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CLINICAL SPECTRUM OF HYPONATREMIA IN MEDICINE ICU

Medicine

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ABSTRACT

Hyponatremia is the most commonly encountered electrolyte abnormality in a hospital setting. Recent studies on hyponatremia have been limited to the patients with severe hyponatremia and there has been no consensus on optimal management of hyponatremia. High mortality among the patients of hyponatremia is secondary to the underlying medical condition, rather than the degree of hyponatremia.

KEYWORDS

hyponatremia in hospitalized patients admitted in ICU

INTRODUCTION:

Hyponatremia is the most common disorder of electrolytes encountered in clinical practice. Although many cases are mild and relatively asymptomatic, hyponatremia is nonetheless important clinically because of the potential for substantial morbidity and mortality.

Despite knowledge of hyponatremia since the mid-20th century, this common disorder remains incompletely understood in many basic areas because of its association with a plethora of underlying disease states, and its causation by multiple etiologies with differing pathophysiological mechanisms.

The approval of the first vasopressin receptor antagonist (vaptan) in 2005 heralded the beginning of a new era in the management of hyponatremic disorders.

The incidence of hyponatremia is roughly 12% (Paniker GI & Joseph S) in ICU hospitalized patients but precise incidence of hyponatremia varies depending on the conditions leading to and the criteria used to define it.

Optimal treatment strategies have not been well defined, both due to these reasons, and because of marked differences in symptomatology and clinical outcomes based on the acuteness or chronicity of the hyponatremia.

Nandani Chatterjee et al, In study conducted for a period of 1 year in tertiary care hospital in Eastern India. The total number of patients admitted in that period was 1221,out of them 201 patients 16.4% had a serum Na of <135mEq/L. The most common underlying predisposing factor for hyponatremia was gastro-intestinal fluid loss followed by cerebrovascular accidents and pulmonary sepsis.

Another study by Thomas Vurgese et al ;In a study done on frequency and etiology of hyponatremia in adult hospitalized patients in medical wards of a general hospital, the commonest cause of hyponatremia was concluded as SIADH due to pneumonia. Overall incidence of hyponatremia was 3.6%. Out of these 56% were males and 44% were females. The commonest age group affected was 45-64 years. The mean serum sodium levels were 122mmol/L in 59% patients.

Mahavir Agarwal et al, In a comparative study of the "Clinico-etiological profile of hyponatremia at presentation with developing in-hospital" common symptoms were concluded as confusion (14%), headache(40%) and malaise(38.6%). Decreased intake followed by increased losses were concluded as the most common. 31.4% developed hyponatremia during their stay in the hospital. Drugs, Fluid overload and inappropriate Ryle's tube feeding more commonly precipitated hyponatremia.

Miyashita J et al, "In study on impact of hyponatremia and SIADH on mortality in critically ill patients with aspiration pneumonia" concluded that hyponatremia due to SIADH was strongly associated with increased mortality in critically ill patients (29%) of221 patients.

Chatterjee et al' on "Descriptive study of hyponatremia" (Incidence 16.4%) found out in there study of 100 patients, Male sex was predominant (63%), which was similar to the study done by Huda et al'. However the study done by Ashraf et al' showed a female predominance (71%). Age distribution were between 11 – 80 years of which majority were above 41 years and mean age was 55.05 ± 2D. 68% were between ages 41 – 70 years, commonest cause for SIADH in his study was respiratory infections (Pneumonia, Pulmonary Tuberculosis) and Stroke.

Taking an idea from the previous studies,aim of this study was to assess the incidence of hyponatremia in hospitalized patients admitted in ICU of Deptt Of Medicine, All india institute of medical science patna. To describe the etiological factors, clinical manifestations associated with hyponatremia and the treatment modalities for hyponatremia and documentation of treatment related complication. For all the patients clinical and demographic detail, final diagnosis, investigations and management were recorded onto a standard data collection sheet as per the study performa and later transferred to a Microsoft Excel spreadsheet for analysis.

Data were recorded on a predesigned performa and managed in a Microsoft Excel spreadsheet. All the entries were double-checked for any possible keyboard error. Data so collected were systematically analyzed. Data were presented as frequency distribution and simple percentages. Descriptive statistics i.e. mean and standard deviation were calculated for the continuous variables. Categorical variables were expressed as percentages.

AIMS AND OBJECTIVES

1. To assess the incidence of hyponatremia in hospitalized patients admitted in ICU of Deptt of Medicine, Aiims patna.
2. To describe the etiological factors responsible for hyponatremia inhospitalized patients.
3. To describe clinical manifestations associated with hyponatremia
4. To describe the treatment modalities for hyponatremia and document treatment related complications.

