Case Report

Carbamazepine-induced hyponatremia – A wakeup call

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Abstract

Carbamazepine-induced hyponatremia is a rare condition. The patients may or may not be symptomatic. Epilepsy is considered a social taboo. Hence, patients do not reveal history of being on antiepileptic agents. Carbamazepine is a known antiepileptic and psychotropic agent. It is commonly used for the treatment of seizures and psychiatric disorders. We present a case of a 60-year-old female patient presenting in emergency department with history of carbamazepine-induced hyponatremia. It raises antidiuretic hormone (ADH) levels. This leads to increased sensitivity of renal tubules to ADH levels. She was diagnosed as a case of syndrome of inappropriate ADH and was treated accordingly. She was asymptomatic and was ambulatory. She recovered significantly. Hence, it is essential to monitor sodium levels in patients on carbamazepine therapy and also on drugs with similar mechanism of action.

Keywords: Anti diuretic hormone, antiepiletic agent, seizures

Introduction

Carbamazepine is an antiepileptic agent which can cause hyponatremia, but it is rarely documented. Hyponatremia, both symptomatic and asymptomatic, has been found to be directly related to the increased mortality and morbidity of the primary disease.[1] Most of the patients of hyponatremia become symptomatic at serum sodium less than 120 mEq/dL approximately.[2] Females of geriatric age group are particularly susceptible to this side effect. The underlying comorbidities, lack of follow-up, and the usage of multiple drugs in this age group can lead to complications with even a slight decrease in serum sodium levels. Monitoring of serum electrolytes, which is a low-cost blood investigation, in both symptomatic and asymptomatic patients is essential to avoid such complications.

Case Description

A 60-year-old female patient presented with history of swelling of bilateral feet since the past 1 month. She gave history of two episodes of focal seizures with secondary generalization 2 months back for which she had consulted a neurologist. She was started on carbamazepine (200 mg thrice daily). She was hypertensive since 2 years for which she was taking telmisartan (40 mg) regularly. There was no history of diuretic intake, vomiting, diarrhea, and shortness of breath. On examination, she was conscious and oriented. Her blood pressure was 130/90 mm hg, pulse rate 84 beats/min, and respiratory rate 18/min. Pedal edema was present. Pallor, cyanosis, clubbing, and lymphadenopathy were absent. Other causes of syndrome of inappropriate antidiuretic hormone (SIADH) were also ruled out such as malignancy, pulmonary diseases, and central nervous system pathology by doing relevant investigations. Iatrogenic causes of hyponatremia, hypothyroidism, and glucocorticoid deficiency were also ruled out.

Laboratory investigations were suggestive of hyponatremia (serum sodium was 118 meq/L), serum potassium was 3.4 mmol/L, and thyroid secreting hormone was 2.3mIU/L. Her serum glucose was 97 mg/dL and serum blood urea was 161 mg/dL. Blood urea nitrogen was 7.52 mmol/L, serum creatinine was 0.76 mmol/L, and serum uric acid was 4.91 mg/dL. Urine osmolality was 317.3 mOsm/kg of water and serum osmolality

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was 270.27 mOsm/kg of water. Her lipid profile was normal. Clearly, urine osmolality was more than plasma osmolality. Urinary sodium was 49.70 mmol/L and serum cortisol was 12 μg/dL. As urinary sodium was more than 20 mmol/L, causes like primary polydipsia and exercise induced were ruled out. Her urine output was around 1.5 L. She was diagnosed as a case of SIADH as she presented with clinical euvolemia, urine osmolality was more than 100 mOsm/kg, and urinary sodium was more than 40 mmol/L with normal thyroid, adrenal, and renal functions. There was evidence of hypokalemia and acid-base disorder. The differential diagnoses were adrenal insufficiency, hypothyroidism, cerebral salt wasting syndrome, hyperlipidemia, and primary polydipsia. The treatment included stopping of carbamazepine as suspected cause of hyponatremia. For seizures, she was started on levetiracetam (500 mg thrice daily). Oral tolvaptan (30mg once daily) and fluid restriction were advised. Her serum sodium on day 3 of starting medication was 122 mEq/L. On day 4, it was 125 mEq/L. Thereafter, after 7 days of treatment on follow-up, it was 135 mEq/L.

