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SCIENTIFIC LETTER

Hyperchloremia and hypernatremia in critically ill children☆

Hipercloremia e hipernatremia en niños en estado crítico

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Dear Editor,

Hyperchloremia and hypernatremia are relatively common alterations in critically ill children.[1,2] In the adult population, hyperchloremia and sodium alterations are associated with a high mortality rate.[3] However, few studies have analyzed the incidence rate and repercussions of chlorine and sodium alterations in critically ill children.[1,4]

A retrospective study was conducted including 250 patients hospitalized in the Pediatric Intensive Care Unit (PICU) for 7 months to study the incidence rate of early hyperchloremia and hypernatremia in critically ill children and their association with acute kidney injury (AKI) based on the pediatric criteria established by the Kidney Disease: Improving Global Outcomes (KDIGO) organization: infection (based on the diagnoses of the patient's discharge summary), and mortality. The study was approved by the center clinical research ethics committee (code 294/17). A total of 151 children with sodium and chlorine levels measured at admission were studied. The patients' mean age was 2.3 years and the interquartile range was between 0.5 and 10.8 years.

Chlorine values between 95 mEq/L and 110 mEq/L, and sodium values between 135 mEq/L and 145 mEq/L were considered normal. Qualitative variables were compared using Fisher's exact test while the quantitative ones were compared using the Mann–Whitney *U* test. *p* values <.05 were considered statistically significant. A multivariate logistic regression analysis was conducted to analyze both the factors associated with AKI (KDIGO stage 2 or 3) and the need for extrarenal depuration techniques (EDT).

In the early blood tests performed 13 patients (8.6%) had hyperchloremia, 4 (2.6%) had hypochloremia, 24 (16%) hypernatremia, and 15 (10%) had hyponatremia. A total of 5 of these patients (33% of the total) had hyperchloremia e hypernatremia at admission. Only 1 patient had hyperchloremia >120 mEq/L and hypernatremia >160 mEq/L.

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Table 1 Association between early hyperchloremia and other variables.

	Variable	Early hyperchloremia, %	No hyperchloremia, %	Statistical significance (*p*)
Number of patients		13	138	
Age	<1 year	30.7	35.5	1.000
	> 1 year	69.2	64.4	
Sex	Male	38.5	58.7	.241
	Female	61.5	41.3	
Diagnosis	Cardiac	38.41	51.4	.225
	Respiratory	15.4	21.7	
	Neurological	30.8	10.9	
	Other	15.4	15.9	
Condition	Medical	46.1	50	1.000
	Surgical	53.8	50	
Acidosis	Yes	66.7	43.2	.379
	No	3.3	56.8	
AKI	Yes	15.4	10.1	.631
	No	84.6	89.9	
EDT	Yes	23.1	7.9	.104
	No	76.9	92.1	
Infection	No	7.3	92.7	.050
	Nosocomial	23.1	76.9	
Mortality	Yes	7.7	2.2	.307
	No	92.3	97.8	

AKI, acute kidney injury; EDT, extrarenal depuration technique.

No statistically significant associations were reported between hyperchloremia and any of the variables studied (Table 1). Barhight et al.[4] studied critically ill children and found that 56% of the patients who required EDT during admission had already had hyperchloremia at some point in the past. In our study we did not find a statistically significant association between hyperchloremia and AKI (that 16 patients did show, 10.5%) or with the need for EDT even through hyperchloremia was more common in the 13 patients who required EDT (8.6% of the total) compared to those who did not. A total of 3 (7.5%) of the 40 patients with infection at admission had hyperchloremia, 6 (6.1%) of those who did not have an infection, and 3 (21.4%) of the 13 who eventually developed a nosocomial infection ($p = .019$) (6 bacteremias, 4 respiratory infections, 2 surgical wound infections, 1 urinary tract infection, and 1 cellulitis). We could not explain this finding and, since the size of the sample is small, larger studies are required to confirm our data and establish whether hyperchloremia at admission is a factor that contributes to the development of nosocomial infection or is just an associated factor or an indicator associated with disease severity.

Hypernatremia was significantly more common in children with heart conditions and during postoperative periods (Table 2). This is somehow logical since most patients with heart conditions were hospitalized after surgery, and at the operating room often receive significant amounts of saline solutions. An association was found between hypernatremia at admission and AKI (Table 2). A total of 6 patients with early hypernatremia (25%) developed AKI vs 7.4% of children without it. Also, an association was found between early hypernatremia and the need for EDT. Consistent with our findings, a multicenter prospective study conducted in adults confirmed the existence of sodium alterations in almost 50% of the patients who required EDT being hypernatremia more common than hyponatremia at the beginning of the EDT.[5] In our study, in the logistic regression analysis, the diagnosis of heart disease, postoperative admission, and hypernatremia at admission explain 89.3% of the cases of AKI, and 90.7% of the cases requiring CEDT, $p < .001$. However, when the 3 factors were analyzed, only hypernatremia at admission was associated significantly with the development of AKI ($p = .029$), increasing risk by 4.345 times (1.158–16.299), and the need for CEDT ($p = .013$), increasing risk by 5.958 times (1.447–24.540). There is no such thing as a clear explanation of the association between hypernatremia and the development of AKI, although an increased osmolarity can induce renal perfusion alternations. On the contrary, the frequency of infection at admission was significantly lower in children with hypernatremia.

No significant differences were seen in the incidence rate of AKI, infection or mortality between children with hypernatremia and hyperchloremia and the rest of the patients.

Several studies have found an association between hyperchloremia and mortality in critically ill children,[1,4,6] although the mechanism of action is not clear to this point. In our study we did not find a statistically significant association between hyperchloremia or hypernatremia and mortality, although the number of dead patients in our study (4 patients, 2.6%) is very small.

Some of the limitations of our study are its retrospective, single-center nature, and its relatively small sample. The scores of clinical severity or other factors that can impact the infection, AKI, and mortality were not analyzed. However, it is useful as a preliminary study to plan larger multicenter, prospective trials to establish the correlation between hyperchloremia and hypernatremia at PICU admission and understand the prognosis of critically ill children.

Table 2 Association between early hypernatremia and other variables.

	Variable	Early hypernatremia, %	No hypernatremia, %	Statistical significance (*p*)
Number of patients		16	135	
Age	<1 year	41.6	33.3	.486
	>1 year	58.3	66.6	
Sex	Male	50	58.7	.502
	Female	50	41.3	
Diagnosis	Cardiac	91.7	42.9	<.001
	Respiratory	8.3	23.8	
	Neurological	0	15.1	
	Other	0	8.2	
Condition	Medical	12.5	56.3	<.001
	Surgical	87.5	43.7	
Acidosis	Yes	43.5	44.8	.672
	No	56.5	55.2	
AKI	Yes	25	7.9	.024
	No	75	92.1	
EDT	Yes	25	6.3	.011
	No	75	93.7	
Infection	No	15.3	84.7	.440
	Nosocomial	23.1	76.9	
Mortality	Yes	0	3.2	1.000
	No	100	96.8	

AKI, acute kidney injury; EDT, extrarenal depuration technique.

In conclusion, between 8% and 16% of critically ill children have hyperchloremia and hypernatremia at the PICU admission. Early hyperchloremia is associated with a higher rate of nosocomial infection. Hypernatremia at admission is more common in children with heart conditions and, after surgery, it is associated with the development of AKI and with the need for EDT.

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Conflicts of interest

None reported.

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