Case Study

Tramadol Dependence and Withdrawal Syndrome: A Case Report

Arun Ashokan[1], C. Sreekanth[2]

[1]Resident, Department of Emergency Medicine, Bangalore Baptist Hospital ORCID: 0009_0000_6329_3857,
[2]Consultant, Department of Emergency Medicine, Bangalore Baptist Hospital, ORCID: 0009_0000_6329_3857

How to cite this article: Arun Ashokan, C. Sreekanth. Tramadol Dependence and Withdrawal Syndrome: A Case Report. Indian Journal of Forensic Medicine and Toxicology/Volume 20 No. 2, April-June 2026.

Abstract

Tramadol is a synthetic analgesic that appears to have two mechanisms of action: a reuptake inhibition of serotonin and noradrenaline and a weak μ-opioid receptor agonism. Even though its potential for abuse is well reported, the drug is readily available off on the market and is not regarded as a controlled substance in many nations, in contrast to the majority of other opioids. The patient in this case report developed severe tramadol dependence after taking large doses of the drug to treat his musculoskeletal pain. We suggest that It should be made a controlled substance at the administrative levels due to the possibility of dependence and severe withdrawal symptoms.

Key Words: Tramadol, Drug withdrawal, Seizure, Drug abuse, Drug dependence.

Introduction

Tramadol is a synthetic analgesic that appears to have two mechanisms of action: a weak μ-opioid receptor agonism and a reuptake inhibition of serotonin and noradrenaline. It is as effective as morphine or meperidine for treating mild-to-moderate pain, but it is less effective for treating severe or chronic pain. The primary active metabolite of tramadol, o-desmethyltramadol (M1 metabolite), also has an agonistic activity at the μ-opioid receptor, albeit with a greater affinity[1]. Despite the abundance of preclinical, clinical, post marketing, and epidemiological data showing comparatively little, but not zero, misuse/dependence, concerns remain over its potential for abuse and proper regulatory classification. Tramadol is readily available off on the market and is not regarded as a controlled substance in many nations, in contrast to the majority of other opioids[2]. Tramadol withdrawal symptoms can include anxiety, paranoia, depersonalization, derealization, and auditory hallucinations in addition to the usual opiate withdrawal symptoms[3]. Opioids are frequently sold over-the-counter in India due to the country's loose drug laws, which raises the possibility of opioid abuse. However, there are very few documented cases of tramadol dependence from India[4]. Both therapeutic and toxic dosages of tramadol have been known to induce seizures. In one research, a young woman taking tramadol for migraine episodes frequently experienced withdrawal seizures as a result of frequent and excessive ingestion[5]. When tramadol was initially prescribed to treat a fractured tibia, the young male

Corresponding Author: Arun Ashokan, Resident, Department of Emergency Medicine, Bangalore Baptist Hospital.

E-mail: Arunemdoc@Gmail.Com

Submission date: January 7, 2026 **Acceptance date:** February 19, 2026 **Published date: April 23, 2026**

patient in this case study self-medicated with the medicine, which led to the development of tramadol dependence and withdrawal seizures.

Case Report

35-Year-old male, smoker, known case of hypertension on irregular medications presented to ER at 4 pm. History of one episode of jerky movements of all four limbs associated with up rolling of eyes and tongue bite at 11.30 am. The episode lasted less than 10 mins, followed by confusion about 30 mins. No history of any trauma, fever, altered sensorium, headache, vomiting, chest pain, or any focal deficits. Patient was taken to nearby hospital from they received primary care and then referred. Patient received loading dose of Levetiracetam from the outside hospital.

During assessment in ER, airway was patent, breathing – RR –16/min, SPO2 – 96% on room air, air entry was equal bilaterally. In circulation all peripheral pulses felt normal, HR – 82/min, BP – 180/100 mmHg. Disability – GCS: 14/15 (E3V5M6), GRBS: 102 mg%, pupils bilaterally 2 mm and reactive to light. There were no bite marks or Injection marks after exposing the patient.

Patient had no known allergies, was on treatment for hypertension with Amlodipine 5 mg which he was not taking regularly. Relatives gave history of taking analgesic tablets for leg pain. He was sleeping post night duty, at that time brother noticed he is having jerky movements of limbs with up rolling of eyes and tongue bite. On detailed history elicitation patent gave history of consumption of Tramadol tablets 5-10 /day for leg pain post fracture of tibia 2 years back. Last taken 10 tablets one day prior to the onset of seizures.

