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A STUDY OF OUTCOME OF ELDERLY PATIENTS ADMITED IN MEDICAL ICU HAVING HYPONATREMIA IN A TERTIARY CARE CENTER

Medicine

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ABSTRACT

Introduction: Hyponatrmia is a common problem in hospitalized patients, especially among elderly patients. It occurs in about 30% patients irrespective of causes and age group.Hyponatremia is defined as plasma sodium level less than 135 mEq/lit. Timely diagnosis and treatment are the most important factors for improving neurological status and reduced hospital stay. Unless taken care of sufficiently, hyponatremia has a major impact on outcome of the hospitalized patients

Materials and methods: A total of 100 patients were selected in the period of study is 15 months. With a clinical diagnosis of type of hyponatremia, and other blood investigations reports patients are classified into hypovolemic , isovoluemic or hypervolemic hyponatremia. Patients' outcome to treatment was recorded.

Results: Among the patients studied, 13 patient had serum sodium levels of less than 105 mmol/l, 26 patients had serum sodium level of 105-115 mmol/l and 61 patients had serum sodium levels of 115-125 mmol. There was no statistically significant difference between the mean age of the group of patients who improved and expired nor was there any statistically significant difference between the group with or without Non CNS symptoms (p = 0.16) with response to outcome but the response to treatment and survival was better among females than compared to males (p=0.0012) and there appearsed to be higher mortality in the patients with admission serum sodium < 105 mmol/l.

Conclusion: The response to treatment and survival was better among females than compared to males (p=0.0012) among all patients with hyponatremia and there appeared to be higher mortality in the patients with admission serum sodium < 105 mmol/l. There was also a statistically significant difference in corrections of mean serum sodium in the different groups with regards to improvement

KEYWORDS

hyponatremia, cerebral demylination,serum and urine osmolality

INTRODUCTION

Hyponatrmia is a common problem in hospitalized patients, especially among elderly patients. It occurs in about 30% patients irrespective of causes and age group.

Hyponatremia is defined as plasma sodium level less than 135 mEq/lit. It occurs mainly due to abnormality in water homeostasis, ADH regulation defect and renal mishandling of filtered sodium. Syndrome of inappropriate ADH occurs due to many underlying clinical conditions like neoplasms, CNS disorders, and pulmonary disorders.

Timely diagnosis and treatment are the most important factors for improving neurological status and reduced hospital stay. The exact etiology of hyponatremia is not possible to detect in every patient. The clinical presentation of severe hyponatremia ranges from mild, nonspecific symptoms, such as nausea, headache, and lethargy, to severe neurological symptoms such as seizure and coma. Unless taken care of sufficiently, hyponatremia has a major impact on outcome of the hospitalized patients

MATERIALS AND METHODS

Elderly patients (60 years and older) having hyponatremia admitted in medical ICU between1st of April 2016 and 31st of June 2017. A total of 100 patients were selected. The period of study is 15 months.

The following data were collected-

a) Required routine/ specific investigations relevant to evaluate as per the admission diagnosis.
b) Serum Sodium levels – At admission, every day during rapid correction/symptomatic period, then as and when indicated.
c) In patients who fulfill the selection of severe hyponatremia (serum Sodium ≤ 125 mMol/L) , the following investigations were done before treatment-

1) Serum Osmolality
2) Urine Osmolality
3) Urine spot Sodium
4) Serum Cortisol level – where indicated
5) Serum T3, T4, TSH – where indicated
6) Imaging studies – as relevant to the admission diagnosis.

d) Treatment as per general prevalent practice in ICU
e) Outcome following treatment.

Diagnosis of Hyponatremia: Hyponatremia- Serum Sodium level ≤ 135 mMol/L, Severe Hyponatremia-Serum Sodium ≤ 125 mMol/l

METHODS: All elderly patients admitted to medical ICU, 3-5 ml of venous blood was collected in a yellow top vaccutainer, and 5-10ml of urine (spontaneous void or catheter specimen) is collected in clean bottle. Routine blood and urine investigations as appropriate the diagnosis like, Complete blood count, renal function tests, electrolytes, liver function tests, urine routine, chest radiograph and other imaging studies as needed are done. When the electrolytes reports are available, patients are enrolled in the study if they are having serum sodium less than 125mmol/L and the plasma and urine sample are sent for measurement of serum osmolality and urine osmolality by freezing point depression osmometer. Serum electrolytes and urine spot Sodium are measured by ion sensitive electrode method.

