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The Changing Pattern of Hypernatremia in Hospitalized Children

Michael L. Moritz, MD*, and J. Carlos Ayus, MD‡

ABSTRACT. *Objectives.* **Past studies have revealed that hypernatremia occurs primarily in infants with diarrheal dehydration. With improved infant feeding practices and the advent of pediatric critical care medicine, the pattern of hypernatremia in children has likely changed. The purpose of this study was to evaluate the current pattern of hypernatremia in hospitalized children.**

Methods. **Medical records were reviewed for 68 patients admitted to a large urban children's hospital during a 3-year period, all with a serum sodium greater than 150 mEq/L. The etiologies, predisposing factors, and morbidity and mortality associated with hypernatremia were evaluated.**

Results. **The average patient age was 3.9 years (range, 1 day to 19.7 years), and the peak serum sodium concentration was 159 mEq/L (range, 151–184 mEq/L). Hypernatremia was hospital acquired in 60% of children. The majority of children (71%) were admitted for reasons other than hypernatremia. In 76% of the patients, inadequate fluid intake was the main cause of hypernatremia. Gastroenteritis contributed to the hypernatremia in only 20% (14 out of 68) of children. Eleven of these were infants <1 year of age with hypernatremia on admission. Eighty-eight percent of patients (60 out of 68) suffered from neurologic impairment, critical illness, chronic disease, or prematurity before developing hypernatremia. The overall mortality was 16%. Patients in whom hypernatremia was not corrected had a significantly higher mortality than those in whom hypernatremia was corrected (4 out of 8 [50%] vs 7 out of 60 [12%]). Peak serum sodium was no different for survivors than nonsurvivors. No deaths were attributable to cerebral edema caused by correction of hypernatremia. Neurologic complications related to hypernatremia occurred in 15% of patients.**

Conclusions. **Hypernatremia occurs in children of all ages, with the vast majority having significant underlying medical problems. Hypernatremia caused by gastroenteritis in infants has become much less common than previously reported. Hypernatremia is primarily a hospital-acquired disease, produced by the failure to administer sufficient free water to patients unable to care for themselves. Failure to correct hypernatremia may result in a high mortality rate.** *Pediatrics* **1999;104:435–439;** ***hypernatremia, sodium, pediatric, fluid, treatment, mortality.***

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Previous studies have revealed that hypernatremia occurs primarily in infants with diarrheal dehydration.[1–8] During the course of hypernatremic dehydration infants can develop central nervous system dysfunction, consisting of seizures, decreased consciousness and coma, and may suffer brain damage or die from intracranial hemorrhages, infarction, and venous thrombosis.[2,9–14] Improper rehydration has been shown to result in brain dysfunction as a result of cerebral edema.[11,12,15–18] Recognition of these serious problems led to the institution of low solute infant formulas that resulted in a decrease in the incidence of infantile hypertonic dehydration.[7,19–22]

Since Rapoport's[1] first description of hypernatremia in childhood, few investigators have evaluated this condition in an inpatient population.[23] We reviewed the records of children admitted to a large children's hospital to obtain an up-to-date picture of the predisposing factors, the common etiologies, and the associated morbidity and mortality of hypernatremia.

METHODS

Study Population

The medical records department queried a database of 32 000 patients admitted to Texas Children's Hospital in Houston, Texas, from January 1992 through December 1994 to identify all patients with a discharge diagnosis of hyperosmolality. Of the 108 admissions identified with this discharge diagnosis, 68 patients were found to have a serum sodium concentration >150 mEq/L. The remaining patients had hyperglycemia or an incorrect discharge diagnosis. The incidence of hypernatremia in hospitalized children by this method (0.22%) was less than would be estimated by querying the department of pathology chemistry lab database (1.4%) not excluding for values from outpatient departments, the emergency department, and lab errors. The present study population seems to be a representative sample with a peak serum sodium (159 ± 5.1 mEq/L) similar to that found when querying the lab database (157 ± 6.8 mEq/L).

Evaluation

A single physician reviewed all medical records. Patient age was assigned as the time that serum sodium first became >150 mEq/L. Time to correction of hypernatremia was determined from the time therapy was instituted until the time serum sodium concentration was ≤150 mEq/L for at least 24 hours. The reason for hospitalization, the presence of significant underlying medical problems, and associated problems during hospitalization were recorded for each patient.

