Hypernatremic Dehydration in Young Children: Is There a Solution?

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ABSTRACT: **Background:** Hypernatremic dehydration is a common and potentially life-threatening condition in children. There is currently no consensus as to the optimal strategy for fluid management.
Objectives: To describe the relationship between the type, route and rate of fluids administered and the rate of decline in serum sodium (Na^+) concentration.
Methods: We reviewed the medical records of all children under the age of 2 years who were hospitalized with hypernatremic dehydration (serum Na+ ≥ 155 mEq/L) in Shaare Zedek Medical Center during the period 2001–2010. Collected data of 62 subjects included initial and subsequent serum Na^+ levels, and rate and Na^+ concentration of all intravenous and oral fluids administered until the serum Na^+ reached ≤ 150 mEq/L.
Results: Median initial serum Na^+ was 159.5 mEq/L (IQR 157–163, maximal value 170). The median rate of decline in serum Na+ until serum Na+ reached 150 mEq/L was 0.65 mEq/L/hr (IQR 0.45–0.95). Forty-two children received hypotonic oral fluids which accounted for approximately one-quarter of all fluids they received. There was no significant difference in the rate of decline in serum Na+ between those who consumed oral fluids and those who did not. Neither was there a correlation between the rate of IV fluids, receipt of oral fluids or the degree of dehydration, with the rate of decline in serum Na+. No child experienced an apparent short-term adverse outcome.
Conclusions: A cumulative rate of 5.9 ml/kg/hr of IV fluid administration may reduce the serum Na^+ by an acceptable rate (0.65 mEq/L/hr). Fluid therapy comprising up to 25% hypotonic oral fluids and 75% IV fluids high in Na+ concentration was not associated with any short-term adverse outcome in our patient population.

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Hypernatremic dehydration is commonly encountered in infants and young children and may arise from ineffective breastfeeding [1-3], improperly mixed infant formula [4] or gastroenteritis [5,6], or it may be hospital acquired [7]. Mortality or significant neurologic morbidity may result from the hypernatremic dehydration state itself [8], or it may occur as a complication of fluid therapy [6,9-11]. There is currently no consensus as to the optimal strategy for fluid management of hypernatremic dehydration. The traditionally accepted range for the desired rate of decline in serum sodium (Na^+) concentration of 0.4–1.0 mEq/L/hr is relatively wide [2,9,12,13]. The assertion that maintaining a rate of decline below this range helps prevent the development of cerebral edema is derived from scant clinical data [14]. Long-standing recommendations with regard to the optimal Na^+ concentration of intravenous (IV) rehydration fluids and rate of fluid administration vary among authors [2,9,12,13,15-17], are hampered by complex calculations [2,9,12,13,15,16] and, with rare exception [17], are not based on clinical studies. More recently, three clinical studies addressing the above issues were published, but with little consensus in their respective conclusions [6,18,19]. Neither was the effect of concomitant oral intake during the intravenous fluid treatment period assessed. With the aim of better elucidating the relationship between the type and rate of fluids administered, the subsequent rate of decline in serum Na^+ concentration and clinical outcome, we comprehensively reviewed our experience treating hypernatremic dehydration. In the present study we analyzed both the rate and Na^+ concentration of all fluids received by the child, as well as the rate of decline in serum Na^+ levels at 4–6 hour intervals throughout the treatment period.

PATIENTS AND METHODS

A computerized search was conducted to identify all children who were hospitalized in our institution with a discharge diagnosis of hypernatremic dehydration between the years 2001 and 2010. Inclusion criteria were age less than 2 years, initial serum Na^+ in the emergency room of ≥ 155 mEq/L, and a documented reduction in serum Na^+ concentration of at least 10 mEq/L during the treatment course. Exclusion criteria were presence of an underlying chronic cardiac, renal, gastrointestinal or central nervous system condition, treatment with diuretics or albumin, or incomplete data of IV and/or oral fluids administered.

