Original Article

Eur J Gen Med 2017;14(3):63-66
ISSN:1304-3889 eISSN:1304-3897
DOI:10.29333/ejgm/81888

Hypernatremia in hospitalized children

Sevil Yuca[1], Yasar Cesur[2], Huseyin Caksen[3], Derya Arslan[4], Cahide Yilmaz[3], Avni Kaya[4]

ABSTRACT

Objective: Hypernatraemia has serious complications such as brain injury, brain oedema and seizure. In this study, the incidence among children hospitalized hypernatremia, causes, development time, clinical features, and morbidity, and aimed to reveal the effect on mortality.

Method: In this retrospective study, clinical and laboratory data from patients with hypernatremic were recorded. The study period was 33 months. The groups were separated into two groups; group I: Hypernatremia was present at hospital admission, group II: Hypernatremia was acquared after the hospitalization.

Results: Overall incidence of hypernatraemia was 1.3% of all hospitalised children. While 42% of patients were from group I, 58% of patients had acquired hypernatremia during hospital stay. In group I, 61% of patients had infections on hospital admission. The most common cause of hypernatraemia in group II was neurological disorders (53%). The mortality rate was 30.5% (11/36) in patients with hypernatraemia on admission, 67.3% (33/49) in those with hospital-acquired hypernatraemia (P<0.05; significantly greater than for those with hypernatraemia on admission), and 51.7% (44/85) overall. Mean serum sodium level was higher in non-survivors than in survivors (161.7±8.3 mg/dL vs. 160±7.4 mg/dL), but the difference was not statistically significant. Similarly, there was no significant difference in peak serum sodium levels in survivors versus non-survivors, P>0.05.

Conclusion: Hypernatraemia in pediatric age is associated with mortality and morbidity, and should be closely monitored in pediatric patients hospitalized for any reason in order to prevent complication.

Keywords: hypernatraemia, child, mortality

INTRODUCTION

Hypernatraemia is an important electrolyte disorder in hospitalised patients, with an incidence of 1%–3%. It appears mainly in infants or in elderly or mentally handicapped patients, but can present in hospitalised patients for various reason (1-4). It is characterised by water loss or hypertonic sodium gain, which leads to hypertonic hyperosmolality. If something about the reason of hypernatraemia is not clear, measurement of urine osmolality in relation to plasma osmolality and urine sodium concentration may help for differential diagnosis (5). Hypernatraemia has serious complications such as brain injury, brain oedema and seizure, with a reported mortality rate of 40%–60% (6-9).

In our country, diarrhea-induced hypernatremic dehydration is important especially during the summer months (10). Also, hypernatremia reported in the neonatal period due to cultural factors in some areas (11). In this study, we investigated the incidence, clinical characteristics, survival probability, outcomes, concomitant electrolyte abnormalities and differences among 85 patients who are either admitted to hospital with hypernatraemia or who have had hypernatraemia during hospital stay.

MATERIALS AND METHODS

Patients

The study took place in paediatric clinic of Yuzuncu Yil University Hospital over a period of 33 months. We retrospectively obtained patients' clinical and laboratory data from hospital records. In addition to serum sodium level the data included serum glucose, urea, creatinine, uric acid, potassium, chloride, calcium as well as urine osmolality, creatinine and urine sodium. Patients were divided into two groups—those with hypernatraemia on admission (group I) and those with hospital-acquired hypernatraemia (group II). The study protocol was approved by the Ethics Committee of YuzuncuYil University and the administration of the local educational authority.

Definition and classification of hypernatraemia

Children with serum sodium >150 mEq/L were diagnosed with hypernatraemia. In all cases, a detailed medical history was obtained with special attention given to recent use of drugs that are associated with hypernatraemia (e.g. lactulose, sodium, bicarbonate and dexamethasone).

Laboratory tests

Laboratory analyses were carried out by automated chemical analysis in our biochemistry laboratory. Serum biochemical parameters were measured using colorimetric spectrophotometry (COBAS INTEGRA 800; Roche Hitachi Modular Analytics System, Germany). Serum sodium, potassium, glucose, urea, creatinine, uric acid, chloride and calcium were measured with ISE reference electrolyte (Roche Diagnostics GMBH, Germany). Urinalysis was performed using a colorimetric spectrophotometer (iQ 200 and Aution Max AX-4280 analysers; Iris, Chatsworth, CA, USA). Urine sodium and potassium concentrations were measured using flame emission photometry (InstrumentationLaboratory, Lexington, MA, USA). Our reference values for those parameters were as; sodium 135-145 mEq/L, potassium 3.7-4.9 mEq/L, glucose 70-100 mg/dL, urea 15-36 mg/dL, creatinine 0.3-1 mg/dL, uric acid 2.8-5.8 mg/dL, chloride 99-107 mEq/L and calcium 8.5-10.6 mg/dL