Patients were classified as having an associated medical problem before the development of hypernatremia if they had a chronic disease or an underlying neurologic impairment, or if they were critically ill, premature, or expremature infants. Patients were classified as critically ill if they were intubated for reasons

other than prematurity before developing hypernatremia. Infants were classified as being premature if their birth weight was <2500 g, their gestational age was <35 weeks, and they had not been discharged to home since birth. Expremature infants had been discharged to home before admission.

Patients were classified as having underlying neurologic impairment if there was documentation of structural brain damage, increased intracranial pressure or hemorrhage, developmental delay, mental retardation, or fixed neurologic deficits before the development of hypernatremia. When present, the underlying neurologic status and reason for impairment were recorded. The final neurologic status was recorded at discharge and was classified as impaired if the above criteria were met, or if there were any focal abnormalities on neurologic examination.

The causes contributing to hypernatremia were recorded for each patient. These were: limited fluid intake, increased extrarenal or urinary water losses, and excess sodium administration. Limited fluid intake was a contributing factor if there was documentation of decreased oral fluid intake, fluid restriction of <800 $mL/m^2/24\ h$,[24] or inadequate access to fluids in patients who were otherwise able to tolerate oral fluids. Urinary water losses were considered increased if there was a concentrating defect, such as nephrogenic or central diabetes insipidus, or if a solute diuresis because of glucose, urea, or a loop diuretic was present. A quantity of sodium ≥5 mEq/kg/d administered in a concentration exceeding 150 mEq/L was considered a contributing factor to hypernatremia. Complications of hypernatremia were recorded, as were the cause of death and pertinent autopsy findings when available.

Statistical Analysis

Data were analyzed using the SigmaStat statistical software package (Jandel Scientific Software, San Rafael, CA). Descriptive data were reported as the mean ± SD or as mean + range. Ordinal data were analyzed using the Mann-Whitney rank sum test. Nominal data were analyzed using the Fisher's exact test. A P value < .05 was considered significant.

RESULTS

Hypernatremia occurred in 68 children of all ages (Table 1). Twelve children (18%) were premature infants. In the remaining children, only 19 of 56 (34%) were <1 year of age. Hypernatremia was hospital acquired in 41 of 68 patients (60%). The majority of children (71%) were admitted for reasons other than hypernatremia.

The primary factors that contributed to hypernatremia were inadequate fluid intake (76%, 52 out of 68), followed by gastrointestinal losses (44%, 30 out of 68), high urinary water losses (44%, 30 out of 68), and sodium excess (26%, 18 out of 68). Gastroenteritis, historically the major cause of hypernatremia in children,[1–5,9,25,26] was a contributing factor in only 14 children. It predominantly affected full-term infants <1 year of age (57%, 11 out of 19), and patients with hypernatremia on admission (48%, 13 out of 27). Excessive urinary water losses, on the other hand, predominantly affected children >2 years of age (52%, 15 out of 29), and patients with hospital-acquired hypernatremia (54%, 22 out of 41). Diabetes insipidus was the major reason for excessive urinary water losses (43%, 13 out of 30), occurring in 9 children with central diabetes insipidus and 3 with nephrogenic diabetes insipidus. Excess intake of sodium predominately contributed to hypernatremia in the critically ill (53%, 9 out of 17). There were no cases of hypernatremia as a result of errors in infant formula preparations, pharmacy errors, salt poisoning, or breastfeeding malnutrition.

Associated Medical Problems

Sixty patients (88%) had an associated medical problem before developing hypernatremia. A chronic disease was the most common associated medical problem (57%, 39 out of 68). Neurologic impairment was present in 26 patients (38%). In 22 of these patients, limited fluid intake contributed to hypernatremia. Many of these children were profoundly disabled, and thereby dependent on caregivers to meet their fluid needs. Seventeen children were critically ill (22%); 11 of them had high urinary water losses.

The birth weight in premature infants was 844 ± 336 g, (range, 485-1730 g). Eleven were born after <28 weeks of gestation. In 10 of the 12 premature infants, insufficient fluid intake contributed to hypernatremia. Eight ex-premature patients accounted for 11 admissions. Six of these patients had complications of prematurity, such as short gut syndrome ($n = 4$), severe gastroesophageal reflux ($n = 2$), or neurologic impairment ($n = 4$), that either increased free water losses or decreased fluid intake.

Morbidity and Mortality

The overall mortality was 16% (11 patients) (Table 2). Four children died while hypernatremic; all were critically ill. Two of these children became hypernatremic on the day of death as a result of sodium bicarbonate administration for acidosis. The other 2 were hypernatremic for 9 days and 46 days because of fluid restriction. The mortality was substantially higher among patients who remained hypernatremic, than among those in whom hypernatremia was corrected (4 out of 8 vs 7 out of 60; $P < .05$).

