What Is the Safe Approach for Neonatal Hypernatremic Dehydration?

A Retrospective Study From a Neonatal Intensive Care Unit

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Objectives: The aims of this study were to evaluate the prevalence, complications, and mortality of hypernatremic dehydration in neonates and to compare the effect of correction rate at 48 hours on mortality and on neurological outcome in the short term.

Methods: This retrospective study was conducted between January 2007 and 2011 in the neonatal intensive care unit. Term neonates were included. The patients were grouped as follows: group 1 = 150 to 160 mmol/L, group 2 = 161 to 170 mmol/L and group 3 = 171 to 189 mmol/L.

Results: Among 4280 neonates, 81 cases (1.8%) had hypernatremic dehydration. Groups 1, 2, and 3 consisted of 55, 23, and 3 patients, respectively. Mortality rates were as follows: 3.6%, 17.3%, and 66.6%. Mean serum sodium (Na) correction rates at 0 to 24 hours and 24 to 48 hours were 0.48 ± 0.2 versus 0.38 ± 0.31 mmol/L per hour (group 1) and 0.49 ± 0.21 versus 0.52 ± 0.28 mmol/L per hour (group 2), respectively. In 32 patients (58.1%) from group 1 and in 13 patients (56.5%) from group 2, correction rate of 0.5 mmol/L per hour or less was achieved. Twenty-two patients developed convulsions, which was the most common complication during therapy. Serum Na greater than 160 mmol/L at admission (odds ratio, 1.9; 95% confidence interval, 1.3–3.7) and serum Na correction rate of greater than 0.5 mmol/L per hour (odds ratio, 4.3; 95% confidence interval, 1.2–6.5) were independent risk factors for death or convulsion. There was a significant difference between groups 1 and 2 in Denver Developmental Screening Test II results (64.1% vs 30.7 %, $P = 0.001$).

Conclusion: Hypernatremic dehydration is an important problem that should be managed properly to avoid adverse outcomes.

Key Words: term neonates, hypernatremic dehydration, management, complications

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In the neonatal period, dehydration that occurs as the result of many problems is one of the most common causes of rehospitalization.[1] According to the serum osmolality, dehydration is classified into 3 forms as hypernatremic, normonatremic, and hyponatremic dehydration. Hypernatremic type is a potentially lethal form because it adversely affects central nervous system, leading to devastating consequences such as intracranial hemorrhage, thrombosis, and even death.[2,3] Recently, along with many other etiologies, early discharge and failure of breast-feeding are increasingly documented as major causes of hypernatremic dehydration (HD).[4–6]

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High serum sodium (Na) concentration, which is associated with diminished fluid or excessive Na intake, or excessive fluid loss, is usually caused by inadequate breast-milk feeding in otherwise healthy newborns. Adequate management improves the outcome. Given the lack of trials for determining the optimal therapy on the issue, HD is a challenging problem not only for the emergency department physicians but also for the pediatricians/neonatologists.[7,8]

The aims of our study were to evaluate the prevalence, complications, and mortality of HD and to compare the effect of hypernatremia correction rate at 48 hours on mortality and on neurological outcome at 6 months in hypernatremic neonates without any underlying disease.

METHODS

This study was carried out retrospectively in term neonates with HD, admitted to the neonatal intensive care unit (NICU) of Cumhuriyet University in Sivas, Turkey, between January 2007 and January 2011.

Our NICU serves as a teaching facility and a tertiary center that provides intensive care to nearly 800 neonates annually with 2 neonatologists, 4 pediatric residents, and 20 neonatal nurses.

In this study, we explored the files of healthy, term neonates who were only breast-fed and discharged from hospital postnatally without any disease. From these newborns, the ones who had HD (plasma Na levels of ≥150 mmol/L along with dehydration) because of inadequate breast-feeding were included.[9–11] Neonates were excluded from the study if they had chromosome anomalies, metabolic/endocrine disorders, congenital anomalies, missing data, asphyxia, and sepsis; any source of water loss (diarrhea; ostomy; nasogastric, orogastric, or ventricular drainage); and if they were less than 37 weeks of gestation or resuscitated at birth.

Data of neonates (demographic, clinical, and laboratory characteristics with perinatal history; complications; fluid management; neurological outcomes) were recorded on the study form by a trained doctor. The study protocol was approved by the local ethics committee.