[1] *Selcuk University Faculty of Medicine, Department of Pediatric Endocrinology, Konya, Turkey.*
[2] *Yuzuncu Yil University Faculty of Medicine, Department of Pediatric Endocrinology, Van, Turkey.*
[3] *Yuzuncu Yil University Faculty of Medicine, Department of Pediatric Neurology, Van, Turkey.*
[4] *Yuzuncu Yil University Faculty of Medicine, Department of Pediatrics, Van, Turkey.*

Correspondence: *Sevil Ari Yuca*
Barıs cad. Prestij Residence 5.giris No:1, Konya, Turkiye
Telefon: +90 533 523 90 50
Fax: +90- (432) 235 34 34

E-mail: sevilyuca@yahoo.com

Received: 8 Apr 2016, Accepted: 14 Jun 2016

Table 1: *Symptoms of overall patients on hospital admission*

	Group I n=36 (%)	Group II n=49 (%)	Total n=85 (%)	P value
Symptoms				
Diarrhea	9 (25)	12 (24.5)	21 (24.7)	>0.05
Vomiting	8 (22)	17 (35)	25 (29)	>0.05
Pyrexia (> 38 °C)	7 (19)	8 (16)	15 (17)	>0.05
Convulsion	9 (25)	24 (49)	33 (67)	>0.05
Alterations on consciousness	3 (8)	2 (4)	5 (10)	>0.05
Cardiopulmonary arrest	1 (2.7)	2 (4)	3 (6)	>0.05
Feeding difficulty	2 (5.5)	1 (2)	3 (6)	>0.05
Respiratory distresses	2 (5.5)	2 (4)	4 (4.7)	>0.05
Polyuria- oliguria	2 (5.5)	-	2 (2.3)	>0.05
Gastrointestinal hemorrhages	-	3 (6)	3 (6)	>0.05

calibration of laboratory equipment has been carried out though quality control guidelines of of Yuzuncu Yil University Hospital.

Statistical analysis

The Statistical Package for Social Sciences (SPSS for Windows Version 20, Chicago, IL, USA) program was used for assessment of the results. Kolmogorov-Smirnov test was applied for the eligibility of the normality of the data distribution. Results were expressed as mean±SD. Comparisons between individual groups were performed using Student's t test. Correlations between laboratory parameters were assessed with linear regression analysis. P<0.05 was considered to indicate statistical significance.

RESULTS

Six thousand two hundred and five patients (52% boys, 48% girls) were admitted to our clinic during the 33-month study period. The incidence of hypernatraemia on admission was 0.5%; the incidence of hospital-acquired hypernatraemia was 0.8%. The overall incidence of hypernatraemia was 1.3%. Eighty-five patients fulfilled the inclusion criterion of serum sodium concentration. Of these, 36 (42.4%) were hypernatraemic on hospital admission and 49 (57.6%) were found to be hypernatraemic during follow-up. Sixty patients (70.6%) were infants (aged <2 years) at diagnosis. Sixty-one percent of patients who were hypernatraemic on hospital admission and 55% of those with hospital-acquired hypernatraemia were boys. A statistically significant difference according to sex was found in group I (P<0.05) but not in group II (P>0.05).

Symptoms on hospital admission are shown in Table 1. The primary diagnoses in patients with hypernatraemia are listed in Table 2.

There was no significant difference between boy and girls for other biochemical parameters measured. The patients with hypernatraemia had at least one additional electrolyte disorder: either an abnormal glucose level or abnormal uric acid level. However, these additional electrolyte disorders were not shown to be correlated with survival. The main electrolyte disorders in the patient cohort were hyperchloraemia (86%), hypocalcaemia (47%), hyperkalaemia 25 (29.4%) and hyperuricaemia (60%).

To identifyfactors that contributed to the development of hypernatraemia, urine-concentrating ability during hypernatraemia was assessed based on urine osmolality, which was measured in 79 patients. A urine-concentrating defect, defined as osmolality <700 mmol/kg, was present in 67 children: 25 (73.5%) with hypernatraemia on admission and 42(80.7%) with hospital-acquired hypernatraemia (P<0.01).

