ISSN: 2321-8819 (Online) 2348-7186 (Print) Impact Factor: 1.498 Vol. 6, Issue 11, November, 2018

Hyponatremia in Hospitalized Patients

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ABSTRACT

Objective: Alleviation of cerebral oedema, not to correct sodium. Therefore, provision is only to severely symptomatic patients.

Place and Duration of Study: This study was carried out from Jan 2018 to March 2018 at Mayo Hospital, Lahore, Pakistan.

Materials and Methods: Out of 3000 patients, 100(3.3%) patients had hyponatremia defined as having level of serum sodium less than 135mmol/L. Among them male patients were 65(65%) and female patients were 35(35%) with average 55 years of age.

Results: In 24(22.2%) patients severe hyponatremia (Na+ < 120 mmol/L) was detected. Euvolemic was the largest group of hyponatraemic patients with 42(42%), then hypervolemic patients with 33(33%) and thirdly hypovolemia patients with 25(25%). 4(4%) patients out of 100 patients qualify the criteria for Syndrome of Inappropriate Anti Diuretic Hormone (SIADH). During stay at hospital, 2(2%) out of 100 hyponatraemic patients died. No death was secondary to hyponatremia. No patient was Tolvaptan (a V2RA) and only 3(3%) patients out of 100 were given saline. At the time of discharge, 73(73%) patients out of 100 were having serum sodium level more than135 mmol/L.

Conclusion: Among the hospitalised patients of Pakistan, hyponatremia is common. The most common type was euvolemic hyponatremia, a good amount of them was secondary to SIADH. It isa challenge to manage hyponatremia but mostly inpatients we managed hyponatremia in spite of unavailability of 3% saline or V2 receptor antagonist.

Key Words: Hyponatremia,Euvolemic, Syndrome of Inappropriate Anti-Diuretic Hormone Secretion

INTRODUCTION

The presence of hyponatremia in hospitalised patients is quite common across the world. The prevalence differs in various researches and it ranges from 5% to 30%. The aetiology is also different in other clinical settings and number of patients. Mostly in studies, SIADH and euvolemic hyponatremia is the most frequent cause in hospitalised patients. Hyponatremia management has always challenged nephrologists and clinicians. Fresher agents are modifying the mode of hyponatremia management. In Pakistan, the management in hospitalised patients is becoming more difficult because of dearth of hypertonic saline and absence of V2 receptor antagonist. No information relating to hyponatremia prevalence, management and aetiology in hospitalised patients is available.

Cross-sectional study was carried out in a private hospital based in Lahore for determining the aetiological element, prevalence and hyponatremia management. The literature was reviewed for discussing the available choices for managing the various kinds and degrees of hyponatremia in patients hospitalised.

MATERIALS AND METHODS

The patients with serum sodium (Na+) level less than 135 mmol/L (normal range 145 to 45 mmol/L) were made part of the studycarried out from Jan 2018 to March 2018 at Mayo Hospital, Lahore, Pakistan. Patients were also included who werehaving history of chronic hyponatremia or had hyponatremia during earlier hospitalisation. The report of 1st admission serum electrolyte was considered for criteria of inclusion. The patients were also included in whom the hyponatremia developed during hospitalisation. All patients were excluded having pseudo hyponatremia (secondary to Hyperproteinaemia &Hyperlipidaemia) or hyponatremia secondary to hyperglycaemiaor mannitol were excluded therefore including pure patients of hyponatraemic patients only.In order to diagnose different hyponatremia aetiology, the standard diagnostic criteria were used. The volume status of the patients was measured clinically as euvolemic, hypervolemic and hypovolemic.

Suspected patients of pseudohyponatremia were not included in the research and only pure patients of hyponatremia were added. Laboratory tests were performed in hyponatremia patients such as complete blood count, serum electrolytes, serum creatine, renal function test including blood urea nitrogen, thyroid function test, serum uric acid, serum cortisole, random urine sodium, serum osmolality, urine complete, random urine

osmolality and chest x-rays. In selected cases ultrasound KUB, serum BNP and 2D Echocardiogram were performed. The normal range in hospital laboratory (Chughtai's Lab) of serum sodium is 135 to 145 meq/l, urine osmolality is 500–850 mosm/kg water and serum osmolality is 275–293 mosm/kg of water. severe hyponatremia defined as serum Na+ < 120 meq/l and normal Hyponatremia is defined as Na+ < 135 meq/l. As per need the consultation of cardiology, endocrinology and nephrology were requested. For the purpose of exclusion SIADH is diagnosed and Bartter-Schwartz have defined the classic criteria that can be summed up as;

1. Hyponatremia with corresponding hypo-osmolality
2. Urine less than maximally dilute
3. Continued renal excretion of sodium
4. Absence of other causes of hyponatremia
5. Absence of clinical evidence of volume depletion
6. Correction of hyponatremia by fluid restriction

Management of the patients was based on the standard guidelines. The patient was considered as chronic hyponatremia if he was having hyponatremia for more than 48 hours or for unknown duration. Sodium was not enhanced more than 10 to 12 meqin chronic hyponatremia during the 1st 24 hours in order to avoid central pontine myelinolysis. Hyponatremia acute had been defined as development of level of low serum sodium within last 48 hours. Demeclocycline, hypertonic saline and tolvaptan were unavailable. The management of hyponatremia was performed by treating basic reasons, oral salt tablets, water restriction, normal saline with or without sodium bicarbonate and furosemide in different combinations. Hypertonic saline was given to only 4 patients having severe symptomatic hyponatremia 3 of them having serum sodium 105, 109 & 110 mmol/L and the 4th one has less than 100 mmol/L. The arrangement of hypertonic saline is not an easy task normally it is arranged by the family.