Study Groups

The patients were grouped into 3 according to the serum Na concentrations at admission: group 1 = 150 to 160 mmol/L, group 2 = 161 to 170 mmol/L, and group 3 = 171 to 189 mmol/L. As a routine treatment, 0.3% and 0.45% NaCl were administered to patients in groups 1 and 2, respectively. Group 3 consisted of severely hypernatremic patients and was managed with 0.6% to 0.9% NaCl. The management of this group of patients was reviewed separately.

Definition

The percentage of weight loss was calculated using the formula: [(birth weight − weight at admission) / birth weight × 100].

Dehydration was defined as a weight loss of more than 10% of the birth weight at the end of the first week of life or clinical findings of dehydration with hypernatremia.[10,12] Plasma osmolality was calculated with the formula: osmolality (mOsm/L) = 2 × [plasma Na (mmol/L)] + [plasma glucose (mg/dL)] / 18 + [blood urea nitrogen (mg/dL)] / 2.8.[13] Fever was defined as presence of axillary temperature 37.5°C or greater. Hypoglycemia and hyperglycemia were defined as plasma glucose levels of less than 50 mg/dL and greater than 125 mg/dL, respectively.[14] Acute kidney injury (AKI) was diagnosed as serum creatinine levels greater than 1.5 mg/dL for at least 2 consecutive days after the first 24 to 36 hours of life.[15] Metabolic acidosis was defined as serum pH less than 7.20 and HCO_3 of 12 or less or base excess of −10 or less (with normal CO_2 level).[16] Intracranial hemorrhage and brain edema were defined by computed tomography or cranial ultrasonography.[17] The neonatal hyperbilirubinemia practice guideline of the American Academy of Pediatrics was used to identify and manage hyperbilirubinemia.[18] Ultrasound criteria for diagnosis of renal thrombosis included echogenic clot visibility, venous distension by the thrombus, and absence of flow by color or pulsed Doppler scanning. Cranial ultrasound using a broadband 5- to 7.5-MHz transducer was performed because of suspected intracranial pathology.[19] If there was any need of further evaluation, it was confirmed with magnetic resonance venography. Neonatal convulsion was diagnosed clinically and by an electroencephalogram demonstrating epileptiform activity.[20]

Management

All patients were initially examined by treating physicians. Along with perinatal history, all signs and symptoms were recorded.

On admission, serum levels of blood urine nitrogen, creatinine, electrolytes, glucose, bilirubin, aspartate aminotransferase, and alanine aminotransferase were measured. Complete blood count and arterial blood gas analysis were performed. Serum osmolality was calculated.

The patients diagnosed as having HD without any underlying disease were managed according to hospital hydration protocol (Fig. 1).

Follow-up

Vital signs were recorded every 6 hours, and body weights were measured every day. The follow-up criteria were applied. The outcome measures were evaluated according to the correction rate at 48 hours. The correction of hypernatremia was defined as less than 145 mmol/L.[10,21]

Neurological Outcome

At the time of discharge from the NICU, all the patients with HD were referred to the Pediatric Neurology Department as they were at high risk for adverse neurological outcome. The patients were further evaluated with the Denver Developmental Screening Test II (DDST-II) adapted for Turkish children to determine abnormal neurodevelopmental outcome including developmental delays and learning and behavior problems at the age of 6 months.[22,23]

The test includes multiple items to examine the major categories (gross motor, language, fine motor, and personal-social). Denver Developmental Screening Test II allows 3 different comments on general development evaluation: normal, suspicious, and abnormal.

Outcome Measures

Our primary outcomes were to evaluate the prevalence, complications, and mortality of HD in neonates without any underlying disease; our secondary outcomes were to compare the effect of hypernatremia correction rate at 48 hours on mortality and on short-term neurodevelopmental result.

Statistical Analyses

Statistical analysis was performed using the SPSS 13.0 package program (SPSS Inc,Chicago, Ill). Continuous variables were analyzed by independent Student *t* testing if normally distributed or otherwise by Mann-Whitney *U* testing; χ^2 and Fisher exact χ^2 tests were used for categorical variables. Multiple logistic regression analysis was conducted to determine the risk factors for death or convulsion at 48 hours. Statistical significance was defined as $P < 0.05$.

