



Low-Dose Tramadol Induced Seizure: A Case Report

Himadri Sekhar Dasgupta*

Department of Pharmacology, North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences, India

Abstract

Tramadol is a weak mu (μ) opioid receptor agonist that acts by inhibiting serotonin and nor epinephrine uptake. Tramadol undergoes extensive hepatic metabolism by a number of pathways including CYP2D6, CYP3A4 and by conjugation with subsequent renal excretion. The maximum recommended dose is 400 mg/day. One of the most important adverse effect of tramadol is seizure which usually occurs at high dose and often generalized tonic-clonic type and, self-limiting. Here we present a case of patient with inflammatory low backache who developed seizures while on low-dose oral tramadol. After one hour of taking first tablet Tramadol, he developed morbilliform rashes all over the body. One day later he developed generalized tonic clonic seizure followed by loss of consciousness for 5 min. Patient was admitted in the hospital and managed conservatively with Injection lorazepam and Tramadol was stopped. In general if applied in overdose, tramadol can only incite seizures in patients already suffering from some sort of disorder related to seizure or if it is administered along with antidepressants, alcohol etc. But here, only with the use of 37.5 mg oral application, the incidence of seizure happened.

Keywords: Tramadol; Seizure; Low dose; Rash

Introduction

Tramadol is a weak mu (μ) opioid receptor agonist that acts by inhibition of serotonin and nor epinephrine reuptake [1]. Tramadol undergoes extensive hepatic metabolism by a number of pathways including CYP2D6, CYP3A4 and by conjugation with subsequent renal excretion. Tramadol is composed of 1:1 racemic mixture of \pm enantiomers and \pm enantiomers.

\pm Tramadol inhibits serotonin reuptake and (-) - Tramadol inhibits Norepinephrine reuptake. The major metabolite of \pm Tramadol activates mu (μ) receptor [2]. The range of blood levels in adults is approximately 100 ng/ml to 300 ng/ml (0.1 μ g/ml to 0.2 μ g/ml). The recommended dose of 400 mg/day is considered as maximum approved dose [3]. Tramadol hydrochloride is a lipophilic substance that completely penetrates the barrier between blood and brain. The level of plasma besieges peak around 1.5 h after taking and 5 h to 6 h is the half life of plasma exclusion. One of the complications of the tramadol use is the seizure which is most often generalized tonic-clonic [3]. Here we are presenting a case report of a 29-year-old male patient, who had an episode of seizure, following single oral dose of Tramadol.

Case Presentation

A 29 year old male patient came to the orthopedic OPD, with history of low back pain following fall from height. He was prescribed oral tablet tramadol hydrochloride 37.5 mg twice daily for five days. After one hour of taking first dose of tablet tramadol, he developed morbilliform rashes all over the body. One day later he developed generalized tonic clonic seizure followed by loss of consciousness for 5 min. The patient was rushed to emergency department and managed conservatively with injection lorazepam and tramadol was stopped. He had no history of similar episode in the past. On examination the patient was conscious, oriented to time, place and person. The temperature was 39°C, the heart rate 136 beats per min, the blood pressure 130/80 mmHg, and the oxygen saturation 98% while the patient was breathing ambient air. On neurological examination, the patient's mental status was normal. There was no involvement of cranial nerve. Motor testing revealed full symmetric strength in the arms and legs. Deep-tendon reflexes were 2+ and symmetric. Other systematic examinations were also normal. Blood levels of electrolytes, glucose, vitamin B12 (cobalamin) were normal, as were results of tests of kidney, liver, and thyroid function. The complete blood count, erythrocyte sedimentation rate, and creatine kinase level were normal. His Electrocardiogram (ECG) revealed atrial fibrillation with controlled ventricular rate (Figure 1). Computed Tomography (CT) of the head, performed after the intravenous administration of contrast material, was normal. An Electroencephalogram (EEG) was done after neurology

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*Correspondence:

Himadri Sekhar Dasgupta, Department of Pharmacology, North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences, India, Tel: +91-6033096725;
E-mail: himadridg3@gmail.com

