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Original Article

Evaluation of thyroid and adrenal functions in patients with hyponatremia

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ABSTRACT

Background: Hyponatremia is frequently detected as a cause in patients admitted to command Hospital Kolkata with altered sensorium. We evaluated these patients to rule out two common endocrine causes as etiological factors i.e. hypothyroidism and hypoadrenalism. **Method:** We studied 100 patients over a period of two years in all seasons who were admitted to hospital with altered sensorium and found to have hyponatremia as a cause, after ruling out other causes of altered sensorium as per inclusion and exclusion criteria. They were subjected to thyroid and adrenal evaluation in addition to detailed history, clinical examination and lab evaluation as per study protocol. **Results:** Total 100 patients were enrolled in the study. The age of patients varied from 31 years to more than 70 years. Majority of patients were between the age group of 41–60 years (49 patients). Males were predominant in the study. Only 8 patients were detected to have hypothyroidism requiring replacement therapy and only 2 patients had adrenal insufficiency. 48 patients had drug induced hyponatremia and 42 idiopathic hyponatremia. No seasonal variation was noted. **Conclusion:** Thiazide diuretic intake as antihypertensive drug was found to be a major cause of hyponatremia. Most of the patients in this group were using thiazide diuretics. In idiopathic group the cause of hyponatremia can be hypothesized as multifactorial. The hot and humid climate of Kolkata and other coastal regions made them more vulnerable to develop hyponatremia. Hypothyroidism and hypoadrenalism were not found to be major causes of unexplained hyponatremia.

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Introduction

Hyponatremia is common in inpatients and outpatients and remain an under diagnosed condition. Its causes are numerous and invariably elusive. Hyponatremia is an important and common electrolyte abnormality that can be seen in isolation or as most often the case, a complication of other medical illnesses.¹ The normal serum sodium level is

135–145 mEq/L. Hyponatremia is defined as a serum level of less than 135 mEq/L and is considered severe when the serum level is below 125 mEq/L.² Patients may be brought to medical attention owing to symptoms directly referable to low serum sodium concentrations or due to a manifestation of other medical co morbidities. Patients may manifest clinical symptoms due to the cause of hyponatremia or the hyponatremia itself.

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Hyponatremia is often found to be a cause of altered sensorium after evaluation of patients admitted to a tertiary care hospital Kolkata. All such patients primarily presented with altered sensorium. Hot and humid climate and poor salt intake are often attributed as the cause of hyponatremia in these cases.

Keeping in view the high incidence of hyponatremia as noted in this hospital the study was undertaken to evaluate hypothyroidism and hypoadrenalism as a cause of hyponatremia in such patients as these two endocrine conditions though rare are often associated with hyponatremia. Symptoms of hyponatremia range from nausea and malaise, with mild reduction in the serum sodium, to lethargy and decreased level of consciousness, headache, seizures and coma.³ Neurologic symptoms most often are due to very low serum sodium levels (usually <115 mEq/L) and the severity of neurologic symptoms correlates well with both the rapidity and the severity of the drop in the serum sodium.⁴

Material and method

This study was carried at command hospital (EC) Kolkata from June 2007 to July 2009. A total 100 patients of unexplained hyponatremia as defined above were selected based on inclusion and exclusion criteria.

Inclusion criteria

All the patients with altered sensorium in which no apparent cause was detected at the time of admission. Only hyponatremic patients were evaluated further as per study protocol.

Exclusion criteria

1. Pregnant ladies, children and post operative patients were excluded from the study.
2. Patients with other co morbidities, known to be associated with hyponatremia e.g.

Cerebrovascular accident, diabetic ketoacidosis etc were also excluded. A total 100 patients ($n = 100$) fulfilling the inclusion and exclusion criteria were enrolled in the study. All these patients were admitted to the hospital. Informed consent was taken from the attendants or the patient when they became conscious. A detailed history (From attendants and patient when he/she became conscious) and physical examination was carried out as per study protocol with special focus on clinical features of hypothyroidism and hypoadrenalism. All the old medical documents were perused for prescription and to find any co morbidity.

Methodology

All the patients who fulfilled the criteria of the study were evaluated further. The diagnosis of hyponatremia was made after evaluating (serum sodium less than 135 mEq/L) two venous blood samples taken 1 h apart. Depending upon the serum sodium levels patients were treated with intravenous or oral sodium replacement as per standard guidelines. Their

clinical response was recorded in the case sheet. Their serum sodium levels were then tested six hourly. All the investigations were done in the hospital laboratory. All the values were compiled in a format along with the relevant other lab investigations.

