Rhabdomyolysis and acute kidney injury due to suicide attempt with tramadol: A rare case report

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Abstract
Although acute kidney injury (AKI) is a very rare complication of tramadol (TR) poisoning, overdose use in recent years should be considered. We present a 21-year-old man with metabolic acidosis, seizures, elevated serum creatine phosphokinase (CPK), creatinine, and rhabdomyolysis due to tramadol poisoning.

KEYWORDS
acute kidney injury, rhabdomyolysis, seizures, tramadol toxicity

1 | INTRODUCTION

Tramadol (TR) is a synthetic analgesic that is widely used. It was approved in various countries in the 1980s and became the most common drug in the world.1,2 It is used alone or in combination with other NSAIDs (nonsteroidal anti-inflammatory drugs) to treat depression-related conditions and pain, such as low back pain, spinal cord injury, and postoperative pain management.3 TR weakly binds to μ-opioid receptors and, in addition, inhibits the reabsorption of the neurotransmitters such as serotonin and norepinephrine.4,5 The standard therapeutic dose of tramadol is 50 mg orally, 50–100 mg by injection, and 100 mg rectally. The total daily dose should not exceed 400 mg. Therapeutic blood levels in adults range from 0.1 to 0.3 mg/L. The fatal dose of tramadol is unknown. An acute overdose of tramadol is generally considered non-life-threatening, and most fatalities are associated with polysubstance overdose.6 Nausea, vomiting, dizziness, fatigue, dry mouth, sweating, and postural hypotension are some of the early side effects of therapeutic TR toxicity. In overdose, tachycardia, seizures, central nervous system depression, coma, and respiratory depression have also been reported.7 However, in credible sources, AKI is not usually considered as a common complication of TR toxicity, and information about its occurrence or how it is treated is limited to some extent, but there have been reports of AKI following TR toxicity in recent years.8-10 In this report, we describe a patient who develops rhabdomyolysis and AKI following TR poisoning and show
that these patients can be treated with timely supportive treatment without the need for invasive procedures such as hemodialysis.

## 2 | CASE PRESENTATION

On June 20, 2021, a 21-year-old man was referred due to a suicidal attempt with the ingestion of 2,250 mg of TR (10 tablets of 225 mg). One hour after ingestion, the patient developed generalized tonic–clonic seizures. He was in the postictal phase at the time of admission to the emergency department, and the Glasgow Coma Scale (GCS) was 11/15 (E3, V4, M4).

He was in good health before and had no history of kidney complications or risk factors for AKI. He had a history of consuming TR (2–3 tablets of 200 mg) per day during the previous month without taking any other drugs or alcohol, had no history of seizures during this period, but had febrile convulsions in childhood.

On examination, the pupils were symmetrically dilated (5 mm in diameter) and reactive to light, with a respiratory rate (RR) of 18 breaths/min with acceptable chest movements during respiration without any symptoms of respiratory distress. The blood pressure (BP) was 125/83 mm Hg, and the electrocardiogram (ECG) showed sinus tachycardia, at a heart rate (HR) of 140 beats/min. There were no signs of trauma or injuries to the head, face, or limbs. After becoming fully conscious, he complained of pain in the shoulders, which on examination and X-ray showed no signs of fracture or dislocation.

In the emergency department, the patient had two generalized tonic–clonic seizures, in which diazepam ampoules were administered to control them and injectable depakine 200 mg/Bid was prescribed to prevent them. After performing the initial proceedings, the patient was transferred to the poisoning ward. Paraclinical evaluation showed metabolic acidosis and increased serum creatine phosphokinase (CPK), creatinine, and urea, and due to that with the possible diagnosis of rhabdomyolysis in the field of seizures, a consultation with a nephrologist was requested (Table 1). Although hemodialysis was considered for the patient, conservative treatment was started by administering 200 cc/hour fluids (normal saline solution) and 1–2 meq/Kg NaHCO3, and due to the healthy reporting of the kidneys on ultrasound and the improvement of symptoms with supportive care, he did not require hemodialysis.