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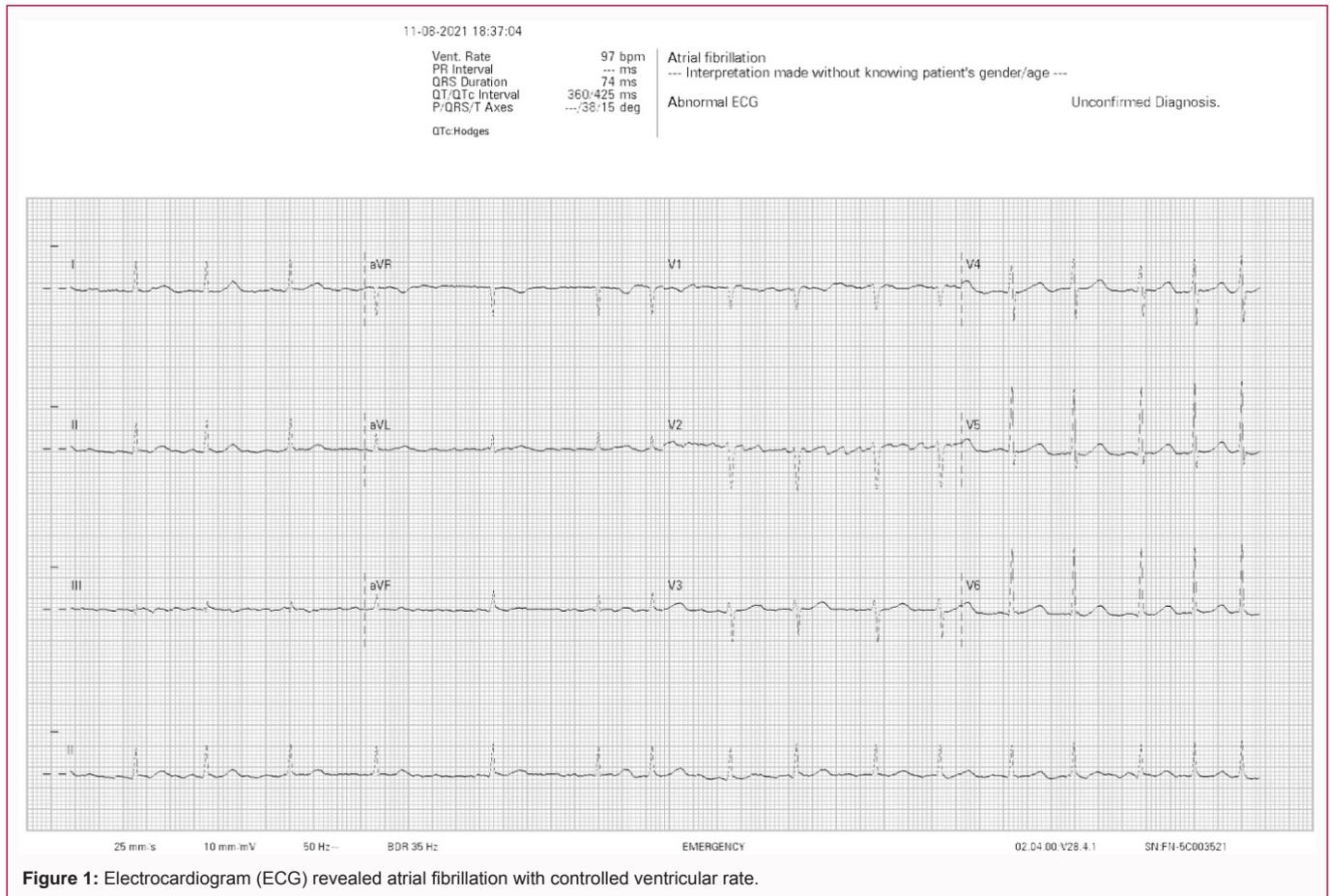


Figure 1: Electrocardiogram (ECG) revealed atrial fibrillation with controlled ventricular rate.

