



# Generalized Tonic Colonic Seizure Followed by Loss of Consciousness Early After Using Low Dose of Tramadol: A Case Report

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## Abstract

**Introduction:** Despite high efficacy and safety of tramadol as a pain relieving analgesic, some minor side effects have been reported following its consumption. However, very rarely, serious and life-threatening side effects may appear following administration of tramadol.

**Case Presentation:** This research describes a case of tramadol poisoning that appeared with acute seizure needing emergent and intensive cares. In the described case, using a low dose of tramadol (200 mg, orally), the patient experienced generalized tonic colonic seizure followed by loss of consciousness and shoulder dislocation due to trauma, requiring admission to the intensive care unit.

**Conclusions:** As shown in the study, even using a low dose of tramadol might lead to acute generalized seizure with loss of consciousness and the need for intensive care.

**Keywords:** Tonic Colonic Seizure, Consciousness, Tramadol

## 1. Introduction

Tramadol is a synthetic 4-phenyl-piperidine analogue of codeine with a centrally acting analgesic effect (1). Compared to common opioid analgesics, such as morphine or pethidine, tramadol has a balanced drug efficacy and safety (2). In comparison with morphine, the analgesic potency of tramadol is approximately 10% of that of morphine, along with considerable lower side effects (3). Moreover, tramadol has an acceptable postoperative pain-relieving effect compared to other analgesics, even in the parenteral route, particularly in those with increased risk of postoperative cardiopulmonary complications (4). On the other hand, adding tramadol to some anesthetic drugs, such as lidocaine can be appropriate in surgeries because of accentuating sensory and motor blockade effects without any increase in complications (5). In total, this drug has been approved as a well-tolerated analgesic drug in patients, who are candidate for different surgical procedures or those with high load of acute or chronic pains following severe trauma, chronic malignant conditions, and colic or neuropathic pain (6). Despite its high efficacy, some minor side effects have also been reported following the use of tramadol, including nausea and vomiting, constipation, dysphoria, or even mild respiratory depression

(7). All of these side effects seem to be dose-dependent and thus considering an optimal dose of drug leads to minimization of its-related side effects. However, serious and life-threatening side effects may very rarely appear following administration of tramadol (8). Herein, this report describes a case of tramadol poisoning that appeared with acute seizure, needing emergent and intensive care.

## 2. Case Presentation

The described case was a 32-year-old male that was advised to use tramadol (200 mg, orally), as a single dose, because of appearing severe headache. About half an hour since using the drug, the patient experienced generalized tonic colonic seizure that lasted about five minutes and thus the patient was hospitalized. On admission, the patient was sleepy and was complaining of pain in both the hands, particularly in the shoulders. The patient had no significant history of special disease, drug abuse or addiction. In laboratory tests, urine screening test confirmed the use of tramadol. Arterial blood gas analysis showed mixed acidotic disturbances (PH = 7.23, PCO<sub>2</sub> = 56 mmHg, and HCO<sub>3</sub> concentration = 19 mmol/L). Due to loss of consciousness, the patient was intubated and admitted to

the intensive care unit. The subject was extubated after 48 hours of intensive care. Given that the patient still complained of pain in both shoulders and also limited movement of the upper limbs, X-ray examination was requested indicating bilateral fractures and dislocation of both shoulders. Thus, he was a candidate for surgery that was successfully managed.

### 3. Discussion

Although some reports are available on seizure as a rare side effect of high dose tramadol, the occurrence of this complication following a low dose has not been reported previously. Interestingly, some evidences have emphasized that seizure following the use of tramadol is not dose-dependent (9). In the present report, the researchers described a case that used a single dose of tramadol 200 mg orally that led to acute generalized seizure requiring intensive care management. Simultaneously, because of probable traumatic injuries, he also had shoulder trauma that was assessed by imaging and managed surgically. In a similar report by Nakhaei et al. (10), of all patients, who referred to the emergency ward with shoulder dislocation, 24.4% had tramadol induced seizures and also showed a significant relationship between the number of dislocation and tramadol use. In another report by Farajidana et al. (11) of patients with tramadol-induced seizures, 79.7% had referred within the first 6 hours after drug use. They also indicated that the prevalence of trauma was 24.6% with the most frequent site of trauma being the face followed by shoulders. Along with studies that assessed the clinical consequences of tramadol poisoning, some others focused on the main determinants of tramadol-related seizure. In a study by Taghaddosinejad et al. (12), seizure was significantly correlated with higher reported dose, and tramadol only to overdose, however, it was neither related to higher tramadol blood concentrations, nor related to time elapsed, age, gender, history of addiction, and observed Glasgow Coma Scale of patients. Thus, in their study, tramadol-induced seizure was shown to be dose dependent.

As shown in the current study, even using a low dose of tramadol might lead to acute generalized seizure with loss of consciousness and need of intensive care. Commonly, it has been shown that taking high dose of tramadol (as the therapeutic range) can induce seizure attacks within the first 24 hours with overall incidence of 84% (13, 14).

