

# Hypoxic-ischemic encephalopathy in a young man due to tramadol overdose



Zahra Ataee\*, Bita Dadpour

Medical Toxicology Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

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\***Corresponding author:** Zahra Ataee, Medical Toxicology Research Center, Mashhad University of Medical Sciences.  
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## Abstract

**Objective:** Tramadol is a synthetic analgesic with two mechanisms. The opioid and non-opioid mechanisms are responsible for tramadol side effects. Non-opioid side effects of tramadol are due to the reuptake inhibitions of serotonin and norepinephrine. Some of the side effects include anaphylactoid reactions, CNS depression, hypoglycemia, hypotension, respiratory depression, seizures, and serotonin syndrome. Seizure may happen in therapeutic doses. If the frequency of tramadol seizures increases, ischemic brain injury and hypoxic-ischemic encephalopathy can be induced.

**Case Report:** We report a young man with a history of tramadol abuse that was admitted with status epilepticus in Imam Reza hospital in Mashhad, Iran. Due to his altered mental status, he was intubated and antiepileptic agents were prescribed. He was transferred to ICU. After regaining consciousness, he was extubated and with the prescription of rehabilitation support he was discharged.

**Conclusion:** Tramadol is a synthetic analgesic agent with less potential for dependence. It is important to mention that the overdose of this drug is common. This drug has two mechanisms. This paper reports a case that developed generalized tonic clonic seizures due to tramadol and hypoxic ischemic encephalopathy. With adequate treatment and supportive care, patient's mental status improves and he/she can be discharged.

**Keywords:** Tramadol, Status epilepticus, Hypoxic ischemic encephalopathy, Antiepileptic

## Introduction

Tramadol is a synthetic analgesic agent that is used for moderate to relatively severe pain with neuropathic and nociceptive mechanisms like renal colic (1). Tramadol has two mechanisms namely opioid and non-opioid mechanisms. The opioid mechanism is like other opioids and binds to  $\mu$ -opiate receptors and suppresses the perception of pain (2). On the other hand, non-opioid mechanism is the inhibitor of serotonin and norepinephrine reuptake (3). Anaphylactoid reactions, CNS depression, hypoglycemia (4), hypotension, respiratory depression, seizures, and serotonin syndrome are the most important side effects of tramadol (5). Evidence shows that seizures of tramadol happen on the first day of use (6) and they are not cured by naloxone, but they are suppressed by benzodiazepines.

Animal research studies show that the inhibition of gamma aminobutyric acid receptors may induce the severity of tramadol seizures (7,8). Seizure of tramadol may happen in therapeutic doses especially with the use of alcohol, tricyclic anti-depressant, selective serotonin reuptake inhibitor, serotonin-norepinephrine reuptake inhibitor, anorectics, other opioids, neuroleptics, monoamine

oxidase inhibitor inhibitors, and drugs which may lower seizure threshold.

In recent years, the abuse of tramadol is on the rise and it is one of the drugs to be searched on the net (9). In recent years the prevalence of tramadol overdose in Iran has increased (10-12). The seizure risk in tramadol overdose is about 15%-35% (10,13). Status generalized tonic-clonic seizures produce severe ischemia in brain and brain stem as well as medulla which can lead to hypoxic ischemic encephalopathy. Severity and duration of hypoxia and the neurologic past medical history can determine a patient's prognosis (14). In this paper we review the effects of tramadol seizure in a young patient.

## Case Report

A 21-year old man was referred to the emergency due to frequent seizures and decreased level of consciences. He had overdosed some tramadol oral tablets and was referred to emergency department with recurrent tonic clonic seizures and decreased consciousness. The information obtained from the patient concerning drug history, past medical history and social history was negative. In physical exam, he was not alert and he had recurrent



seizures. Blood pressure, heart rate, respiratory rate and temperature were normal. Pupils were mydriatic. Other physical exams were normal. There were not any signs of trauma. He was intubated and admitted in intensive care unit. Antiepileptic agents were prescribed. Urine toxicology test discerned tramadol. Brain computerized tomography scan showed edema and we prescribed mannitol, dexamethasone and depakin consequently. After 5 days his consciousness level improved and after 15 days he was extubated. Finally, he was referred to the ward, but he had bizarre behavior and after some days with the prescription of supportive and rehabilitation measures he was discharged.

## Discussion

Tramadol is an effective analgesic agent for moderate to severe pain with a low level of addiction (15). Tramadol works with two different mechanisms: opioid and non-opioid. These two mechanisms cause good effects and side effect for tramadol (16). One of the most common side effects in overdose or therapeutic dose is seizure (17). Sometimes the frequency of seizures increases, but if seizures are treated as soon as possible, the resultant would be better prognosis (18).

Mortality of status epilepticus is about 7%-39% (19), and research shows that opioids like tramadol and morphine can induce status epilepticus (20) (Figure 1). Hypoxic-ischemic encephalopathy results from some events such as poisoning (drug overdose) (14). There is a great deal of evidence concerning its side effects. Talaie et al in 2009 reported that the prevalence of tramadol seizure is about 46.2% (12). Mehrpour in 2005 suggested that tramadol can induce status epilepticus (21). The study conducted by Boostani and Derakhshan in 2012 showed that tramadol seizure is generalized tonic-clonic and it happens in 24 hours of tramadol intake, but if tramadol is used with alcohol-antipsychotics-antidepressants, the risk of seizure can be increased (22). A study conducted by Taghaddosinejad et al in 2011 showed that the prevalence

of tramadol seizure is related to tramadol dose, but it is not related to blood concentration (23). Talaie et al in 2009 indicated that tramadol seizure is not dose dependent (12).

## Conclusion

This study is about one of the most important side effects of tramadol over dose. This study is about one of the most important side effects of tramadol over dose: hypoxic-ischemic encephalopathy following recurrent seizures induced by Tramadol overdose. He was treated and after some days with the prescription of supportive and rehabilitation measures he was discharged. In recent years the use of tramadol without caution has increased and it is available easily. In this regard, physicians must know how to treat the side effects of this drug.

## Authors' contributions

ZA and BD contributed equally in study design, drafting article, reading critically and accepted finally proof.

## Ethical Issues

Patient's informed consent was obtained regarding the use of personal data for this report.

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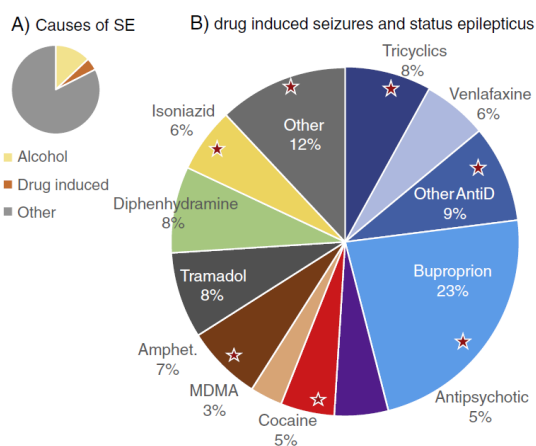


Figure 1. Causes of status epilepticus and drug induced seizures.

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