World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Case Report
ISSN: 2583-6579
SJIF Impact Factor: 6.916
Year - 2026
Volume: 5; Issue: 6
Page: 422-429

RAPID OVERCORRECTION OF HYPONATREMIA FOLLOWING UNEXPECTED AQUARESIS DURING HYPERTONIC SALINE THERAPY IN AN OXCARBAZEPINE-TREATED PATIENT: A CASE REPORT

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Article Received: 08 April 2026 | | ***Article Revised: 29 April 2026*** | | ***Article Accepted: 19 May 2026***

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DOI: https://doi.org/10.5281/zenodo.20445236

How to cite this Article: Dr. Jyoti Goyal, Dr. Bhawesh Kumar Thakur, Dr. Anil Jain, Dr. Nickle Sasidharan, Dr. Jitendra Soni (2026) RAPID OVERCORRECTION OF HYPONATREMIA FOLLOWING UNEXPECTED AQUARESIS DURING HYPERTONIC SALINE THERAPY IN AN OXCARBAZEPINE-TREATED PATIENT: A CASE REPORT. World Journal of Pharmaceutical Science and Research, 5(6), 422-429.

ABSTRACT

Background: Oxcarbazepine is a well-recognized cause of drug-induced hyponatremia and may precipitate breakthrough seizures despite adequate compliance with antiepileptic therapy. While rapid sodium overcorrection is commonly described with vasopressin antagonists such as tolvaptan, sudden overcorrection during conventional 3% hypertonic saline therapy due to unexpected aquaresis is less frequently highlighted in literature. **Case Presentation:** We report a case of severe symptomatic hyponatremia in a patient with seizure disorder receiving multiple antiepileptic drugs including oxcarbazepine. The patient presented with breakthrough seizures and serum sodium of 118 mEq/L. Hypertonic 3% saline was initiated for symptomatic hyponatremia. Within a few hours, urine output increased abruptly from 100–150 mL/hour to 300–400 mL/hour, suggestive of sudden free water diuresis (aquaresis). Despite early discontinuation of hypertonic saline, serum sodium increased rapidly by nearly 20 mEq/L within less than 16 hours. Rescue therapy with 5% dextrose and desmopressin was initiated to prevent further overcorrection and reduce the risk of osmotic demyelination syndrome. **Discussion:** This case highlights an important but under-recognized phenomenon of rapid sodium auto-correction associated with sudden aquaresis during hypertonic saline therapy. Although this phenomenon is well described with tolvaptan and reversal of SIADH physiology, it is less commonly reported during routine 3% saline administration. The case emphasizes that abrupt increase in urine output may serve as an early bedside warning sign of impending overcorrection. **Conclusion:** Close monitoring of urine output is essential during correction of severe hyponatremia with hypertonic saline. Sudden polyuria should prompt urgent reassessment of sodium correction trajectory and consideration of early intervention with desmopressin-based strategies to prevent osmotic demyelination.

KEYWORDS: Hyponatremia, Oxcarbazepine, Hypertonic saline, Aquaresis, Polyuria, Sodium overcorrection, Desmopressin, Osmotic demyelination syndrome.

INTRODUCTION

Hyponatremia is one of the most frequently encountered electrolyte abnormalities in neurological and critical care practice. Severe acute hyponatremia may manifest with seizures, altered sensorium, cerebral edema, respiratory failure, and death. Oxcarbazepine is a well-known cause of drug-induced hyponatremia and acts predominantly through SIADH-like mechanisms with increased renal responsiveness to vasopressin.[1,2]

Symptomatic hyponatremia is commonly treated with 3% hypertonic saline. However, one of the major therapeutic challenges is inadvertent rapid sodium correction following sudden emergence of free water diuresis (aquaresis). Excessive sodium correction increases the risk of osmotic demyelination syndrome (ODS), a potentially devastating neurological complication.[3]

Rapid overcorrection due to spontaneous aquaresis is widely recognized during treatment with vasopressin antagonists such as tolvaptan.[4] However, similar rapid correction occurring during standard hypertonic saline therapy is less frequently documented in literature. We report a clinically important case of severe oxcarbazepine-associated hyponatremia in which sudden unexpected aquaresis during 3% saline therapy resulted in marked sodium overcorrection despite early discontinuation of hypertonic saline.

