



Combination of Diuretics and SSRIs Leading Severe Hyponatremia: A Case Report

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Abstract

Hyponatremia is one of the most encountered electrolyte imbalances among all medical fields. It has a wide range of symptoms as well as complications from fatigue to loss of consciousness. Although a lot of factors can cause low sodium levels, combining specific medications can lead severe hyponatremia in a rapid onset which can cause high mortality and morbidity. The objective of this case report was to underline that prescribing specific medications disregarding their side effects can cause this common electrolyte imbalance but in a more severe manner. In this case report, we present a 46-year-old male patient with serum sodium level of 104 mEq/L who consumed hydrochlorothiazide for hypertension and was under treatment with Selective Serotonin Reuptake Inhibitors (SSRIs) for major depression. Patient had tonic-clonic seizures at the second hour of the treatment and intubation was needed due to loss of consciousness and hypoxia. After proper replacement of sodium with hypertonic solutions in intensive care unit for nine days, extubation was indicated. Even in healthy young males, hyponatremia due to two separately prescribed medications can lead life threatening hyponatremia. Physicians should be aware of the side effects of diuretics, especially hydrochlorothiazides and SSRIs and their combinations.

Keywords: Diuretics; Hydrochlorothiazide; Hyponatremia, SSRI

Introduction

Hyponatremia is defined when sodium levels are decreased less than 135 mEq/L [1]. It is the most common electrolyte imbalance detected among all medical fields. It has an incidence of 0.97% and prevalence of 2.48% in general population [2]. The prevalence of hyponatremia among hospitalized patients is 15% to 30% [3]. Most of the time the severity of hyponatremia is mostly mild or moderate and the patients are generally asymptomatic. Main symptoms include nausea, vomiting, headache, lethargy, fatigue, apathy, disorientation, drowsiness, agitation, muscle cramps and convulsions. Physical examination shows findings of dehydration, decreased level of consciousness, ataxia, decreased deep tendon reflexes, presence of pathological reflexes, pseudobulbar paralysis, increased intracranial pressure syndrome, hypothermia, Cheyne Stokes respiration [4]. Severe hyponatremia primarily presents with central nervous system symptoms and findings [4]. Renal or cerebral water wasting, loss of sodium via gastrointestinal system or skin, specific medications and many more factors can cause hyponatremia. In our case, we present a patient with severe hyponatremia secondary to combination of two specific medications usage which necessitated intubation due to generalized seizures.

Case Presentation

A 46-year-old male patient, who was diagnosed with hypertension a month ago, applied to the emergency department of our hospital with complaints of headache lasting for 10 days and lately developed confusion. Further questioning implied that the patient had had many emergency room admissions due to severe hypertension attacks for a month. Medication for hypertension he used for a week included spironolactone 25 mg per oral (po), once a day (qd); hydrochlorothiazide 25 mg po, qd; perindopril indapamide 5 mg/1.25 mg po, qd. He had taken 100 mg captopril right before he applied to the emergency room.

Physical examination findings were confusion, limited cooperation and coordination. Blood pressure was 158/70 mmHg, pulse was 76 beats per minute with normal sinus rhythm, saturation was 99%, and temperature was 36.6°C at the time of admission. No specific findings were noted on the respiratory and gastrointestinal system examination. He had not had nausea, vomiting and diarrhea at the onset of symptoms. Laboratory results were as serum sodium of 104 mEq/L, glucose

