Original Research Article

Study of etiology, clinical features and outcome following treatment of hyponatremia in elderly in intensive care unit

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Abstract

Background: Hyponatremia is a common electrolyte disturbance in the hospitalized elderly sick patients.

Objectives: To study etiology, clinical features and outcome following treatment of hyponatremia in elderly hospitalized patients.

Materials and methods: All elderly patients being admitted to ICU were screened for hyponatremia and 100 patients with severe hyponatremia (<125 meq/L) were included in this study, these patients were investigated as per the protocol and were treated as per the standardized regimen.

Results: 100 patients with severe hyponatremia (<125 mEq/L) were studied. There was female preponderance of cases (55%). The common causes of hyponatremia were SIADH (30%) and drugs (24%) of which diuretics (79%) was a major chunk. The common CNS symptoms were drowsiness, lethargy and irrelevant talk. The common co-morbid conditions were hypertension (62%) and diabetes mellitus (51%). Females tolerated hyponatremia better than males with mortality of 9.09% in females and 33.33% in males (p=0.0026). 20 (20%) patients succumbed to their primary illness with a possible contribution attributable to hyponatremia or its treatment.

Conclusion: Hyponatremia is common in females and they seem to better tolerate it than their male counterparts. Early detection, strict adherence to treatment protocol is required. Diuretics should be used with caution in elderly.

Key words

Hyponatremia, Ederly patient, SIADH, Diuretics, Outcome.

Introduction

Hyponatremia is defined as a serum sodium concentration of less than 135 mEq per L, which is the most common dyselectrolytemia in the geriatric age group [1] and observed in almost 50% of geriatric admissions. The prevalence of hyponatremia in elderly population is about 18-22.3% [2-4]. Studies suggest that hyponatremia may be present in 34.3% patients in Intensive Care Units [5]. This incidence is more in elderly due to impaired ability to maintain water and electrolyte homeostasis in response to dietary, environmental and physiological changes occurring with age affecting the renal system.

Hyponatremia can be classified on the basis of serum osmolality, volume status and urinary sodium into hypotonic, isotonic and hypertonic types. Hypotonic hyponatremia is further classified as hypovolemic, euvolemic and hypervolemic as follows [6]: 1. Hypovolemic hyponatremia: decreased total body sodium and decreased total body water, the sodium deficit exceeding water deficit. 2. Euvolemic hyponatremia: normal body sodium with increase in total body water. 3. Hypervolemic hyponatremia: increase in total body sodium with greater increase in total body water.

Common causes of hyponatremia in geriatric hospitalized patients includes drugs (thiazide and loop diuretics, proton pump inhibitors, NSAIDS), coexisting morbidities (congestive cardiac failure, chronic kidney and liver disease, respiratory infections, volume overload, dehydration etc.) [7-12]. The clinical manifestations of hyponatremia vary from asymptomatic to mild symptoms like lethargy, malaise to severe neurological manifestations like seizures, altered sensorium [2]. The number and severity of symptoms increase with the degree of hyponatremia and the rapidity with which it develops. Severe and rapidly evolving hyponatremia may present with seizures, coma, permanent brain damage, respiratory arrest, brainstem herniation, and death [13].

Management of hyponatremia is etiology specific after assessing volume status of the patient. Patients with acute symptomatic hyponatremia are candidates for aggressive treatment [14-18]. The main controversy in the literature surrounds treatment of chronic symptomatic hyponatremia because central pontine myelinolysis may result if the condition is corrected too rapidly [14-18]. Key to successful management is frequent monitoring of serum electrolytes to ensure adherence to the guidelines outlined. Clinicians should have a clear appreciation of the roles that iatrogenic interventions and lapses in nutrition and nursing care frequently play in upsetting the homeostatic balance in elderly patients particularly those who are in long-term institutional and inpatient settings [19].

With this background we undertook this study to investigate etiology, clinical features and outcome following treatment of hyponatremia in elderly patients admitted to Medical Intensive Care Unit as there are very limited studies available in our country so as to improve the management of hyponatremia in elderly patients and to decrease the morbidity and mortality.