With a clinical diagnosis of type of hyponatremia, and other blood investigations reports patients are 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 following guidelines and formula. Patients' outcome to treatment was recorded.

Microsoft excel was used for data tabulation and SPSSv22 was used for data analysis.

RESULTS:

Among the patients studied, 13 patient had serum sodium levels of less than 105 mmol/l, 26 patients had serum sodium level of 105-115 mmol/l and 61 patients had serum sodium levels of 115-125 mmol/l(Table-1).

Table 1- distribution of population according to degree of hyponatremia

DEGREE OF HYPONATREMIA (mmol/l)	NO. OF PATIENT
<105	13
105 – 115	26
>115	61

Table 2- Distribution of type of hyponatremia with outcome

Types Of Hyponatremia	Improved	Expired	Total No Of Patient
Isovolemic Hypo-osmolar	47	9	56
Hypervolemic Hypo-osmolar	20	5	25
Hypovolemic Hypo-osmolar	11	6	17
Isovolemic-iso-osmolar	1	0	1
Hypervolemic-iso-osmolar	1	0	1

Among the 100 patient 80 patients survived and improved and 20 patient succumbed, all of whom died due to the severity of presenting illness (Table-3)

Table-3: The distribution of patient in each age group who survived and improved and who expired

STUDY OUTCOME	FREQUENCY
IMPROVED	80
EXPIRED	20

Table-4: age distribution of patients with regards to outcome

Outcome			
Age Group	Improved	Expired	Total
20-40 YRS	9	2	11
40-60YRS	19	5	24
60-80 YRS	38	11	49
80-100 YRS	14	2	16
Total	80	20	

p-0 .85

There is no significant difference between the various studied age groups with regards to outcome groups (p value=0.854)(Table-4)

The age of the patient who improved ranged from 20- 100yrs with a mean age of 62.54± 15.79 yrs. Among the patient who expire the age ranged from 20-100 yrs. with a mean of 65± 15.19 yrs. There is no statistically significant difference between the mean age of the group of patients who improved and expired. (p value = 0.811)(Table-5)

Table-5: Mean age of the study population with regards to outcome

OUTCOME	NO OF PATIENTS	MEAN AGE	STD. DEVIATION
IMPROVED	80	62.54	15.79
EXPIRED	20	65.70	15.197

Among the 80 patients who improved 49 were female and 29 were male. And among the 20 patients, who expired, 14 were male and 6 were female. This indicates that among the 45 male patients admitted 29 (68.89%) patients improved and 15 (31.11%) patients expired, and among 55 female patients 49 (89.1%) improved and 6 (10.9%) expired(Table-6). Hence, the response to treatment and survival is better among females than compared to males (p=0.0012)

Table-6:Sex distribution with regards to outcome

OUTCOME			
GENDER	IMPROVED	EXPIRED	TOTAL
FEMALE	49	6	555
MALE	31	14	445
TOTAL	80	20	

Table-7: Outcome with age distribution for male

OUTCOME			
Age	improved	Expired	Total
20-39	3	1	4
40-59	8	2	10
60-79	14	9	23
80-99	6	2	8
Total	31	14	45

Table-8: Outcome with age distribution for female

OUTCOME			
Age	improved	Expired	Total
20-39	6	1	7
40-59	11	3	14
60-79	24	2	26
80-99	8	0	8
Total	49	6	55

Among the patients who presented with CNS symptoms of hyponatremia, 65 patients (80.2%) improved and 16 patients (19.8%) expired. Those patients who did not have any CNS symptoms at admission 15 (78.9%) improved and 4 (4.17%) expired(Table-8). This indicated that there is no stastistically significant difference between the outcome of the groups with and without CNS symptoms (p value 0.899).

Table-9:Outcome with regards to CNS symptoms

	IMPROVED	EXPIRED	TOTAL
WITH CNS SYMPTOMS	65	16	81
WITHOUT CNS SYMPTOMS	15	4	19
	80	20	100

Among the patients with severe hyponatremia, 85 patients who had symptoms other than CNS symptoms, patients 66 (77.64%) improved and 19 patients (22.35%) expired. And among the 15 patients who did not have non CNS symptoms 14 patients (93.33%) survived and 3 patients (6.67%) expired(Table-10). There is no statistically significant difference between the group with or without Non CNS symptoms (p = 0.161)

Table-10:Outcome with regards to non-CNS symptoms

	Improved	Expired	Total
With Non Cns Symptoms	66	19	85
Without Non Cns Symptoms	14	1	15
Total	80	20	100

Among the patients with severe hyponatremia, there were 43 patients who had history of recent admission within 4 weeks. Though with relation to outcome 34 patients (79.07%) had improved and 9 patients (20.9%) expired. Patients who did not have any history of recent hospitalization 57 patients 46 patients (80.7%) of them improved and 11 patients (19.2%) expired (Table-11). There is no statistically significant difference between the groups with relation to history of recent hospitalization with regards to outcome (P value 0.84). Though there are a significant number of patients who have history of recent hospitalization.