RESULTS

During the study period, 4280 neonates were admitted to NICU. Among them, 97 had HD. Sixteen patients were excluded from the study. Prevalence of HD was 1.8% (81/4280). All the patients were fed with breast milk. Fifty-nine patients were born in our hospital; 51 patients were discharged from the hospital within the first 48 hours of life.

The age of the infants varied between 2 and 21 days, and Na concentration range was 150 to 189 mmol/L at rehospitalization.

A. Emergency phase

1. All patients with any sign and/or symtom of shock require immidiate attention (Shock management)
2. The correction of vascular volume should be accomplished with 0.9% NaCl (10-20 ml/kg) over half an hour.

B. Rehydration phase

1. Rehydration fluid is 5-10% dextrose with 0.3% -0.45% NaCl (In very high Na levels, consider ≥6% NaCl)
2. Total body water deficit (in L) = [(current Na level in mmol/L ÷ 145 mmol/L) - 1] x total body water (0.73x weight (in kg).The volume of replacement fluid needed to correct the total water deficit (in L) = total body water deficit x [1 ÷ 1 - (Na concentration in replacement fluid in mmol/L ÷ 154 mmol/L)]. Total fluid amount is the sum of total water deficit and maintenance fluid at 48 to 72 hours
3. The recommended rate of sodium correction is 0.5 mmol/L/h or 10-12 mmol/L/day in 24-48 hours.
4. Dehydration should be corrected (serum levels < 145 mmol/L) over 48-72 hours.
5. If the serum sodium concentration is more than 200 mEq/L, peritoneal dialysis should be considered.
6. If the patient is urinating, add 40 mmol/L KCl to aid water absorbtion into cells.

C. Follow up

1. Serum electrolytes should be monitoried with 4-6 h intervals to avoid rapid correction of hypernatremia.
2. Clinical examination should be repeated, vital signs and weight should be checked closely.

FIGURE 1. Treatment and follow-up protocol of HD.

TABLE 1. Demographic, Clinical, and Laboratory Characteristics

Variables	Group 1 (n = 55)	Group 2 (n = 23)	*P*
Birth weight,* g	3450 ± 283	3470 ± 275	0.62
Birth weight on admission,* g	2910 ± 291	2750 ± 460	**0.01**
The degree of dehydration*	16.8 ± 4.4	20.4 ± 6.4	**0.01**
The day of admission†	5 (2–17)	8 (2–21)	**0.03**
Male, n (%)	26 (47.2)	11 (47.8)	0.93
Vaginal delivery, n (%)	39 (70.9)	15 (65.2)	0.57
Maternal age,* y	28.07 ± 6.32	21.2 ± 4.2	**0.04**
First child (yes), n (%)	17 (30.9)	16 (69.5)	**0.02**
Education level of mother, n (%)			
Illiterate	5 (9)	2 (8.6)	0.72
Primary school	23 (41.8)	12 (52.1)	
Middle school	13 (23.6)	4 (17.3)	
High school	8 (14.5)	3 (13)	
University	6 (10.9)	2 (8.6)	
Symptoms at admission,‡ n (%)			
Fever	11 (20)	9 (39.1)	**0.01**
Poor feeding	7 (12.7)	5 (21.7)	
Jaundice	9 (16.3)	8 (34.7)	
Restlessness and irritability	5 (9)	4 (17.3)	
Serum Na level,* mEq/L	156.5 ± 2.6	164 ± 3.06	**0.01**
Serum creatinine level,† mg/dL	1.25 (0.4–8)	1.58 (0.5–4.5)	**0.04**
Serum blood urea nitrogen level,† mg/dL	40 (4–263)	95 (18–178)	**0.03**
Plasma osmolality,† mOsm/L	330 (307–385)	435 (350–490)	**0.04**

*Mean ± SD.

†Median (range).

‡Infants could have 1 or more symptoms.

Values in bold face indicate Statistically significance.

Groups 1, 2, and 3 consisted of 55, 23, and 3 patients, respectively. Demographic, clinical, and laboratory characteristics of the patients were shown in Table 1.