Materials and methods

This cross sectional observational study was conducted in Government Medical College and Hospital, Nizamabad, Telangana State between 1st October 2016 to 30th September 2017. All elderly patients admitted to MICU were screened

for hyponatremia and 100 patients with severe hyponatremia (<125 mEq/l) were included in this study. Written Informed consent was obtained from the patients and institutional ethics clearance was taken. Relevant history including h/o compulsive water drinking, past medical history, drug history specially of diuretics, symptoms and clinical examination were recorded in all patients. On admission voluemic status of the patient was assessed by examination. All patients were subjected to serum sodium levels (on admission, every day during rapid corrections/ symptomatic period, then as and when indicated), serum osmolality/ urine osmolality (by freezing point depression osmometer), urine spot sodium (by ion sensitive electrode method), serum cortisol level (when indicated), serum T3,T4, TSH (where indicated), imaging studies (as relevant to the admission diagnosis), other routine investigations like complete blood count, renal function tests, serum electrolytes, liver function tests, urine routine, chest radiograph were done. With a clinical diagnosis of type of hyponatremia and other blood investigations reports patients were classified into hypo, iso or hypervolemic hyponatremia. Based on the type of hyponatremia and severity of symptoms patients were started on correction of hyponatremia by taking into account the standard guidelines and formulae. All patients were followed till discharge from the hospital and outcomes were categorized as improved or expired.

Inclusion Criteria

- Patients of age 60 years and above
- Patients of serum sodium level less than 125mEq/L

Exclusion Criteria

- Patients of less than 60 years
- Patients of serum sodium level more than 125 mEq/L
- Patients with dyslipidemia and hypoprotienemia

Diagnosis of Hyponatremia

Hyponatremia: Serum sodium <135mEq/L
Severe Hyponatremia: Serum sodium <125mEq/L

Statistical methods

The excel and SPSS (SPSS Inc, Chicago) software packages were used for data entry and analysis. The results were averaged (mean± standard deviation) for continuous variable parameters, numbers, and percentage for discrete variables are presented. The following methods of statistical analysis were used in this study.

Results

Of the total 1440 elderly patients hospitalized during the study period for 1st October 2016 to 31st September 2017, 518 (36%) patients had hyponatremia (serum sodium <135 mEq/L) and 100 (6.9%) patients (study group) had severe hyponatremia (serum sodium <125mEq/L)

Among the 100 study patients, 55 (55%) patients were female and 45 (45%) patients were male, which indicates preponderance of hyponatremia among elderly female patients. Maximum patients (53%) were in the age group of 60 to 69 years (**Table – 1**).

Table - 1: Age and Sex distribution of patients (N=100).

Age group	Male	Female	Total
60-69	25(25.00%)	28(28.00%)	53(53.00%)
70-79	10(10.00%)	15(15.00%)	25(25.00%)
80-89	09(9.00%)	11(11.00%)	20(20.00%)
90-100	01(1.00%)	01(1.00%)	02(2.00%)
Total	45(45.00%)	55(55.00%)	100(100.00%)

Among the study group on admission 65% of patients were euvolemic, 25% overloaded and 10% were dehydrated. 15 patients had very sever hypontremia with serum sodium levels less than 105 mEq/l, 32 patients had serum sodium levels between 105 to 115 mEq/l and 53 patients had serum sodium levels between 115 to 125 mEq/l
The most common cause of hypontremia in our study was SIADH (30%) followed by drug induced (24%) (**Table – 2**).

Table - 2: Etiology of hyponatremia amongst study patients.

Etiology		No. of Patients	%
SIADH		30	30.00
Renal		21	21.00
GI Loss		13	13.00
Drugs	Diuretics	19	24.00
	Others	5	
Endocrine		4	4.00
Cardiac(IHD/CCF)		3	3.00
Cerebral Salt wasting		3	3.00
Cirrhosis of liver		2	2.00

The most common comorbid disease in our study was hypertension, (62%), followed by diabetes mellitus (51%) (**Table – 3**).

Table - 3: Comorbid diseases amongst study patients.

Comorbidity	No. of Patients	%
Hypertension	62	62.00
Diabetes mellitus	51	51.00
Ischemic Heart Disease/CCF	18	18.00
Renal Failure	22	22.00

The mean serum sodium level on admission was 113.89mEq/l, and after correction it was 129.54 mEq/l. 76 patients on admission had CNS symptoms attributed to hyponatremia whereas 24 patients had no CNS sympotms (**Table – 4**).