The children's medical records were thoroughly reviewed and various clinical and biochemical data were collected and entered into a computerized data sheet. These data included age and gender, duration of illness prior to hospital presentation, etiology of hypernatremia – either acute gastroenteritis or

insufficient breastfeeding (defined as any exclusively breastfed neonate with hypernatremic dehydration and without symptoms of acute gastroenteritis), and weight on presentation and at hospital discharge.

Follow-up data were recorded from presentation until the serum Na^+ reached ≤ 150 mEq/L or, if the initial serum Na^+ was < 160 mEq/L, until the serum Na^+ declined by at least 10 mEq/L. Data collected included repeated serum chemistry and blood gas values, rate, route and Na^+ concentration of all fluids administered (including those given as diluent for IV medication and fluids given to maintain arterial line patency), as well as clinical and neurological state.

Fluid management for the children in our study was not guided by any standardized guideline or regimen. The length of time that the initial normal saline bolus was administered, all subsequent changes in the Na^+ concentration, and the rate of the intravenous fluids administered were decided upon according to the clinical judgment of the treating physicians. The decision to administer oral fluids was made by the treating physician and was based on the child's clinical condition and ability to ingest fluids. We recorded the data regarding the administered fluids in a continuous fashion so that the total amount of fluid and Na^+ received at any given time point could be assessed.

STATISTICAL ANALYSIS

Continuous data were described in terms of the mean and standard deviation (SD) for normally distributed variables, or median and interquartile range (IQR) when distribution was non-normal, and categorical data as percentages. Correlations between continuous variables were analyzed using the Pearson correlation coefficient. Differences between groups were analyzed using the chi-square test for categorical variables, and Student *t*-test or ANOVA for continuous variables. Multivariate analysis of factors influencing the rate of decline in serum sodium (as the dependent variable) was done by linear regression. Statistical significance was defined as $P < 0.05$. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS/Windows ver. 19.0, SPSS, Chicago, IL).

Since this study was performed by retrospective chart review, an exemption from full institutional review board approval was issued.

RESULTS

Sixty-six children met the primary inclusion criteria; 4 were excluded due to incomplete data. Fifty children (80.6%) had acute gastroenteritis and 12 (19.4%) suffered from insufficient breastfeeding. The mean duration of illness prior to hospital presentation was 3.4 days. The baseline clinical and biochemical data for all 62 subjects are given in Tables 1 and 2. The median initial serum Na^+ was 159.5 mEq/L (IQR 157–163), with a maximal value of 170 mEq/L. There was no statistically significant difference in the initial serum Na^+ between subjects younger and older than 2 months (158 vs. 160 mEq/L respectively, $P = 0.07$). The median percentage of dehydration (determined by the difference between the admission and discharge weight) was 9.46% (IQR 5.8–12%). There was no correlation between the log-transformed percentage of dehydration and the log-transformed height of the initial serum Na^+ (Pearson coefficient -0.13, $P = 0.33$). Most patients (87%) had abnormally elevated serum creatinine levels on presentation (i.e., > 0.4 mg/dl) and 27% had a serum creatinine ≥ 1.0 mg/dl.

Table 1. Demographic and clinical data of the 62 subjects

	N (%)	Mean (SD)	Range
Age (months)		6.8 (5.27)	0–24
0–2	18 (29)		
2–24	44 (71)		
Gender			
Female	25 (40.3)		
Male	37 (59.7)		
Cause			
Gastroenteritis	50 (80.6)		
Insufficient breastfeeding	12 (19.4)		
Duration of illness*		3.4 (2.6)	1–15
Dehydration level**			
Very mild	4 (6.6)		
Mild	11 (18.0)		
Moderate	12 (19.7)		
Severe	34 (55.7)		
Mental status			
Alert	39 (62.9)		
Apathetic	13 (21.0)		
Obtunded	4 (6.5)		
Unresponsive	5 (8.1)		
Seizures***	1 (1.6)		
PICU admission	15 (24.2)		