The most common factors that contributed to impaired renal concentrating ability were neurological disorders (n=6/15) and acute renal deficiency caused by bacteraemia (n=5/9) in each group. Other causes were solute diuresis caused by uraemia (n=2), organic acidaemia (n=1), hyperglycaemia

Table 2: *Primary Diagnoses in Patients with Hypernatremia*

	Group I n=36 (%)	Group II n=49 (%)	Total n=85 (%)	P value
Etiology of hypernatremia				
Infection causes	22 (61)	17 (35)	39 (46)	<0.05
Sepsis	7 (32)	12 (63)	19 (49)	
Bronchopneumonia	7 (32)	4 (26.3)	11 (28)	
Gastroenteritis	8 (36)	1 (10.5)	9 (23)	
Neurological disorders	8 (22)	26 (53)	34 (40)	<0.05
Infections of CNS (meningitis or encephalitis)	4 (50)	14(54)	17 (20)	
Stroke	2 (25)	5 (19)	7 (8)	
Brain edema or encephalopathy	-	7 (27)	7 (8)	
Anatomic disorders	2 (25)	-	2 (2.3)	
Other causes	6 (17)	6 (12)	12 (14)	>0.05
Congenital metabolic disorders	2	2	4	
Nephrogenic diabetes insipidus	1	-	1	
Renal tubular acidosis	1	-	1	
Chronic hepatic failure	1	-	1	
Diabetes mellitus	1	-	1	
Acute myeloid leukemia	-	1	1	
Acute viral hepatitis	-	1	1	
Chronic renal failure	-	2	2	

(n=1), diabetes mellitus (n=1), mannitol administration (n=1, brain oedema), or nephrogenic diabetes insipidus (n=1).

The mortality rate was 30.5% (11/36) in patients with hypernatraemia on admission, 67.3% (33/49) in those with hospital-acquired hypernatraemia (P<0.05; significantly greater than for those with hypernatraemia on admission), and 51.7 % (44/85) overall.

The median age in survivors on study enrolment was lower than in non-survivors: 4 and 1.5 months, respectively. Mean serum sodium level was higher in non-survivors than in survivors (161.7±8.3 mg/dL vs. 160±7.4 mg/dL), but the difference was not statistically significant. Similarly, there was no significant difference in peak serum sodium levels in survivors versus non-survivors p>0.05.

DISCUSSION

The incidence of hypernatraemia was 1.3% of all hospitalised children in our clinic.

Previous studies on the prevalence of hypernatraemia in hospitalised patients have focused on geriatric and adult patients (2, 4, 9, 12), as well as that has been published in pediatric patients (3, 5-7, 13). We aimed to evaluate the incidence, causes and treatment of hypernatraemia in a pediatric population. Hypernatraemia may occur in children of all ages, with the vast majority having significant underlying medical problems. Neonatal hypernatraemic dehydration may be caused by inadequate nutrition and artificial feeds that lead to an elevated level of sodium (11, 14). It has been reported previously that hypernatraemia in infants is caused by gastroenteritis (15-18). Recently, hypernatraemia has been primarily a hospital-acquired disease, caused by failure to administer sufficient free water to patients unable to care for themselves (19).

Seventy-one percent of our patients with hypernatraemia were younger than 2 years old but were not newborn infants. Hypernatremia can detect in hospitalized patients that in the first accepted to hospital or during in the hospital. Underlying infections were the primary reason for hospitalisation in 61% patients who had hypernatraemia on hospital admission; 51% of those with hospital-acquired hypernatraemia had neurological disorders. Although gastroenteritis was responsible for 25% of the cases of hypernatraemia on admission, it occurred in only one patient with hospital-acquired hypernatraemia. Gastroenteritis contributed to hypernatraemia in 11.7% of all patients. Therefore, the incidence of hypernatraemia caused by acute gastroenteritis in infants was much lower than that in previous studies (18). Apart from acute gastroenteritis, 47% of children with hypernatraemia on admission had diarrhoea and vomiting; this increased to 59% in children with hospital-

acquired hypernatraemia (Table 1). Hypernatraemia was caused by infection in 45.8% of cases, and neurological disorders in 38.8%. On the other hand, 23% of patients (20 out of 85) suffered from neurological impairment, critical illness, and chronic disease before developing hypernatraemia. Our patients were younger than 1 year old (62%) and therefore they did not drink water freely. This situation could potentially lead to hypernatraemic dehydration.

