

## BRIEF REPORTS

# A Case of SSRI-Induced Hyponatremia

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Hyponatremia complicates 1% of hospital admissions and can be associated with serious central nervous system effects. We report a case of a 38-year-old woman with hyponatremia resulting in seizures and coma. Medications are one of many causes of hyponatremia. This case emphasizes the need to consider selective serotonin reuptake inhibitors (SSRIs) as a potential source of hyponatremia in all age groups.

### Case Report

An unresponsive 38-year-old woman with a history of schizophrenia, depression, and tobacco abuse was transported by Emergency Medical Transport to the emergency department of a large community hospital after suffering an apparent generalized tonic-clonic seizure, which was witnessed by her family at home. For 2 to 3 days before the seizure, the family reported the patient complained of fatigue, nausea, and intermittent emesis.

Approximately 30 days earlier, the patient had started taking paroxetine (Paxil) for depression and trimethoprim-sulfamethoxazole (Septra) for bronchitis. The patient's medication regimen before admission also included risperidone (Risperdal), ibuprofen, and an albuterol inhaler.

### Physical Examination

On arrival at the emergency department, the patient's temperature was 98.4°F, blood pressure was 132/88 mm Hg, and pulse was 72 beats per minute. The patient was unresponsive and on a ventilator. Her pupils were equal, round, and reactive to light. A doll's eye test was negative, corneal reflexes were

faint, and she had a positive gag response, tongue lacerations, and broken teeth. Her neck was supple. Her heart rate and rhythm were regular, with no gallops, murmurs, or rubs. Breath sounds were symmetric without crackles. The findings during an abdominal examination were unremarkable. Her extremities were cool. Neurologically, she was unresponsive, and her extremities were flaccid. She had up-going toes. Laboratory studies disclosed the following values: serum sodium was 108 mEq/L, potassium 2.7 mEq/L, chloride 83 mEq/L, bicarbonate 19 mEq/L, blood urea nitrogen 4 mg/dL, and glucose 192 mg/dL. A computed tomogram of the head showed small lateral ventricles consistent with cerebral edema. No bleeding or focal mass was noted.

### Hospital Course

The initial diagnosis was new-onset seizure of unknown origin. One dose of mannitol was administered. In addition, she was given a loading dose plus a maintenance dose of phenytoin. The patient was managed with rapid-cycle ventilation to keep her mildly alkalotic. Once her serum chemistry screening results were reviewed, the diagnosis was changed to seizures secondary to hyponatremia. The hyponatremia was corrected at a rate of 0.5 mEq/h with normal saline and furosemide. After a lumbar puncture, she was treated for possible infection with 2 g of ceftriaxone while cerebral spinal fluid, blood, and urine culture results were pending. Her trimethoprim-sulfamethoxazole and paroxetine were discontinued.

Cerebral spinal fluid, urine, and blood cultures were negative. The patient's serum sodium level slowly returned to normal within 36 hours, and the phenytoin was discontinued without any further seizure activity. She was extubated, her cognitive function returned to baseline, and she continued to maintain normal sodium levels with the discontinuation of her paroxetine.

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### Brief Literature Search

A MEDLINE search was performed, using the MeSH terms "selective serotonin reuptake inhibitors" and "hyponatremia," for articles published between 1980 and 2000. One review article<sup>1</sup> cited 30 published articles between 1966 and 1995. Eighty-three percent of these 30 articles involved patients older than 65 years. Five additional articles published between 1996 and 2000 were found. In summary, these 35 articles reported a correlation between SSRI use and hyponatremia. The median time to onset of hyponatremia was 13 days (range 3–120 days). In all cases the patient's condition returned to normal 2 to 28 days after discontinuation of the SSRI. In 5 of the cases a rechallenge of the medication was reported. Three patients developed hyponatremia again. The 2 others tolerated the rechallenge.

Although some articles reported possible alternative explanations for the hyponatremia, many reported a strong temporal association between SSRI use and hyponatremia, a lack of an alternative explanation, and reversal of the process with discontinuation of the SSRI, suggesting a causal relation. The literature reviewed rated a definite or probable causal link in 40% of the cases. The remainder of the cases showed a probable causal link between SSRI use and hyponatremia. The findings of this case report have been reported to the pharmaceutical company and the Food and Drug Administration.

### Discussion

The correction of the patient's hyponatremia, combined with the discontinuation of her paroxetine, resulted in resolution, without recurrence, of her hyponatremia and the elimination of seizure activity. A literature search found a strong association between SSRI use and hyponatremia, with the annual incidence of hyponatremia in patients using paroxetine at 3.5/1,000. Alternative explanations are possible, but the most probable cause of the altered electrolyte status in this patient was SSRI use. Although risperidone also can cause decreased sodium levels, that the hyponatremia did not recur after restarting the risperidone makes a stronger case for paroxetine as the offending agent. Most cases of SSRI-induced hyponatremia involve the elderly, which could be related to altered antidiuretic hormone regulation or action of the antidi-

uretic hormone on the kidneys. Impairment of the maximal diluting and concentrating ability of the kidney<sup>2,3</sup> and increased antidiuretic hormone secretion might contribute as well. Another possible explanation for the propensity for hyponatremia in the elderly is their increased antidiuretic hormone response to osmolar stimuli compared with young control patients.<sup>4</sup>

This case of hyponatremia in a young woman raises the question of what factors might predispose a younger patient to SSRI-induced hyponatremia? Additive drug effects and drug interactions are two potential sources. Dopamine antagonists, such as haloperidol and domperidone, have been shown in animal models to increase thirst and to facilitate antidiuretic hormone secretion.<sup>5–7</sup> Diuretics are thought to predispose patients to hyponatremia.<sup>8</sup> SSRIs inhibit a number of cytochrome P-450 isoenzymes. Through inhibition of the metabolism of drugs used concomitantly, such as neuroleptics, SSRIs might increase the effect of these other drugs on water and electrolyte balance. Certain disease processes might also predispose patients to hyponatremia, including such pulmonary processes as pneumonia, malignant neoplasms, and psychiatric conditions, such as schizophrenia.<sup>8</sup>

### Conclusion

SSRI use should be considered in the differential diagnosis of hyponatremia. Hyponatremia can complicate SSRI use in the young as well as the older patient, especially if other risk factors are present. In the case described, the patient had multiple concurrent risk factors. Clinicians should be alert for SSRI-induced hyponatremia, not only in the elderly patient, but also in the younger patient, particularly if the onset of symptoms has a close temporal association with the start of SSRI treatment.

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