Oxcarbazepine Induced Hyponatremia: A Case Report

Ashima Basheer[1], Rittu R.L[2], Dr.Dhanya Dharman[3], Dr Shaiju S Dharan[4]
[1,2] *Pharm D Intern, Department of Pharmacy Practice, Ezuthachan College of Pharmaceutical Sciences, Marayamuttom, Trivandrum*
[3] *Associate Professor, Department of Pharmacy Practice, Ezuthachan College of Pharmaceutical Sciences, Marayamuttom, Trivandrum*
[4]*HOD/Principal of Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Trivandrum*

Abstract- **Oxcarbazepine is a well-known and effective anti-convulsant used for patients with underlying seizure disorder. It is a structural analog of carbamazepine, it follows a different metabolic pathway in which it is converted to a different active metabolite. Side effects associated with this medication are vast, in this report we will look in on the renal adverse effects, Syndrome of inappropriate anti-diuretic hormone secretion (SiADH). SiADH is a condition in which the body is making too much anti-diuretic hormone which results in too much water absorption and cause hyponatremia with neurologic sequelae. Here is a 67-year-old female patient with complaint of increased talk, insomnia for 3 months. On admission in hospital under psychiatry the patient was treated with T.Zenoxa (Oxcarbazepine) 450mg 1-0-1 and on following days patient Na decreased 135, 130, 124 mEq/L which indicated to be hyponatremic secondary to having SiADH.**

Keywords: Hyponatremia, SiADH, Adverse effects, Anti-convulsant

INTRODUCTION

Oxcarbazepine (OXZ) is an antiepileptic drug developed as a keto derivative of carbamazepine (CBZ) [1]. It is widely used as a mood stabilizer in patients with bipolar disorder [1]. OXZ monotherapy is as effective as compared with CBZ, lithium and valproic acid in treating bipolar patients and has fewer side effects [1]. Hyponatremia has been reported to occur in 3–51% of epileptic or psychiatric patients taking OXZ [3]. It works by binding to the voltage-gated sodium channels in their inactive form and thereby preventing sustained or repetitive firing of an action potential [4]. Because of- its mechanism of action, oxcarbazepine toxicity is associated with neurologic, cardiovascular, and anticholinergic symptoms [5].

Hyponatremia, is an electrolyte imbalance without clinical significance which may sometimes lead to serious complications when not treated appropriately [6]. One of the main cause of hyponatremia is the Syndrome of Inappropriate Antidiuretic Hormone (SIADH) secretion which has been associated with some drugs such as carbamazepine (CBZ) [8]. Because of its antidiuretic effects, CBZ has been used successfully used to treat diabetes insipidus centralis [8]. Altered sensitivity to serum osmolality by hypothalamic osmo receptors appears to be similar but an increased sensitivity of the renal tubules to circulating ADH cannot be excluded [7]. CBZ has led to hyponatremia in patients with epilepsy, neuralgia, mental retardation, and psychiatric disorders with a frequency varying from 4.8 to 40% [9]. Oxcarbazepine which is structurally related to CBZ, has shown similar hyponatremic effects [10]. Experience with OXZ is still limited, and there is no definite explanation for a possible difference in antidiuretic potency [10]. In rare cases, water intoxication has been reported, necessitating treatment discontinuation [10].

CASE REPORT

A 67-year-old female patient was admitted under psychiatry on 26/08/2022 for the reason of increased talk, insomnia for 3 months. The patient has history of Type II DM, BP, uterine prolapse, hypothyroididm and psoriasis. Her objective evidence revealed Hb-10.1 g/dL, WBC -56000 cells/mm^3, CRP-1.1 mg/L, neutrophill count – 63.7%, Lymphocytes - 29.3%, Monocytes -3.5 %, Platelet count- 2.76 lack cells/cmm and Sodium-135mEq/L and on following days sodium value was decreased to 130 mEq/L ,124 mEq/L simultaneously. On admission in the hospital the patient was treated with T.Dicorate E R (Divalproex)

500 mg 1/2-1/2 -1, T.Lonazep (Clonazepam) 0.5 mg 1/2-1/2-2, T.Sizopin (Clozapine) 25mg 0-0-1, T.Atrax (Hydroxyzine) 25 mg 1-0-1, T.Zenoxa (Oxcarbazepine) 450mg 1-0-1, T.Sizodon Plus (Risperidone + Trihexyphenidyl) 1-1/2-1, T.Sernace (Haloperidol) 1.5mg 1-1-1, T.Janumet (Sitagliptin + Metformin) 1/2-0-0.

On following days the patient sodium level was found decreasing from 135-130-124 mEq/L. The Doctor was informed regarding and T.Zenoxa (Oxcarbazepine) 450 mg 1-0-1 was stopped and added T.Addna (Salt capsule) 1g 1-1-1.

DISCUSSION

Oxcarbazepine is a anti-convulsant which is administered orally as an extended-release tablet or as an oral suspension to treat seizures, nerve pain, and bipolar disorder. OXZ stimulates the collecting tubule V2 receptor-G protein complex independent of anti-diuretic hormone (ADH), leading to increased renal tubular water absorption [1]. These channels are found on the collecting ducts and they carry water across the membrane into the bloodstream [2]. In this report, we will focus on the renal complication, SiADH [3]. SiADH is an entity that involved excessive production of ADH, also known as vasopressin. This hormone allows the body to retain water. One of the most common complication of SiADH is hyponatremia. Hyponatremia can present with symptoms such as nausea, vomiting, headaches, confusion, fatigue, restlessness, and muscle weakness. If severe enough it may also lead to seizures and possibly coma [2].

Oxcarbazepine-induced SiADH is a result of an increase in ADH, which increases sensitivity of the aquaporin 2 channels in the renal tubules, resulting in hyponatremia [3]. The choice of management is fluid restriction which has been proven to be correct for hyponatremia [4]. If severe hypertonic saline and demeclocycline are also given to improve the symptoms[4].

One of the most common side effects of oxcarbazepine is nausea and vomiting [5,6]. Hyponatremia caused by oxcarbazepine has been linked to patients with epilepsy, neuralgia, and psychological disorders. Other side effects of oxcarbazepine include seizures, respiratory distress, lethargy, headache, and altered mental status [6].

SiADH is caused by one of the following four major categories: pulmonary disorders, malignancy, neurologic disorders, and medications. Other medications commonly associated with SiADH include chlorpropamide, carbamazepine, and cyclophosphamide. Studies have shown that chlorpropamide increases sodium permeability in the loop of Henle, causing more water absorption in the collecting ducts by increasing the number of ADH receptors, whereas oxcarbazepine, which is structurally related to carbamazepine, increases the sensitivity of the ADH receptors. Nausea and vomiting have been shown to correlate with sodium levels below 125 to 130 mEq/L [8]. Coma and respiratory distress have been correlated with serum sodium levels below 115 to 120 mEq/L [9]. Other symptoms include gait disturbances, memory and cognitive disturbances, fatigue, dizziness, confusion, and muscle cramps [10].

CONCLUSION

Being a severe adverse event and because of the increasing the use of OXC in bipolar disorder, psychiatrists should pay attention to this preventable side effect. The causes of SiADH are broad, and clinicians should change the treatment of hyponatremia to the cause of SiADH for better patient outcomes. Moreover, hyponatremia as a result of SiADH is common and attempts should be made to find the underlying cause instead of pursuing fluid restriction to reduce patient re-hospitalization and hospital length of stay.

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