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ORGINAL STUDY

Incidence and Outcome of Severe Hyponatremia in Children and Young Adults

A Single Institution Experience

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مدى انتشار انخفاض الصوديوم الشديد ونتائجه
عند الأطفال والشباب تجربة معهد

الملخص: الهدف: هناك هدفين رئيسيين للدراسة وهما تقييم مدى انتشار انخفاض الصوديوم الشديد ومعرفة نتائج هذا الانخفاض عند المرضى الراقدين في المستشفى من الأطفال والشباب. **الطريقة:** بصورة استعادية حسبنا مدى انتشار انخفاض الصوديوم الشديد (أقل من ١٢٥ ملي مول/ ليتر) ونتائجه عند المرضى الراقدين في المستشفى تحت سن ١٨ سنة. والذين أدخلوا لمرات متتابعة خلال سنة تقويمية واحدة. تم استبعاد حالات نقص الصوديوم غير الحقيقي الناجمة عن الأمور الفنية. تم تسجيل المعلومات الديموغرافية والعلامات السريرية والمعطيات المختبرية والعلاج والنتائج. **النتائج:** من مجموع ٣٥٦١ مريضا مرقدا تحت سن ال١٨ سنة. كان هناك ٢٠ مريضا مصابا بانخفاض الصوديوم الشديد. كان من بين الأعراض والعلامات الأكثر **انتشارا:** الغثيان والتقيؤ وعدم الاستقرار وضعف الإحساس بالمحيط الخارجي والنوبات الصرعية. أما الأعراض المصاحبة لذلك فكانت أمراض الجهاز العصبي المركزي وذات الرئة والأورام الخبيثة. تقدير حالة الحجم كانت أكثر من الطبيعي (٧ حالات) وأقل من الطبيعي (٧ حالات) وطبيعي (٦ حالات). لوحظ نقص الحجم لأسباب طبية في ٦٠ ٪ من الحالات - (استخدام الأدوية المدرة للبول) في ٥ حالات. (والسوائل ذي التركيز القليل) في ٧ حالات. بلغت حالات الوفاة ٢٠٪. **الخلاصة:** يجب مراقبة المرضى الذين يعطون سوائل قليل التركيز عن طريق الوريد بصورة دقيقة لكشف حالة انخفاض الصوديوم. السبب الرئيسي لحالات نقص الصوديوم في هذه الدراسة هو طبي المنشأ.

ABSTRACT ***Objective:*** Our two main objectives are to assess the incidence and the outcome of severe hyponatremia in young hospitalized patients. ***Method:*** We retrospectively reviewed the incidence and outcome of severe hyponatremiac (Na <125 mmol/l) inpatients less than 18 years of age, admitted as consecutive admissions during one calender year. Psuedohyponatremia and artifactual hyponatremia were excluded. Patients' demographics, clinical features, laboratory, treatment and outcomes were recorded. ***Results:*** Of 3561 admissions of patients less than 18 years of age, 20 developed severe hyponatremia. Nausea, vomiting, irritability, clouded sensorium and seizures were the most common symptoms and signs. Underlying central nervous system disease, pneumonia and malignancy were major co-morbid conditions. The initial volume status was determined as hypervolemia (n=7), hypovolemia (n=7) and euvolemia (n=6). Iatrogenic (diuretics 5 and hypotonic fluids 7) hyponatremia accounted for 60% of all cases. Mortality was 20%. ***Conclusion:*** Patients receiving intravenous hypotonic fluids should be closely monitored for the development of hyponatremia. The common etiology of hyponatremia in our studied cohort of patients is iatrogenic.

