Hyponatremia in ICU
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Abstract

Background: Hyponatremia is defined as serum sodium level <135 meq/L. It is the most common electrolyte abnormality seen in hospital admissions worldwide. The proportion is even higher in the ICU setting. A wide variety of factors influence the outcome of the hyponatremic patient. Present study is designed to approach to analyse etiology, clinical features, co-morbid factors, severity of hyponatremia, rate of correction, and impact of treatment on outcome of these diverse group of patients in ICU.

Aims: 1) To find proportion of patients presenting with hyponatremia and requiring medical ICU admission in a tertiary care set up. 2) To study the etiology and clinical features of hyponatremia in patients requiring ICU admission. 3) To compare and study the effect of various factors on the outcome of hyponatremic patients in the ICU.

Methods: This study was a cross-sectional observational study in tertiary care hospital. All indoor general medicine ward admissions over a period of 18 months were screened for the presence of hyponatremia and patients requiring Medical ICU care and satisfying inclusion criteria were studied. Serial serum electrolytes and urine sodium were tested for all patients in the ICU satisfying the inclusion criteria. Type of fluid given and daily correction of serum sodium of all patients were noted. Outcome was measured in terms of mortality, duration of stay in ICU, number of days required for sodium correction and complications of treatment if any. Patients were followed up till hospital discharge or death.

Results: In this study, 5.2% of total admissions had hyponatremia. Among the ICU admissions, the different symptoms attributed to hyponatremia included nausea (69.3%), malaise (80%), drowsiness (61.3%), confusion (41.3%), lethargy (24%), frequent falls (1.3%), convulsions (2.7%), altered sensorium (41.3%) and delirium (9.3%). SIADH was the most common cause of hyponatremia in these patients (32%). Serum sodium levels of patients on admission ranged from 82 – 133 meq/L, with average serum sodium being 124 meq/L. Overall mortality among the hyponatremic ICU admissions was 26/75, 34.6%, which was higher than the total ICU mortality of 26% in same duration (p = 0.1). There was a significant increase in duration of stay in ICU in patients with various co-morbidities (p=0.003). There was a significant association between Glasgow Coma Scale (GCS) and serum sodium levels, (p = 0.002). Blood pressure and hydration status did not significantly influence outcome. Lower serum sodium on admission was associated with a lower survival (p= 0.041). Sodium correction of < 5 m eq/day was associated with an increased mortality(p = 0.04), whereas sodium correction of > 10 m eq/day was not associated with increased mortality, but an increased risk of EPM, which was seen in one patient.

Conclusion: Most common cause of hyponatremia in ICU patients is SIADH. Longer duration of stay is seen in the presence of different co-morbidities. A lower GCS and a lower serum sodium on admission is associated with lower survival. Type of fluid used for hyponatremia correction did not influence the outcome. Under correction of hyponatremia in first 24 hours or inadequate correction was associated with a poorer outcome. Overcorrection was not associated with any survival benefit, but was associated with risk of EPM.

Introduction

Hyponatremia is defined as serum sodium level <135 meq/L. It is the most common electrolyte abnormality seen amongst hospitalized patients worldwide.1 Prevalence of hyponatremia in hospital admissions vary between 3.4% to 39.4%2-4 and even higher in ICU setup. The commonest cause of euvolemic hyponatremia found among different studies is the syndrome of inappropriate antidiuretic hormone (SIADH),1,5 however many studies have also found diuretic therapy, congestive cardiac failure and liver disease to be the most common causes.6

Assessment of the volume status is helpful in determining the type of hyponatremia as it occurs because of a relatively greater amount of total body water as compared with total body solute.7 It is important to rule out pseudohyponatremia secondary to hyperglycemia and hyperlipidemia. Urine sodium, serum and urine electrolytes are important basic investigations needed to arrive at the etiology of hyponatremia. Hypovolemic hyponatremia is associated with clinical symptoms and signs of volume depletion. Hyponatremia without signs of volume depletion or overload is classified as euvolemic. Patients with clinically detected increased ECF volume are classified as hypervolemic hyponatremia.8,9