Table - 4: CNS Symptoms on admission amongst study patients.

CNS Symptoms	No. of Patients	%
Lethargy	29	29.00
Drowsy +Irrelevant talk	31	31.00
Drowsy+ Slow	33	33.00
Seizures	4	4.00
Headache	8	8.00
Disturbed sleep	3	3.00
Confusion	2	2.00
Unresponsiveness	7	7.00`
No CNS symptoms	24	24.00

84 patients had non CNS symptoms attributed to hyponatremia on admission **Table – 5**).

Table - 5: Non CNS Symptoms on admission amongst study patients.

Non CNS Symptoms	No. of Patients	%
Vomiting	31	31.00
Diarrhea	13	13.00
Anorexia	31	31.00
Hiccups	04	4.00
Pain abdomen	11	11.00
Fever/ Sweat	14	14.00

Among 100 patients studied 80 (80%) patients improved 20 (20%) patients expired, all of them died due to severity of presenting illness.

The age of the patients who improved ranged from 60 to 90 years with mean age of 71.96±9.63. Among the patients who expired the age ranged from 60 to 90 years with mean age of 72.4±9.29. There is no statistically significant difference between the mean age of the group of patients who improved and expired (**Table – 6**).

Table - 6: Mean age of the study patients according to outcome.

Outcome	N	Mean	Std. dev	Min.	Max.
Improved	80	71.96	9.63	60	90
Expired	20	72.40	9.29	60	90
Diff(1-2)		-0.438	9.5595		

t-value: 0.19, p value: 0.8529

Among the 80 patients who improved 50 were female and 30 were male. And among the 20 patients who expired 15 were male and 5 were female. This indicate that among the 45 male patients admitted 30 (66.67%) patients improved and 15 (33.33%) patients expired whereas among 55 female patients admitted 50 (90.91%) improved and 5 (9.09%) expired, which shows that although sever hyponatremia is more common among females the response to

treatment and survival is better among females than males (p=0.0026) (**Table – 7**).

Table - 7: Sex distribution amongst study patients according to outcome.

Outcome	Male	Female	Total
Improved	30(66.67%)	50(90.91%)	80
Expired	15(33.33%)	05(9.09%)	20
Total	45	55	100

Statistics	DF	Value	Prob
Chi-sqaure	1	9.0909	0.0026

With relation to the type of hyponatremia and outcome there is no significant difference between the groups with regards to outcome (p=0.2559) (**Table – 8).**

Table - 8: Type of hyponatremia amongst study patients according to outcome.

Type of Hyponatremia	Outcome		Total
	Improved	Expired	
Hypervolemic-Hyposmolar	20(25.00%)	2(10.00%)	22
Hypervolemic-Isoosmolar	1(1.25%)	0(0.00%)	1
Hypovolemic-Hyposmolar	10(12.5%)	6(30.00%)	16
Isoovolemic-Hypoosmolar	47(58.75%)	11(55.00%)	58
Isoovolemic-Isoosmolar	2(2.50%)	1(5.00%)	3
Total	80	20	100

Statistics	DF	Value	Prob
Chi-sqaure	4	5.32	0.2559

Among the patients who presented with CNS symptoms of hyponatremia, 57patients (75%) improved and 19 patients (25%) expired and among those patient who did not have any CNS symptoms on admission 23 (95.83%) improved and 1 (4.17%) expired this indicates that among patients who have CNS symptoms 25% patients succumbed to their illness whereas 95.83% patients who do not have any CNS symptoms survived (p=0.0261) (**Table – 9**).

Table - 9: CNS symptoms amongst study patients according to outcome.

Outcome	CNS Symptoms on admission		Total
	Yes	No	
Improved	57(75.00%)	23(95.83%)	80
Expired	19(25.00%)	01(4.17%)	20
Total	76	24	100

Statistics	DF	Value	Prob
Chi-sqaure	1	4.9479	0.0261

Among the patients who had non CNS symptoms 67 patients (79.76%) improved and 17 patients (20.24%) expired. Among the patients who did not have non CNS symptoms 13 patients (81.25%) survived and 3 patients (18.75%) expired. There is no statistically significant difference between the groups with or without non CNS symptoms (p=0.8915), (**Table – 10**).