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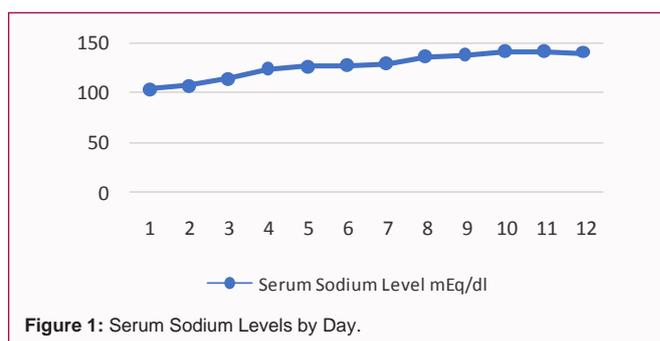
level of 122 mg/dl, potassium level of 3.5 mEq/L, chloride was 67 mEq/L, blood urine nitrogen was 19 mg/dl, creatinine was 0.96 mg/dl. Blood gas levels showed that pH: 7.5, HCO₃: 25 mEq/L. Blood count was WBC: 15,000, Hb 13 g/dl and PLT 330,000/ul. According to clinical examination, patient was assessed as euvoletic. Since his serum osmolality was 221 mosm/kg it was decided that patient had been having euvoletic hyponatremia and internalized to the internal medicine clinic. Sodium gap was calculated, and 3% hypertonic serum infusion had been started. When the hypertonic infusion was at the second hour, patient had a generalized tonic-clonic seizure. The patient had gotten unconscious and became hypoxic due to aspiration. Consequently, he was intubated and transferred to intensive care unit of internal medicine clinic. Phenytoin infusion had been started as the first line intervention. Cranial imaging of the patient showed no pathological findings while thoracic imaging indicated air bronchograms and diffuse consolidations. Patient diagnosed with aspiration pneumonia and treatment of 4,5 gr piperacillin – tazobactam four times a day had been started.

Intubated patient was followed up for nine days. Sodium depletion was replaced carefully during this period with 3% hypertonic sodium chloride solution. When sodium levels reached to 139 mEq/L, patient had become conscious again and ventilation requirement was no longer needed; patient was extubated. After 3 more days of follow up in intensive care unit with sodium replacement therapy with hypertonic sodium infusion and antibiotic regimen for aspiration pneumonia, satisfying results were obtained from laboratory tests indicating pneumonia regression and acceptable serum sodium levels. Patient's sodium levels by day were demonstrated on Figure 1. Patient had gotten clinically better, was no longer in need for intensive care unit admission and discharged to internal medicine clinic.

Investigations for etiology of the hyponatremic case had been started ultimately. Spot urine sodium was <20 mEq/L. Thyroid function was normal as the results were as follows: TSH was 1.18 uIU/ml, free T3 level was 3.05 pg/ml and free T4 was 0.97 ng/dl. No pathologic results of urine sampling were noted other than ketone bodies which were 2+. Patient's morning cortisol level was 10.2 mcg/dl and ACTH level was 51 pg/ml. Therefore, intravenous ACTH stimulation test was performed. Adrenal insufficiency was ruled out due to the satisfactory results of cortisol response. Patient's lab results for functions of hypophysial hormones were within normal ranges. As a result of all laboratory testing, patient's evaluation for etiology of the normovolemic hypotonic hyponatremia was ended up with drug related hyponatremia as known as drug induced hyponatremia. Patient's all prescribed medications were stopped, and hypertension management was done with 30 mg nifedipine two times a day per oral. Following blood pressure levels were within normal ranges. Serum sodium levels were noted in normal ranges during the inpatient followed up. No additional seizures were observed. After completion of the antibiotic regimen for aspiration pneumonia which was confirmed with laboratory results and clinical recovery, patient was discharged with satisfying outcomes.

Discussion

Hyponatremia as one of the most common electrolyte imbalances is caused by numerous factors disturbing the balance between water and sodium. The diagnosis and the treatment are essentially based on the etiologic factors. First and the foremost, main etiological factors causing hyponatremia should be assessed properly. In some cases, various factors, especially multiple drug usage, can



cause hyponatremia at once. Careful history taking and physical examination can make a physician distinguish whether the patient is hypovolemic, normovolemic or hypervolemic. Additionally, history of the patient can reveal that if the condition is acute or chronic, and the patient is symptomatic or asymptomatic [4]. In patients diagnosed with hyponatremia, serum osmolality should be calculated, and etiology of the imbalance should be investigated. In our case, patient had become symptomatic in a short period of time which was obtained by a detailed patient history pointing out that the patient's condition was acute. Additionally, patient had severe symptoms which also occurred acutely and had high mortality rates.

