

# Therapy with Hypertonic Saline in Combination with Anti-Convulsants for Hyponatremia-Induced Seizure: A Case Report and Review of the Literature

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## Abstract

*Seizures are an uncommon but serious complication of hyponatremia which can lead to permanent brain damage and even death.<sup>1,2</sup> It is recommended that patients with hyponatremic-induced seizures be treated with 3% hypertonic saline, however, a rapid rate of correction may result in central pontine myelinolysis (CPM), a severe neurological disorder characterized by mutism, dysarthria, spastic quadriparesis, and pseudobulbar palsy.<sup>2</sup> The patient in this case developed a hyponatremia-induced generalized tonic-clonic seizure which was aborted by rapid therapy with diazepam, followed by hypertonic saline and phenytoin. Subsequent replacement of hypertonic saline with normal saline and salt tabs in combination with phenytoin allowed gradual correction of serum sodium without any subsequent seizures or neurological complications.*

## Introduction

Hyponatremia is defined as serum sodium less than 137 mEq/L.<sup>1</sup> It is a frequent problem, especially in the elderly, affecting as many as 7% of healthy elderly persons.<sup>1</sup> Early signs of hyponatremia include: apathy, weakness, cramps, anorexia, nausea, vomiting, and headache which occur at levels of 125 mEq/L or less.<sup>1,2,5,7</sup> Advanced manifestations include impaired response to verbal and painful stimuli, hallucinations, and urinary incontinence.<sup>7</sup> Other serious complications are hyper/hypothermia, central diabetes insipidus, pulmonary edema, respiratory arrest, coma, seizures, permanent brain damage, and death from increased intracranial pressure or brain herniation.<sup>2,5,6,8</sup> Most brain damage is associated with untreated hyponatremic encephalopathy in a limited number of clinical settings: postoperative state, polydipsia-hyponatremia syndrome, pharmacologic agents (analgesics, antidepressants, antineoplastics, diuretics, hypnotics, oral hypoglycemic agents, narcotics, sedatives, and tranquilizers), congestive heart failure, and AIDS.<sup>6</sup>

Studies show that 3-10% of patients with serum sodium levels below 130 mEq/L have seizures,<sup>3,4</sup> particularly when serum sodium is lower than 115 mEq/L or there is a rapid decrease in serum sodium

concentration (less than 12 hrs<sup>9</sup>).<sup>7</sup> Other factors that may lower the seizure threshold are electrolyte and glucose imbalance, ischemic encephalopathy, medications, and medication withdrawal.<sup>7</sup>

Symptomatic hyponatremia is a medical emergency since even small increases in brain volume (5%) can lead to substantial morbidity (4-15%)<sup>4,5,6</sup> and mortality.<sup>5,6</sup> Records show that correction by water restriction alone results in unacceptable morbidity and mortality,<sup>6</sup> and treatment with hypertonic saline is associated with survival and recovery in symptomatic patients.<sup>5,6</sup>

This report describes the case of a patient who had a hyponatremia-induced generalized tonic-clonic seizure and recovered without any subsequent seizures or neurological complications after treatment with diazepam, hypertonic saline, and phenytoin.

## Case Report

A 69-year-old, Japanese female with a history of hypertension and sialadenitis treated with methylprednisolone (2 sets of 4 mg titrating dose) was seen in the office for routine evaluation and found to have a serum sodium of 121 mEq/L. Later that day, she felt "jittery" and nauseated. Methylprednisolone was discontinued due to her nausea. The following day, the day of admission, she vomited twice. She drank 4 large glasses of water after vomiting the first time. That night in the emergency room, she presented with nausea, vomiting, polydipsia, and "jitters". Her sodium measured 108 mEq/L. She subsequently had a witnessed generalized tonic-clonic seizure with cyanosis and was immediately given 5mg of diazepam IV, followed by infusion of 3% hypertonic saline at 25 ml/hr. The entire seizure lasted approximately 3 minutes. Phenytoin load of 750 mg IV at a rate of 40 mg/min was then given with a maintenance dose of 250 mg IV qd.