Due to fever (T = 38°C) without shortness of breath, myalgia, or abdominal pain with a diagnosis of aspiration pneumonia during seizures, ceftriaxone 1 gr/Bid and clindamycin 900 mg/Tds were prescribed. Finally, after 10 days of the above supportive treatment, the patient found a normal urinary output and was discharged in good general condition and normal laboratory tests. This research was carried out in accordance with the principles outlined in the Helsinki Declaration. Also, CARE guidelines and methodology have been followed in this study.

## 3 | DISCUSSION

Clinically, pain is postoperatively seen in cases including malignancy and chronic neuropathy.11 Among the analgesics, TR is commonly used due to its high efficacy and safety and was the second most common drug to be studied on a user-based website alongside oxycodone.12

### TABLE 1 Results of initial tests and comparison with measured values 10 days after treatment

| Parameter | Initial blood sample | Blood sample 10 days after treatment |
|-----------|----------------------|--------------------------------------|
| **CPK**   | Male: 39–308 U/L     | Cr Male: 0.74–1.35 mg/dl             |
|           | Females: 26–192 U/L  | Female: 0.59–1.04 mg/dl              |
| **Cr**    | Male: 20,000         | 5.7                                  |
|           | Females: 688         | 2.2                                  |
| **BUN**   | 6–24 mg/dL           | 90                                   |
| **K**     | 3.5–5.0 mEq/L        | 4.2                                  |
| **Na**    | 135–145 mEq/L        | 138                                  |
| **Ca**    | 8.5–10.5 mg/dl       | 9.1                                  |
| **pH**    | 7.35–7.45            | 7.24                                 |
| **pCO2**  | 35–45 mm Hg          | 28.9                                 |
| **HCO3**  | 22–28 mEq/L          | 12.5                                 |

Abbreviations: BUN, blood urea nitrogen; CPK, Creatine phosphokinase; Cr, creatinine; pCO2, partial pressure of carbon dioxide.
Furthermore, in recent years, easy and widespread access, overadministration, and euphoria of this drug have led to a rapid increase in TR use and intoxication in Iran. It has both opioid and nonopioid mechanisms and has fewer side effects than other opium at regular doses. TR is a norepinephrine and 5-HT reuptake inhibitor and has an active metabolite, O-desmethyltramadol, which is catalyzed by CYP2D6, a µ-opioid receptor agonist.

The expression of CYP2D6 is highly variable in different individuals; therefore, the analgesic effect of TR is inconsistent among individual patients. Among the complications, seizures have been identified as a complication that occurs at both toxic and high therapeutic doses, and it is difficult to define the minimum dose required to induce seizures. While high concentrations of TR can attenuate γ-aminobutyric acid (GABA) receptors, the exact mechanism of tramadol-induced seizures has not been established. TR causes muscle damage by causing seizures that increase all CPK isoforms (MB, M, and B). Renal failure is a rare complication of poisoning that can be directly or indirectly caused by TR following seizures and rhabdomyolysis due to poisoning. In a study conducted in 2019 by Abdul Rahman et al., it was shown that the risk of suicide among adolescents with substance use disorders is high and that there is a direct relationship between substance use disorders and suicidal ideation. Tramadol users also accounted for 40% of the sample.

Our reported patient is a young man who developed generalized tonic–clonic seizures after taking 2,250 mg of TR with suicidal ideation, followed by metabolic acidosis and increased serum CPK, urea, and creatinine. Due to the possible diagnosis of AKI following poisoning, supportive treatment with intravenous fluids and bicarbonate was immediately started for him. Although we intended hemodialysis for the patient from the beginning, all our efforts were made to eliminate the need for invasive procedures, and fortunately, in the end, without the need for hemodialysis and only with supportive treatment, the clinical symptoms and laboratory tests improved.

4 | CONCLUSIONS

Acute kidney injury is a rare and important complication of TR intoxication that requires prompt treatment and is usually not considered. Therefore, it can challenge the treatment of poisoning, and according to our case report, it can be concluded that this side effect can be treated only with supportive care and without hemodialysis.

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CONFLICT OF INTEREST
The authors confirm that this article content has no conflict of interest.

AUTHOR CONTRIBUTIONS
ZZ was involved in the interpretation and collection of data and manuscript editing. MS was involved in writing, editing, and preparing the final version of the manuscript. FG was involved in critically revising the whole manuscript. AM and MS are responsible for collecting data and submitting the manuscript. All authors reviewed the paper and approved the final version of the manuscript.