Table - 10: Non CNS symptoms amongst study patients according to outcome.

Outcome	Non CNS Symptoms on admission		Total
	Yes	No	
Improved	67(79.76%)	13(81.25%)	80
Expired	17(20.24%)	03(18.75%)	20
Total	84	16	100

Statistics	DF	Value	Prob
Chi-sqaure	1	0.0186	0.8915

Patients with severe hyponatremia with sodium level less than 105 mEq/l on admission had a mortality of 33.3%, where as those with serum sodium between 105 to 125 mEq/l had a mortality of 17.6%, though the values are statistically not significant (p=0.1635), there appears to be a trend towards higher mortality among the patients with admission serum sodium less than 105 mEq/l (**Table – 11**).

The mean sodium correction irrespective of outcome for patients with admission serum sodium <105mEq/l was 26.53mEq/l, whereas for

those with admission serum sodium of 105 - 115mEq/l it was 14.81 mEq/l and for those with admission serum sodium between 115 - 125mEq/l it was 12.3 mEq/l. This implies that serum sodium of the patient in the study was corrected to a level between 125 - 130 mEq/l irrespective of the outcome (**Table – 12**).

Table - 11: Admission serum sodium levels amongst study patients according to outcome.

Outcome	Serum sodium values on admission		Total
	<105mEq/l	>105mEq/l	
Improved	10(66.70%)	70(82.4%)	80
Expired	05(33.3%)	15(17.6%)	20
Total	15	85	100

Statistics	DF	Value	Prob
Chi-sqaure	2	1.94	0.1635

Table - 12: Admission serum sodium levels amongst study patients according to outcome.

Sodium values at admission	N Obs	Mean	Std. dev	Min.	Max.
<105	15	-26.53	8.77	-37.00	-6.00
105-115	32	-14.81	24.19	-30.00	113.00
>115	53	-12.30	4.53	-20.00	-2.00

F-value: 5.68, p value: 0.0046

Among the improved patients who had admission serum sodium of <105 mEq/l, the mean change in serum sodium level was 27.2 mEq/l and among the patients with admission serum sodium 105-115 mEq/l it was 19.25 mEq/l and for patient with serum sodium of 115 -125 mEq/l it was 13.29 mEq/l, this implies that patients were given correction for serum sodium upto a level of 130mEq/l. There is a statistically significant difference in corrections of serum sodium in different groups with regard to imporvement (**Table – 13**).

Among the patients who expired the mean correction for patients with admission serum sodium value of <105 mEq/l was 25.2 mEq/l, for those with serum sodium between 105-115 mEq/l it was 16.25 mEq/l and for patients with sodium levels of 115-125 mEq/l it was 8.55 mEq/l there is no significant difference between the correction given for different gropus (**Table – 14**).

Table - 13: Mean sodium correction among improved patients.

Sodium values at admission	N Obs	Mean	Std. dev	Min.	Max.
<105	10	-27.20	7.61	-34.00	-8.00
105-115	28	-19.25	6.67	-30.00	-4.00
>115	42	-13.29	4.17	-20.00	-5.00

Table - 14: Mean change in serum sodium level among expired patients according to values at admission.

Sodium values at admission	N Obs	Mean	Std. dev	Min.	Max.
<105	5	-25.20	11.65	-37.00	-6.00
105-115	4	16.25	64.64	-22.00	-113.00
>115	11	-8.55	3.96	-15.00	-2.00

F-value: 2.46, p value: 0.1151

Discussion

In the present study the incidence of hyponatremia was 36%, with severe hyponatremia (<125mEq/L) being 6.9%, which was more common in elderly females (55%) as compared to males (45%), concordant with the findings of Miller M, et al. [20] and Rao, et al. [21].

