24 hours of age and treated for at least 10 days after birth, at the Vietnam National Children's Hospital from July 2018 to June / 2019.*

Results: *Total accumulated chlorine intake reached 49.95 ± 11.07 mmol / kg in the first 10 days. The amounts of chlorine intake in unintentional fluids and in intravenous nourishing fluids are the two main sources of chlorine in the first 10 days after birth. There was a correlation between high chlorine intake in the first 10 days (> 47 mmol / kg) and metabolic acidosis.*

Conclusion: *High chlorine intake > 47 mmol / kg in the first 10 days after birth is associated with metabolic acidosis in premature infants less than 32 weeks.*

Key words: *Chlorine intake, premature infants, metabolic acidosis.*

1. INTRODUCTION

Chlorine is the most concentrated anion in extracellular fluid, playing a role in maintaining osmotic pressure, balancing water, and neutralizing the charge of ions in the blood. However, the optimal chlorine intake in premature infants has been very little studied. In clinical practice, chlorine intake in premature infants is rarely controlled and clinicians are usually only interested in sodium and potassium intake. However, the sources of chlorine for babies in the perinatal period are many: isotonic saline solution (NaCl 0.9%) is often used to compensate the circulating volume in neonatal resuscitation units; Electrolytes such as sodium, potassium, and amino acids in intravenous nourishing fluids are usually provided as chlorinated salts. High chlorine intake is associated with metabolic acidosis in adults as well as in children [1], [2]. Acidosis is strongly related to a number of complications in premature infants such as hypotension, intracranial hemorrhage [3]. Therefore, we conducted a study to: describe the amount of chlorine intake in the first 10 days after birth in premature infants less than 32 weeks

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in the neonatology department of the Vietnam National Children's Hospital and investigate the relationship between high chlorine intake and metabolic acidosis in the above group of children.

2. STUDY METHODS

2.1. Study subjects

Including all premature infants <32 weeks treated in the Neonatal Intensive Care Unit of Vietnam National Children's Hospital admitted within 24 hours of age and treated until at least 10 days after birth. Patients who died in the first 10 days after birth or were hospitalized after 24 hours of age were not included in the study.

2.2. Study Methods

Study Design: Descriptive Study.

- All patients are given full or partial intravenous nourishment for the first 10 days according to nutritional practice at the neonatology department of the Vietnam National Children's Hospital.

- Total sodium and chlorine intake per day for the first 10 days (mmol/kg/day) includes sodium and chlorine in intravenous nourishing fluids, milk and unintentional fluids (including drug mixtures, bolus solutions for lowering blood pressure or correction of electrolyte disturbances, alkaline acidosis ...). Total chlorine intake was defined as high when> 47 mmol/kg during the first 10 days. These threshold values are computed based on the ROC curve.

- Patients are tested for blood gas at least 1 time/day.

Data processing

Data is processed with SPSS 20.0 software. The difference was statistically significant when p <0.05.

3. STUDY RESULTS

From July 2018 to June 2019, we collected 95 premature infants less than 32 weeks eligible for the study. Mean gestational age was 28.6 weeks (±1.7), mean birth weight was 1195.3 grams (±353.6).