Complications at Admission

Eighteen patients (22.2%) were admitted with AKI, which was the most common complication at admission. Five patients without any cerebral lesions (total 7 patients, 8.6%) presented with convulsions. The number of patients with complications was given in Table 2.

Fluid Therapy

Groups 1 and 2

Five patients in group 1 (9%) and 7 patients in group 2 (30.4%) needed bolus of 0.9% NaCl for hypovolemic shock management. For rehydration, 0.3% NaCl and 0.45% NaCl were administered to 55 patients (group 1) and to 23 patients (group 2), respectively. Although there was not a significant difference in mean serum Na correction rate at 0 to 24 hours (0.48 ± 0.2 vs 0.49 ± 0.21 mmol/L per hour), mean correction rate at 24 to 48 hours was statistically significant between groups 1 and 2, respectively (0.38 ± 0.31 vs 0.52 ± 0.28 mmol/L per hour, $P = 0.034$).

The groups were divided into 2, according to the correction rate of serum Na levels at 48 hours. In 32 patients (58.1%) from group 1 and in 13 patients (56.5%) from group 2, the correction rate of 0.5 mmol/L per hour or less was achieved (Fig. 2). A total of 54 infants had normal serum Na levels at 48 hours (42 from group 1 and 12 from group 2).

Group 3

All the patients had bolus of 0.9% NaCl because of hypovolemic shock management. Then 0.6% NaCl was given as rehydration fluid. At 6 hours, the patient with intracranial hemorrhage (serum Na 189 mmol/L at admission) and the patient with cerebral thrombosis and AKI (serum Na 182 mmol/L at admission) had a correction rate of 0.8 mmol/L per hour and 0.7 mmol/L per hour, respectively. Because the correction rate was more than 0.5 mmol/L per hour, the treatment was changed to 0.9% NaCl. The mean correction rates of these 2 patients at 24 hours were 0.55 and 0.48 mmol/L per hour, respectively.

TABLE 2. Complications in Patients With HD at Admission

Complications*	Group 1 (n = 55)	Group 2 (n = 23)	Group 3 (n = 3)
AKI	7 (12.7)	10 (43.4)	1 (33.3)
Hyperbilirubinemia†	6 (10.9)	6 (26)	2 (66.6)
Hypoglycemia	4 (7.2)	5 (21.7)	2 (66.6)
Convulsion	2 (3.6)	3 (13)	2 (66.6)
Hyperglycemia	—	1 (4.3)	—
Cerebral thrombosis	—	—	1 (33.3)
Intracranial hemorrhage	—	—	1 (33.3)

Figures in parentheses indicate percentages.

*Patients might have suffered from more than 1 complication.

†Hyperbilirubinemia requiring phototherapy.