RESULTS

Out of 3000 patients hospitalised, 100(3.3%) patients had hyponatremia defined as having level of serum sodium less than 135mmol/L. Among them male patients were 65(65%) and female patients were 35(35%) with average 55 years of age. Out of 100 patients, 27(27%) were having the serum sodium level less than 120. Mostly patients having mild hyponatremia preventing the causative drug or the treatment of basic causes along with water restriction fixed sodium. In hypovolemia patients, correction of fluid loss by hyponatremia with normal saline assisted correct serum sodium. The hyponatremia causes are as follow:

3 patients having adrenal insufficiency and hypothyroidism were given thyroxin and steroids to correct sodium. Patient having basic polydipsia was advised to avoid fluid and it corrected sodium. But after two weeks with hyponatremia secondary to bad compliance with fluid the patient was again hospitalised and was referred to psychiatry. The management of hyponatremia secondary to idiopathic SIADH, congestive heart failure (CHF), chronic live diseased (CLD)was the most difficult. In spite of the use of furosemide, the level of serum sodium remains 128 to 136 in patients. 4 severe hyponatremia patients (having serum sodium less than 100,105,109 and 110 mmol/L) required about one litre of 3% saline to correct sodium and causes to take sodium at secure range of 115 to 120 mmol/L. Mostly patients respond to normal saline with sodium bicarbonate for the creation of hypertonic IV fluid (tonicity 1.5 to 2.5%). The bicarbonate solution was particularly used for patients having some level of metabolic acidosis. The preparation of fluid is based on the nephrologist's recommendation depending on the level of serum bicarbonate, sodium and require correcting sodium. There was low sodium of unclear aetiology in ourpatients, but they responded to hold pregabalin. Physician restarted pregabalin and returned to OPD with low sodium level of 121 that again responded to hold pregabalin. No complication was developed in patients resulting from hyponatremia or its treatment. Patients mostly were managed in general ward with an exception of few patients having severe and acute hyponatremia which need to be managed in ICU. Around 50% patient were lost for the purpose of follow up but mostly patients had level of serum sodium in normal range with few exceptions of chronic liver disease, advance congestive heart failure and idiopathic Syndrome of Inappropriate Anti-Diuretic Hormone.

DISCUSSION

The presence of hyponatremia in a group of hospitalised patients was 3.3%. In other epidemiological researches the prevalence has been shown between 5 to 30% in different clinical settings depending on various aetiological risk element. In the current research, the level of hyponatremia prevalence is less as compared to values reported in mostly western literature. Slight low occurrence be considered as secondary to the fact that the study involved all patients inclusion of

surgical, obstetrics and gynaecology, medical and hospitalised for limited period. otherwise mostly patients were healthy and for short period hospitalisation for delivery of new born or elective surgery or for procedure such as angiogram to exclude acute coronary syndrome etc. Recently, the prevalence of 4.7% has been reported by Sandar Win, Komal Patel, Maria V De Vita et al. in the patients hospitalised. The prevalence of 4.2% according to current data is in consistent with the prevalence reported by them. In the hyponatremia aetiological terms, it has been found that likewise others, SIADH is the most frequent cause of hyponatremia in patients. Chronic liver disease is also common reason of hyponatremia. Perhaps this would be secondary to the fact that in Pakistan and South East Asia there is prevalence of hepatitis B&C, chronic liver disease and cirrhosis. The findings of the current research are in line with other researches with respect to the elements of aetiology. Hyponatremia management is still a challenge and requires good knowledge, pharmacological measures, non-pharmacological, multi-disciplinary approach and hypertonic saline availability, vasopressin receptor antagonist etc. hyponatremia in patient has been connected with high morbidity and mortality but the question is whether mortality is connected itself with hyponatremia or there are some underlying diseases which remains unclear. The assessment of the volume status of the patient is imperative in evaluating the type of hyponatremia that would assist in finding what type of management is needed. More fast correction by using of hypertonic saline may be needed if the patient hasserious hyponatremia symptoms (for example seizures) in order to avoid complications and cerebral oedema. Treatment of patients having severe hyponatremia may be challenging and difficult as the tolvaptan is unavailable and hypertonic saline is not available freely. All the patients were managed except few who needed 3% saline. After literature review and while relying on the experience these are the possible recommendation. Underlying cause treatment: stopping of diuretics such as selective serotonin uptake blockers hydrochlorothiazide and other likely drugs. Treatment of hyponatremia underlying correctable cause. Water restriction: it works in all circumstances and it must be 1st recommendation regardless of aetiology. Among the patients it works as wonder with primary polydipsia. The water restriction can be assessed relying on the patient's urine osmolality, level of sodium and current water consumption. Normally the daily fluid restriction is 1 to 1.5 Litre.

