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Case Report

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Tramadol-induced hyponatremia: case report highlighting the mechanism and review of literature

Abstract

We report a case of postoperative hyponatraemia following routine Coronary artery Bypass Grafting (CABG) surgery. The patient had been given the weak opioid tramadol for postoperative pain relief. After 48 hours, patient was complaining of severe headache, nausea, and progressive hyponatremia not responding to resuscitation fluids. Once tramadol was discontinued, the serum sodium level started to return to normal level. Through its effects on serotonergic neurotransmission in the central nervous system, we hypothesize that tramadol may have been directly involved in this patient's biochemical disorder.

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Ahmed Akl,[1,2,3] Meshari Alwagdani,[1] Ahmed Abdel Aziz,[4] Ramadan A Saad,[5,6] Ghassan Baslaim,[4] Fahmi Aldhaheri[1]

[1]Internal medicine department, Dr. Soliman Fakeeh Hospital, Saudi Arabia
[2]Internal medicine department, Fakeeh college of medical sciences, Saudi Arabia
[3]Nephrology department, Urology & Nephrology canter, Mansoura, Egypt
[4]Cardiothoracic Surgery department, Dr. Soliman Fakeeh Hospital, Saudi Arabia
[5]Physiology department, faculty of medicine, Ain Shams University, Egypt
[6]Physiological sciences department, Fakeeh College for medical sciences, Saudi Arabia

Correspondence: Ahmed Akl, MD, FACP, FASN, Consultant of Nephrology & Transplantation
Associate Professor, FCMS, ISN Education Ambassador, Nephrology department, Urology & Nephrology canter, Mansoura, Egypt, Email aiakl201@yahoo.com

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Introduction

Opioid analgesic therapy is widely used nowadays in all fields of medicine. Inappropriate antidiuretic hormone secretion [SIADH] is a common complication of opioids and may be the cause of the hyponatremia secondary to opioid therapy. Nausea and hypotension secondary to opioid therapy may promote Antidiuretic hormone (ADH) release and induce hyponatremia. Another mechanism explained this hyponatremia is by stimulating thirst centre which induced more water intake and possible hyponatremia.[1] Hyponatremia is defined when serum sodium <135 mEq/L[2].

Tramadol is a commonly used centrally acting analgesic. Tramadol increases ADH secretion by acting on opiate receptors directly, and indirectly by increasing serotonin secretion which in turn increases the release of ADH. Both mechanisms may induce the hyponatremia after opioid therapy.[3]

Case report

A 65-year-old male with ischemic heart disease and multiple comorbidities including hypertension, diabetes and hyperlipidaemia. The patient suffered from recurrent anginal pain and had undergone percutaneous coronary stenting 4 years ago. Recently, the patient presented to our cardiology department with progressive anginal pain. Computerised tomography and coronary angiography revealed critical coronary stenosis, and patient was scheduled for coronary artery bypass grafting (CABG) surgery. After surgery, the patient was clinically stable, and tramadol was added for pain control. Seventy-two hours later, serum sodium dropped from 148 mEq/l to 125 mEq/i, serum osmolality was 262 mOsm/kg and the patient complained of headache, nausea and one attack of vomiting. Intravenous normal saline 0.9% resuscitation failed to correct hyponatremia and serum sodium dropped to 122 mEq/l even after the discontinuation of furosemide, blood sugar was 262 mg/dl, after correction by adding 2 mEq of sodium for every 100 mg/dl blood glucose increase above 100 mg/dl the net serum sodium was 125 mEq/l. The thyroid function was normal with normal TSH level, lipid profile was normal at time of hyponatremia. Intravenous hypertonic saline was initiated after calculating the sodium deficit. Serum creatinine was 0.9 mg/dl, Bun 18 mg/dl, Serum albumin 2.9 g/l.