Hospital-acquired hypernatraemia often results from inadequate fluid prescription in patients who have increased free-water losses combined with an inability to increase oral water intake freely in response to hypertonicity. Increased free-water losses also may be caused by impaired renal concentrating capacity as well as increased extra-renal fluid losses, enteral losses and insensible losses (1, 13, 20).

An acute and large elevation in plasma sodium concentration to >158–160 mmol/L is usually necessary for symptoms to develop (5). Intense thirst as an important back-up defense may be absent, especially in patients with altered mental status, with hypothalamic lesions that affect the thirst center, or in infants and elderly persons. Non-specific symptoms such as anorexia, muscle weakness, restlessness, nausea and vomiting tend to occur early. More serious central nervous system dysfunction follows, with altered mental status, lethargy or irritability, stupor, coma, myoclonus, asterixis, chorea, or tonic–clonic or absence seizures. Also, acute brain shrinkage can induce vascular rupture with cerebral bleeding and subarachnoid haemorrhage (13). In our study, 33 patients (38.8%) had convulsions on admission, and cerebral haemorrhagic disorders, oedema and altered consciousness were common in group II. Other electrolyte disturbances, such as hyperglycaemia, hyperkalaemia, hyperphosphataemia, hypermagnesaemia and hypocalcaemia, may be accompanied to hypernatraemia (2, 21). The most frequent concomitant electrolyte imbalances were hyperchloraemia (86%), hyperuricaemia (55%), hypocalcaemia (47%) and hyperkalaemia (29.4%) in our cases. These data indicate that most cases had hypertonic dehydration; the additional electrolyte abnormalities were not related to survival.

Hypernatraemia is frequently associated with volume depletion; therefore, it is essential that the management of hypernatraemia provide adequate free water to correct serum sodium level. Thus, water resuscitation with normal saline or colloid should be instituted to correct free water deficit. After initial volume expansion, the composition of parenteral fluid therapy largely depends on the cause of hypernatraemia. Oral hydration should be instituted as soon as it can be safely tolerated. The rate of correction of hypernatraemia is dependent on the severity and cause of hypernatraemia. When hypernatraemia is corrected rapidly, it can lead to cerebral oedema (8-22). In severe hypernatraemia (>170 mEq/L), serum sodium level should not be decreased to <150 mEq/L in the first 48–72 h. Seizures during the correction of hypernatraemia are not uncommon in children and might be a sign of cerebral oedema. Seizures are usually self-limited and not a sign of long-term neurological sequelae (22).

In the present study, eight (9.4%) patients who had hypovolemic dehydration and shock were administered 0.9% NaCl during the first 1 or 2 h, followed by fluid maintenance that was appropriate for the patient's age. If patients had no sign of hypovolemic shock after this course, we gave any supplemental electrolytes before initiating fluid replacement. We administered fluid at age-appropriate levels and waited until serum sodium decreased to normal levels. The mean serum sodium level in patients who were hypernatraemic on admission (160.6±7.8 mg/dL) was not significantly different from that in patients with hospital-acquired hypernatraemia (161.4± 7.9 mg/dL). Hypernatraemia was corrected in 66% of patients within 72 hours; unfortunately, 21% of these patients died during follow-up. Mean time to improvement of hospital-acquired hypernatraemia was 2.4 days (range 1–20 days). The mean time to death for patients with intractable disease was 5.6 days (range 1–29 days) after diagnosis of hypernatraemia. These patients had long-term renal dysfunction and neurological deficit. The mortality rate was higher in patients with intractable hypernatraemia (20 out of 20 [100%]), as compared to 38.5% in patients with hypernatraemia that readily improved. Cerebral oedema during correction of hypernatraemia was not observed. Neurological complications, which occurred in nine (10.6%) patients, were more related to underlying neurological disorders than to hypernatraemia.

In our study, the mortality rate was higher than previously reported (3, 11, 12, 23). However, the high mortality rate could not be directly attributed to hypernatraemia. When we reviewed the patients' medical records carefully, hypernatraemia contributed to mortality in only 4.5% of patients that hospitalized in the children's service. We thought that most deaths occurred from severe infection and neurological disorders, which were in many cases the underlying causes for hypernatraemia.