CASE PRESENTATION

A 38-year-old female with a known seizure disorder presented to the emergency department with breakthrough generalized tonic–clonic seizures despite good compliance with her prescribed antiepileptic medications, including levetiracetam, lacosamide, and oxcarbazepine. There was no history of fever, headache, vomiting, recent infection, or any focal neurological deficit. She had no significant past medical history of hypertension, diabetes mellitus, chronic kidney disease, liver disease, or other chronic illnesses.

On arrival, the patient was in a postictal state. Her vital signs were stable, with blood pressure of 126/84 mmHg, heart rate of 108 beats/minute, respiratory rate of 23 breaths/minute, and oxygen saturation of 96% on room air. She remained drowsy for approximately 30 minutes following the seizure episode and gradually became conscious, though mildly confused, over the next 3–4 hours. She subsequently regained full orientation and normal cognition. Systemic examination was unremarkable, and there were no signs of meningeal irritation or focal neurological deficits. Clinical assessment suggested a euvolemic state.

Initial laboratory investigations revealed severe symptomatic hyponatremia with a serum sodium level of 118 mmol/L. Serum potassium was 3.1 mmol/L, serum creatinine was 0.5 mg/dL, and blood urea was 12 mg/dL. Serum osmolality was 250 mOsm/kg (reference range 275–295 mOsm/kg), consistent with hypotonic hyponatremia. Urine studies demonstrated concentrated urine with urine osmolality of 456 mOsm/kg and elevated urine sodium levels (38mEq/l) supporting the diagnosis of syndrome of inappropriate antidiuretic hormone secretion (SIADH). Urinalysis showed a urine pH of 5.0, specific gravity of 1.011, and no glycosuria. In view of the euvolemic hypotonic hyponatremia and chronic oxcarbazepine use, a diagnosis of oxcarbazepine-induced SIADH was considered most likely.

Electrocardiography and echocardiography were unremarkable. Contrast-enhanced MRI showed no significant abnormalities in the brain parenchyma, ventricular system, or extracerebral cerebrospinal fluid spaces.

Because the patient presented with seizures attributable to severe hyponatremia, treatment with 3% hypertonic saline was initiated at a rate of 30 mL/hour in the critical care unit. Fluid restriction was advised, and close biochemical monitoring was planned with serial serum sodium measurements every 8 hours. At presentation, urine output was approximately 100–150 mL/hour. However, approximately 3–4 hours after initiation of hypertonic saline, urine output increased dramatically to nearly 400–500 mL/hour, suggestive of spontaneous aquaresis and restoration of free water clearance.

The first repeat serum sodium measurement, obtained approximately 8 hours after initiation of therapy, revealed a rapid rise in serum sodium from 118 mEq/L to 138 mEq/L, representing an increase of 20 mEq/L within 8 hours. Recognition of this unexpectedly rapid correction prompted immediate discontinuation of hypertonic saline. Given the substantial risk of osmotic demyelination syndrome (ODS), rescue therapy was initiated promptly with intravenous 5% dextrose and desmopressin. Intravenous 5% dextrose was administered at a rate approximating urine output plus an additional 100 mL/hour, and desmopressin one puff (10 mcg) was administered intranasally in each nostril twice a day for 2 days till the time aquaresis stopped and sodium stabilized.

Subsequent serial monitoring demonstrated gradual relowering and stabilization of serum sodium levels. Serum sodium decreased to 134 mEq/L after 4 hours of starting 5% dextrose and desmopressin spray. Every 4 hourly sodium monitoring is done and sodium was 131, 132 and 134 in subsequent 4 hourly readings for next 12 hours. Hence in first 24 hours sodium increased to 16 mmol/l despite of all the efforts to relower the sodium. Relowering therapy continued. At the end of 48 hours sodium reading was 134 mmol/l. With the help of 5% dextrose and desmopressin total sodium correction was 16 after 48 hours which is very well in the limit of advised correction. Patient was shifted to room and next day reading that is 72 hours after initial correction was 140mmol/l. (Figure 1).

The patient subsequently underwent close neurological and biochemical monitoring throughout hospitalization. She was transferred from the intensive care unit to the general ward on hospital day 3 and discharged on day 8 in a neurologically stable condition. No clinical manifestations suggestive of osmotic demyelination syndrome developed during the hospital stay. Repeat MRI brain to look for features of ODS was not done. She was in follow up with neurologist for optimization of her antiepileptics and there was no neurological sequelae or recurrence of hyponatremia were observed during the next 2-month follow-up.

Table 1: Timeline of Events During Hyponatremia Correction and Development of Aquaresis.

