

## Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH) as a Rare Manifestation of Oxcarbazepine Poisoning– A Case Report

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### Abstract

Oxcarbazepine is an anti-epileptic drug in which the metabolite 10-Monohydroxy Derivative (MHD) is the pharmacologically effective compound. Oxcarbazepine is a prodrug and that the formation of the active MHD metabolite is a rate-limiting process which may contribute to the relative low toxicity of the drug in overdose. There are only a few published human data available concerning the acute toxicity of the antiepileptic drug oxcarbazepine.

We present a case of oxcarbazepine toxicity with severe hyponatremia and Generalized Tonic- Clonic Seizure (GTCS) due to Syndrome of Inappropriate Antidiuretic Hormones (SIADH).

**Keywords:** Hyponatremia; Oxcarbazepine; SIADH; MHD; GTCS

### Introduction

Oxcarbazepine is a relatively new drug, which is used as an antiepileptic as well as for bipolar effective disorders, and is structurally and chemically similar to the well established antiepileptic drug carbamazepine [1,2].

The carbonyl group of the oxcarbazepine is reduced by presystemic 10-ketoreduction to form 10-Monohydroxy Derivative (MHD), which is the metabolite responsible for the pharmacological effect [3].

One of the presumed mechanisms of action of MHD is thought to be blockage of voltage-sensitive sodium channels, thereby stabilizing hyperexcited neural membranes, inhibiting repetitive neuronal firing and diminishing the propagation of synaptic impulses. Syndrome of Inappropriate Antidiuretic Hormones (SIADH) is a rare complication of oxcarbazepine toxicity [4,5]. Oxcarbazepine has lower incidence of side effects than carbamazepine, causing less hepatic induction and is not known to cause hepatotoxicity. The most common adverse reaction associated with oxcarbazepine are- dizziness, headache, diplopia, vomiting, abnormal vision, and tremor. Less common adverse reaction is hyponatremia ( $\text{Na}^+ < 125 \text{ mEq/L}$ ) [6]. There are very few published data for acute toxicity of oxcarbazepine.

### Case Report

A 32 year old male, known case of bipolar disorder with paranoid schizophrenia was admitted to medicine intensive care unit, 3 hours after ingestion of approximately 40 tablets of 600 mg oxcarbazepine

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**Received:** July 24 2017; **Accepted:** August 08 2017; **Published:** August 15 2017

(maximal therapeutic dose is 2400 mg day) with complaints of nausea, vomiting, and dizziness.

On examination patient was drowsy, responding intermittently to verbal command and moving all four limbs. Blood pressure was 100/60 mm of Hg, pulse was 65 / min regular. Neurological examination (Glasgow coma scale was- 09/15), tendon and pupillary reflexes were normal. Plantars were bilateral flexors. There were no signs of nystagmus, ataxia or dysarthria.

The ECG was within normal limits (sinus rhythm). X ray chest was within normal limits.

Endotracheal intubation was done in view of low Glasgow coma scale for airway protection.

Thirty minutes after admission, patient had an episode of generalized tonic- clonic seizure which was treated by diazepam (intravenous 5 mg once).

Blood investigations revealed serum sodium levels of 109 mEq/L. Plasma osmolality was 215 mOsmol/Kg, Urine osmolality was 128 mOsmol/Kg and Urinary sodium was 45 mEq/L suggesting SIADH induced hyponatremia. Other electrolytes, arterial blood gases, thyroid profile, kidney and liver functions were normal.

Hyponatremia was treated as per protocol. Tablet Tolvaptan 15 mg once a day was given. The sodium levels were corrected at a rate of not more than 8-10 mEq/l over 24 hours. Post correction sodium levels after 48 hours was 134 mEq/L.

Patient's GCS improved after 20 hours of MICU admission. (Glasgow coma scale was-15/15).

No ECG changes or arrhythmias occurred and the patient remained haemodynamically and respiratory stable. Also the sodium serum



**Figure 1:** Post- extubation X-Ray showing no obvious abnormality.

Clinical Assessment on Admission	Clinical Assessment on Discharge
<p><b>General Examination</b>  GCS- 09/15  Afebrile  Pulse- 65/ min Regular  Blood Pressure- 100/60 mm of Hg  Systemic Examination:  CNS- Drowsy, responding intermittently to verbal command and moving all four limbs. Tendon and pupillary reflexes were normal. Plantars were bilateral flexors. There were no signs of nystagmus, ataxia or dysarthria.  CVS- S1S2 present, No Murmurs present  R/S- Air Entry B/L equal with no Adventitious sounds heard  P/A- Soft, non- tender with No organomagely</p>	<p><b>General Examination</b>  GCS- 15/15  Afebrile  Pulse- 82 / min Regular  Blood Pressure- 116/72 mm of Hg  Systemic Examination:  CNS- Conscious and oriented. Tendon and pupillary reflexes were normal. Plantars were bilateral flexors. There were no signs of nystagmus, ataxia or dysarthria.  CVS- S1S2 present, No Murmurs present  R/S- Air Entry B/L equal with no Adventitious sounds heard  P/A- Soft, non- tender with No organomagely</p>

**Table 1:** Clinical Assessment on Admission vs Clinical Assessment on Discharge.

concentration, as well as other electrolytes, arterial blood gases, kidney and liver functions remained normal. Patient was extubated after 36 hours of MICU admission.

Post-extubation x- ray chest was within normal limits.

Four days after admission the patient fully recovered and was discharged on Tablet Tolvaptan 15 mg once a day for 7 days after being seen by the Psychiatrist.

## Discussion

Studies suggest that one-third of all cases of hyponatremia are caused by the syndrome of inappropriate Secretion of Antidiuretic Hormone (SIADH) [7]. SIADH was first described by Bartter and Schwartz [8]. Physiologically vasopressin [also known as Arginine Vasopressin (AVP) or Antidiuretic Hormone (ADH)] acts in response to an increase in serum osmolality to retain water at the kidney nephron. Patients with SIADH have unregulated secretion of vasopressin despite hypotonicity of the serum. Consequently, polydipsia and high concentration of serum vasopressin leads to antidiuresis eventually resulting in hyponatremia.

Recently vasopressin receptor antagonists like oral tolvaptan and parenteral conivaptan are used in the management of SIADH. In the European Union, tolvaptan-the only orally administered vaptan-is approved for use in adults with hyponatremia secondary to SIADH [9].

Quite surprisingly, despite its clinical relevance, electrolyte imbalance has received very little attention in the scientific literature, with only a very few reviews specifically dealing with electrolyte disturbances, seizures and drug overdoses published so far. Seizures represent an important clinical manifestation of electrolyte disorders and are more frequently observed in patients with hyponatremia. In fact, treatment of seizures secondary to electrolyte imbalances is determined by the underlying cause of the disturbance, and in most cases administration of Anti- epileptic drugs is not necessary as long as the underlying disturbance is rectified [10].

## Conclusion

This report describes a severe overdose with the antiepileptic drug

oxcarbazepine causing SIADH induced severe hyponatremia leading to generalized tonic- clonic seizure.

This indicates that the drug response for oxcarbazepine varies on individual basis and hence close monitoring of patients with oxcarbazepine intoxication is advised.

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