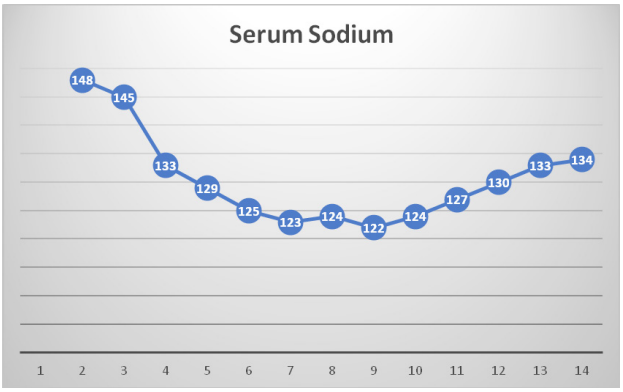

Figure 1 Shows the serial monitoring of serum sodium and creatinine.

After reviewing the literatures, Tramadol-induced hyponatremia was hypothesized, and tramadol was discontinued. In 24 hours, serum sodium was corrected to 130 mEq/L, and to 134 mEq/l on the following day. The patient was discharged home however, he

was readmitted one week later for his leg wound care. His sodium level was fluctuating, and one week after second discharge from the hospital his serum sodium was 136 mEq/l.

Discussion

Postoperative electrolyte disorders are the most common complications following major surgery especially hip and knee surgery for elderly patients.[4] Brain damage is the most common consequence of severe hyponatremia.[5]

Hyponatremia can be simply classified into three types; hypovolemic type following long term thiazide diuretics, euvolemic one may be due to syndrome of inappropriate antidiuretic hormone (SIADH).[6] Hypervolemic type is defined by a significant deficit in free water excretion, which results in excessive water retention as compared to sodium levels. An enlarged extracellular volume and dilutional hyponatremia arise from this imbalance.[7]

Different entities can cause of SIADH such as, nervous disorders, lung disorders, malignancy, and side effects of some drugs. Clinical diagnosis of SIADH is associated with the occurrence of hypotonic hyponatraemia, natriuresis, absence of oedema or volume depletion and normal renal and adrenal functions.[8]

During the patient's first hospitalisation, lab analysis confirmed hyponatremia which may be due to inappropriate loss of sodium in urine. This natriuresis may have been due to his current therapy with diuretics but is also a feature of SIADH. However, this hyponatremia did not improve after discontinuation of his diuretic, indicating that there was an additional factor contributing to the problem.

In one case, it was suggested that ADH activity was increased due to low fractional water excretion, and it would appear that biochemical abnormality was caused by excess water retention resulting in a dilutional hyponatraemia.[9]

SIADH can be brought about by an assortment of medications, especially antipsychotics and serotonin reuptake inhibitors (SSRIs).[6] The SSRIs commonly prescribed to treat depression, are particular inhibitors of the presynaptic serotonin reuptake transporter, which prompts an intense expansion in serotonin at the synaptic cleft.[10] Various case reports and clinical examinations have reported the SSRIs as main reason for hyponatremia, especially in the older persons.[11–14]

A manufactured narcotic, Tramadol acts centrally through binding to mureceptors, giving a moderate relief of pain, it is widely used due to its little side effects as respiratory depression and dependence.[15] Tramadol has mu-agonist activity, also inhibits the central reuptake of serotonin (5-hydroxytryptamine) and noradrenaline.[16] Both neurotransmitters activate the pain inhibitory pathway in the spinal cord.[17]

Hyponatraemia owing to tramadol is an incidental effect. A solitary case report in the writing archives a 76-year-elderly person with Colles fracture and on Tramadol as an analgesic. His biochemical report showed hyponatraemia.[18] Analysis of the lab report for this patient revealed below normal serum osmolarity which was consistent with high ADH secretion. Discontinuation of tramadol quickly brought about a notable biochemical improvement. In a report from the French pharmacovigilance database 1152 patients develop serious side effects related to tramadol including hyponatremia.[19]

Opioids can directly enhance antidiuretic hormone secretion, which could explain part of our patient's tramadol response, but this usually requires greater dosages[20] and more strong agonists.[21]

Conclusion

In conclusion, medications that elevate serotonin synaptic concentration may cause ADH secretion in people who are not dehydrated. As a result, tramadol alone appears to be capable of causing dilutional hyponatraemia related to SIADH in some people.

Acknowledgments

None.

Conflicts of interest

The author declares there is no conflict of interest.