On physical exam, the patient was fatigued, yet able to respond to spoken words and follow commands. She did not recall having a seizure. Blood pressure was 120/60 mmHg, pulse 68/min, respirations 21/min and temperature 96.5 F. Skin had reduced turgor. Pupils were equal and reactive to light and extraocular movements were intact. There were no intranasal lesions, no mucosal irregularities or irritation of the oral cavity. Facial movements were symmetrical. A 3cm mobile, firm, tender, right submandibular mass was noted. Lung exam revealed few crackles bilaterally. Trace edema was noted in her extremities. On neurological exam, patient was alert and oriented to person and time. She performed well on the mini-mental status exam except for serial sevens. Cranial nerves II-

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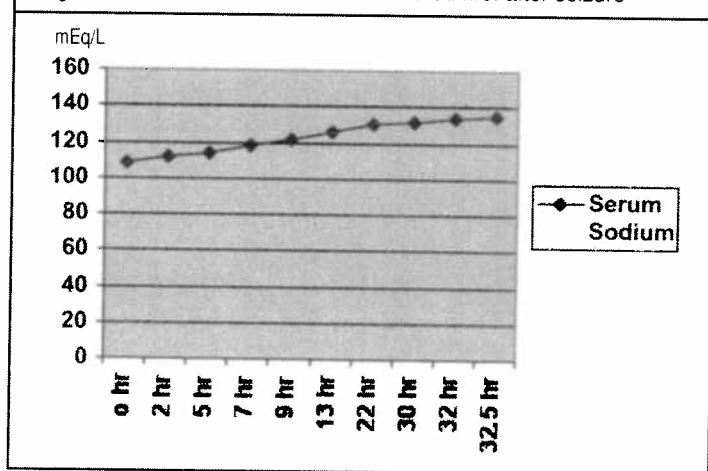
XII were intact. Muscle size, tone, and strength were normal and symmetrical. Babinski signs were observed bilaterally. Reflexes were normal. Touch sensation was also normal.

Laboratory values obtained included serum glucose 126 mg/dL, sodium 108 mEq/L, potassium 4 mEq/L, chloride 78 mEq/L, BUN 5 mg/dL, creatinine 0.4 mg/dL, osmolality 234. Urine osmolality 374 mOsmol/kg and sodium 79 mg/dL. TSH 1.69  $\mu$ U/ml, free T4 1.50 mg/dL. Serum cortisol 17.6  $\mu$ g/dL and 27.2  $\mu$ g/dL. WBC 13.8, Hgb 13.6, Hct 39.6, Plt 323. EKG showed prolonged QT intervals of 448 mili seconds and a U wave. CXR was normal. CT scan without contrast was negative for any intracranial process, although it showed an enhancing mass involving the right submandibular gland measuring 3x4x4 cm with areas of multi-lobulation.

The patient was admitted to ICU and sodium levels were checked every two hours. After two hours, her sodium rose to 112 mEq/L at which time the hypertonic saline was discontinued. Her intravenous infusion was replaced with normal saline IV at a rate of 150 ml/hr and salt tabs 1g po tid. Her serum sodium gradually increased to 130 mEq/L at 22 hours post-seizure (figure 1).

The following day she was transferred to the Progressive Care Unit, the salt tabs were discontinued and phenytoin was changed to 100 mg po tid. The patient remained stable and her sodium levels remained in the 130-136 mEq/L range over the next week. The day before discharge, she underwent right submandibular gland excision, which revealed a hemorrhagic ulcer with acute and chronic cellulitis, microabscesses, necrotizing sialadenitis, and reactive lymphadenitis without atypia or malignancy. On the day of discharge, the patient was stable, without neurological sequelae and sodium was 130 mEq/L. On follow-up exam, there was no evidence of any neurologic abnormalities.

Figure 1.— Serum Sodium Levels from 0-32 hrs. after seizure



## Discussion

In this case, the patient experienced nausea and vomiting at sodium levels of 121 mEq/L as well as a seizure and pulmonary edema at a sodium level of 108 mEq/L. The cause of her hyponatremia was unknown. Although hyponatremia and seizure are not well-known side effects of methylprednisolone<sup>7</sup>, it was the primary suspect in this patient's case since the patient does not have any history of hyponatremia, epilepsy, or any of the risk factors for lowering the seizure threshold.