MATERIALS AND METHODS

Source Of Data

The study was conducted in the ICU of Department of Medicine, All india institute of Medical, Science, Patna. All admitted patients whose serum electrolytes (serum sodium) had been estimated, were identified from the biochemistry laboratory records. Those patients with a serum sodium concentration less than 135 meq/L at any point during the admission were included in the study.

Inclusion Criteria:

All adult (age >18 yrs) patients admitted to ICU of Deptt of Medicine, AIIMS Patna, with documented hyponatremia, defined as serum sodium concentration ([Na+]) less than 135 meq/L, were included in the study.

Exclusion Criteria:

Patients with pseudohyponatremia (defined by hyponatremia in the

absence of any obvious etiology and presence of hyperproteinemia and/or hypertriglyceridemia) were excluded from the study.

METHODOLOGY

Clinical Assessment

(a)Detailed history- This included history of symptoms of hyponatremia, predisposing factors and pre- existing illnesses if present. The definition ofsymptomatic hyponatraemia was based on a clinical assessment of symptomatology including the presence of altered sensorium, postural dizziness, lethargy and seizures.

Sensorium changes comprised acute confusional states, memory disturbances stupor, delirium and/or coma in the absence of dementia, psychiatric illness and substance abuse. Drugs that can increase the non-osmoticrelease of antidiuretic hormone (ADH) or potentiate its renal action (ADH stimulating drugs) were recorded. History of illnesses causing hyponatremia such as congestive heart failure, chronic kidney disease, chronic liver disease, hypothyroidism and other conditions which are associated with SIADH such as small cell lung carcinoma, CNS disease, pulmonary diseases were taken and recorded. History of fluid loss as in vomiting, diarrhea, diuretic use, excessive sweating was taken in all patients.

(b)Physical examination- Detailed clinical evaluation was done in everypatient. Hydration status of the patient was determined by clinical examination.The signs of hypovolemia included tachycardia, orthostatic falls in bloodpressure, decreased skin turgor, dry mucous membranes and decreased peripheral perfusion with a delayed capillary refill more than three seconds. Hypervolemic state was defined by the presence of anasarca, ascites, symmetrical and pitting pedal edema and raised jugular venous pressure (JVP). Accordingly patients were divided into hypervolemic, hypovolemic and euvolemic states.At the time of diagnosis of hyponatremia detailed CNS examination was done to document the signs of raised ICP (bradycardia, hypertension and papilloedema), mental status of the patient and other focal neurological deficit.CNS examination was repeated after the correction of hyponatremia and thepresence of symptoms such as dizziness, lethargy, altered sensorium andseizures were attributed to hyponatremia unless there was a coexisting medicalcondition or medication effect to account for these symptoms. Patients werescreened for osmotic demyelination syndrome ODS based on clinical grounds (i.e. the development of confusion, agitation and flaccid or spastic paralysis during or after correction of hyponatraemia) and magnetic resonance imaging was done as confirmatory test.

Investigations

(a) Complete blood count – Hemoglobin (Hb), total leukocyte count (TLC),differential leukocyte count (DLC) and platelet count.
(b) Urine routine examination (RE) and microscopic examination (ME) andspecific gravity.
(c) Serum sodium – serum sodium was done 6-8 hourly in patients with severehyponatremia on 3% saline infusion. In symptomatic patients not on hypertonic saline serum sodium was done daily till the correction of hyponatremia. In asymptomatic patients it was done every alternate day. Serum electrolytes were measured by an ion selective electrode system
Rosche 9180 electrolyte analyzer.
(d) Serum blood urea nitrogen (BUN) and glucose levels – for calculation ofserum osmolality
(e) Serum osmolality was calculated by the formula:

SIADH diagnostic criteria- The diagnostic criteria used were as described byVerbalis-

Essential Criteria

1. Extracellular fluid (ECF) effective osmolality below 270 mOsm/kg water.
2. Inappropriate urinary concentration (>100 mOsm/kg).
3. Clinical euvolemia (absence of signs of hypovolemia and hypervolemia)
4. Increased urinary [Na+] while on a normal salt and water intake.
5. Absence of adrenal, thyroid, pituitary or renal insufficiency or diuretic use.

Supplemental Criteria

1. Abnormal water load test (inability to excrete at least 90% of 20 ml/kg waterload in 4 h and/or failure to dilute urinary osmolality to below 100mOsm/kg).
2. Plasma AVP level inappropriately raised relative to plasma osmolality.
3. No significant correction of plasma [Na+] with volume expansion but improvement after fluid restriction.

