

Low-Dose Tramadol-Induced Seizure: A Case Report

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Abstract

Tramadol is a weak mu (μ) opioid receptor agonist that acts by inhibiting serotonin and norepinephrine uptake. Tramadol undergoes extensive hepatic metabolism by a number of pathways, including CYP2D6 and CYP3A4, and by conjugation with subsequent renal excretion. The maximum recommended dose is 400 mg/day. One of the most important adverse effects of tramadol is a seizure, which usually occurs at high doses and is often generalized tonic–clonic type and self-limiting. Here, we present a case of a patient with inflammatory low backache who developed seizures while on low-dose oral tramadol. After 1 h of taking the first tablet of tramadol, he developed morbilliform rashes all over the body. One day later, he developed generalized tonic–clonic seizures followed by a loss of consciousness for 5 min. The patient was admitted to 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 seizures 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

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Introduction

Tramadol is a weak mu (μ)-opioid receptor agonist that acts by inhibiting serotonin and norepinephrine reuptake.¹ Tramadol undergoes extensive hepatic metabolism by a number of pathways, including CYP2D6 and CYP3A4, and by conjugation with subsequent renal excretion. Tramadol is composed of a 1:1 racemic mixture of (+) -enantiomers and (–) -enantiomers.

(+) -Tramadol inhibits serotonin reuptake and (–) -tramadol inhibits norepinephrine reuptake. The major metabolite of (+) -tramadol activates the mu (μ) receptor.² The range of blood levels in adults is approximately 100 ng/mL to 300 ng/mL (0.1–0.2 μ g/mL). The recommended dose of 400 mg/day³ is considered as the maximum approved dose. Tramadol hydrochloride is a lipophilic substance that completely penetrates the barrier between the blood and the brain. The level of plasma besieges a 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 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 seizures, following a single oral dose of tramadol.

Case History

A 29-year-old male patient came to the Orthopedic OPD, with a history of low back pain following a fall from height. He was prescribed oral tablets of tramadol hydrochloride 37.5 mg twice daily for five days. After 1 h of taking the first dose

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of tablet tramadol, he developed morbilliform rashes all over the body. One day later, he developed generalized tonic-clonic seizures followed by a loss of consciousness for 5 min. The patient was rushed to the emergency department and managed conservatively with injection lorazepam and tramadol was stopped. He had no history of similar episodes in the past. On examination, the patient was conscious and oriented to time, place, and person. The temperature was 39°C, the heart rate was 136 bpm, the blood pressure was 130/80 mm Hg, and the oxygen saturation was 98% while the patient was breathing ambient air. On neurological examination, the patient's mental status was normal. There was no involvement of the 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, and vitamin B₁₂ (cobalamin) were normal, as were the 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 a 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 consultation and revealed a normal study. Cardiology consultation was taken for atrial fibrillation and was advised for transthoracic echocardiography, which revealed a normal study. The repeat ECG was done on day 2 of admission and showed normal sinus rhythm (Figure 2). The 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 in both opioid and monoaminergic (serotonergic and nonadrenergic) pathways in the central nervous system (CNS). Tramadol is commonly used in place of other potent opioid analgesics for the treatment of moderate to moderately severe pain associated with osteoarthritis, rheumatoid arthritis, 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

