

## Tramadol, Seizure Caused by an Overdose and Acute Renal Failure: A Case Report

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**Abstract:** *Background:* Tramadol is the most common narcotic drug used in the world. In recent years, its use is increasing in Iran. In most cases, its abuse was for suicidal attempt. *Case:* The patient is a 22-year old young man who was transferred to the medical center after taking 94 pills of tramadol 100 mg. He was in a deep coma for 2 days and 3 seizure attacks. He was intubated due to severe respiratory distress and he was admitted in the ICU. Two days after being admitted to the ICU, the patient was done hemodialysis. The patient was hospitalized for 19 days in the ICU. After six months, his general condition remained. *Conclusion:* The results of this study can be used to design the effective strategies on the prevention of abuse, as well as efforts to increase the awareness of young people about the drug tramadol and limiting its access and distribution.

**Key words:** Tramadol • Drug Poisoning • Overdose • Suicide

### INTRODUCTION

Poisoning as one of the major causes of death in most countries is very important in terms of public health [1]. The most common combined toxicity is drug toxicity [2]. Toxic factor is different in various parts of Iran. In Tehran, Mashhad and Babol drug toxicity is common with sedatives [1]. Tramadol is the most consuming narcotic drug that is prescribed in the world [3] and its consumption has been on the rise in recent years in Iran. Suicidal impulse level has been reported as the most reason of consumption [4]. In Iran, 7.4 % has been reported to be the mortality by tramadol poisoning mainly due to seizures [5]. Tramadol is a centrally effective drug used for the treatment of moderate to severe pain, including cancer pain, the pain of surgery, muscle and joint pains [6, 7]. Its effectiveness is less than morphine and pethidine and is stronger than ibuprofen and acetaminophen [8]. Tramadol dosage should be adjusted according to the patient's pain and allergy. Standard therapeutic doses are 50 mg orally, 50-100mg injection and 100 mg rectally [9]. The total daily dose amount does not exceed from 400 mg. Tramadol blood in adults range from

0.1 to 0.3 mg [9]. Tramadol has a dual effect mechanism, the weak effect on  $\mu$  receptors and inhibits the reuptake of serotonin and noradrenaline that are neurotransmitters and are widely metabolized by the liver and excreted primarily in the urine [10]. The side effects of poisoning with the tramadol are drowsiness, nausea, vomiting, restlessness, headache, constipation [11]; rare side effects include seizures, disorders of respiratory system, liver and kidney [10]. Other symptoms of poisoning with tramadol are loss of consciousness and eventually coma leading to 10% hospitalization of poisoned patients in intensive care units for a long time [12]. According to tramadol is a narcotic quasi-legal analgesic commonly consumed and failure of liver and kidneys is an uncommon complication of tramadol poisoning, in this study, we introduced the successful management of overdose of tramadol.

**Case:** The patient is a 22-year-old young man who has been addicted to crack for 4 years and has been clean for a year. He was mechanic and did not have any family history of addiction and suicide. Informed consent was obtained from patient. While the eyes reverse, cyanosis was seen in the head and neck, mydriasis and did not

Table 1: Patient's Laboratory data on admission

WBC:8700	Na:145	BUN:74	Bil T:0.5
RBC:3.92	K:3.8	Cr:5.7	Bil D:0.3
Hb:10.5	P:6	ALK:178	Hco3:19.7
HCT:30.5	Ca:8	AST:381	Pco2:34
MCV:77.8	Mg:1.9	ALT:211	Pao2:59
PLT:145000			GLU:75