Salt Intake: it can be used to increase the level of serum sodium. There should be removal of salt restriction and salt can freely be used in diet. The use of salt (NaCl) can be in form of tablets or capsules. Every single tablet or capsule has normally 500mg of salt. There is need to monitor closely the volume status and blood pressure. Oral rehydrating solution must not be used unless potassium is low because it gives increased contents of potassium. Normal Saline: mostly the offered treatmentto hypovolemic hyponatremia patients is replacement of both water and salt by way of intravenous infusion of salt solutions. Unless there is obvious proof of dehydration and hypovolemia, the normal or hypotonic fluids must be evaded. It may result in worse hypervolemic hyponatremia. In case of Syndrome of Inappropriate Anti-Diuretic Hormone, the normal use of saline is dependent on urine osmolality which is normally fixed. Hyponatremia may be corrected by the assistance of urine osmolality if it is less than 308 mmol/L. if the urine osmolality is over 308 (normally over 450 mOsm/kg H_2O in Syndrome of Inappropriate Anti-Diuretic Hormone) then hypotonic or normal saline would worsen the hyponatremia because of fixed urine osmolality and retention of free water after excretion of urine at increased osmolality. Sodium bicarbonate addition can support in enhancing the solution tonicity and it would assist in correcting hyponatremia. Furosemide can be of assistance for normal saline to rapidly improvise hyponatremia by dumping more water in urine as damage is caused by furosemide to renal tubular responsiveness to ADH.

Demeclocycline: recommendation in case of Syndrome of Inappropriate Anti-Diuretic Hormone has been made but did not prove fruitful secondary to poor efficacy and side effects. In all analysis the demeclocycline effects are not significant and there is decline in its role because of the invention of new V2 receptor antagonists such as tolvaptans. Furthermore, it is unavailable in Pakistan. Hypertonic saline: it is quite useful in case ofsevere symptoms and acute hyponatremia need to be promptly corrected. Centres such as Shifa, SIUT and Shaukat Khanum are preparing 3% saline but it cannot be found free from the pharmacies. With respect to replacement, required deficit of sodium can be assessed with the use of the formula. Na+ (mEq given as 3%) = (Na+ desired) – (Na+ measured) X estimated TBW. By this way the sodium amount in mEq can be given as 3% saline over time t. in 1 litre of 3% saline there are 513 mEq of sodium. The determination of hypertonic saline volume to be given over time t, divide the

No. of sodium mEq to be given by 513 mEq/L. thereafter give the volume over time t. the efficacy of 3% saline can be enhanced by the addition of Lasix.

The patient having sodium serum of 105 and pointed neurological signs of changed mental status, hypertonic saline is decided (3% saline, OSM=1026) must be given primarily with respect to the pointed hyponatremia and neurological signs. That's the method of assessing the wanted sodium increase of 15 mmol/L during first thirty hours. Na+ deficit = 0.6 × 70 × (120-105), = 630 meq =1200mL of 3% saline At 40 ml/h over 30 h to raise the plasma Na+ concentration by 0.5 meq/L/h. sodium is enhanced by 6 to 8 meq/L with normally 50 to 100 ml/hr for 4 to 6 hours which is normally sufficient for the reduction of signs severely V2 Receptor Antagonist: in USA the oral Tolvaptan is available easily and is recommended and approved for hyponatremia management secondary to chronic liver disease , Syndrome of Inappropriate Anti-Diuretic Hormone and congestive heart failure. Canada is the exclusive country for the availability of Tolvaptan, the only V2R antagonist. A 4-years research of salt trials is recognised as Saltwater, it has been revealed that rise in the level of sodium serum was maintained for long time. Unluckily there is no availability of tolvaptan is in Pakistan. But whenever subject to availability of dose it should be started from 15 mg and can use maximum dose of 60 mg daily as required. During the use of tolvaptan, fluids or water are un-restricted to evade fast correction of sodium. It is resulting in free water loss or aquaresis by stopping ADH receptor. It is pointed out and FDA has approved for hyponatremia because of Syndrome of Inappropriate Anti-Diuretic Hormone, Chronic liver disease or cirrhosis and congestive heart failure when aquaresis relatively diuresis is required because of hyponatremia. By the retention of sodium and resulting free loss of water, it corrects sodiumand give treatment to overload fluid particularly in chronic liver disease and congestive heart failure.

CONCLUSION

Hyponatremia is commonly found in Pakistani hospitalised patients. The most common type is euvolemic hyponatremia, a great number of which was secondary to Syndrome of Inappropriate Anti-Diuretic Hormone. There is a challenge to manage hyponatremiabut hyponatremia is managed in mostly current patient in spite of unavailability of 3% saline or V2 receptor antagonist.

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