Treatment approach to hyponatremia depends on the type of hyponatremia. Patients with hypovolemic hyponatremia are mainly treated by repleting the ECF volume with Normal Saline (NS). Water restriction and 3% saline are the mainstay of treatment of euvolemic and hypervolemic hyponatremia. Acute
hyponatremia (developing in < 48 hrs) can present with severe symptoms of hyponatremic encephalopathy and can culminate into brain herniation and death if not intervened immediately. Consensus is that acute symptomatic hyponatremia can be treated by a bolus of 3% NaCl given over 10 minutes, to raise the serum sodium by 4 – 6 meq/L. Chronic hyponatremia is to be treated at slower rates, as neurological sequelae are associated with more rapid rates of correction. Patients with euvoletic hyponatremia due to SIADH, hypothyroidism, or secondary adrenal failure will respond to successful pharmacologic therapy to increase an increase in plasma Na concentration. However, not all causes of SIADH are immediately reversible, necessitating pharmacologic therapy to increase the plasma Na concentration. Finally, patients with hyponatremia due to beer potomania and low solute intake respond very rapidly to intravenous saline and the resumption of a normal diet.

Materials and Methods

Following were the aims and objective of study
1. To find proportion of patients presenting with hyponatremia and requiring medical ICU admission in a tertiary care set up.
2. To study the etiology and clinical features of hyponatremia in patients requiring ICU admission.
3. To compare and study the effect of various factors (including different co morbidities) and treatment (rate of correction) on the outcome of hyponatremic patients in the ICU.

It is a cross-sectional observational study in tertiary care hospital. All indoor general medicine ward admissions over a period of 18 months were screened for the presence of hyponatremia (serum Na 135 meq/L) and patients requiring ICU care and satisfying inclusion criteria were studied. Patients who develop hyponatremia later on during the course in ward (after 24 hours of admission) and patients with pseudohyponatremia (Patients with hyperlipidemias, paraproteinemias and those having redistributive hyponatremia (mannitol therapy, hyperglycemia) were excluded. Sample size was 75 patients.

Detailed history and clinical examination was noted which included demographic factors, history of symptoms of hyponatremia, like nausea and vomiting, headache, confusion, gait disturbances, tendency to fall, loss of energy and fatigue, restlessness and irritability, muscle weakness, spasms or cramps, seizures, coma and history of co-morbid health conditions, similar history in the past. Detailed examination was done with specific emphasis on volume status and CNS examination. Serum electrolytes and urine sodium were tested for all patients in the ICU satisfying the inclusion criteria. Routine hematological and biochemical investigations were carried out which included CBC, electrolytes, renal and liver function tests and ABG. Special tests like serum osmolarity, urine osmolality, thyroid function tests, basal cortisol, CT, MRI, CSF examination, etc were carried out only when they were indicated. Patients were classified in euvoletic, hypovolemic and hypervolemic types of hyponatremia based on clinical findings. In euvoletic patients, the Bartter and Schwartz criteria was used to confirm diagnosis of SIADH.

Outcome was measured in terms of mortality, duration of stay in ICU, number of days required for sodium correction, complications of treatment if any (osmotic demyelination syndrome, fluid overload, requirement of ventilator support, morbidity due to underlying disease). Patients were followed up till hospital discharge or death. All statistical analysis was performed by using 10.0 version of statistical Software SPSS. Continuous variables were summarized by using summary statistics (number of observations, mean and standard deviation). Categorical values were summarized by using frequencies and percentages. Association between outcome with different parameters were estimated by using Chi Square test and Student’s t test as per relevance.

Results

Out of 24,675 admissions in the medical wards during this period, 1283 patients (5.2%) had hyponatremia on the day of admission (Defined as serum sodium <135meq/L). Of these, 78 hyponatremic patients were admitted in the MICU. Three were excluded in view of pseudohyponatremia (hyperlipidemia). Forty six (61.3 %) of the cases were males and median age was 48 years. Presenting symptoms of hyponatremia are shown in Table 1.