*No. of days with symptoms prior to presentation

**Dehydration level was based on the percentage of body weight lost, which was calculated by the difference in weight between admission and discharge: very mild ≤ 3%, mild 3–6%, moderate 6–9%, severe ≥ 9%

***The seizure occurred prior to onset of treatment

PICU = pediatric intensive care unit

Table 2. Biochemistry values of the 62 subjects at hospital presentation

	Median (IQR)	Range
Sodium (mEq/L)	159.5 (157–163)	155–170
Potassium (mEq/L)	4.15 (3.7–4.7)	2.6–66
Glucose (mg/dl)	109.5 (86.7–140.2)	49–299
Calcium (mg/dl)	10.0 (9–10.1)	8.4–11.1
Blood urea nitrogen (mg/dl)	28.0 (18–44.5)	2–111
Creatinine (mg/dl)	0.64 (0.5–1.0)	0.3–2.7
pH	7.26 (7.19–7.3)	6.96–7.45
PCO_2 (mmHg)	33.0 (28.0–36.0)	15.0–54.5
HCO_3 (mg/dl)	14.5 (11.5–18.3)	5.7–23.1

The median cumulative rate of IV fluids (ml) administered per kg per hour at 2, 4, 8, 12 and 24 hours after the commencement of IV fluids was 19.2 (IQR 16.1–22.7%), 6.4 (IQR 5.2–11.2%), 6.2 (IQR 5.2–7.1%), 5.8 (IQR 5.1–7.3%) and 5.9 (IQR 4.5–7.3%), respectively. The mean time from the commencement of IV fluid therapy until the serum Na^+ reached ≤ 150 mEq/L was 23.7 hours (± 11.7 hours, range 4.0–54 hours.). The median rate of decline in serum Na^+ until it reached 150 mEq/L was 0.65 mEq/L/hr (IQR 0.45–0.95). The median rate of decline in serum Na^+ over the first 12 hours was 0.33 mEq/L/hr (IQR 0.06–0.83), and the maximum rate was 1.75 mEq/L/hr.

IV FLUID INTAKE

The initial IV fluid given to all children was normal saline as a bolus. Subsequently, the median Na^+ concentration of the IV solution was 154 mEq/L, 141 mEq/L, 137 mEq/L and 122 mEq/L at 2, 4, 8 and 12 hours from onset of treatment, respectively. The median Na^+ concentration of the IV fluids was less than the median serum Na^+ concentration by 5.5 mEq/L (IQR 3.0–9.2), 8.0 mEq/L (IQR 3.0–13.6), 35.0 mEq/L (IQR 5.0–73.0), 59.0 mEq/L (IQR 19.7–77.2) and 73.4 mEq/L (IQR 52.0–81.7) at the onset of IV fluid administration, and at 2, 4, 8 and 12 hours later, respectively [Figure 1]. At 24 hours after onset of IV fluid therapy the median Na^+ concentration of the IV solution was 81.4 mEq/L, which was 69 mEq/L less than the median serum Na^+ at that point. Serum sodium declined faster than 0.5 mEq/L/hr in 76% of the acute gastroenteritis group and in 41.7% of the insufficient breastfeeding group ($P = 0.03$).

ORAL FLUID INTAKE

Over the entire course of treatment 42 children (67.7%) received oral fluids, starting at a mean of 10.2 (± 7.5) hours after commencing IV fluid therapy. The median serum Na^+ when oral fluids were initiated was 156.5 mEq/L (IQR 154–161). The median Na^+ concentration of the oral fluids ranged between 3.7 and 20.3 mEq/L throughout the treatment period. In total, 42 children received 66.5 ml/kg of oral fluids until the serum Na^+ reached ≤ 150 mEq/L. During the first 12 hours oral fluids accounted for 22% of total fluids administered (± 14.6%) and for 26.3% (± 16.5%) of all fluids received until the serum Na^+ was 150 mEq/L or less. Eight infants were nursed during the treatment period so the amount of oral fluids they received could not be calculated. Among the 19 children who consumed oral fluids during the first 12 hours of IV fluid treatment, the median rate of decline in serum Na^+ was 0.5 mEq/L/hr, compared to 0.8 mEq/L/hr among the 30 children who did not consume oral fluids ($P = 0.51$).