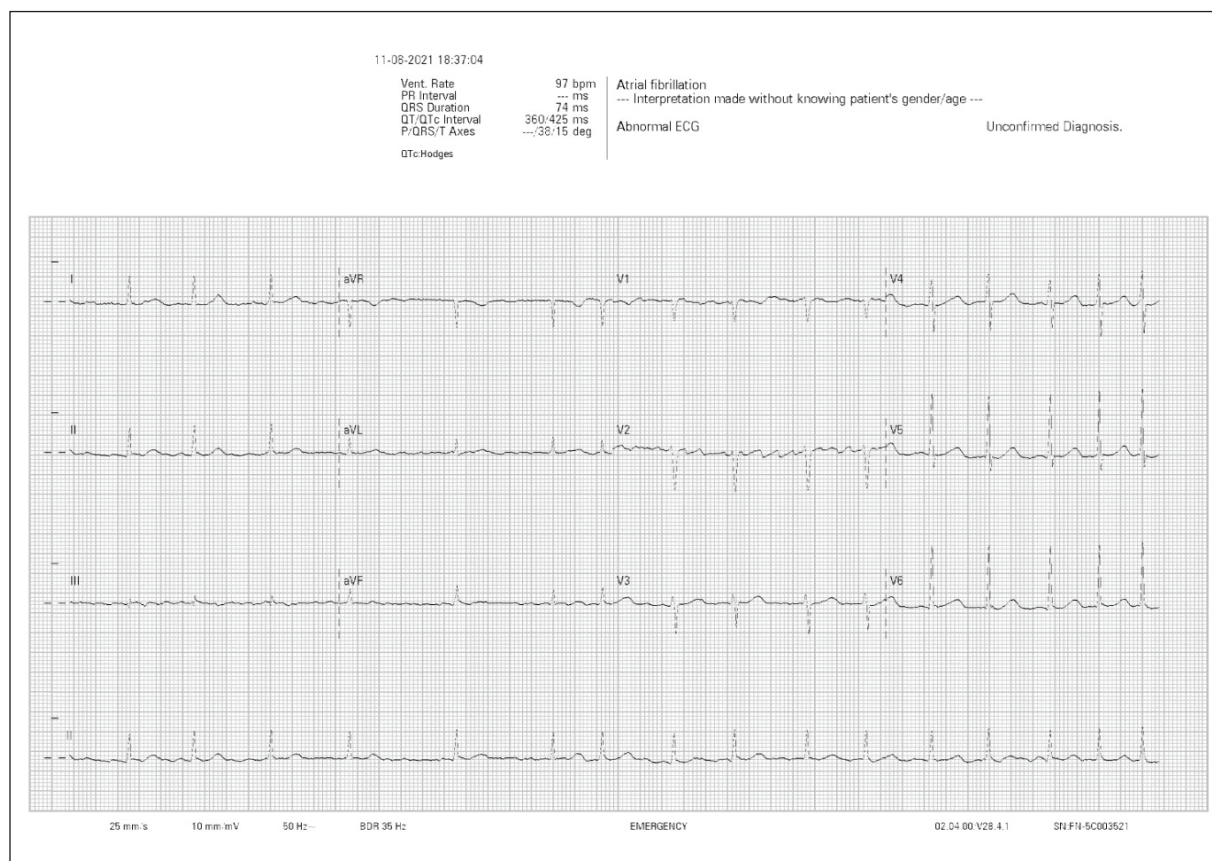


Figure 1. Electrocardiogram Suggestive of Atrial Fibrillation in Controlled Ventricular Rate.

Source: Neigrihms medicine In patient Department.

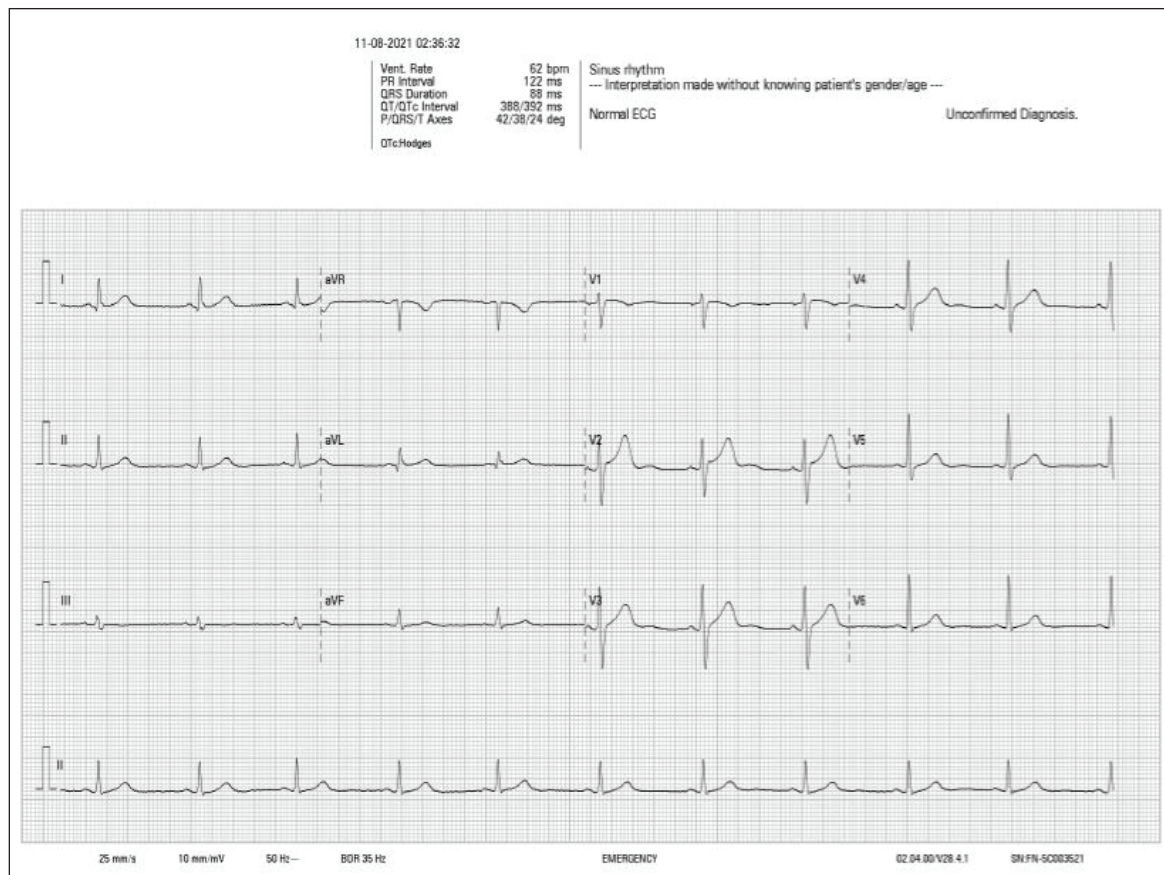


Figure 2. Electrocardiogram in Normal Sinus Rhythm.

Source: Neigrihms medicine In patient Department.

with antidepressants, alcohol, etc., instigates seizure.^{6,7} It was also disclosed from other studies that tramadol also instigates seizures when used as monotherapy in an approved dose. It has also been found that the appearance of seizures 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 seizures found that all of the patients had tonic-clonic seizures within 12 h of oral intake of tramadol in supratherapeutic and recommended doses. Among those, 13% had a history of epilepsy, which was well controlled and did not recur before one year of their evaluation. Tramadol-induced seizures may be associated with agitation, tachycardia, confusion, and hypertension, leading to serotonin syndrome.¹⁰ In the present case, the continuing tachycardia ranging from 120 to 140

bpm was found to be the only salient observation that could be accountable for low serotonergic action.

Conclusion

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

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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