Current treatment recommendations for symptomatic hyponatremia include close monitoring, preferably in ICU,<sup>6,10</sup> and correction

with 3% hypertonic saline and intravenous furosemide to raise sodium at a rate of 0.6-2 mEq/L/hr.<sup>1,5,6,10</sup> During therapy, electrolytes should be checked every two hours, until the patient is neurologically stable.<sup>6</sup> Patients with seizures require immediate anticonvulsant-drug therapy and adequate ventilation.<sup>5</sup> If the patient continues to have seizures after anticonvulsant therapy, it is recommended that the sodium be raised by 4-5 mEq/L over the first hour or until seizure activity has ceased.<sup>6</sup> A rapid increase of 3-7 mEq/L is enough to stop seizures induced by hyponatremia<sup>5</sup>, however, too rapid of a correction can lead to CPM. Guidelines for discontinuing hypertonic saline include a sodium increase of 20 mEq/L or sodium levels of 120-125 mEq/L.<sup>2,6</sup> The patient's serum sodium measured 121 mEq/L less than 48 hours prior to admission, therefore, it was thought the symptoms were due to acute hyponatremia. Due to the urgent nature of the situation, hypertonic saline was infused at 25 ml/hr. Four hours later, the patient's serum sodium increased by 4 mEq and without further seizures, therefore the patient was felt to be stable and the hypertonic saline infusion was discontinued to prevent rapid correction. However, the serum sodium continued to rise and exceeded the recommended rate of correction.

Controversy remains over the rate of correction. However, most authorities agree that sodium levels should not be elevated by more than 8-12 mEq/L during any 24 hr period.<sup>1,2,4,5,6</sup> Some studies show that increases of more than 12 mEq/L in 24 hrs were too rapid and resulted in CPM.<sup>2,10</sup> Other studies show CPM only develops when 1) a patient is inadvertently made hyponatremic during therapy, 2) sodium levels increase by 25 mEq/L in the first 24-48 hrs, 3) the patient suffers a hypoxic event, or 4) has severe liver disease.<sup>2,5,6,10</sup> It is also recommended that serum sodium not be corrected to eunatremic or hypertremic levels.<sup>6</sup>

## Conclusion

Hyponatremia-induced seizures are a rare but serious condition that may result in permanent brain damage and death either as a primary cause or as a complication of therapy. In symptomatic patients, correction with hypertonic sodium chloride should be prompt, but strictly controlled for avoidance of neurological complications. Immediate administration of anticonvulsant drugs diazepam and phenytoin allowed gradual correction of hyponatremia and prevention of myelinolysis.

## References:

- Kugler, J: Hyponatremia and Hypernatremia in the Elderly. *American Family Physician* 2000, 61:3623-3630.
- Laureno, R. MD and Karp, B. MD: Myelinolysis after Correction of Hyponatremia. *Annals of Internal Medicine* 1997, 126:57-62.
- Hirsberg, B. and Ben-Yehuda, A.: The Syndrome of Inappropriate Antidiuretic Hormone Secretion in the Elderly. *American Journal of Medicine* 1997, 103: 270-273.
- Ellis, SJ: Severe Hyponatremia: Complications and Treatment. *QJM* 1995, 88: 905-909.
- Adroge, H. MD and Madias, N. MD: Primary Care: Hyponatremia. *New England Journal of Medicine* 2000, 342:1581-1589.
- Fraser, C. MD and Arieff, A. MD: Epidemiology, Pathophysiology, and Management of Hyponatremic Encephalopathy. *American Journal of Medicine* 1997, 102: 67-75.
- Delanty, N; et al: Medial Causes of Seizures. *The Lancet* 1998, 352:383-388.
- Andrew, RD: Seizure and Acute Osmotic Change: Clinical and Neuophysiological Aspects. *Journal of Neurological Science* 1991, 101: 7-18.
- Arieff, AI; et al: Neurological Manifestations and Morbidity of Hyponatremia: Correlation with Brain Water and Electrolytes. *Medicine* 1976, 55:121-129.
- Miller, M.: Hyponatremia: Age-Related Risk Factors and Therapy Decisions. *Geriatrics* 1998, 53: 32-48.
- Thomas, E. MD: Seizures and Epilepsy in the Elderly. *Archives of Internal Medicine* 1997, 157: 605-614.
- Oster, J. MD and Singer, I. MD: Hyponatremia. Hypoosmolality and Hypotonicity: Tables and Fables. *Archives of Internal Medicine* 1999, 159: 333-336.
- Bylesjo, I; et al: Epidemiology and Clinical Characteristics of Seizures in Patients with Acute Intermittent Porphyria. *Epilepsia* 1996, 37: 230-235.
- Ayus, JC and Arieff, AI; Abnormalities of Water Metabolism in the Elderly. *Seminars in Nephrology* 1996, 16: 277-288.