Seven patients died after hypernatremia was corrected (Table 2), 5 were premature infants (birth weight, 700 ± 59 g) and 2 were older children. Hypernatremia was corrected at a rate of 0.29 ± 0.25 mEq/L/h (range, 0.13–0.79 mEq/L/h) for all patients with corrected hypernatremia. The fall in se-

TABLE 1. Demographic Characteristics of Pediatric Patients With Hypernatremia

Patient no.	68
Age y (range)*	3.9 ± 5.1 (1 day to 19.7 y)
Male sex, *n* (%)	39 (57)
Hypernatremia at admission, *n* (%)	27 (40)
Hospital-acquired hypernatremia, *n* (%)	41 (60)
Peak sodium concentration, mEq/L (range)	159 ± 5.1 (151–184)*
Hypernatremia corrected, *n* (%)	60 (88)
Time to correction of hypernatremia, days (range)	2.2 ± 1.6 (0.2–7.3)*
Mortality, *n* (%)	11 (16)

* Mean ± SD.

TABLE 2. Mortality Among Pediatric Patients With Hypernatremia

Age (Years)	Peak Serum Sodium (mEq/L)	Time After Correction of Hypernatremia (Days)	Cause of Death
0.06	163	27	Lipoid pneumonia
0.01	158	90	Multisystem organ failure
0.01	154	48	Pulmonary interstitial emphysema
0.01	153	10	Necrotizing enterocolitis
0.01	154	18	Sepsis
12.2	156	24	Ventricular tachycardia
11.5	151	7	Cardiomyopathy
11.3	184	0	Disseminated intravascular coagulation, sepsis
2.1	160	0	Sudden hypotensive episode with bradycardia
1.6	160	0	Septic shock
9.2	154	0	Cardiogenic shock

rum sodium was 12 ± 5 mEq/L (range, 8–19 mEq/L). Death occurred 7 to 90 days after the correction of hypernatremia. No deaths were attributable to cerebral edema because of correction of hypernatremia. The peak serum sodium concentration was similar in survivors and in those who died (159 mEq/L). Diarrheal dehydration was not the cause of death in any of the patients.

Ten patients (15%) developed neurologic complications related to hypernatremia (Table 3). Four patients developed seizures that resolved after the correction of hypernatremia. Eight patients had long-term neurologic sequelae. In 6 patients the neurologic sequelae were most likely caused by their underlying disease rather than to hypernatremia. Two infants with diarrheal dehydration who were previously normal had an impaired neurologic status with hypertonicity at discharge.

DISCUSSION

Hypernatremia has been reported to be a disease that primarily occurs in infants with diarrheal dehydration.[1–5,16,25] Our study showed that, currently, in a tertiary care center, hypernatremia occurs in children of all ages. When excluding premature infants, it primarily occurs in children >1 year of age (37 out of 56, 66%). Only 11 children in our study were infants with gastroenteritis. The reason that the average age of patients in our study was greater than would be expected from previous reports could be explained by a decrease in the incidence of infantile hypernatremic diarrheal dehydration.[7,19,21] This decrease has been attributed to widespread use of low-solute infant formulas, and the improved availability of oral rehydration solutions.[27]

Most of the patients described in our study developed hypernatremia after admission to the hospital. This is similar to recent reports in adults and children. In a large study of 162 elderly patients, 57% developed hypernatremia while being in the hospital. In another study of 103 adults, 83% became hypernatremic after hospitalization.[28,29] In a series of 29 children with a serum sodium concentration ≥165 mEq/L, 56% percent developed hypernatremia while in the hospital.[23] Most of the children in our study who developed hypernatremia after admission to the wards were either critically ill or premature.

The majority of patients in our series had an associated medical problem. Neurologic impairment was the major predisposing factor, occurring in 26 of the 56 patients who were not premature. This observation is not without precedent.[1,3,4,11,12,30] Franz and Segar[4] showed that 12 of 68 patients with hypernatremic dehydration had preexisting brain damage, whereas Macaulay and Watson[11] showed that 14 of 89 infants who survived hypernatremia had preexisting brain damage. Inadequate access to water is the factor that most likely accounts for this high incidence. Greater attention to providing adequate free water to these children, and assessing their fluid balance and serum sodium concentration during times of illness, is clearly required.