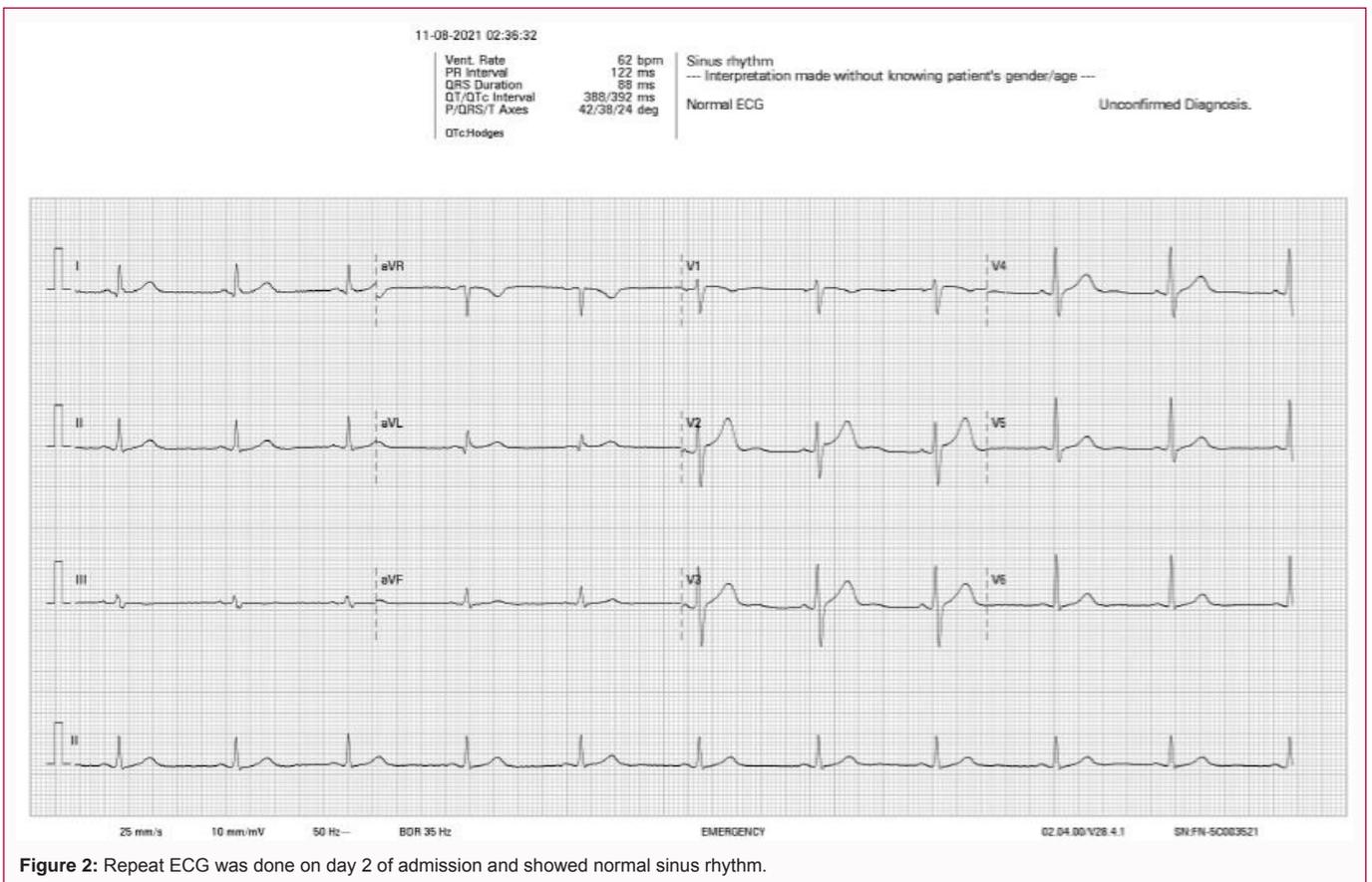


Figure 2: Repeat ECG was done on day 2 of admission and showed normal sinus rhythm.

consultation and revealed normal study. Cardiology consultation was taken for atrial fibrillation and was advised for transthoracic echocardiography which revealed normal study. The repeat ECG was done on day 2 of admission and showed normal sinus rhythm (Figure 2). Patient improved with the conservative management and was discharged uneventfully and was found to be doing well at regular follow-ups.