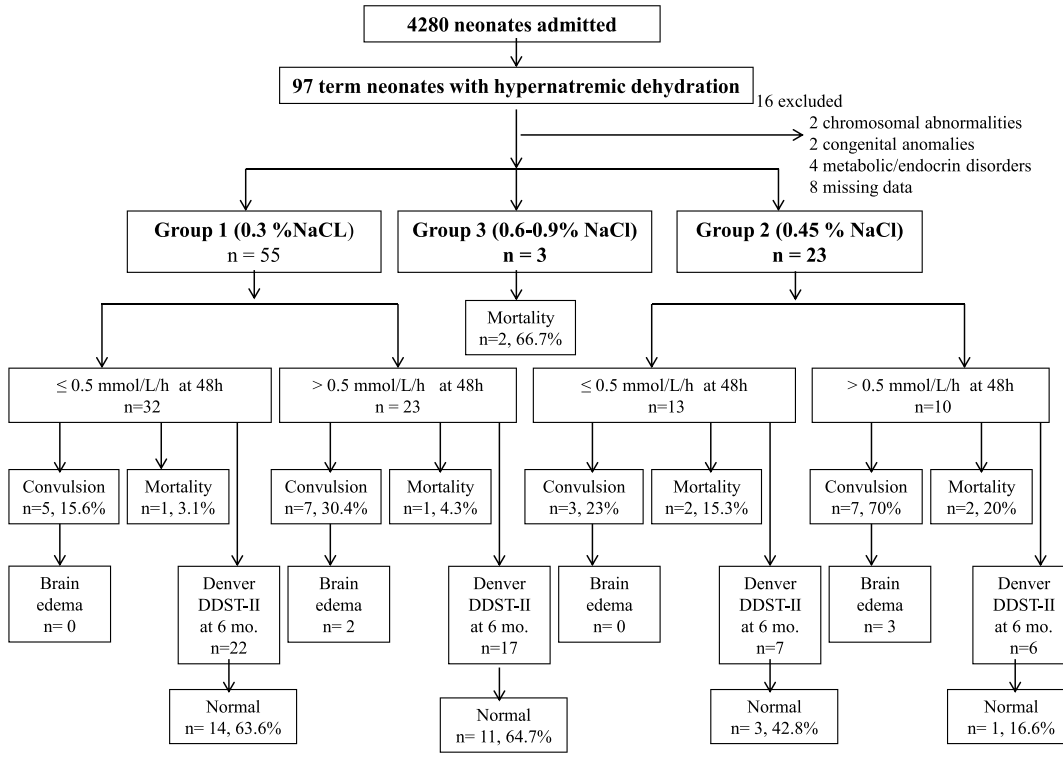

FIGURE 2. Convulsion and mortality during therapy, DDST-II results at 6 months.

Within 24 hours, both of them were intubated because of respiratory failure and brain edema. On the second day of admission, both of them died. The correction rate in the other patient (serum Na 172 mmol/L at admission) was 0.35 mmol/L per hour at 24 hours. The rehydration fluid was changed to 0.45% NaCl after 24 hours. Serum Na level was less than 145 mmol/L per hour at 68 hours. He did not have any complication during fluid therapy.

Complications During Therapy

Twenty-two patients developed convulsions, which was the most common complication during therapy. Among them, 17 patients did not have any cerebral lesions. There was a statistically significant difference in convulsion between groups 1 and 2 (21.8% vs 43.5%, $P = 0.001$). Also, the patients with serum Na correction rate of greater than 0.5 mmol/L per hour had more risk of convulsions, compared with those with serum Na correction rate of 0.5 mmol/L per hour or less (42.4% vs 17.8%, $P = 0.001$).

Mortality

Two patients from group 1, 4 patients from group 2, and 2 patients from group 3 died. Mortality rates were as follows: 3.6%, 17.3%, and 66.6%. There was a statistically significant difference in mortality between groups 1 and 2 (3.6% vs 17.3%, $P < 0.001$). The difference in mortality between patients with serum Na correction rate of 0.5 or less and greater than 0.5 mmol/L per hour was insignificant (6.6% vs 9%, $P = 0.16$).

To find the independent risk factors for death or convulsion at 48 hours, logistic regression analysis was used. Serum Na level at admission, degree of dehydration at presentation, Na concentration of the fluid administered, and serum correction rate of hypernatremia were evaluated. Serum Na of greater than 160 mmol/L at admission (odds ratio, 1.9; 95% confidence interval, 1.3–3.7; $P = 0.024$) and serum Na correction rate of greater than 0.5 mmol/L per hour (odds ratio, 4.3; 95% confidence interval, 1.2–6.5; $P = 0.03$) were independent risk factors for death or convulsion.

Duration of hospitalization was statistically significant between groups 1 and 2 (5.2 ± 2.1 vs 7.8 ± 3.7 days, respectively) ($P = 0.04$).

Neurological Outcome

The 39 patients in group 1, 13 patients in group 2, and 1 patient from group 3 were evaluated with using DDST-II at 6 months. Fourteen patients from group 1 and 6 patients from group 2 were lost to follow-up at the sixth month. The number of patients with normal DDST results was given in Figure 2. The only surviving patient in group 3 had abnormal DDST-II results at 6 months.

There was a significant difference between groups 1 and 2 in DDST-II results at 6 months (64.1% vs 30.7%, $P = 0.001$). However, when patients with serum Na correction rate of 0.5 mmol/L per hour or less were compared with those with serum Na correction rate of greater than 0.5 mmol/L per hour, significant difference was not noted (58.6% vs 52.1%, $P = 0.78$, respectively).