RESULTS

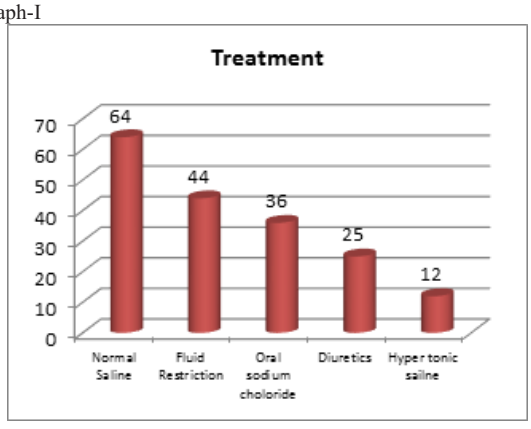
Incidence - A total 7562 patients were admitted to the medical emergency and wards out of which 614 patients were transferred ICU of Dept of Medicine, All india institute of Medical, Science, Patna, between the period one year 102 patients out of the admitted patients in ICU developed hyponatremia giving an incidence ratio of **17.58%.**

Treatment

1. **Oral Sodium Chloride Supplementation** – Oral sodium chloride supplementation was given in 36 patients. All the patients receiving hypertonic saline were given oral sodium chloride supplementation after symptomatic improvement and when oral intake could be resumed.
2. **Normal saline (0.9% NaCl)** – Normal saline was given in 64 patients either for correction of hyponatrmia or as a part of fluid therapy.
3. **Hypertonic saline** – 3% saline was used only for severe hyponatremia patients or those with neurological symptoms. Total 12 patients required hypertonic saline infusion.
4. **Diuretics** – 25 patients were given loop diuretics for promoting free water excretion which included patients of dilutional hyponatremia (CHF, cirrhosis of liver, renal disorder) and patients with SIADH.
5. **Water restriction** – Fluid restriction equal to urine output of previous 24 hours was advised in 44 patients either for correction of hyponatremia or as a part of treatment of the basic disease as in CHF or CKD.

The various strategies adopted for the patients for correction of hyponatremia has been summariazed in Graph-I.

Graph-I



6. **Potassium Replacement** – Total 13 patients developed hypokalemia due to comorbid conditions like vomiting and diarrhoea or due to diuretic use. These patients were given oral potassium supplements.

7. The aim was to correct the serum sodium levels gradually by increasing sodium levels at 8-10 meq/L/day. This aim was achieved in most of the patients.

8. Duration of correction of hyponatremia – Mean duration of correction of hypnatremia ranged from 3 days to 17 days and mean duration of correction was 6 days.

9. Treatment related complications- As detailed below one patient treated with hypertonic saline developed osmotic demyelination syndrome with characteristic clinical and MRI features. No other complications were noted in other patients.

10. Ten patients had persistent hyponatremia at the time of discharge from the hospital. It was associated with diuretic use in 3, CHF in 2, SIADH in 2, liver disease in 1, poor intake in 1 and colostomy fistula in 1 patient.

Complications of treatment of hyponatremia - One patient of severe hyponatremia during the study had a rare renal salt wasting state. This

patient had presented initially to another instiitute with progressively increasing quadriparesis with preserved deep tendon jerks, intermittent carpopedal spasms and one episode of generalized seizures following a short febrile illness and acute gastroenteritis. The patient was treated with hypertonic saline for severe hyponatrmia (serum sodium 113 meq/L) for two days outside our hospital. However there was no improvement in the clinical status of the patient and hyponatremia persisted despite treatment with hypertonic saline.

On detailed evaluation she was found to have concomitant hypokalemia (2.4 meq/L), hypomagnesemia (0.80 mg/dl) and hypocalcemia (5.90 mg/dl) with urinary magnesium wasting and metabolic alkalosis. She was diagnosed to have renal salt wasting secondary to Gitelman's syndrome, an autosomal recessive disease characterized by mutations in the gene coding for the thiazide-sensitive Na-Cl cotransporter in the distal tubule. Her quadriparesis failed to improve despite correction of all the electrolyte deficiencies. MRI brain was done which 65 showed characteristic bat's wing appearance of central pontine myelinolysis (CPM) which was presumably related to the hypertonic saline treatment.

Mortality –A total of 19 (19%) patients in this study died during the study period from factors other than hyponatremia. Most common cause was advanced cirrhosis of liver, present in 9 patients. 2 patients died due to urinary tract infection leading to sepsis. Other causes responsible for death were HIV infection with tubercular meningitis in 5 patients, carcinoma ovary with multiple metastasis in one patient and end stage kidney disease in 2 patient. Out of 31 patients of severe hyponatremia in our study 7 patients died, thus giving a mortality of 22.58 % among the patients of severe hyponatremia.