Time	Time from Admission	Serum Sodium (mEq/L)	Change in Sodium from Baseline (mEq/L)	Urine Output (mL/hour)	3 % Nacl	5 % Dextrose	Desmopressin	Neurological Status / Clinical Events	Clinical Interpretation	Urine Osmolality	Serum Osmolality
11:20 Pm	At Presentation	118	-	100-150 ml / Hr for first 4 hours	Started at 30 ml per hour	No	No	No deficits, slightly dull in postictal state	Severe symptomatic hyponatremia	456 mOsm/kg	250 mOsm/kg
	3–4 Hours	Not done	-	400 -500 ml / Hr for 4-8 hours	continued	No	No	No deficits, conscious oriented	Rapid free water clearance suspected	-	-
	6–8 Hours	138	20	400-500 ml /Hr for 2 hours	3 % Nacl Stopped after 8 hours	No	No	Persistent polyuria/ High risk for Osmotic Demyelination Syndrome	Ongoing spontaneous water diuresis	-	-
	8–12 Hours	134	16	Decreased from 10^{th} hour to 150 -200 ml per hour for next4-5 hours	Reassessment of correction strategy	Urine output plus 100 ml per hour	10 ugm nasal spray in both nostrils	Neurologically stable, urine output decreased	High-risk correction phase/ Attempt to re-lower sodium	-	-
	<16 Hours	131	13	80-100 ml per hours	Continued monitoring	continued	no	Urine output decreased further	Attempt to re-lower sodium continued	-	-
	After 20 Hour	132	14	70-80 ml per hour	Serial sodium and urine monitoring	continued	Nasal spray repeated	Urine output normalized	Attempt to re-lower sodium continued under close monitoring of sodium	-	-
	>24 Hour	134	16	60-70 ml per hour	Serial sodium and urine monitoring	continued	no	Close neurological observation	Prevention of further aquaresis	-	-
	>48 Hour	134	16	70-80 ml per hour	Serial sodium and urine monitoring	stopped	Nasal spray repeated	Close neurological observation	Prevention of further aquaresis	-	-
	At 72 hours while shifting to Ward from ICU	140	22	Self-voiding	Shifted to Ward	stopped	no	Neurologically stable	Recovery without clinical ODS and plan to shift in step down	-	-

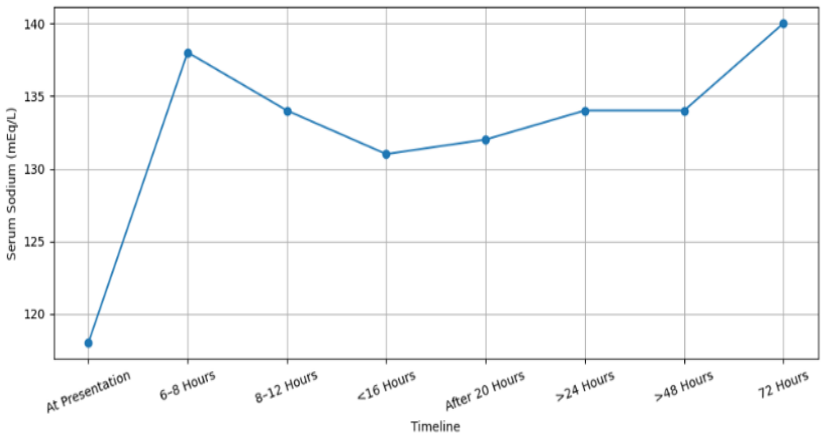
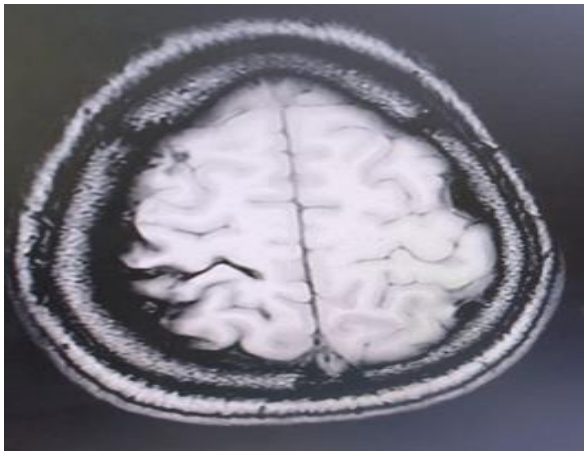
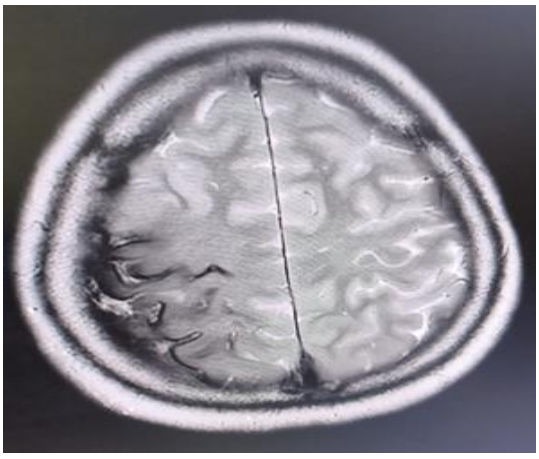