On next day of admission, fasting samples of thyroid profile total (T3, T4, TSH) and serum cortisol were taken. Thyroid profile was done by Radioimmunoassay and intra-assay and inter-assay coefficient of variation were considered for different kits used in our laboratory. Hypothyroidism was defined in patients with raised TSH and low free T4/T3 levels. The normal values as per hospital lab were T3 = 0.5–1.2 ng/ml, T4 = 4.5–11 µg/dl and TSH = 0.5–6.2 µIU/ml. Only those patients who had serum cortisol levels less than 15 µgm/dl (Normal values as per lab = 10 to 20 µgm/dl) were subjected to ACTH stimulation test (only 5 patients). ACTH test was performed in 5 patients by giving 250 µg IV ACTH and taking blood for serum cortisol before and after 1 h of ACTH injection.

Results

Total 100 patients were enrolled in the study. The age of patients varied from 31 years to more than 70 years. Majority of patients were between the age group of 41–60 years (49 patients) Males were predominant in the study. Only 19 patients had severe hyponatremia (<125 mg/L). Eight patients were detected to have hypothyroidism and only 2 patients had adrenal insufficiency. 48 patients had drug induced hyponatremia and 42 idiopathic hyponatremia (Table 1, Fig. 1). No seasonal variation was noted.⁵ Eight (8%) patients who were detected to have hypothyroidism, all of them required thyroid hormone replacement therapy (Fig. 2). All these patients had overt hypothyroidism clinically and biochemically at the time of evaluation when presented with altered sensorium and subsequently detected to be hyponatremic. The five hypocortisolemic patients who had serum cortisol levels less than 15 µg/dl were provisionally diagnosed to have hypoadrenalism initially. All these patients were then subjected to ACTH stimulation test. Three out of these five patients showed an absolute increase in the cortisol levels above 20 µg/dl and were not labeled as hypoadrenalism. Two patients showed no increase in the serum cortisol levels and subjected to insulin tolerance test showing no significant increase in cortisol level and were diagnosed as cases of adrenal insufficiency (Fig. 3).

Discussion

Hyponatremia was frequently observed as a cause of altered sensorium in patients who were admitted to command

Table 1 – Showing the patient distribution as per etiologies of hyponatremia.

Hypothyroidism	8
hypoadrenalism	2
Idiopathic	42
Drugs	48

Fig. 1 – Pie chart showing the percentage of patients as per etiologies of hyponatremia.

hospital Kolkata. Certain drugs, exposure to hot and humid climate, and dilutional hyponatremia are known frequent causes of hyponatremia. More incidence of such cases as was observed in admitted patients with altered sensorium prompted us to study and rule out two common endocrine causes of hyponatremia i.e. Hypothyroidism and hypoadrenalism.

Majority of patients had drug induced hyponatremia (48%) (Table 1, Fig. 1). Most of these patients were elderly and were taking medications for hypertension (Diuretics as Thiazide, indapamide and spironolactone in various dosages) which was revealed on history when patient became conscious and on scrutinizing the medical documents when made available. One patient was taking Tab Carbamazepine for glossopharyngeal neuralgia in the dosages of 1200 mgs per day. Other patients were using antipsychotic drugs mainly sertraline and amitriptyline. These patients in addition were also exposed to hot and humid climate of Kolkata and other coastal areas. All these drugs produce hyponatremia by different mechanisms^{6–8}.

Idiopathic group of hyponatremic patients were elderly and had a habit of drinking water with poor salt intake in hot and

Fig. 3 – Details of hypocortisolemic patients.

humid climate of Kolkata for most of the time in the year. The most probable causes attributable to hyponatremia is these patients are excessive sweat salt loss due to hot and humid climate and excessive water intake without salt, leading to dilutional hyponatremia. Increased water intake usually does not lead to hyponatremia unless there is also impairment in water excretion however various mechanisms contribute to hyponatremia in these cases. Eight (8%) of patients were incidentally detected to have hypothyroidism and all of them required eltroxin replacement therapy (Fig. 2). All these patients had overt hypothyroidism clinically and biochemically at the time of evaluation when presented with altered sensorium and subsequently detected to be hyponatremic.

Various mechanisms have been attributed as the cause of hyponatremia in hypothyroidism. The principal abnormality in the patient with normal fluid intake appears to be the inability to maximally suppress antidiuretic hormone. This is most likely due to reduced cardiac output in this disorder, which can lead to the release of antidiuretic hormone via the carotid sinus baroreceptors.^{9,10}

The glomerular filtration is also decreased in hypothyroidism. This can directly diminish free water excretion by diminishing water delivery to the diluting segments. Decreased delivery may be particularly important in those cases in which hyponatremia develop despite appropriate suppression of ADH release.¹¹ The incidence detected in our study is comparable to various other studies.