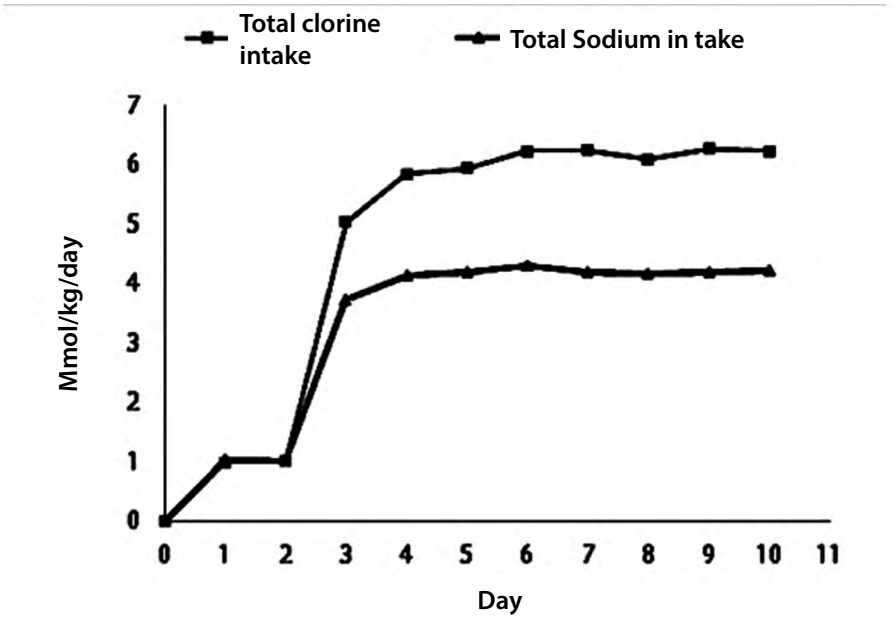

Figure 1. Average total chlorine and sodium intake over the first 10 days

Comment: The cumulative average total chlorine intake was 2.02 ± 1.45 mmol/kg in the first 2 days and 49.95 ± 11.07 mmol/kg in the first 10 days. More chlorine intake than sodium intake for the first 10 days. This difference (AC | _ N) added up to 14.7 ± 6.4 mmol/kg over 10 days.

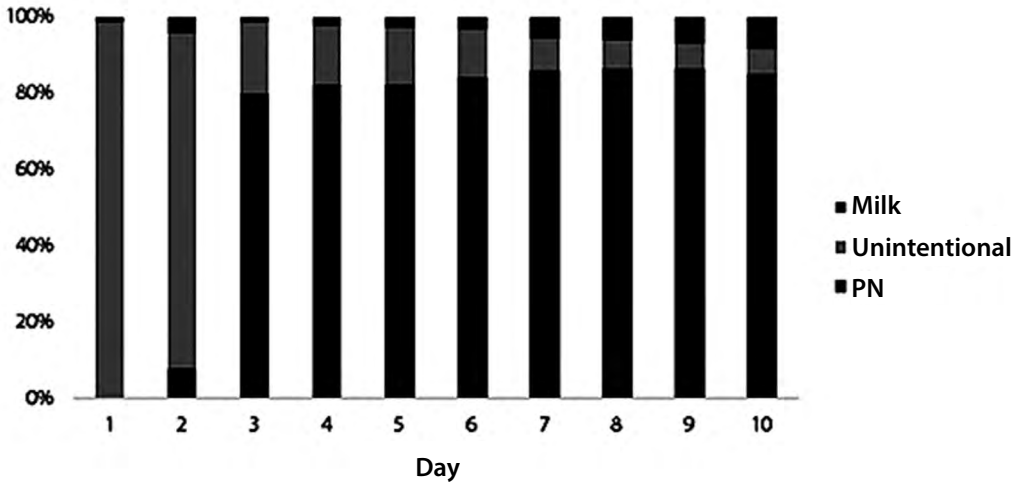

Figure 2. Main chlorine sources in the first 10 days after birth

Comment: The amount of unintentional chlorine intake is the main chlorine supply component in the first 2 days after birth, accounting for 98.2% of the total chlorine intake in day 1, 87.4% in day 2. From day 3, the amount of chlorine contained in the IV nourishing fluid is the main ingredient, accounting for 79.7% in day 3 and stable in the range 84 to 86% from day 6 onward. Intestinal chlorine intake is very low, reaching a maximum amount of 0.54 mmol/kg on day 10 (accounting for 8.7% of total chlorine intake).

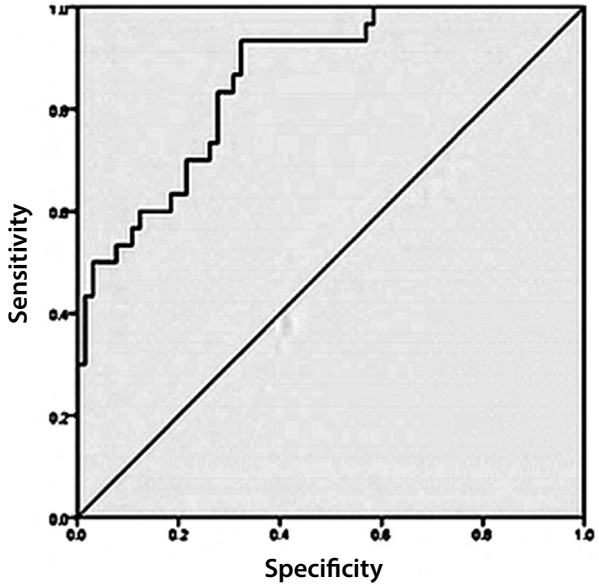

Figure 3. Area under the ROC curve of chlorine intake

Comment: The area under the ROC curve = 0.858 with p <0.001 is statistically significant, so the high or low chlorine intake is capable of determining the metabolic acidosis status expressed by the BE index <-10 mmol/l, with a cut-off point of 47 mmol/kg, the sensitivity is 93.3% and the specificity is 67.7% and at this point the Youden index = 0.61 is the highest.