There was no statistically significant difference in the mean duration of hospitalization between infants who received IV fluids only and those who received IV and oral fluids (5.25 days vs. 5.86 days respectively, $P = 0.53$).

In order to identify which factors affect the rate of decline in serum Na^+, we used multivariate analysis of the data at the onset of, and at 12 and 24 hours of therapy. The level of the initial serum Na^+ correlated positively with the rate of decline in serum Na^+. At 12 hours, a higher Na^+ concentration of the IV fluids was associated with a slower decline in serum Na^+. There was no correlation between the administration rate of IV fluids, receipt of oral fluids or the percentage of dehydration, with the rate of decline in serum Na^+ [Figure 2]. The rate of decline in serum Na^+ also did not significantly vary between the acute gastroenteritis and insufficient breastfeeding groups (0.90 vs. 0.59 mEq/L/hr, $P = 0.14$).

Multivariate analysis of the data after 24 hours of IV fluid treatment revealed that the only variable that correlated with the rate of decline in serum Na^+ at 24 hours was the rate of decline at 12 hours.

There were no deaths, nor any apparent short-term adverse neurologic outcomes among any of the subjects. Only one child had a seizure, which occurred prior to the initiation of fluid administration. Although a formal neurodevelopmental assessment was not performed prior to hospital discharge, nor subsequently, routine examination of each child at the time of discharge revealed that they appeared to have maintained the same level of neurologic and developmental function as before their illness.

Figure 1. Decline in medium serum sodium during the first 48 hours of treatment

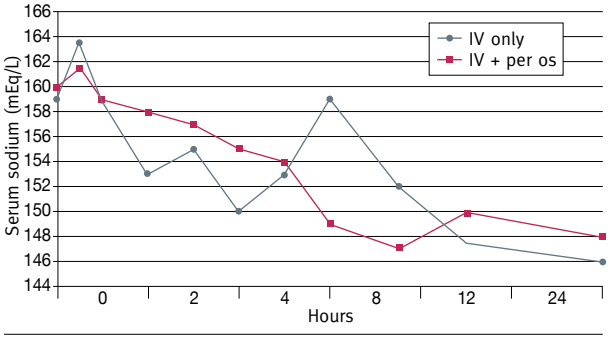
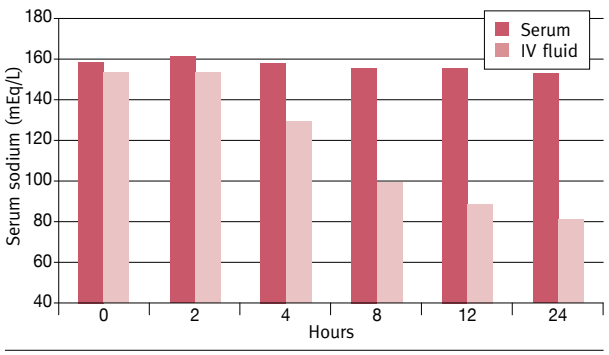


Figure 2. Comparison of median sodium concentration of the serum and IV fluids during first 24 hours of treatment



DISCUSSION

Hypernatremic dehydration in infants may be caused by acute gastroenteritis or insufficient breastfeeding. Lactation failure results in a persistently elevated Na^+ concentration in the breast milk, which, coupled with insufficient milk volume leads to hypernatremic dehydration [20]. In acute hypernatremic dehydration, the extracellular fluid space becomes hypertonic relative to the intracellular space and draws fluid across the osmotic gradient out of the cells. When the condition persists for more than 1–3 days (chronic hypernatremia), cerebral adaptation induces the production of "osmoprotective" molecules which restore the intracellular brain volume. It is then understandable why rapid rehydration or administration of fluid that is relatively too hypotonic could lead to cerebral edema.