Pathophysiologically, the metabolites of tramadol produced by liver via o-demethylation have a major role in appearing serotonergic syndrome that has been suggested to be responsible for seizure. In other words, these metabolites may induce serotonin activity that explains occur-

rence of seizure related to tramadol uptake. In addition, the use of selective serotonin reuptake inhibitors can also induce seizure occurrence, another reason for increased risk for seizure following tramadol consumption (15). However, the risk for generalized seizure after taking low dose of tramadol has remained uncertain and should be assessed further.

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### Footnotes

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### References

1. Dayer P, Desmeules J, Collart L. [Pharmacology of tramadol]. *Drugs*. 1997;**53 Suppl 2**:18-24. doi: [10.2165/00003495-199700532-00006](https://doi.org/10.2165/00003495-199700532-00006). [PubMed: [9190321](https://pubmed.ncbi.nlm.nih.gov/9190321/)].
2. Lehmann KA. [Tramadol in acute pain]. *Drugs*. 1997;**53 Suppl 2**:25-33. [PubMed: [9190322](https://pubmed.ncbi.nlm.nih.gov/9190322/)].
3. Byrne K, Nolan A, Barnard J, Tozer M, Harris D, Sleigh J. Managing Postoperative Analgesic Failure: Tramadol Versus Morphine for Refractory Pain in the Post-Operative Recovery Unit. *Pain Med*. 2017;**18**(2):348-55. doi: [10.1093/pm/pnw084](https://doi.org/10.1093/pm/pnw084). [PubMed: [28204722](https://pubmed.ncbi.nlm.nih.gov/28204722/)].
4. Klotz U. Tramadol—the impact of its pharmacokinetic and pharmacodynamic properties on the clinical management of pain. *Arzneimittelforschung*. 2003;**53**(10):681-7. doi: [10.1055/s-0031-1299812](https://doi.org/10.1055/s-0031-1299812). [PubMed: [14650359](https://pubmed.ncbi.nlm.nih.gov/14650359/)].
5. Imani F, Entezary SR, Alebouyeh MR, Parhizgar S. The maternal and neonatal effects of adding tramadol to 2% lidocaine in epidural anesthesia for cesarean section. *Anesth Pain Med*. 2011;**1**(1):25-9. doi: [10.5812/kowsar.22287523.1271](https://doi.org/10.5812/kowsar.22287523.1271). [PubMed: [25729652](https://pubmed.ncbi.nlm.nih.gov/25729652/)]. [PubMed Central: [PMC4335753](https://pubmed.ncbi.nlm.nih.gov/PMC4335753/)].
6. Lassen D, Damkier P, Brosen K. The Pharmacogenetics of Tramadol. *Clin Pharmacokinet*. 2015;**54**(8):825-36. doi: [10.1007/s40262-015-0268-0](https://doi.org/10.1007/s40262-015-0268-0). [PubMed: [25910878](https://pubmed.ncbi.nlm.nih.gov/25910878/)].
7. Vazzana M, Andreani T, Fangueiro J, Faggio C, Silva C, Santini A, et al. Tramadol hydrochloride: pharmacokinetics, pharmacodynamics, adverse side effects, co-administration of drugs and new drug delivery systems. *Biomed Pharmacother*. 2015;**70**:234-8. doi: [10.1016/j.biopha.2015.01.022](https://doi.org/10.1016/j.biopha.2015.01.022). [PubMed: [25776506](https://pubmed.ncbi.nlm.nih.gov/25776506/)].

8. Beakley BD, Kaye AM, Kaye AD. Tramadol, Pharmacology, Side Effects, and Serotonin Syndrome: A Review. *Pain Physician*. 2015;**18**(4):395-400. [PubMed: [26218943](#)].
9. Beyaz SG, Sonbahar T, Bayar F, Erdem AF. Seizures associated with low-dose tramadol for chronic pain treatment. *Anesth Essays Res*. 2016;**10**(2):376-8. doi: [10.4103/0259-1162.177181](#). [PubMed: [27212778](#)]. [PubMed Central: [PMC4864678](#)].
10. Nakhaei Amroodi M, Iri A, Akhoondi S. The definition of recurrent shoulder dislocation in tramadol induced seizure patients. *Med J Islam Repub Iran*. 2015;**29**:298. [PubMed: [26913261](#)]. [PubMed Central: [PMC4764268](#)].
11. 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. [PubMed: [22582482](#)].
12. Taghaddosinejad F, Mehrpour O, Afshari R, Seghatoleslami A, Abdollahi M, Dart RC. Factors related to seizure in tramadol poisoning and its blood concentration. *J Med Toxicol*. 2011;**7**(3):183-8. doi: [10.1007/s13181-011-0168-0](#). [PubMed: [21735309](#)]. [PubMed Central: [PMC3550210](#)].
13. Boyd IW. Tramadol and seizures. *Med J Aust*. 2005;**182**(11):595-6. [PubMed: [15938692](#)].
14. Jovanovic-Cupic V, Martinovic Z, Nestic N. Seizures associated with intoxication and abuse of tramadol. *Clin Toxicol (Phila)*. 2006;**44**(2):143-6. doi: [10.1080/1556365050014418](#). [PubMed: [16615669](#)].
15. Mason BJ, Blackburn KH. Possible serotonin syndrome associated with tramadol and sertraline coadministration. *Ann Pharmacother*. 1997;**31**(2):175-7. doi: [10.1177/106002809703100208](#). [PubMed: [9034418](#)].