CONSENT
Written informed consent was obtained from the patient to publish this report in accordance with the journal’s patient consent policy.

DATA AVAILABILITY STATEMENT
The data are available to the corresponding author and can be obtained upon request.

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REFERENCES
1. Soleymani F, Shalviri G, Abdollahi M, et al. Pattern of use and adverse drug reactions of tramadol; a review of 336, 610, 664 insured prescriptions during 5 years. Int J Pharmacol. 2011;7(7):757-760.
2. Taghaddosinejad F, Mehrpour O, Afshari R, et al. Factors related to seizure in tramadol poisoning and its blood concentration. J Med Toxicol. 2011;7(3):183-188.
3. Tetsunaga T, Tetsunaga T, Tanaka M, et al. Efficacy of tramadol–acetaminophen tablets in low back pain patients with depression. J Orthop Sci. 2015;20:281-286.
4. Loughrey M, Loughrey C, Johnston S, et al. Fatal hepatic failure following accidental tramadol overdose. Forensic Sci Int. 2003;3:232:134.
5. Clarot F, Gouille J, Vaz E, et al. Fatal overdoses of tramadol: Is benzodiazepine a risk factor of lethality? Forensic Sci Int. 2003;134:57-61.
6. Grond S, Sablotzki A. Clinical pharmacology of tramadol. Clin Pharmacokinet. 2004;43:879-923.
7. Ahmadimanesh M, Shadnia S, Rouini MR, et al. Correlation between plasma concentrations of tramadol and its metabolites and the incidence of seizure in tramadol-intoxicated patients. Drug Metab Pers Ther. 2018;33(2):75-83.
8. Mike TB, DeVault H, Blackford MG, et al. Acute tramadol ingestion with transient acute kidney injury in an adolescent female. J Pediatr Pharmacol Ther. 2021;26(4):411-413.
9. Afshari R, Ghooshkhannehe H. Tramadol overdose induced seizure, dramatic rise of CPK and acute renal failure. J Pak Med Assoc. 2009;59(3):178.
10. Wang SQ, Li CS, Song YG, et al. Multiply organ dysfunction syndrome due to tramadol intoxication alone. *Am J Emerg Med*. 2009;27(7):903-e5.

11. Dogar SA, Khan FA. Tramadol-paracetamol combination for postoperative pain relief in elective single-level microdisectomy surgery. *J Neurosurg Anesthesiol*. 2017;29:157-160.

12. Wightman RS, Perrone J, Erowid F, Erowid E, Meisel ZF, Nelson LS. Comparative analysis of opioid queries on erowid.org: an opportunity to advance harm reduction. *Subst Use Misuse*. 2017;1-5.

13. Okazi A, Taghadosinejad N, Mazrouei N, et al. Occurrence and recurrence of seizures and related factors in patients with tramadol ingestion. *IJMTFM*. 2018;8(3):101-8.

14. Raffa RB, Buschmann H, Christoph T, et al. Mechanistic and functional differentiation of tapentadol and tramadol. *Expert Opin Pharmacother*. 2012;13:1437-1449.

15. Hartrick CT, Rozek RJ. Tapentadol in pain management: a mu-opioid receptor agonist and noradrenaline reuptake inhibitor. *CNS Drugs*. 2011;25:359-370.

16. Shadnia S, Soltaninejad K, Heydari K, et al. Tramadol intoxication: a review of 114 cases. *Hum Exp Toxicol*. 2008;27:201-205.

17. Hara K, Minami K, Sata T, et al. The effects of tramadol and its metabolite on glycine, γ-aminobutyric AcidA, and N-methyl-d-aspartate receptors expressed in Xenopus oocytes. *Anest Analg*. 2005;100(5):1400-5.

18. Mohammadpour A, Ashkezari MD, Farahmand B, et al. Demographic characteristics and functional performance of the kidneys and hearts of patients with acute tramadol toxicity. *Drug Res (Stuttg)*. 2019;69(4):207-210.

19. Ismail Abd El-Rahman A, Ahmed Abdullah Mekki A, Mohamed Sadek I, Atallah Gad Salama M. Suicidality in a sample of Egyptian adolescents with substance use disorder. *Al-Azhar Med J*. 2019;48(4):397-406. doi:10.21608/amj.2019.64947

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