Analysis of the fluid management of our 62 patients may be valuable since none developed apparent signs of cerebral edema or other short-term neurologic sequelae (even patients who initially presented with an altered mental status). During the first 24 hours of therapy the children received IV fluids with a high concentration of Na^+, starting with normal saline as a bolus followed by a slow descent in the Na^+ concentration to 122 mEq/L at 12 hours and 88 mEq/L at 24 hours. This allowed for a relatively small difference in Na^+ concentration between the serum and the intravenous fluids particularly during the first 8 hours of treatment when the serum Na^+ was highest, and thus also the risk for cerebral edema.

Since the median dehydration was 10%, fluid resuscitation was a necessary part of treatment. Yet none received a volume of more than 20 ml/kg/hour, and by 24 hours of therapy the cumulative fluid rate had dropped to 5.9 ml/kg/hour. The administration of intravenous fluids at a relatively low rate may also have contributed to the favorable outcome in our subjects. Our cumulative rate approximates that of Fang et al. [19] who, in a retrospective study of 97 children with hypernatremic dehydration, half of whom developed cerebral edema, found that a cumulative IV fluid administration rate at 24 hours of ≤ 6.8 ml/kg/hour was protective against this complication.

Since the median rate of decline in serum Na^+ was 0.65 mEq/L/hr (IQR 0.45–0.95), our result differs from the findings of two recent reports based on which slower correction of the serum Na^+ was recommended. Bolat et al. [18] reviewed the management of 81 neonates with hypernatremic dehydration due to inadequate breastfeeding and found that correcting the serum Na^+ by a rate of > 0.5 mEq/L/hr was a risk factor for death or seizures. Likewise, Fang et al. [19] concluded that a Na^+ correction rate of > 0.5 mEq/L/hr is associated with the development of cerebral edema. By contrast, Robertson and team [6] did not find an association between the rate of decline in serum Na^+ and clinical outcome. That no apparent short-term complications occurred in our study group suggests that a rate of decline in serum Na^+ up to 0.65 mEq/L/hr may be safe.

If slow reduction of serum Na^+ is a key to preventing adverse outcomes, the question then becomes, what affects the rate of decline? Our multivariate analysis suggests that the main determinant is the Na^+ concentration of the IV fluid, further emphasizing the importance of administering IV fluids with a Na^+ concentration that is only minimally less than the serum Na^+ concentration.

To the best of our knowledge this study is the first to account for both IV and oral fluid intake during the treatment period. Blum et al. [21] reported the successful rehydration of 18 infants with hypernatremic dehydration who received exclusively oral fluids. An electrolyte solution containing 60 mEq/L of Na^+ was used and no adverse events occurred. The fluids received by the 42 infants in our study contained very little Na^+ and accounted for approximately one-quarter of the total fluid intake.

Among the limitations of this study are its retrospective design and the relatively small sample size. Further, since none of the subjects had an initial serum Na^+ > 170 mEq/L, our findings may not be applicable to the most severe cases of hypernatremic dehydration. Lastly, as previously mentioned, a formal neurodevelopmental assessment was not performed prior to hospital discharge, nor at a later date for long-term follow-up. We therefore cannot exclude the possibility of subtle neurodevelopmental deficits sustained from the dehydration or its management.

CONCLUSIONS

This retrospective review of the treatment of 62 cases of hypernatremic dehydration in young children suggests that a cumulative IV fluid administration rate of 5.9 ml/kg/hr may reduce the serum Na^+ at an acceptable rate (0.65 mEq/L/hr). Administering IV fluid that is only minimally lower in Na^+ than the serum Na^+ level, especially in the first hours of treatment, may be an important strategy in the management of hypernatremic dehydration. Lastly, we found that the above IV fluid treatment strategy coupled with hypotonic oral fluids comprising up to one-quarter of the total fluids administered did not result in apparent short-term adverse clinical effects in our study population.

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