In 8 of our patients, the neurologic status was worse at the time of discharge than on admission. Six of these patients had other medical problems, such as prematurity and metabolic diseases, making it difficult to determine what role hypernatremia played in their neurologic deterioration. Previous reports have shown that children with hypernatremia can develop neurologic impairment. Macaulay and Watson[11] observed that 33 of 114 infants with hypernatremia (29%) went on to show evidence of brain damage. In

TABLE 3. Neurologic Sequelae in Children With Hypernatremia

Age	Underlying Illness	Peak Serum Sodium	Neurologic Sequelae
4 d	Hyperammonemia	151 mEq/L	Seizures during hypernatremia. Increased tone at discharge.
3 y	Mitochondrial disease	181 mEq/L	Seizures during hypernatremia. Do not resuscitate at discharge.
13.6 y	Hydrocephalus, seizure disorder	166 mEq/L	Seizures during hypernatremia.
4 d	25-week's gestational age	152 mEq/L	Myoclonic jerks during hypernatremia. Ventriculomegaly.
88 d	Diarrheal dehydration	163 mEq/L	Hypertonicity at discharge.
40 d	Diarrheal dehydration	153 mEq/L	Hypertonicity at discharge.
1 d	26-week's gestational age	172 mEq/L	Intraventricular hemorrhage.
14.2 y	Pan-hypopituitarism	174 mEq/L	Obtunded during correction of hypernatremia.
17	Astrocytoma, Pan-hypopituitarism	167 mEq/L	Increased right-sided weakness at discharge.
55 d	25-week's gestational age	156 mEq/L	Developmental delay at discharge.

17 of these patients, the brain damage was unrelated to or antedated hypernatremia. Dunn and Butt[23] found that 7 of 17 children who survived severe hypernatremia (Na ≥165), had a worsened neurologic status at follow-up. These observations are consistent with experimental data in rats that revealed that acute hypernatremia can lead to permanent histologic brain damage, consisting of myelinolysis of the white matter and necrosis of neurons.[31] In our study, 12% of patients had long-term neurologic damage. The percentage is lower than that reported previously.[5,23] This may be attributable to the relatively few infants in our series with infectious diarrhea and the lower average peak serum sodium in our series than in those of others.

The overall mortality of 16% (11 out of 68) in our series is 16 times higher than the 1% overall mortality of Texas Children's Hospital in 1996. This mortality is, however, similar to that reported by others in patients with hypernatremia.[2,5,27] Our study is unique in that there were no deaths related to diarrheal dehydration. All the deaths in our study occurred either in premature or critically ill infants. Three of 7 (42%) premature infants with birth weights <750 g died, a percentage similar to that for the institution as a whole, and 1 in 4 (25%) premature infants with a birth weight between 750 g to 1000 g died compared to 22% for the institution. The mortality among critically ill patients with hypernatremia was 10 times higher than the mortality among patients without hypernatremia admitted to the intensive care unit during a 1-year period (41% [7/17] vs 7.3% [15/346]; $P < .001$). As already indicated, the mortality was the highest in children with uncorrected hypernatremia: 4 of our 6 deaths among nonpremature infants occurred while hypernatremia was present. Although hypernatremia was not the sole factor that contributed to their death, prolonged uncorrected hypernatremia seemed to be a contributing factor to their demise. This observation is consistent with that made by other investigators. Mandal et al[32] found that in hospitalized adults with hypernatremia, the average serum sodium at the time of death was 152 mEq/L. Dunn and Butt[23] found that of 10 hypernatremic children who died, 5 died with a serum sodium >150 mEq/L. Moritz et al[33] observed that delayed or inadequate treatment of hypernatremia was a significant comorbid factor that contributed to death. Thus, although hypernatremia does not increase the mortality in premature infants, the development of hypernatremia seems to increase the mortality in the critically ill child with hypernatremia compared with the one without.

No deaths among our patients appeared to result from rapid correction or overcorrection of hypernatremia. Animal data revealed that rapid correction (≤24 hours) of both acute or chronic hypernatremia can result in cerebral edema.[31] This may not apply to our patients who had a lower peak serum sodium concentration and an average time to correction of hypernatremia of 48 hours.

CONCLUSION

In summary, hypernatremia occurs in children of all ages. It is primarily a hospital-acquired disease. The majority of these children have significant underlying medical problems such as a chronic disease, neurologic impairment, a critical illness, or prematurity. The major cause of hypernatremia is failure to administer sufficient free water to patients who are unable to care for themselves. Critically ill children who develop hypernatremia have a significantly increased mortality, with most deaths occurring before correction of hypernatremia. Few complications seem to be related to therapy. In most children, hypernatremia could be prevented by frequently assessing fluid and electrolyte balance and by providing adequate free water to these patients.

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