DISCUSSION

Hyponatremia is the most common electrolyte disturbance seen in hospital practice. It is more common in the elderly patients with multiple medical comorbidities. Hyponatremia has been associated with considerable morbidity and mortality in many chronic diseases, most notably in patients with congestive heart failure and cirrhosis of liver.

Hyponatremia also leads to increased health care cost and the majority of these costs are attributable to the incremental resource utilization for patients who were not admitted specifically for hyponatremia, but whose hospitalization was prolonged due to hyponatremia.

In previous studies incidence of hyponatremia in hospitalized patients was found to be about 1% to 6% and specifically for ICU set up it was found to be between 15% to 30% depending upon the basic facilities and infrastructure of the ICU setup. 5-year retrospective study of 2,188 patients, Bennani et al found the incidence of hyponatremia to be 14% at the time of admission to the intensive care unit while DeVita et al found the incidence of hyponatremia in ICU to be 29.6%. In this study incidence of hyponatremia in ICU patients was 17.58 %. Incidence of hyponatremia has been shown to have direct correlation with age.

In our study 65% of the patients were 50 to 80 yrs old. Multiple co-morbidities like Hypertension and Diabetes Mellitus are present in this age group treatment of which predisposes a patient to hyponatremia. Use of diuretics is also more common among the elderly patients, which has been a major cause of hyponatremia in hospitalized patients. Hawkins et al noted that increasing age, after adjusting for sex, was independently 70 associated with both hyponatremia at presentation and hospital-acquired hyponatremia.

In the present study prevalence of hyponatremia was more in male patients with male: female ratio of **1.56 : 1** (61 males and 39 females). This is due to the fact that the number of patients admitted in the male medical and surgical wards outnumbered the patients admitted in the corresponding female.

Major clinical manifestations of hyponatremia were lethargy (33%) and postural dizziness (28%) which occurred with equal frequency in both severe and moderate hyponatremia.

In this study **54%** patients had varied neurological manifestations of hyponatremia however only one of the patients had seizures.

In this study 19 (19%) of the patients had hyponatremia due to renal disorders out of which 17 patients had pre-existing renal disease, one patient had acute renal failure and one patient was diagnosed to have Gitelman's syndrome. Total 8 (8%) patients had liver disorder (7 patients with pre-existing liver disease and 1 had acute viral hepatitis) and another 8 (8%) patients had hyponatremia due to heart failure.

Thus 33 (33%) of the patients in this study had pre-existing renal isorder, heart failure or chronic liver disease. 26 out of these 32 patients were admitted to the hospital due to non-compliance with treatment and inappropriate fluid intake leading to volume expansion and dilutional hyponatremia.

In our study 7 out of 31 patients of severe hyponatremia were on thiazide diuretic. Saeed et al, studied hyponatremia in hospitalized patients and in 19 out of 57 patients (33.3%) it was associated with diuretic use.

In a study by Huda et al, 14 out of 22 (63.6%) patients of hyponatremia on diuretics were taking thiazide diuretics. Our hyponatremic patients who were taking a loop diuretic had at least one other cause for the hyponatremia in the form of liver disease, heart failure, vomiting or post-operative status. Loop diuretics are frequently used to treat conditions such as congestive cardiac failure and cirrhosis in which hyponatremia occurs due to hypervolemia, while thiazide diuretics are being prescribed routinely for management of primary hypertension especially in the elderly age group.

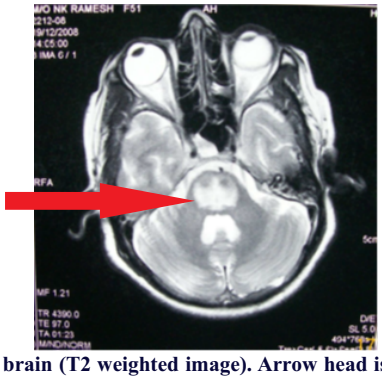


Fig. MRI brain (T2 weighted image). Arrow head is showing T2 hyperintensity in pons showing bat's wing appearance suggestive of ponine demyelination.

SUMMARY &CONCLUSION

Out of 7562 patients admitted in medicine emergency of All india institute of Medical, Science, Patna.**614** patients were transferred to ICU for their critical illness and treatment during study period (june 2019 to 31st July 2020). 102 patients among the admitted patients in ICU developed various degrees of hyponatremia giving the incidence of **17.58%**.

This study included 100 patients of hyponatremia in hospitalized patients in medicine ICU of AIIMS, Patna and data were recorded on a predesigned performa and managed in a Microsoft Excel spreadsheet. All the entries were double-checked for any possible keyboard error. Data so collected were systematically analyzed.

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