The symptoms of hyponatremia mostly depend on the onset and the severity of the imbalance. Mortality is caused by cerebral edema, which is precipitated by acute decrease in serum sodium levels, or by osmotic demyelination syndrome due to the aggressive replacement of sodium in chronic hyponatremia patients. Hence it is crucial to get a proper history of the patient to determine whether the hyponatremia developed in a short or long period of time. Our patient's serum sodium levels were very low as he applied for an emergency care with very low sodium levels (104 mEq/L).

The variety of the drugs causing hyponatremia is increasing constantly. Underlying mechanism of the drugs leading hyponatremia mainly can be divided into three categories which are drugs physiologically acting as Antidiuretic Hormone (ADH), stimulating the secretion of ADH and creating a synergistic effect of ADH on renal response [4].

In a study conducted by Fenoglio et al. [5], which focused on the most reported drugs causing iatrogenic hyponatremia, they revealed that 75.5% of the patients had syndrome of inappropriate ADH secretion. Selective serotonin reuptake inhibitors (n=15), antiepileptics (n=7), proton pump inhibitors (n=7) or hormones, antipsychotics, antineoplastics were taken by those patients. Additionally, 12.2% of the participants who were diagnosed with hypoosmolar hypovolemic hyponatremia, thiazide diuretics were submitted as the main etiology. Our patient was newly diagnosed with hypertension and was taking his medications which were spironolactone, hydrochlorothiazide, perindopril, indapamide. Moreover, he was taking hydroxyzine and sertraline for his major depression which was prescribed by his physician.

In another study, Movig et al. compared the risk of hyponatremia caused by SSRI's and other antidepressants. Also, they compared combined use of diuretics with SSRI's or with other antidepressants. The results indicated that SSRI's were 4 times more potential to cause hyponatremia than other antidepressants. Additionally, the use of diuretics combined with SSRI's in elderly population had the highest risk ratio among others [6]. Although our patient was relatively

younger than the patients in the study; severe hyponatremia was caused by combined medications he was using for his hypertension and his depression which all were prescribed by physicians.

Time onset of hyponatremia has a wide range from the first day of the consumption up to few months. In one study conducted by Liu BA and his friends, the mean time interval was estimated at 13 days [7]. The time interval was also short in our study which was about seven days; as the patient developed prominent symptoms after starting his antihypertensive treatment with hydrochlorothiazide.

In hospitalized patients with hyponatremia secondary to SSRI usage, 10% of those needed intensive care and mortality rates are up to 7% [8]. Thus, exclusion of other etiologic factors causing hyponatremia and early diagnosis and treatment are crucial. As mentioned above, our patient was in severe depletion of sodium which led him had tonic-clonic seizures, become hypoxic and unconsciousness which all are signaling high rate of mortality, separately.

Checking the serum sodium levels both before and after the treatment is recommended in patients who have multiple chronic diseases and under the treatment with multiple medications since they have higher risk for drug related hyponatremia. [9,10]. First treatment approach is discontinuation of the possible drug and providing supportive therapy. In patients under SSRI medication, diuretic prescription should be avoided to minimize the risk of hyponatremia [5,6].

Conclusion

Physicians should keep this in mind that commonly used drugs such as SSRIs or diuretics are causing severe hyponatremia with acute onset which leads mortality and morbidity. In a patient with acute hyponatremia symptoms careful questioning about medication history should be done. We strongly recommend that combination of SSRI with diuretics, especially with hydrochlorothiazide shouldn't be prescribed to any patient since they have severe complications by decreasing the serum sodium levels rapidly.

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