Table-11 :Outcome with regards to recent admission

	Improved	Expired	Total
H/o Recent Admission	34	9	43
No H/o Recent Admission	46	11	57
Total	80	20	100

Among the patients with severe hyponatremia those with sodium levels less than 105 Mmol/L at admission had a mortality of 30.77% than compared to those with serum sodium levels between 105 – 115 mMol/L who had a mortality of 15.38% and >115 mmol/l who had a mortality of 19.97% (Table-12) . Though the values are statistically not significant (P = 0.52) there appears to be trend towards higher mortality in the patients with admission serum sodium < 105 mmol/l.

Table-12:Outcome with regards to serum sodium level

SODIUM IN mmol/l	IMPROVED	EXPIRED	TOTAL
<105	9	4	13
105-115	22	4	26
>115	49	12	61
TOTAL	80	20	100

Among the patients admitted with severe hyponatremia, the correction of serum sodium irrespective of outcome for the level of admission serum sodium < 105 mMol/L was a mean of 25.38 mMol/L, for those with admission serum sodium levels 105 – 115 mMol/L was 19.12 mMol/L and for those patients with serum sodium as admission between 115 – 125 mMol/L was 13.11 mMol/L(Table-13). This implies that the serum sodium of the patients in the study was corrected to a level between 125 – 130 mMol/L. irrespective of the outcome

Table-13:Outcome with regards to serum mean sodium correction

Sodium Level At Admission	No. Of Patient	Mean Sodium Correction
<105	13	25.38
105-115	26	19.12
>115	61	13.11
TOTAL	100	16.27

P -0 .001

Among the patients admitted with severe hyponatremia who survived and improved, the mean change in sodium level in patients who had a admission serum Na value of < 105 mMol/L was 26.11 mMol/L, for admission serum Na value between 105 – 115 mMol/L was 19.82 mMol/L, and for patients with admission serum Na Level between 115 – 125 mMol/L was 13.53 mMol/L (Table-14). that implies that that patients were given correction for serum sodium up to a level of 130 mMol/L. There is a statistically significant difference in corrections of serum sodium in the different groups with regards to improvement (p-0.002)

Table-14: Mean Change in Serum level among Improved patients according to Serum values at admission when outcome was improved

Sodium At Admission In Mmol/l	No Of Patient	Mean Sodium Correction
<105	9	26.11
105-115	22	19.82
>115	49	13.53

Among the patients admitted with severe hyponatremia who expired. The mean correction for patients who had admission serum sodium value of < 105 mMol/L was 23.75 mMol/L, for those with Na values between 105 – 115Mmol/L was 15.25 mMol/L and for the patients with Na values between 115 – 125 mMol/L was 11.45 mMol/L (Table-15). There is no significant difference between the corrections given for the different groups.

Outcome=expired: Mean Change in Serum level among expired patients according to Serum values at admission

Table-15: Mean Change in Serum level among expired patients according to Serum values at admission when outcome was expired

Sodium At Admission In Mmol/l	No Of Patient	Mean Sodium Correction
<105	4	23.75
105-115	4	15.25
>115	12	11.45

DISCUSSION

All patients were treated according to a standardized regimen based on recommendation in various studies. Patients with CNS symptoms were treated with intravenous 3% saline infusion to raise there serum sodium levels by 0.5 mMol/L per hour to a maximum of 12 mMol/L increase in serum sodium per day. Patients who did not have any CNS symptoms were treated based on severity of their presenting illness with either Intravenous hypertonic saline or oral correction with salt supplementation. Though cerebral demyelination is described as a rare complication associated with symptomatic hyponatremia[1].

Animal data have shown that correction of hyponatremia by>20–25 mEq/l can result in cerebral demyelination [2]. This has resulted in a mistaken belief that a rapid rate of correction is likely to result in cerebral demyelination.