Discussion

Tramadol is a “bimodal” agent that possesses activity at opioid and monoaminergic (serotonergic and non-adrenergic) pathways in the CNS. Tramadol is commonly used in place of other potent opioid analgesics for treatment of moderate to moderately severe pain associated with osteoarthritis, rheumatoid arthritis, and low back pain and neuropathic conditions [4,5]. There are controversies about the seizure inducing effect of tramadol. Some earlier studies suggested that Tramadol when given in overdose in patients with extant disorder of seizure or when used along with antidepressants, alcohol etc. instigates seizure [6,7]. It was also disclosed from other studies that Tramadol also instigates seizure when used as monotherapy in approved dose. It has also been found that appearance of seizure following tramadol use is not dose dependant [8]. However, in our patient the seizure occurred at a dose of 37.5 mg oral tramadol hydrochloride. Tramadol-induced seizures have been reported to be generalized tonic-clonic in nature, without aura and focal deficit, as seen in our patient. Tramadol has very less abuse potential when compared to other opioids. So, it is prescribed very commonly in clinical practice. A recent cross-sectional study conducted by Labate et al. [9] in 2005 examined 106 patients with tramadol induced seizure found the entire patient had tonic clonic seizure within 12 h of oral intake of tramadol in suprathreshold and recommended doses. Among those, 13% had history of epilepsy which was well controlled and didn't recur before one year of their evaluation. Tramadol induced seizure may be associated with agitation, tachycardia, confusion and hypertension, leading to serotonin syndrome [10]. In the present case, the continuing tachycardia ranging from 120 bpm to 140 bpm was found to be the only salient observation that could be accountable to low serotonergic action.

Conclusion

Tramadol has been otherwise a safe drug over many years; however with evidence of serious reaction like seizure even at low doses, the scientific community should consider ensuring strict pharmacovigilance with respect to its use especially in the developing countries where such monitoring systems are inadequate.

References

1. Sansone RA, Sansone LA. Tramadol: Seizures, serotonin syndrome, and co-administered antidepressants. *Psychiatry (Edgmont)*. 2009;6(4):17-21.
2. Raffa RB, Friderichs E, Reimann W, Shank RP, Codd EE, Vaught JL, et al. Complementary and synergistic antinociceptive interaction between the enantiomers of tramadol. *J Pharmacol Exp Ther*. 1993;267(1):331-40.
3. Boostani R, Derakhshan S. Tramadol induced seizure: A 3-year study. *Caspian J Intern Med*. 2012;3(3):484-7.
4. Duhmke RM, Derry S, Wiffen PJ, Bell RF, Aldington D, Moore RA. Tramadol for neuropathic pain in adults. *Cochrane Database Syst Rev*. 2017;6(6):CD003726.
5. Cepeda MS, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis: A systematic review and metaanalysis. *J Rheumatol*. 2007;34(3):543-55.
6. Marquardt KA, Alsop JA, Albertson TE. Tramadol exposures reported to statewide poison control system. *Ann Pharmacother*. 2005;39(6):1039-44.
7. Farajidana H, Hassanian-Moghaddam H, Zamani N, Sanaei-Zadeh H. Tramadol-induced seizures and trauma. *Eur Rev Med Pharmacol Sci*. 2012;16(Suppl 1):34-7.
8. Talaie H, Panahandeh R, Fayaznouri M, Asadi Z, Abdollahi M. Dose-independent occurrence of seizure with tramadol. *J Med Toxicol*. 2009;5(2):63-7.
9. Labate A, Newton MR, Vernon GM, Berkovic SF. Tramadol and new-onset seizures. *Med J Aust*. 2005;182(1):42-3.
10. Beakley BD, Kaye AM, Kaye AD. Tramadol, pharmacology, side effects, and serotonin syndrome: A review. *Pain Physician*. 2015;18(4):395-400.