Keywords: Iatrogenic hyponatremia, high morbidity

Hyponatremia (serum sodium <135 mmol/l) has an incidence ranging from 15-20% in hospitalized patients.[1] Severe hyponatremia is less common and studies addressing this particular issue in pediatric inpatients are few.[2-13] Although the incidence of severe hyponatremia is not very high, this particular patient population is clinically significant due to associated predisposing conditions and adverse outcomes.[2] Severe hyponatremia is also known to be a marker of serious illness in sick children.[3]

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Table 1. ***Patients' demographics, clinical features, laboratory, treatment and outcome***

No.	Age	Sex	Pre- Fluids	Lowest Na	Volume Status	Treatment	Co-morbidities	Symptoms	Outcome
1	8	M	None	110	⇧	D	DCM	SOB	Died
2	5	M	Hypo	123	⇩	NS	DM	N, V, I	Discharged
3	3	M	Hypo	107	⇩	NS	SCD	N, V	Discharged
4	9	M	None	124	⇔	FR	BMT	N, V	Discharged
5	9	M	None	122	⇔	None	Surg, CNS	I	Discharged
6	8	M	Hypo	124	⇩	NS, ABX	SCD	N, V, Sz	Discharged
7	7	M	None	122	⇩	NS	CLD	Ac, Hem	Discharged
8	6	F	Hypo	120	⇩	NS	SCD	Pain	Discharged
9	2	M	Hypo	111	⇧	D, HS	Pneumonia	N, V, I	Discharged
10	1	M	Hypo	123	⇧	ABX	Down Synd, A-V Shunt, Sepsis	N, V, Sz	Discharged
11	2	M	None	123	⇩	NS	Pneumonia	N	Discharged
12	2	M	Hypo	122	⇧	D	Fanconi synd, Rickets	None	Discharged
13	<1	M	Hypo	117	⇔	ABX	Preterm, Sepsis	None	Discharged
14	<1	F	None	117	⇔	NS	Asphyxia, SAH	Sz	Died
15	<1	M	NS	107	⇧	D	CAH	V, I	Discharged
16	<1	F	None	120	⇧	HS	Inborn error of metabolism	Sz	Died
17	<1	M	Hypo	123	⇧	D	CNS	V	Discharged
18	<1	M	Hypo	117	⇔	None	Preterm	Sz	Discharged
19	<1	F	Hypo	123	⇔	ABX	CNS,Sepsis	Sz	Discharged
20	<1	M	None	120	⇔	None	Heart block, renal failure, DM	None	Died

M= Male; F= Female; Pre-Fluids= Fluids administered before the development of hyponatremia; Hypo= Hypotonic fluids; ⇧=Hypervolemic; ⇩= Hypovolemic; ⇔= Euvolemic; D= Diuretics; NS= Normal saline; FR=Fluid restriction; ABX=Antibiotics; D=Diuretics; DCM= Dilated cardiomyopathy; DM=Diabetes mellitus; BMT= Bone marrow transplant; Surg= Surgical procedure performed; CNS= Central Nervous system disease; SCD= Sickle cell disease; CLD= Chronic liver disease; SAH= Subarachnoid hemorrhage; CAH= Congenital Adrenal Hyperplasia; SOB=Shortness of breath; N=Nausea; V=Vomiting, I=Irritability; AC=Altered level of consciousness; Hem=Hematemesis; Sz=Seizure

METHOD

We retrospectively studied hospitalized patients <18 years old with severe hyponatremia (arbitrarily defined as serum sodium less than 125 mmol/l) admitted to Sultan Qaboos University Hospital from 1st January 1998 to 31st December 1998. These patients were identified through the computerized hospital information system (HIS). Patients where hyponatremia was considered to be artifactual (single serum sodium measurement of <125 mmol/l, which on repeat assessment within 6 hours, was normal >135 mmol/l without any therapeutic intervention) were excluded. Serum sodium was measured by indirect ion-selective electrode method (Beckman) and quality control values were set within 2%.

Demographic data, physical signs and symptoms, laboratory data, treatment before and after the diagnosis of severe hyponatremia, associated comorbid conditions and outcome were collected. Total number of pediatric admissions and deaths were also obtained for comparison.