Of the 95 studied patients, 49 patients (51.6%) had chlorine intake> 47 mmol/kg during the first 10 days.

Table 1. Relationship between chlorine intake and HCO_3^-

Factor		Blood HCO_3^-				p	OR (95% CI)
		< 12 mmol/l n=9		> 12 mmol/l n=55			
		n	%	n	%		
Chlorine intake for 10 days	>47 mmol/kg	8	88.9	41	47.7	0.03	8.78 (1.05 - 73.26)
	<47 mmol/kg	1	11.1	45	52.3		1

Comment: High chlorine intake> 47 mmol/kg in the first 10 days increases the risk of low blood HCO3- below 12 mmol/l to 8.78 times.

Table 2. Relationship between chlorine intake and blood BE

Factor		Blood BE				p	OR (95% CI)
		<-10 mmol/l n=30		> -10 mmol/l n=65			
		n	%	n	%		
Chlorine intake for 10 days	>47 mmol/kg	28	93.3	21	32.3	<0.01	29.33 (6.38-134.90)
	<47 mmol/kg	2	6.7	44	67.7		1

Comment: High chlorine intake > 47 mmol/kg in the first 10 days increases the risk of blood BE lower than -10 mmol/l by 29.33 times.

4. DISCUSSION

The average cumulative chlorine intake was 49.95 ± 11.07 mmol/kg during the first 10 days. On average, the amount of chlorine intake each day is about 5 mmol/kg. The mean total chlorine intake included in this study within the recommended chlorine intake threshold is 0 to 5 mmol/kg/day in neonates [4]. The two main sources of chlorine are intravenous nourishing fluids and unintentional fluids. Our study subjects are critically ill patients, so most of them were given fasting, either exclusively intravenous feeding or minimal trophic feeding and partial vein feeding. Therefore, the amount of chlorine intake from the intravenous nourishing fluid accounts for a large proportion while the amount of chlorine intake from milk is negligible. Chlorine intake more than sodium intake and this difference ($\Delta_{Cl - Na}$) accumulated reached 14.7 ± 6.4 mmol/kg over 10 days.

The mechanism of metabolic acidosis caused by high chlorine intake was explained through Stewart's acid-base physiology model [5], [6]. According to Stewart, blood bicarbonate concentraten and blood pH are determined by four systems: partial CO2 pressure (pCO2), total concentraten of weak acids (proteins of which are mainly albumin), the presence of other acids such as lactic acid, ketoacid and strong ionic difference (SID). Strong ionic difference is defined as the difference between the concentraten of measured strong anions and measured strong cations, which are mainly Na, K and Cl in the blood. SID = $[Na^+ + K^+ + Ca^{2+} + Mg^{2+}]$ - [Cl + lactate]. The SID value is mainly equal to the total concentraten of HCO3 and albumin. A decrease in SID will cause a decrease in pH. Therefore, an increase in blood chlorine that is not related to sodium will decrease the SID of the blood and decrease the pH. Stewart's theory of the physiological acid-base equilibrium has been used

in many different studies [7]. In our study, high chlorine intake (> 47mmol/kg in the first 10 days, average 4.7mmol/kg/day) increases the risk of low blood HCO_3^- <12 mmol / l by nearly 9 times. and increased risk of BE <-10 mmol/l by 29 times, these are two indicators of severe metabolic acidosis.

5. CONCLUSION

Research shows that high chlorine intake >47mmol/kg in the first 10 days after birth is associated with metabolic acidosis. Therefore, strict control of blood chlorine intake and monitoring of electrolyte balance in intravenous nourishment in premature infants in the first days of life will contribute to the reduction of metabolic acidosis as well as complications such as lowering blood pressure, cerebral hemorrhage.

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