On CNS examination there was no neck stiffness, cerebellar signs were negative. There were no focal neurological deficits but bilateral plantar reflex was extensor. Other system examinations were within normal limits.

MRI Brain Seizure protocol done in ER showed multiple discrete hyperintensities in deep white matter of frontal, parietal and occipital lobes which were non-specific, probable post-ictal oedema (Figure:1) The blood investigations were largely within normal limits. Haemoglobin, total white cell count, differential counts (neutrophils and lymphocytes), PCV, sodium, potassium, creatinine, calcium, magnesium, and phosphorus are all within standard reference ranges, with no major abnormalities evident (Table:1). Patient was admitted to critical care unit for further monitoring and management.

Table 1: Results of relevant laboratory investigations.

Laboratory investigation	Result
Total Count (TC)	8000cells/µL
Haemoglobin (Hb)	12.3g/dL
Neutrophils (N)	66%
Lymphocytes (L)	22%
PCV	38.7%
Sodium (Na^+)	138mmol/L
Potassium (K^+)	3.5mmol/L
Creatinine	1.2mg/dL
Calcium	8.7mg/dL
Magnesium	2.41mg/dL
Phosphorus	3.3mg/dL

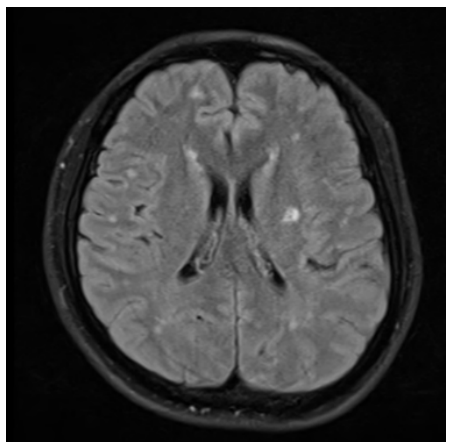

Figure 1: MRI Brain showing multiple discrete hyperintensities.

24 hours post admission patient became restless which gradually worsened. Patient had insomnia, tachycardia, pupils were 2 mm bilateral and reacting to light.MRI brain with contrast was performed which showed multiple small T2 FLAIR hyperintense foci in deep and periventricular white matter involving bilateral frontal and parietal lobes with involvement of bilateral semi-ovale. Which likely represent microvascular changes secondary to opioids in view of history. A CSF analysis was performed but no

abnormalities were detected. Baseline clinical opiate withdrawal scale (COWS) score was 8.

Patient was administrated with 2 doses of 0.4 mg of Naloxone and started on IV buprenorphine 300 mcg. There was slight improvement of symptoms with the treatment. Other supportive measures including sedatives continued for 2 days. Clonidine was added to the medications to control blood pressure. After a hospital course of 6 days patient got discharged from the hospital. Buprenorphine IV got replaced by Tablet 5 mg during Discharge.

Discussion

Tramadol is a synthetic opioid that is a weak MOR agonist. Noradrenaline and serotonin reuptake inhibition also contribute to analgesia. used primarily to treat mild to moderate pain, with little success in treating severe pain. The oral bioavailability of the medication is 68%. It is metabolized in liver and excreted in urine. When taken orally, the medication begins to effect within an hour, peaks in two to three hours, and lasts for six hours in total[6].

The drug frequently causes headaches, dizziness, dry mouth, nausea, vomiting, drowsiness, and respiratory depression. In people with a predisposition, tramadol can both induce and worsen seizures. Patients using MAOIs with SSRIs may experience serotonin syndrome due to the impact on serotonin reuptake. Tramadol abuse and dependence have been documented, despite its unknown potential for abuse[7].

Inhibition of serotonin and norepinephrine reuptake is linked to neurotoxicity following tramadol exposure. The reduced seizure threshold may be explained by the strong inhibition of GABA-A receptors at high tramadol dosages. Seizures are also believed to be caused by histaminergic, dopaminergic, opioid, and GABAergic neurotransmission. At high concentrations, tramadol and its metabolite M1 inhibit GABAA receptors; at clinical dosages, they inhibit NMDA receptors[6].

There are typical and atypical signs and symptoms of tramadol withdrawal. According to their frequency, tramadol withdrawal symptoms include gastrointestinal discomfort, anxiety, bone pain, depression, diarrhoea, sleeplessness, epiphora, nausea, agitation, rhinorrhoea, and excessive sweating. Severe anxiety, panic attacks, atypical CNS symptoms like delusion, confusion, depersonalization, and paranoid thoughts (2.27% prevalence), abnormal sensory experiences like tinnitus, tingling, prickling, and numbness (4.25% prevalence), and haptic, visual, and auditory hallucinations (20% prevalence) are examples of atypical symptoms. It should be noted that atypical symptoms only occur in one out of every eight instances, while typical symptoms are typically observed during the withdrawal phase[8].