References

1. Langfeldt LA, Cooley ME. Syndrome of inappropriate antidiuretic hormone secretion in malignancy: Review and implications for nursing management. *Clin J Oncol Nurs*. 2003;7:425–430.
2. Sahay M, Sahay R. Hyponatremia: A practical approach. *Indian J Endocrinol Metab*. 2014;18(6):760–771.
3. Le Berre JP, Desrame J, Lecoules S, et al. Hyponatremia due to tramadol. *Rev Med Interne*. 2007;28:888–889.
4. Tambe AA, Hill R, Livesley PJ. Postoperative hyponatraemia in orthopedic injury. *Injury*. 2003;34: 253–255.
5. Fraser CL, Arieff AI. Epidemiology, pathophysiology and management of hyponatremic encephalopathy. *American Journal of Medicine*. 1997;102:67–77.
6. Moore K, Thompson C, Trainer P. Disorders of water balance. *Clinical Medicine*. 2003;3:28–33.
7. Gines P, Guevara M. Hyponatremia in cirrhosis: pathogenesis, clinical significance, and management. *Hepatology*. 2008;48:1002–1010.
8. Baylis PH. The syndrome of inappropriate antidiuretic hormone secretion. *International Journal of Biochemistry and Cell Biology*. 2003;35:1495–1499.
9. Knapp LT, Berghorn KA, Hoffman GE. Osmolality-dependent steroid feedback regulation of vasopressin gene expression. In: Saito T et al., editors. *Neurohypophysis: Recent Progress of Vasopressin and Oxytocin Research*. Amsterdam: Elsevier Science BV, 1995;131–41.
10. Kam PC, Chang GW. Selective serotonin reuptake inhibitors: Pharmacology and clinical implications in anaesthesia and critical care medicine. *Anaesthesia*. 1997;52:982–988.
11. Movig KL, Leufkens HG, Lenderink AW, et al. Association between antidepressant drug use and hyponatraemia: case control study. *British Journal of Clinical Pharmacology*. 2002;53:363–369.
12. Fisher A, Davis M, Croft-Baker J, et al. Citalopram-induced severe hyponatremia with coma and seizure: case report with literature and spontaneous reports review. *Adverse Drug Reactions and Toxicological Reviews*. 2002;21:179–187.
13. Fifgeld D. SSRI-related hyponatraemia among aging adults. *Journal of Psychosocial Nursing and Mental Health Services*. 2003;41:12–16.
14. Rosner MH. Severe hyponatremia associated with the combined use of thiazide diuretics and selective serotonin reuptake inhibitors. *American Journal of the Medical Sciences*. 2004;327:109–111.
15. Joshi GP, White PF. Management of acute and postoperative pain. *Current Opinion in Anesthesiology*. 2001;14:417–421.
16. Gobbi M, Mennini T. Release studies with rat brain cortical synaptosomes indicate that tramadol is a 5-hydroxytryptamine uptake blocker and not a 5-hydroxytryptamine releaser. *European Journal of Pharmacology*. 1999;370:23–26.

17. Grond S, Sablotzki A. Clinical pharmacology of tramadol. *Clinical Pharmacokinetics*. 2004;43:879–923.

18. Anonymous. Tramadol. First report of hyponatraemia in an elderly patient: case report. *Reactions Weekly*. 2004;1019:14.

19. Moulis F, Rousseau V, Abadie D, et al. Effets indésirables « graves » du tramadol : bilan 2011–2015 de pharmacovigilance en France. Therapie. 2013;68(2):77–84.

20. Florence Moulis, Vanessa Rousseau, Delphine Abadie, et al. Serious adverse drug reactions with tramadol reported to the French pharmacovigilance database between 2011 and 2015. *Therapie*. 2017;72(6):615–624.

21. Hardman JG, Limbird LE, Goodman GA. *Goodman and Gilman's – the Pharmacological Basis of Therapeutics*. 10th edn. New York: McGraw-Hill, 2001.

22. Kokko H, Hall PD, Afrin LB. Fentanyl-associated syndrome of inappropriate antidiuretic hormone secretion. *Pharmacotherapy*. 2002;22:1188–1192.

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