There was almost equal distribution of all the three types of Hyponatremia, with 25 being euvoletic, 27 being hypervolemic and 23 being hypovolemic type of hyponatremia. All the patients with euvoletic hyponatremia had SIADH, except one, who had psychogenic polydipsia. Commonest cause of SIADH was pulmonary pathology (17 patients). Two patients had CNS infection. Other causes included GBS (3 patients), NMDA Receptor encephalitis (1 patient) and idiopathic SIADH (1 patient). Of the 27 patients with hypervolemic hyponatremia, 14 had AKI, 6 had CKD, 5 had congestive heart failure, 2 had cirrhosis of liver. Of the 23 patients with hypovolemic hyponatremia, 8 had cerebral salt wasting, 4 had AKI, 8 had dehydration due to different causes, 2 had diuretic induced hyponatremia, and one had salt losing nephropathy. In this study, 28% of the patients had systolic blood pressure (SBP) <100 mmHg on admission, 63.3% had SBP between 100 and 140 mmHg, and 18.6% had SBP ≥ 140 mm Hg. Also, 38.6% of the patients had CVp < 6, and 61.3 % had CVp ≥ 6 (significantly higher, p < 0.05). GCS ≤10 was seen in 36% of patients, whereas 64% had a GCS > 10.

Serum sodium levels of patients on admission ranged from 82 – 133 meq/L, with average serum sodium being 124meq/L. Number of patients with Urine sodium ≤ 20 was 9, and those with urine sodium > 20 were 66. Average serum osmolarity was 265. Average Hb was 11 g/dL. Forty one percent of the patients had serum creatinine of > 1.5 mg/dL. One patient who presented with delirium was detected to have hyponatremia related

Table 1: Proportion of different symptoms of hyponatremia

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No. of cases</th>
<th>% of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>52</td>
<td>69.3</td>
</tr>
<tr>
<td>Malaise</td>
<td>60</td>
<td>80.0</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>46</td>
<td>61.3</td>
</tr>
<tr>
<td>Lethargy</td>
<td>31</td>
<td>41.3</td>
</tr>
<tr>
<td>Confusion</td>
<td>18</td>
<td>24.0</td>
</tr>
<tr>
<td>Frequent falls</td>
<td>1</td>
<td>01.3</td>
</tr>
<tr>
<td>Convulsions</td>
<td>2</td>
<td>02.7</td>
</tr>
<tr>
<td>Altered sensorium</td>
<td>31</td>
<td>41.3</td>
</tr>
<tr>
<td>Delirium</td>
<td>7</td>
<td>09.3</td>
</tr>
<tr>
<td>Coma</td>
<td>-</td>
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</tr>
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</table>
significant association between CVP on admission and survival (0.9), duration of correction of hyponatremia (0.1) and duration of stay in ICU (0.053). There was a significant association between GCS and serum sodium levels, with them being directly proportional to each other (p = 0.002 by student t test). Lower GCS was associated with a significantly lower survival (p by student t test = 0.038) (Figure 2). Also, patients with a shorter duration of correction of hyponatremia had a higher GCS, compared to those who took longer time (>5 days) for correction of hyponatremia (p = 0.06). No significant association was found between GCS and duration of ICU stay (p = 0.4). There was a significant association between serum sodium on admission and survival, with lower sodium levels associated with lower survival (p = 0.04 by student t test). Also, patients with a lower sodium level on admission, had a significantly longer duration of correction of hyponatremia (p = 0.03 by student t test). However, there was no significant association between serum sodium on admission, and the duration of stay in ICU (p = 0.4). No association was found between serum creatinine on admission and survival (p = 0.9) as well as duration of stay in ICU (p = 0.2), however, patients with lower creatinine had a significantly shorter duration of correction of hyponatremia (p = 0.014 by chi square test) (Table 2). Of the 75 patients, only 8 required 3% NaCl for correction, and the remaining were treated with normal saline. Sodium correction on day 1 ranged from 4 to 17 meq/L.