Recent data have now shown that the rate of correction has little to do with development of cerebral demyelinating lesions, and that lesions seen in hyponatremic patients are more closely associated with other co-morbid factors or extreme increases in serum sodium [3,4,5,6,7,8]. Consistent with these data, in our study also we did not encounter any complications related to relative rapid correction with a maximum correction of 12 mMol/L / day.

In our study a statistically better response in terms of survival was demonstrated among patients who presented with CNS symptoms of hyponatremia and responded to treatment than compared to those who did not show any CNS symptoms of hyponatremia. This data is consistent with the data in the literature [9,10]. Appropriate correction of hyponatremia in patients with symptomatic hyponatremia is recommended in accordance to the guidelines for correction of hyponatremia. In general, the plasma sodium should not be corrected to >125–130 mEq/l. Assuming that total body water comprises 50% of total body weight, 1 ml/kg of 3% sodium chloride will raise the plasma sodium by ~1 mEq/l [9,10].

Among the patients included in the study there was slight preponderance of elderly females (55%) as compared to males (45%). When the mortality outcomes were compared with respect to gender distribution it was noticed that females though had higher risk or hyponatremia, they responded better to treatment with a mortality of 10.9% as compared to 31.11% in males with hyponatremia. This was statistically significant (p= 0.012). There is evidence to support the idea that adaptation of the elderly female rat brain to hyponatremia is largely dependent on physical factors (i.e., brain-to-skull size ratio). The Na-K-ATPase pump is one of the major biochemical mechanisms by which the brain adapts to hyponatremia, to prevent brain edema.

In this study it was seen that that 48 out of 55 females were elderly and the mean age of the female who improved was 62.33 but who expired was 59.50 .Thus, because elderly females have decreased mortality, one might have speculate that the Na-K-ATPase pump function would be increased with advancing age. Moreover, because it is known that estrogen and progesterone inhibit the sodium pump and that these hormones are decreased in the elderly, the assertion was that these factors alone were sufficient to explain the decreased mortality and morbidity from symptomatic hyponatremia seen in elderly females subjects., however data suggest that the Na-K-ATPase pump function is significantly decreased in female rats with advancing age and, as such, survivability of hyponatremia in elderly females may be independent of the sex hormones and the Na-K-ATPase activity.The reason for this age-related decrease in the sodium pump function is unclear. Factors such as the female sex hormones, which are known to inhibit the Na-K-ATPasepump[11,12,13], are significantly diminished after menopause. As such, estrogen and progesterone would be unlikely to contribute to the age-related decrease in sodium pump function that was observed in the older age group. Additionally, if the age-dependent decrease in the sodium pump function was primarily mediated by the sex hormones, one would expect pump activity to increase with advancing age, coincident with the lower circulating levels of estrogen and progesterone. Because the Na-K-ATPase activity decreases with age, it is quite likely that other factors may play a more dominant role in elderly subjects regarding brain adaptation to hyponatremia.Those factors, which are known to play important roles in brain adaptation to hyponatremia in postmenopausal females, include an age-related decrease in estrogen and progesterone and increased intracranial space (physical factors) due to naturally occurring age related atrophy.

Many studies in the past indicate a higher mortality in the patients with severe hyponatremia, with a mortality ranging from 33% to 86%. ([9,14,15]). In this study a mortality of 20% was found in the series or patients studied. And among those who succumbed the cause of death was secondary to severe sepsis or other conditions like progressive cerebrovascular disease, advanced malignancy and acute coronary event. The association of hyponatremia with these patients could be an association or secondary to the medications used by these patients for their pre-existing illness. Though in this study there is a mortality of 30.8% has been demonstrated in the patients with serum sodium at hospitalization < 105 mMol/L. than compared to14.9% in those with a admission serum sodium levels between 105 – 125 mMol/L. there was no statistically significant difference between those groups (p = 0.524).none of the patients had developed complications related to correction of hyponatremia with hypertonic saline.

Taken together the findings suggest that brain sew swelling without the development of significant intracranial pressure to cause brain compression by the skull may result in reduced morbidity and mortality [16].

In our study it was noted that people who died had succumbed to severe sepsis with septic shock, progressive renal failure, and progressive cerebrovascular disease. 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.

CONCLUSION

The response to treatment and survival was better among females than compared to males among all patients with hyponatremia and there appeared to be higher mortality in the patients with admission serum sodium <105 mmol/l. There was also a statistically significant difference in corrections of mean serum sodium in the different groups with regards to improvement. There was no relation between the mean age of the group of patients who improved and expired nor was there any relation between the group with or without non CNS symptoms or history of recent hospital admission with the outcome

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