Figure 1: Trend of serum sodium over time.



T1



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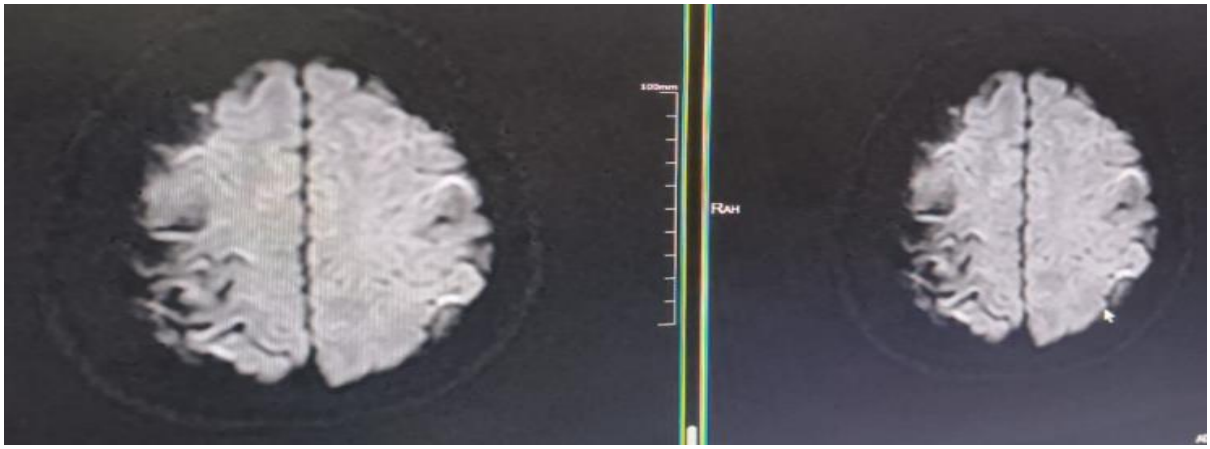

DWI and ADC

Figure: 2 MRI brain.

Impression

- T2 hypointense subdural signals in the right fronto – parietal region without significant mass effect with similar in the right fronto – parietal sulcal spaces and left extradural region with gradient blooming.
- Tiny micro-hemorrhage bleed focus in the right thalamus and lateral ventricles.

- Foci of SWI blooming also seen in right cerebral peduncle, red nucleus, bilateral middle cerebral peduncles and right cerebellar hemisphere as seen before – S/o micro hemorrhages.

DISCUSSION

Oxcarbazepine is a well-recognized cause of hyponatremia and is among the antiepileptic drugs most strongly associated with SIADH-like physiology. The mechanism is believed to involve enhanced renal responsiveness to vasopressin with increased water reabsorption at the collecting duct level. The reported incidence of oxcarbazepine-associated hyponatremia varies widely in literature, with severe hyponatremia occurring more frequently in elderly patients, chronic users, and those receiving combination antiepileptic therapy.[2]

The present case is clinically important because severe symptomatic hyponatremia presented as breakthrough seizures despite good antiepileptic compliance. More importantly, the patient subsequently developed rapid sodium overcorrection associated with abrupt onset of aquaresis while receiving standard 3% hypertonic saline therapy.