Total mortality was 26/75 (34.6%) patients, which was higher compared to total ICU mortality (26%) in same duration. Majority of the patients who did not survive had a sodium correction of <5 meq/L/day on first day. There was a significant correlation between sub-optimal correction of sodium and mortality (p = 0.04). Lower sodium levels on admission were associated with a longer duration of correction of hyponatremia, but the difference was not statistically significant (p = 0.07). However, no association was found between sodium correction on day 1 and duration of stay in ICU (p = 0.2). Also, as can be seen in Figure 3, sodium correction of >10 meq/L/Day (3 patients) although did not increase mortality, caused complication in one,
in the form of development of 65 extra pontine myelinolysis (EPM). Four patients developed hypernatremia, out of which only one had sodium correction per day of > 10 m eq/L. EPM was treated with therapeutic re-lowering of serum sodium, and patient clinically improved over a course of four weeks. Fluid overload was another complication of treatment that was noted in 4 patients (one CKD and 3 AKI), of which one subsequently required hemodialysis.

Discussion

In this study, 5.2 % of the total admissions had hyponatremia. A study done by Chatterjee et al in Kolkata showed a prevalence of hyponatremia of 16.4% (1). However, it included patients who developed hyponatremia after admission also. In this study of 75 hyponatremic patients admitted in the Medical ICU Male: Female ratio was 1.58. Age ranged from 13 to 90 years, with median age being 48 years. Different studies have shown that increasing age is a strong independent risk factor for hyponatremia, however gender is not an important risk factor.44

Among the ICU admissions, the different symptoms attributed to hyponatremia included nausea (69.3%), malaise (80%), drowsiness (61.3%), confusion (41.3%), lethargy (24%), frequent falls (1.3%), convulsions (2.7%), altered sensorium (41.3%) and delirium (9.3%). The most common presenting complaints/ reasons for admission in MICU in this study were breathlessness (44%) and altered sensorium (29.3%), followed by fever (10%), oliguria (6%), drowsiness (4%), acute flaccid paralysis (3%), acute gastroenteritis (2%), jaundice (1%), and poisoning (1%). The different co-morbid conditions / end-organ damage that were assessed included hypertension, diabetes mellitus, chronic kidney disease, acute kidney injury, ischemic heart disease, tuberculosis and HIV. In this study, 28% of the patients had systolic blood pressure (SBP) <100 mmHg on admission, 63.3% had SBP between 100 and 140 mmHg, and 18.6% had SBP ≥ 140 mm Hg. Also, 38.6% of the patients had CVP < 6, and 61.3 % had CVP ≥ 6 (significantly higher, p < 0.05). Glasgow Coma Scale (GCS) ≤10 was seen in 36% of patients.

This study showed a similar distribution among the three types of hyponatremia among the MICU admissions, with the number of patients with hypovolemic hyponatremia being 23, euvolemic being 25 and hypervolemic being 27. Causes of hypovolemic hyponatremia included diarrhea, thiazide induced, cerebral salt wasting, salt losing nephropathy, euvolemic included SIADH and psychogenic polydipsia, and hypervolemic included congestive heart failure, AKI, CKD and liver cirrhosis. According to one study, there was a wide range of aetiologies: diuretic therapy, congestive cardiac failure and liver disease were the most common, and 75.3% of patients had multiple causes.4 Another study showed that thiazides were responsible for severe diuretic-induced hyponatremia (serum sodium level < 115 mEq/L) in 94 percent of 129 cases reported in the literature between 1962 and 1990.15 However, SIADH has been unanimously found to be the most common cause of hyponatremia in different studies.

Serum Sodium levels ranged from 88 to 133 m eq/L with the average being 124.29 m eq/L. Out of the 75 patients, 2 patients had Sr. Na < 110 meq/L (2.6%), 11 patients had Sr. Na of 110 – 119 meq/L (14.6%), 45 patients had Sr.Na of 120 – 129 meq/L(60%) and 17 patients has Sr. Na ≥ 130 meq/L (22.6%).

