Hyponatremia Associated With Tramadol in a Patient With Alcohol Use Disorder and Anxiety Taking Desvenlafaxine

To the Editor: Tramadol, a weak μ-opioid agonist that also inhibits norepinephrine and serotonin reuptake, is used as an analgesic alternative to opioids like oxycodone, although it still has abuse potential, along with risks such as seizures and serotonin syndrome.[1] A reported link exists between tramadol and hyponatremia.[2] Presented here is a case of a woman with alcohol use disorder, on an antidepressant, who exhibited hyponatremia after a course of tramadol for musculoskeletal pain, which resolved after discontinuation of tramadol.

Case report. The patient, a 52-year-old woman with alcohol use disorder and vitamin B_{12} deficiency, presented to a rehabilitation facility after completion of inpatient detoxification with diazepam and divalproex for seizure prophylaxis. She was given 7 days of furosemide 40 mg/d for pedal edema, which resolved. Her complete blood count, thyroid function, transaminases, vitamin B_{12}, and electrolytes including sodium (137 mmol/L; range, 136–145 mmol/L), chloride (97 mmol/L; range, 95–115 mmol/L), blood urea nitrogen, and creatinine levels were within normal limits upon admission, while serum osmolality was slightly low (272 mOsm/kg; range, 275–295 mOsm/kg). The patient had no history of polydipsia and was not observed drinking excess fluids. She was being treated for generalized anxiety disorder with desvenlafaxine 50 mg/d. She also was taking a multivitamin, thiamine 100 mg/d, folic acid 1 mg/d, and hydroxyzine 25 mg as needed for anxiety.

The patient reported persistent severe pain in her coccyx related to a fall prior to admission for detoxification, which did not respond to ibuprofen 800 mg, a course of meloxicam 15 mg/d, or lidocaine patches. A medical consultant recommended tramadol 50 mg every 8 hours as needed (maximum 100 mg/d). The risks, including serotonin syndrome and seizure, were discussed with the patient. For the subsequent 5 days, the patient used the maximum daily dose of tramadol, and her pain began to improve. A second blood test was taken 7 days after the initiation of tramadol. Results showed her serum sodium was 127 mmol/L, chloride was 88 mmol/L, serum osmolality was 251 mOsm/kg, and urine osmolality was 149 mOsm/kg (range, 300–1,300 mOsm/kg). The patient exhibited no mental status changes, lethargy, or confusion. Tramadol was discontinued, and she was advised to restrict free water intake. Five days later, her serum sodium was 133 mmol/L, chloride was 91 mmol/L, and serum osmolality was 263 mOsm/kg. Further laboratory chemistries were not obtained as the patient was scheduled for discharge. The medical consultant recommended follow-up with her primary care provider.

Hyponatremia, defined as serum sodium < 135 mmol/L, can cause confusion, seizures, coma, and death.[3] A review by Fournier et al[2] reported at least a 2-fold increase in hospitalization due to tramadol-induced hyponatremia. Tramadol is thought to cause hyponatremia by syndrome of inappropriate antidiuretic hormone secretion (SIADH).[2] Patients in most published cases of tramadol-induced hyponatremia were over the age of 70 years, consistent with higher risk in older adults.[4–6]

A literature review indicates that antidepressants, including desvenlafaxine, may cause hyponatremia.[7–9] Antidepressants most likely cause hyponatremia by SIADH, which usually occurs within 2–3 weeks of medication initiation.[7,8]

Other than her age, factors increasing our patient's risk for hyponatremia included recent course of furosemide, a loop diuretic, and concurrent desvenlafaxine.[10] These medications, however, did not affect this patient's sodium level, which was within normal limits at admission. Her sodium only decreased after tramadol initiation and began to normalize after discontinuation, strongly suggesting tramadol was the cause of her hyponatremia.

Even with short-term use, tramadol may cause serotonin syndrome, seizures, and hyponatremia. It is recommended to prescribe tramadol with caution, especially in elderly patients and those taking other medications that may affect sodium levels, and to monitor the patient's laboratory results, in particular electrolytes, at baseline and in regular intervals during treatment.[7]

References

1. Miotto K, Cho AK, Khalil MA, et al. Trends in tramadol: pharmacology, metabolism, and misuse. *Anesth Analg*. 2017;124(1):44–51.
2. Fournier JP, Yin H, Nessim SJ, et al. Tramadol for noncancer pain and the risk of hyponatremia. *Am J Med*. 2015;128(4):418–425.e5.
3. Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. *Am J Med*. 2013;126(suppl 1):S1–S42.
4. Hunter R. Tramadol and hyponatraemia. *Aust Prescr*. 2004;27(4):97.
5. Udy A, Deacy N, Barnes D, et al. Tramadol-induced hyponatraemia following unicompartmental knee replacement surgery. *Anaesthesia*. 2005;60(8):814–816.
6. Le Berre J-P, Desramé J, Lecoules S, et al. Hyponatremia due to tramadol. *Rev Med Interne*. 2007;28(12):888–889.
7. De Picker L, Van Den Eede F, Dumont G, et al. Antidepressants and the risk of hyponatremia: a class-by-class review of literature. *Psychosomatics*. 2014;55(6):536–547.
8. Lee Gt, Leung JI. Syndrome of inappropriate secretion of antidiuretic hormone due to desvenlafaxine. *Gen Hosp Psychiatry*. 2013;35(5):574.e1–574.e3.
9. Liew ED, Alderman CP. Syndrome of inappropriate antidiuretic hormone secretion associated with desvenlafaxine. *Int J Clin Pharm*. 2014;36(2):253–255.
10. Liamis G, Milionis H, Elisaf M. A review of drug-induced hyponatremia. *Am J Kidney Dis*. 2008;52(1):144–153.

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