RESULTS

There were 3561 admissions of patients less than 18 years of age in 1998. Twenty one patients had serum sodium of <125 mmol/l but one patient was excluded due to artifactual hyponatremia. The remaining 20 patients were considered having true severe hyponatremia. Out of the 20 patients studied, 16 were male and 4 were females. All patients developed severe hyponatremia during hospitalization. Major co-morbid conditions included central nervous system disease 3, malignancy 2, pneumonia 2, diabetes mellitus 2, hypertension 2, and post-surgery 1. Nausea, vomiting, irritability and seizures were the most common clinical features. Seven patients were considered as hypervolemic (hypertensive, elevated central venous pressure, edema and/ or use of diuretics). Seven patients were dehydrated (judged on the basis of clinical findings of dry mucus membranes, sunken eyes, hypotension and intravenous fluid requirement). Six patients were classified as euvolemic (not falling into either hypovolemic or hypervolemic categories). Use of hypotonic fluids was observed in 11 patients (35%) and diuretics in 5 (25%) prior to development of severe hyponatremia. None of the patients received antidiuretic hormone (ADH) analogs. Two patients were treated with hypertonic fluids; four were treated with isotonic fluids while the rest were managed with discontinuation of inciting agent (hypotonic fluids or diuretics). Of 3561 patients, thirty-one deaths were recorded for non-hyponatremic pediatric and young adult inpatients during the same period and four deaths in twenty patients with severe hyponatremia. Hence the mortality in general pediatric inpatients was 0.87% compared to 20% in patients with severe hyponatremia. Although we did not compare our patients with a cohort of similar co-morbid conditions without hyponatremia, but comparison with unselected non-hyponatremic patients showed mortality rate of 20 times high for hyponatremic patients. One patient was discharged with residual neurological deficits and four patients (2 male and 2 female) died.

DISCUSSION

Hyponatremia has been described with variable frequencies in children and young adults. The described frequency varies according to the level of hyponatremia and age range under study.

Iatrogenic factors are known to account for 40-66% of cases of hyponatremia.[1] Common causes of iatrogenic hyponatremia include excessive water intake[5] or intravenous administration of hypotonic fluids,[6] use of antidiuretic hormone or its analogs,[7] Carbamazepine,[8] diuretics and postoperative hyponatremia.[9] Administration of hypotonic fluids and diuretics were common causes in our series. Postoperative hyponatremia was seen in only one patient.

Neurological symptoms such as irritability and seizures are dependant on the rate of development of hyponatremia. Chronic hyponatremia tends to be less symptomatic because of adaptation of cells in response to slowly developing hypoosmolality.[10] Patients who developed seizures have a higher mortality. Routine anticonvulsants may be ineffective in seizures due to hyponatremia.[11] Use of hypertonic saline to correct hyponatremia, if used judiciously, is known to be safe and effective. However, because of the risk of development of Osmotic Demyelination Syndrome (ODS), hypertonic saline should preferably be reserved for patients with acutely developing hyponatremia who become symptomatic. Acute hyponatremia should be corrected slowly and during the infusion of hypertonic saline serum levels should be monitored closely.

In our series only two patients who had seizures were treated with hypertonic fluids and one of the two died. As these patients did not have autopsies, ODS was not diagnosed. Imaging studies such as CT and

MRI of brain may not show lesions typical of ODS for as long as a month. It may take 10 months for typical CT and MRI changes of ODS to appear.[2]

Mortality associated with hyponatremia is often high. It is difficult to determine the direct effect of hyponatremia to mortality rates due to the usual coexistence of the other high risk co-morbid conditions. Dunn and Butt reported a mortality of 19% in their study of severe hyponatremia in pediatric inpatients,[13] which is comparable to our observation.

CONCLUSION

We confirm that severe hyponatremia in pediatric inpatients is associated with 20-times higher mortality when compared to unselected patients of the same age range. Caution should be exercised in administration of hypotonic feeds or fluids. Patients, who for some reason receive hypotonic fluids, should be monitored for development of hyponatremia. Hypotonic fluids need to be discontinued if hyponatremia develops. For symptomatic hyponatremia, hypertonic fluids should be considered and used judiciously. Serum sodium should be monitored closely during therapy with hypertonic saline.

In the presence of significant comorbid conditions, it is difficult to assess direct contribution of hyponatremia to death. Prospective studies are therefore required to assess accurately the etiology, iatrogenic component, adverse neurological and fatal outcomes, and the cost of care.

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