Discussion

Serum sodium less than 136 mmol/L is defined as hyponatremia. Usually, acute-onset hyponatremia occurs in less than 48 h and is associated with multiple neurological complications such as seizures and coma.[3] Most of the patients of hyponatremia become symptomatic at serum sodium less than 120 mEq/dL approximately.[2] Hyponatremia has been found to occur in less than 1% cases of hospitalized patients. As sodium is the primary electrolyte of extracellular fluid and is the dominant factor of serum osmolality, imbalances in the serum sodium levels can lead to pathological variation in cellular functions.[1,4] Hyponatremia, both symptomatic and asymptomatic, has been found to be directly related to increased mortality and morbidity of the primary disease.[1] There are multiple causes of hyponatremia such as medications like diuretics, antiepileptics, and antipsychotics. Diuretics are the most common cause of hyponatremia. In our case, hyponatremia was caused by carbamazepine. Carbamazepine is commonly used for the treatment of seizures, neuralgia, and psychiatric disorders. Carbamazepine-induced hyponatremia is more common in females, patients of age more than 40 years, low baseline serum sodium levels, psychiatric illness, surgery, and hypothyroidism.[5,6] Our patient had two risk factors – age and gender. Carbamazepine causes increase in antidiuretic hormone (ADH) which leads to abnormal sensitivity of renal tubules to ADH activity. This causes increased expression of aquaporin 2 channels in the renal tubules.[7] The incidence of hyponatremia due to carbamazepine has been found to be 1.8%–40% in previous studies. Although the incidence of hyponatremia with monotherapy of carbamazepine is low, the overall incidence is on the rise.[8] A previous study has also reported a case of a 52-year-old female patient who presented with grand mal epilepsy as a consequence of hyponatremia due to carbamazepine.[9] Other anticonvulsants causing hyponatremia are oxcarbamazepine and lamotrigine. All these drugs alter the vasopressin levels in the renal tubules.[10] The incidence of drug-induced hyponatremia is on the rise as a result of polypharmacy and self-medication especially in the elderly patients.[11] In the majority of cases described in the literature, hyponatremia occurred shortly after initiating the treatment and most of the patients were symptomatic.[6,12] However, Fourlanos highlighted a case series of patients with carbamazepine-induced hyponatremia who were asymptomatic at presentation.[11] Our patient was also asymptomatic. A few case reports described in the past have highlighted the role of genetic predisposition in the development of drug-induced diabetes insipidus. However, this association was not observed in cases of drug-induced hyponatremia such as diuretics. Thus, it was concluded that patients developing hyponatremia as a result of diabetes insipidus with one drug can be affected with another drug affecting vasopressin secretion in the renal tubules.[13] Since epilepsy is considered a social stigma and patients are hesitant to share the history of being on antiepileptic drugs, one can miss this rare cause of hyponatremia. The geriatric patients usually go to a family physician as the first contact for medical services. Drug-induced hyponatremia, although a known entity, is rarely documented. As the geriatric patients have underlying comorbidities and age-related physiological changes, even a minimal change in the electrolytes can lead to morbidities and avoidable mortality. This case highlights the importance of consideration of the side effects of these often prescribed medications in aged population which can be followed up by family physicians.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Adler SM, Verbalis JG. Disorders of body water homeostasis in critical illness. Endocrinol Metab Clin North Am 2006;35:873-94.
2. Lu X, Wang X. Hyponatremia induced by antiepileptic drugs in patients with epilepsy. Expert Opin Drug Saf 2017;16:77-87.
3. Adrogué HJ, Madias NE. Hyponatremia. N Engl J Med 2000;342:1581-9.
4. Palmer BF. Causes and management of hyponatremia. Ann Pharmacother 2003;37:1694-702.
5. Letmaier M, Painold A, Holl AK, Vergin H, Engel R,

Konstantinidis A, *et al*. Hyponatraemia during psychopharmacological treatment: Results of a drug surveillance programme. Int J Neuropsychopharmacol 2012;15:739-48.

6. Kuz GM, Manssourian A. Carbamazepine-induced hyponatremia: Assessment of risk factors. Ann Pharmacother 2005;39:1943-6.
7. Bragança AC, Moyses ZP, Magaldi AJ. Carbamazepine can induce kidney water absorption by increasing aquaporin 2 expression. Nephrol Dial Transplant 2010;25:3840-5.
8. Kuz GM, Manssourian A. Carbamazepine-induced hyponatremia: Assessment of risk factors. Ann Pharmacother 2005;39:1943-6.
9. Holtschmidt-Taschner B, Soyka M. Hyponatremia-induced seizure during carbamazepine treatment. World J Biol Psychiatry 2007;8:51-3.
10. Chan TY. Drug-induced syndrome of inappropriate antidiuretic hormone secretion. Causes, diagnosis and management. Drugs Aging 1997;11:27-44.
11. Fourlanos S. Managing drug-induced hyponatraemia in adults. Aust Prescr 2003;26:114-7.
12. Gandelman MS. Review of carbamazepine-induced hyponatremia. Prog Neuropsychopharmacol Biol Psychiatry 1994;18:211-33.
13. Krysiak R, Okopień B, Haberka M, Herman ZS. Nephrogenic diabetes insipidus induced by colchicines – A case report. Pol Arch Med Wewn 2005;114:882-6.