Only 5 patients in our study were found to have reduced cortisol levels. Those patients who had serum cortisol levels less than 15 $\mu\text{g/dl}$ were provisionally diagnosed to have hypoadrenalism. All these patients were subjected to ACTH stimulation test. Three patients showed an absolute increase in the cortisol levels above 20 $\mu\text{g/dl}$ and were not labeled as hypoadrenalism. Two patients showed no increase in the serum cortisol levels and subjected to insulin tolerance test showing no significant increase in cortisol level and were finally diagnosed as cases of adrenal insufficiency (Fig. 3).

Fig. 2 – Details of hypothyroid patients.

The electrolyte disturbances in primary adrenal insufficiency are due to diminished secretion of cortisol and aldosterone. A major function of aldosterone is to increase urinary potassium secretion. As a result, hypoaldosteronism is associated with hyperkalemia and mild metabolic acidosis. Although aldosterone normally enhances sodium reabsorption, other sodium-retaining factors such as angiotensin II and norepinephrine are able to compensate for the decreased availability of aldosterone.¹² Hyponatremia and hyperkalemia are the two major manifestations of primary adrenal insufficiency. Hyponatremia is mediated by increased release of antidiuretic hormone which results in water retention and a reduction in the plasma sodium concentration¹³ both cortisol and aldosterone deficiency contribute to this problem. The hypersecretion of ADH seen in cortisol deficiency may be in part due to the reductions in systemic blood pressure and cardiac output induced by the lack of cortisol. Cortisol feeds back negatively on CRH and therefore ADH, an inhibitory effect that is removed with adrenal insufficiency.¹⁴ Hypovolemia stimulates the release of ADH via the carotid sinus baroreceptors.¹⁵

Other studies show similar incidence of hyponatremia in hypoadrenalism.¹⁶

It is concluded from this study that hypothyroidism and hypoadrenalism are not major causes of hyponatremia but should be suspected.

Conflicts of interest

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REFERENCES

- Rose BD, Post TW. *Clinical Physiology of Acid-base and Electrolyte Disorders*. 5th ed. New York: McGraw-Hill; 2001:699–716.
- Clayton JA, Le Jeune IR, Hall IP. Severe hyponatraemia in medical in-patients: aetiology, assessment and outcome. *N Engl J Med*. 2000;342:1581.
- Gross P. Correction of hyponatremia. *Semin Nephrol*. 2001;21:269–272.
- Miller M, Morley JE, Rubenstein LZ. Hyponatremia in a nursing home population. *J Am Geriatr Soc*. 1995;43:1410–1413.
- Chakrapani M, Shenoy D, Pillai D. Seasonal variation in the incidence of hyponatremia. *J Assoc Physician India*. 2002;50:559–562.
- Sonnenblick M, Friedlander Y, Rosin AJ. Diuretic-induced severe hyponatremia: review and analysis of 129 reported patients. *Chest*. 1993;103:601.
- Friedman E, Shadel M, Halkin H, Farfel Z. Thiazide-induced hyponatremia. Reproducibility by single dose challenge and an analysis of pathogenesis. *Ann Intern Med*. 1989;110:24.
- Fichman MP, Vorherr H, Kleeman CR, Telfer N. Diuretic-induced hyponatremia. *Ann Intern Med*. 1971;75:853.
- DeRubertis Jr FR, Michelis MF, Bloom ME, et al. Impaired water excretion in myxedema. *Am J Med*. 1971;51:41.
- Hanna FW, Scanlon MF. Hyponatraemia, hypothyroidism, and role of arginine-vasopressin. *Lancet*. 1997;350:755.
- Schmitz PH, de Meijer PH, Meinders AE. Hyponatremia due to hypothyroidism: a pure renal mechanism. *Neth J Med*. 2001;58:143.
- Diederich S, Franzen NF, Bahr V, Oelkers W. Severe hyponatremia due to hypopituitarism with adrenal insufficiency: Report on 28 cases. *Am J Cardiol*. 1997;97:1064–1067.
- Oelkers W. Hyponatremia and inappropriate secretion of vasopressin (antidiuretic hormone) in patients with hypopituitarism. *N Engl J Med*. 1989;321:492.
- Raff H. Glucocorticoid inhibition of neurohypophysial vasopressin secretion. *Am J Physiol*. 1987;252:R635 [Diederich S, Franzen NF, Bahr V, Oelkers].
- Garg LC, Narang N. Effects of hydrochlorothiazide on Na-K-ATPase activity along the rat nephron. *Kidney Int*. 1987;31:918.
- Gonc EN, et al. Hyponatremia can be a presenting finding of multiple pituitary hormone deficiency in children: Report of a case and review of literature. *Clin Pediatr*. 2005;44:623–628.