DISCUSSION

Hypernatremia in healthy neonates usually occurs in the first week of life, typically because of inadequate breast-feeding. A large-scale population study suggested weighing the infants in the first week of life, as recommended by the American Academy of Pediatrics, to allow early identification.[24] Because it may have devastating consequences and is a preventable state of dehydration, every effort to avoid the condition and to treat it appropriately if it occurs is an important goal to achieve.

However, there is not a precise guideline for prevention or optimal treatment.

In literature, it is always emphasized that serum Na correction rate of less than 0.5 mmol/L per hour provides better outcomes; there is not a simple formula for achieving the best results, and fluids containing low Na should be avoided.[25–29] On the other hand, some authors cite the rate of less than 5 mmol/L/d, which is equal to 0.2 mmol/L per hour. Correcting serum Na level at such a low rate is likely to be harmful rather than helpful. Alshayeb et al[30] found that patients with first 24-hour hypernatremia correction rate of less than 0.25 mmol/L per hour had significantly higher mortality.

Little has been published on which fluid regimen to use for intravenous rehydration of newborns with HD, and there is no consensus on the most appropriate electrolyte composition of intravenous fluids, with recommendations ranging from 0.18% to 0.9% saline solutions.[29,31,32] With this article, we aimed to state the difficulties neonatologists, and emergency pediatricians may face at management.

The degree of hypernatremia is very important for prognosis, and treatment should be planned according to serum Na level at admission.[10,33] It is stated in literature that Na concentration above 160 mmol/L is a well-known risk factor for adverse outcomes and mortality.[34] We also found that not only serum Na level greater than 160 mmol/L at admission but also correction rate greater than 0.5 mmol/L per hour are independent risk factors for death or convulsion. The difference in mortality between patients with serum Na correction rate of 0.5 or less and greater than 0.5 mmol/L per hour was insignificant, but the patients with serum Na correction rate of greater than 0.5 mmol/L per hour had more risk of convulsions, compared with those with serum Na correction rate of 0.5 mmol/L per hour or less.

The cause of rapid fall in serum Na level is not fully understood, but the combination of hypotonic fluid with nonosmotic stimuli for antidiuretic hormone (ADH) secretion may cause a marked decrease in serum Na in the early period. It is not clear whether hypernatremia in neonates has increased ADH levels.[35] In this study, contribution of ADH in early improvement of serum Na level could not be evaluated as ADH levels were not measured in our institution.

The DDST-II was applied to evaluate the neurodevelopmental status of neonates with HD at 6 months, because it is easy to use, and no specialist training and no specific instruments are required.[36] In this study, significant difference was observed between 2 groups with respect to the neurodevelopmental status in the short-term follow-up, but we observed that correction rate did not influence neurological outcome at 6 months. However, the accurate assessment of neurodevelopment is not precisely reliable in infancy. Long-term follow-up until at least 2 years of age and use of a specific and more sophisticated tool (such as the Bayley scale) are important in the precise assessment of neurodevelopment, as described in the literature.[37,38] Unfortunately, in our hospital, this equipment and clinical psychologist are not available. On the other hand, this short-term neurodevelopmental assessment is crucial because it may offer clues regarding possible future disabilities.[38,39] Koklu et al[40] demonstrated that neurological deterioration occurred in approximately one third of the HD cases in long-term follow-ups. However, Ergenekon et al[39] reported that there was not a statistically significant difference between admission serum Na levels and developmental test scores. Unlike Ergenekon et al,[39] we found that patients with high Na levels at admission had more risk of neurodevelopmental impairment. This can be attributed to our patients' high mean serum Na level.

Taking into account the small number of patients in our study, we cannot comment more on the subject. We suggest that the infants diagnosed with HD should be followed up for a long period to look out for possible adverse effects of the condition, which might cause decreased academic achievement or behavioral problems in the future.

In addition to previously mentioned ones, this study has some more limitations. The data were collected retrospectively from the hospital medical records, and some information was not available. Detailed neurodevelopmental evaluation could not be performed because of limited facilities of our institution and the patients being lost to follow-up.

CONCLUSIONS

Hypernatremic dehydration is an important problem that should be managed properly to avoid adverse outcomes. The optimal treatment depends on adequate hydration along with close follow-up to achieve the right correction rate with the right fluid. Which fluid is right? What are the long-term consequences? What are our mistakes? What else can be done? These questions may be answered by future prospective studies.

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