Our case had 34-year-old male with history of tramadol abuse for 3 years. He had atypical symptoms like insomnia and agitation. Yates et al. described a 29-year-old woman who initially used tramadol to manage her pain from carpal tunnel syndrome. Over the course of three years, she grew reliant on a daily dosage of 30–50 mg while abstaining from all other medications and opioids. She experienced significant withdrawal symptoms from tramadol, such as headaches, sleeplessness, vertigo, and diarrhoea[9].

Similar history of tramadol withdrawal seizure in a young female was reported in a case report in India. They added that the drug's efficacy at the opioid receptor and the drug's intricate neuropharmacology may be more responsible for the non-specific withdrawal symptoms that were reported and observed[5].

In conclusion, because tramadol acts on opioid receptors, it may cause dependence, although a slight one. As medical professionals, we should be aware of the potential for tramadol dependence and use the drug in an efficient and responsible manner. Tramadol withdrawal symptoms might range from moderate nausea to potentially fatal seizures. We have an ethical obligation to comprehend the kind of side effects that the pharmaceutical industry produces and notify drug regulatory authorities of such incidents so that appropriate scheduling and warnings can be issued.

Conclusion

This example demonstrates how tramadol, even when administered for valid analgesic reasons, has the underappreciated potential to result in dependence and clinically substantial withdrawal.

Tramadol withdrawal may exhibit a combination of opioid and neuropsychiatric symptoms due to its dual opioid and monoaminergic actions, which could result in an incorrect diagnosis in acute care settings. Physicians should use caution when prescribing tramadol, educate patients about the possibility of dependence, and keep an eye out for increasing dosage needs or recurrent episodes of vague symptoms. To avoid difficulties, early detection, planned tapering, and suitable referral to de-addiction services are crucial. Patient safety can be enhanced and sensible analgesic usage encouraged by bolstering prescribing guidelines and raising professional understanding.

The single-patient form of this report limits its generalizability and makes it impossible to draw conclusions about prevalence or causality. Tramadol exposure could not be objectively quantified, withdrawal severity could not be standardized, and there were no long-term results after the intervention. It was not possible to thoroughly investigate potential behavioural and psychosocial factors that contribute to dependence. To further describe risk factors, clinical patterns of tramadol withdrawal, and the best preventative and treatment practices in various clinical settings, more prospective studies and multicentre observational data are required.

Declaration: We declare that we have no financial interests or personal conflicts that may affect the study in this article.

References

1. Close BR. Tramadol: does it have a role in emergency medicine? Emerg Med Australas. 2005 Feb;17(1):73-83. doi: 10.1111/j.1742-6723.2005.00671. x. PMID: 15675908.
2. Raffa RB. Basic pharmacology relevant to drug abuse assessment: tramadol as example. J Clin Pharm Ther. 2008 Apr;33(2):101-8. doi: 10.1111/j.1365-2710.2008.00897. x. PMID: 18315774.
3. Sidana A, Domun I, Arora P. Tramadol withdrawal psychosis. Indian J Psychiatry. 2019;61(6):655. doi: 10.4103/psychiatry.IndianJPsychiatry_11_19
4. Sarkar S, Nebhinani N, Singh SM, Mattoo SK, Basu D. Tramadol Dependence: A Case Series from India. Indian Journal of Psychological Medicine. 2012;34(3):283-285. doi:10.4103/0253-7176.106038
5. Saha A. Tramadol abuse potential and resultant withdrawal seizures. Int J Adv Med. 2014;1(2):1. doi:10.5455/2349-3933.ijam20140815
6. Nakhaee, S., Hoyte, C., Dart, R.C. et al. A review on tramadol toxicity: mechanism of action, clinical presentation, and treatment. Forensic Toxicol 39, 293–310 (2021). https://doi.org/10.1007/s11419-020-00569-0.
7. Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 13e Laurence L. Brunton, Randa Hilal-Dandan, Björn C. Knollmann.
8. Rajabizadeh G, Kheradmand A, Nasirian M. Psychosis following Tramadol Withdrawal.
9. Yates WR, Nguyen MH, Warnock JK. Tramadol dependence with no history of substance abuse. Am J Psychiatry. 2001 Jun;158(6):964. doi: 10.1176/appi.ajp.158.6.964. PMID: 11384913.