Current international hyponatremia guidelines recommend cautious correction of serum sodium to minimize the risk of osmotic demyelination syndrome (ODS). The European Clinical Practice Guideline on Hyponatraemia and expert recommendations by Sterns et al. suggest limiting sodium correction to approximately 8–10 mEq/L within 24 hours in most patients, with even stricter targets in high-risk individuals such as malnourished patients, alcoholics, liver disease patients, and those with profound chronic hyponatremia.[5,6]

A major learning point from this case is that sodium overcorrection was not solely related to administered hypertonic saline. Rather, the principal driver appeared to be sudden emergence of free water diuresis (aquaresis). The patient initially had urine output of approximately 100–150 mL/hour, which rapidly increased to nearly 300–400 mL/hour shortly after initiation of therapy. This abrupt transition strongly suggests reversal of the antidiuretic state with restoration of renal free water clearance.[5,6,7]

Sterns and colleagues have repeatedly emphasized that most episodes of dangerous sodium overcorrection occur not because excessive sodium is administered, but because spontaneous water diuresis develops during treatment. Once the underlying stimulus for vasopressin secretion resolves, suppression of endogenous ADH permits rapid excretion of electrolyte-free water, causing sudden “autocorrection” of serum sodium. This mechanism is particularly important in transient SIADH states, hypovolemic hyponatremia after volume restoration, adrenal insufficiency after steroid replacement, and drug-induced hyponatremia. The present case demonstrates that similar physiology may also occur during treatment of oxcarbazepine-associated hyponatremia.[7,8]

Although rapid overcorrection due to aquaresis is widely recognized with vasopressin antagonists such as tolvaptan, reports specifically highlighting this phenomenon during routine hypertonic saline therapy remain comparatively limited. Tolvaptan-induced overcorrection is well documented because vasopressin antagonism directly produces massive electrolyte-free water excretion. However, this case illustrates that abrupt aquaresis can similarly occur spontaneously during conventional therapy and may continue even after hypertonic saline has been discontinued.[9]

An especially important bedside observation in this case was the sudden increase in urine output preceding rapid sodium rise. Polyuria may therefore serve as one of the earliest clinical warning signs of impending sodium overcorrection. Hourly urine output monitoring is often underemphasized during hypertonic saline administration,

despite its critical role in identifying evolving aquaresis. The present case therefore supports the concept that urine output monitoring should be considered equally important as serial sodium monitoring during treatment of severe hyponatremia. An abrupt increase in urine output should prompt immediate reassessment of serum sodium, consideration of stopping hypertonic saline, measurement of urine osmolality and early initiation of desmopressin if rapid correction is anticipated.

Several recent publications strongly support proactive or rescue use of desmopressin ("DDAVP clamp") to prevent excessive sodium correction. Sood et al. described the combined use of hypertonic saline and desmopressin as a controlled strategy for severe hyponatremia correction. By limiting sudden free water excretion, desmopressin stabilizes renal water handling and allows clinicians to achieve a more predictable sodium rise.[10]

Rondon-Berrios and Sterns further demonstrated that therapeutic relowering of sodium using desmopressin and hypotonic fluids may reduce risk of osmotic demyelination after inadvertent overcorrection. In the present case, prompt administration of 5% dextrose and desmopressin likely helped stabilize sodium correction trajectory and may have contributed to prevention of neurological complications.[6,7]

Another important aspect is that osmotic demyelination syndrome can occur even when initial hyponatremia symptoms improve clinically. Early neurological recovery after sodium correction should therefore not create false reassurance. Delayed neurological manifestations including dysarthria, quadriparesis, pseudobulbar palsy, movement disorders, and altered consciousness may appear several days later. Hence, prolonged neurological observation remains essential in patients experiencing rapid sodium correction.[11]

The present report adds to existing literature by emphasizing a practical and easily observable bedside marker — sudden polyuria during correction therapy. While sodium measurements are intermittent, urine output changes may provide earlier real-time evidence of transition from antidiuretic physiology to uncontrolled free water clearance.

CONCLUSION

This case highlights an aquaresis as clinically important but under-recognized cause of rapid sodium overcorrection during hypertonic saline therapy. Unexpected aquaresis resulted in marked sodium rise despite early discontinuation of 3% saline. Although this phenomenon is well recognized with tolvaptan therapy, it is less commonly emphasized during routine hypertonic saline administration.

The case strongly reinforces the importance of close urine output monitoring during correction of severe hyponatremia. Sudden polyuria should be considered an early warning sign of impending sodium overcorrection and should prompt immediate reassessment of treatment strategy. Early intervention with desmopressin-based rescue therapy may help prevent neurological complications and improve patient safety. This case therefore reinforces several clinically important principles:

1. Rapid sodium overcorrection may occur even with apparently cautious 3% saline administration.
2. Emergence of aquaresis may become the dominant driver of sodium correction.
3. Sudden polyuria is an important early warning sign.
4. Urine output monitoring should be mandatory during hypertonic saline or vaptan therapy.
5. Early desmopressin-based intervention may prevent catastrophic neurological complications.

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