CONCLUSION

We also suggest that serum electrolyte levels should be closely monitored in hospitalised children to avoid hypernatraemia. Especially, the patients that treated with IV fluid are important to closely follow. The management of serum and electrolyte levels should be performed carefully. In particular, neurologically handicapped and young children should be followed for fluid and serum electrolyte balance during hospitalisation. In summary, treating hypernatraemia and its underlying causes is truly vital in paediatric patients. Very little literature on this topic has been published. We believe that it will be useful for physicians to understand the importance of this issue and monitor electrolytes carefully in this group.

REFERENCES

1. Macdonald NJ, McConnell KN, Stephen MR, Dunnigan MG. Hypernatraemic dehydration in patients in a large hospital for the mentally handicapped. BMJ. 1989;299(6713):1426–1429.
2. Liamis G, Tsimihodimos V, Doumas M, et al. Clinical and laboratory characteristics of hypernatraemia in an internal medicine clinic. Nephrol Dial Transplant. 2008;23(1):136–143.
3. Finberg L. Pathogenesis of lesions in the nervous system in hypernatremic states. I. Clinical observations of infants. Pediatrics. 1959(1);23:40–44.
4. Mahowald JM, Himmelstein DU. Hypernatremia in the elderly: relation to infection and mortality. J Am Geriatr Soc. 1981;29(4):177–180.
5. Adrogue HJ, Madias NE. Hypernatraemia. N Engl J Med. 2000;342(20):1493–1499.
6. Kang SK, Kim W, Oh MS. Pathogenesis and treatment of hypernatraemia. Nephron. 2002;92(1):14–17.

7. Macaulay D, W atson M. Hypernatraemia as a cause of brain damage. Arch Dis Child. 1967;42(225):485–491.
8. Ayus JC, Armstrong DL, Arieff AI. Effects of hypernatraemia in the central nervous system and its therapy in rats and rabbits. J Physiol. 1996;492(1):243–255.
9. Palevsky P, Bhagrath R, Greenberg A. Hypernatraemia in hospitalized patients. Ann Inter Med. 1996;124(2):197–203.
10. Bicer S, Col D, Erdag GC, Giray T, Gurol Y, Yilmaz G, Vitrinel A, Ozelgun B. A retrospective analysis of acute gastroenteritis agents in children admitted to a university hospital pediatric emergency unit. Jundishapur J Microbiol. 2014 Apr;7(4):e9148.
11. Koklu E, Gunes T, Ozturk MA, Kose M, Kurtoglu S, Yuksel F. A review of 116 cases of breastfeeding-associated hypernatremia in rural area of Central Turkey. J Trop Pediatr. 2007;53(5):347–350.
12. Beck LH, Lavizzo-Mourey R. Geriatric hypernatremia. Ann Intern Med. 1987;107(5):768–769.
13. Moritz ML, Ayus JC. The changing pattern of hypernatremia in hospitalized children. Pediatrics. 1999;104(1):435–439.
14. Jacobson J, Bohn D. Severe hypernatremic dehydration and hyperkalemia in an infant with gastroenteritis secondary to rotavirus. Ann Emerg Med. 1993;22(10):1630–1632.
15. Chouchane S, Fehri H, Chouchane C, et al. Hypernatremic dehydration in children: retrospective study of 105 cases. Arch Pediatr. 2005;12(12):1697-1702.
16. Banister A, Matin-Siddiqi SA, Hatcher GW. Treatment of hypernatraemic dehydration in infancy. Arch Dis Child 1975;50(3):179–186.
17. Moritz ML, Ayus JC. Preventing neurological complications from dysnatremias in children. Pediatr Nephrol. 2005;20(12):1687–1700.
18. Pizarro D, Posada G, Villavicencio N, et al. Oral rehydration in hypernatremic and hyponatremic diarrheal dehydration. Am J Dis Child. 1983;137(8):730–734.
19. McManus ML, Churchwell KB, Strange K. Regulation of cell volume in health and disease. N Engl J Med. 1995;333(19):1260–1266.
20. Fitzsimons JT. The physiological basis of thirst. Kidney Int. 1976;10(1):3–11.
21. Rosenfeld W, deRomana GL, Kleinman R, Finberg L. Improving the clinical management of hypernatremic dehydration. Observations from a study of 67 infants with this disorder. Clin Pediatr 1977;16(5):411–417
22. Strange K. Regulation of solute and water balance and cell volume in the central nervous system. J Am Soc Nephrol. 1992;3(1):12–27.
23. Morris-Jones PH, Houston IB, Evans RC. Prognosis of the neurological complications of acute hypernatraemia. Lancet. 1967;30(9730):1385–1389.

◇◈◈◈◈◈◇