In the present study the commonest cause of hyponatremia was SIADH (30%), concordant with the previous studies by Rao, et al. [21], P R Patgiri, et al. [22], Thomas vurgese, et al. [23] and Clayton, et al. [8] who found SIADH in nearly half of the patients . Similarly Laczi, et al. [28] reported SIADH as the most common cause of euvolemic hyponatremia in their study in Hungary. A study from Israel concluded that the cause of hyponatremia in elderly is multifactorial and reported SIADH in nearly 45% of the patients [24] however, Sozio, et al. [25] challenged the study as the diagnosis of SIADH is dependent on volume status of the patients

which cannot be assessed in elderly patients reliably, as Kaeley, et al. [26] found SIADH only in 4.2% normovolumic hyponatremic patients.

In present study second most commonest cause of hyponatremia was drug induced (24%), of which diuretics (79%) formed a major chunk, which correlates with the study conducted by Sharabi, et al. [27]. Many studies have reported that drugs specially thiazide diuretics as a major cause of hyponatremia in elderly [28, 29]. However it has been suggested that women compensate the effect of thiazide diuretics by drinking more water [30]. Though JNC VIII recommends diuretics as the first line drug for treatment of hypertension, a word of caution should be maintained while prescribing diuretics in the elderly and when required, doses should be modified according to body weight and should begin with the lowest dose.

In present study, the commonest co morbid disease was HTN (62%) followed by DM (51%) similar to Kaeley, et al. [26], however, Patgiri, et al. [22] found ischemic heart disease (40%) as the commonest comorbid disease followed by HTN (13.3%) and CVA (10%).

In the present study patients had varied CNS symptoms like lethargy (29%), drowsiness with slow response (33%) or drowsiness with irrelevant talk (31%), headache (8%), disturbed sleep (3%), confusion (2%), seizures (4%) or unresponsiveness (7%). This finding is consistent with the available literature [21, 31-33] and Kaeley, et al. [26] who found lethargy as the major clinical manifestation (22.5%) and other severe neurological features only in 10.4% of the patients .However Mahavir Agarwal, et al. [34] found confusion (40%), headache (40%) and malaise (38.6%) as the commonest CNS symptoms. The other common non CNS symptoms were vomiting, diarrhea, decreased appetite, hiccup, pain abdomen and fever with sweating. These symptoms are difficult to interpret as they could be either cause or effect of hyponatremia and are also found in other conditions without hyponatremia.

In the present study a mortality of 20% was found and the cause of death was secondary to severe sepsis or other conditions like progressive cerebrovascular disease, renal failure, advanced malignancy and acute coronary events. However the extent of contribution of hyponatremia to death is debatable as even those patients who succumbed to their illness had received correction for hyponatremia as per the standardized regimen of treatment followed in this study. Many studies in the past indicate a higher mortality in the elderly patients with severe hyponatremia, with a mortality ranging from 33% to 86% [31-33] however studies conducted by Rubio Rivas H, et al. [35] and Nidhi Kaeley [26] showed mortalities of 12.9% and 7.1% respectively.

In the present study when the mortality outcomes were compared with respect to gender distribution it was noticed that females though had higher risk of hyponatremia, they responded better to treatment with a mortality of 9.09% as compared to 33.33% in males. This was statistically significant (p= 0.0026). This finding is consistent with the previous studies [21, 22].

In our study a statistically better response in terms of survival was demonstrated among patients who did not show any CNS symptoms (n=24) of hyponatremia compared to those who presented with CNS symptoms of hyponatremia. However this data is inconsistent with the data in the literature [31, 36]. This inconsistency could be because of small sample size.

Although in this study a mortality of 33.33% has been demonstrated in the patients with serum sodium at hospitalization <105 mEq/L than compared to17.6% in those with a admission serum sodium levels between 105 – 125 mEq/L, there was no statistically significant difference between the two groups (p = 0.1635), similar to previous study [35] however there appears to be trend towards higher mortality in the patients with admission serum sodium <105 mEq/l.

In the present study there, serum sodium was corrected to a level between 125-130mEq/l irrespective of the outcome. There was a statistically significant difference in corrections of serum sodium in the different groups with regards to improvement. However among the patients who expired there was no significant difference between the corrections given for different groups.

Conclusion

Clinicians need to be aware about the common occurrence of hyponatremia in acutely sick elderly, early identification and adherence to standardized correction protocol is essential to avoid complications and to reduce mortality. Meticulous monitoring for dosing of multiple drugs in elderly population would help in preventing hyponatremia.

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