Outcome

Apart from treatment related factors, the influence of co-morbid conditions and clinical factors at presentation has not been studied intensively in literature. In this study, outcome was measured in the form of survival, duration of correction of hyponatremia and duration of stay in ICU. Overall mortality among the hyponatremic ICU admissions was 26/75, 34.6%, which was higher than the total ICU mortality of 26% in same duration. Males had a shorter duration of stay in ICU compared to females (duration < 5 day in males 80% vs females 58.6%, p= 0.02). This study showed that the presence of hypertension, diabetes mellitus, chronic kidney disease did not have any influence on the overall survival of the patients. The presence of different co-morbidities also did not significantly affect the duration of correction of hyponatremia. On studying the effect of different co-morbidities on the duration of stay in MICU, it was found that patients with the presence of various co-morbidities had a significantly longer stay in the ICU (>5 days). One study showed that compared with patients with normonatremia (135-144 mEq/L), those with hyponatremia had more co-morbid conditions.16

A higher proportion of patients who survived had a normal SBP, compared to those who did not survive. Patients with a lower systolic BP on admission had a shorter duration of correction of hyponatremia, compared to patients with a normal or high SBP. Patients with higher SBP on admission had longer duration of stay in ICU. CVP level on admission did not influence survival. Proportion of patients with a CVP >6cm of H2O, had a shorter duration of correction of hyponatremia, compared to those with a lower CVP on admission. In this study patients with lower GCS had poor survival. Also, higher proportion of patients with GCS >10 had a shorter duration of correction of hyponatremia, as well as a shorter stay in the ICU compared to the patients with GCS<10. One study showed that there was no correlation between initial sodium level and ICU stay, as well as between GCS score and the ICU stay.3

There was a significant association between serum sodium on admission and survival, with patients with lower sodium levels on admission having lower survival rates (p=0.04). Also, lower sodium levels were associated with significantly longer duration of correction of hyponatremia but did
not affect duration of stay in ICU. A meta-regression analysis showed that the hyponatremia related risk of overall mortality was inversely correlated with serum sodium. However, according to a 1984 study conducted on hyponatremic hospitalized patients, the relationship between hyponatremia and outcome is probably not causal. Rather, hyponatremia appears to be a marker for severe underlying disease that carries a poor prognosis. According to present study, the admission serum creatinine did not predict the survival or the duration of ICU stay, however, a lower serum creatinine (<1.5) was significantly associated with a shorter duration of correction of hyponatremia, compared to patients with a higher serum creatinine on admission. One study showed that hyponatremia was associated with an adverse outcome in patients with CKD. The duration of correction of hyponatremia was not significantly affected by the type of fluid used in our study group of patients. It neither predicts the survival, nor the duration of stay in ICU. The appropriate fluid must be given depending on the type and severity of hyponatremia. One study showed that more aggressive therapy with 3% saline may improve outcome in symptomatic patients. This study showed that patients with <5 meq/day of sodium correction on day 1 took a longer duration for sodium correction compared to patients who had > 5meq/day correction of sodium. Also, majority of the patients who did not survive had < 5 meq/day correction of sodium. The rate of correction did not have any effect on the duration of ICU stay, as it was influenced by the underlying illness. Four patients developed fluid overload, and one developed extra-pontine myelinosis EPM as a complication of treatment. Studies state that neurological sequelae are associated with faster rates of correction, and correction of chronic severe hyponatremia should be < 10 mmol/l in 24 h. However, another study states that more aggressive therapy with 3% saline may improve outcome in symptomatic patients, and that a slow rate of correction in severe hyponatremia is associated with higher mortality than rapid correction, at least in the short-term. Frequent monitoring of Na is the key to management. Mortality among the hyponatremic patients was 34.6%, which was higher compared to 26% overall mortality in the ICU.

Conclusion

Hyponatremia complicates approximately 5.2% of the hospital admissions, of which 6% of patients require ICU admission. Among the hyponatremic patients that required ICU admission, hypovolemic, euvolemic and hypervolemic types are found in similar number. Most common cause of euvolemic hyponatremia is SIADH. Common clinical features attributed to hyponatremia included malaise, nausea and drowsiness. There is a trend towards higher mortality among hyponatremic patients admitted to the ICU compared to the total ICU mortality. Longer duration of stay is seen in the presence of different co-morbidities, however there is no significant influence on mortality or the duration of correction of hyponatremia. Vital parameters and volume status on admission does not significantly influence the outcome. A lower GCS and a lower serum sodium on admission is associated with prolong ICU stay and lower survival. Type of fluid used for hyponatremia correction did not influence the outcome. Under correction of hyponatremia in first 24 hours or inadequate correction was associated with a poorer outcome. Overcorrection is associated with serious sequel.

References

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