Table 2: Patient's Laboratory data on 16<sup>th</sup> days

WBC:15100	PLT:261000	BUN:79	Ph:7.2
RBC:3.09	Na:144	Cr:5	Hco3:21.2
Hb:8.1	K:3.9	ALK:163	Pco2:30
HCT:25.4	P:7.4	AST:186	Pao2:70
MCV:82.2	Ca:8.5	ALT:65	

react to light, 1 to 2 hours after ingestion of 100 tablets of tramadol. He was moved to if medical center. For the patient Cardiopulmonary resuscitation (CPR) and finally after resuscitation, gastric decontamination was performed. In the first two days he was not alert, he was in deep coma (GCS = 3-4). He had 4 nights hospitalization in the ICU and seizures three times for 4 days. To complete remedial measures he was referred to other centers. A day prior to admission, patient's consciousness was better. Upon arrival at the center, the patient was restless and complained of severe dyspnea and the vital signs were the following: respiratory rate 28 per minute, heart rate 107 per minute, blood pressure 140/90 mmHg and body temperature 39°C. On the patient's general examination, he was feverish and dizzy and had increasing heart rate and respiration rate. On lung auscultation, crackles were heard, preferably in the lower half of the right lung. Pulmonary edema was seen on chest radiograph. Electrocardiogram (ECG), neurologic examination and sonography examination of the abdomen and the pelvis was normal. There was no cyanosis or edema. Acute kidney failure was diagnosed in kidney sonography and due to severe respiratory distress he was intubated and admitted in the ICU. According to the results of the tests nasogastric tube was inserted for the patients. Fluid therapy (Lasix, serum 2/3, 1/3 and etc.), activated charcoal and naloxone were prescribed to the patient.

Initially the patient had oliguria, his urine volume one and a half hour after entering to the sector was about 600cc and within an hour he received a half liter of saline. Oxygen therapy was performed. The patient's examination before dialysis was as follow:

Two days after being admitted to the ICU, the patient was done hemodialysis. Everyday dialysis was done except day six and day thirteen. Eleven days after

hospitalization, the patient had a fever. Hemoglobin (Hb) level fell gradually during treatment. At last, 4 units of blood were injected to the patient. On the 16th day of hospitalization, due to a sharp decline in hemoglobin, the patient did not respond to painful stimuli and the pupils were equal and did not show any reaction to light. The next test was as follows:

Brain CT scan was reported be normal. The patient was hospitalized in the ICU for 19 days. And then because of stabilization of the vital signs and relieving of dyspnea, he was transferred to the internal part. Three days after he was discharged from the hospital he was admitted to another psychotherapy center. The drugs that were used for the patient included Haloperidol, multivitamin, Serum, Vancomycin, Pantoprazole, Meropenem, Octreotide, Ceftriaxone and Amino Acid MP. After six months the patient's general condition was evaluated. The mental condition of patient via behavior therapy was very close to optimal condition. According to the tests carried out, a kidney problem has not been observed and the patient is in a normal physical condition.

## DISCUSSION

According to the report of the UN Office on Narcotic and Crime (UNODC) in 2004, 185 million consumers of different narcotics have been identified that include 3% of the world population [13]. In Germany in 1977, the first use of tramadol was suggested [14] and in some countries, the use of tramadol, since 1980 in America, in France since 1995 and in 1997 adopted for public use. Due to its uses and limitations, tramadol was prescribed to patients after surgery and for healing chronic pain [9-11, 15-18]. In 2001, after the ban on diclofenac injectable prescription, tramadol enters the market as an alternative painkiller to Iran [19, 20]. Tramadol is made based on molecular structure of Narceine which is one of opium alkaloids and it is a synthetic analgesic with central effects [8]. This drug is a sedative that had an effect like narcotics. Most cases of its poisoning are deliberately with high dose. Its lethal seizure is one of the dangerous side effects of tramadol [21], as well as some of its drug interactions, training for general practitioners and restrictions on the distribution and consumption has been recommended [22].

Excessive use in addition to being fatal cause symptoms such as difficulty of breathing, sleepiness, convulsions, cardiac arrest or slow heartbeat, extreme weakness and coma. In our study patient, symptoms such

as respiratory distress, drowsiness, convulsions, tachycardia, hypoxia and coma were observed. In America, out of every 7 people that consume tramadol, a person dependent with it [23]. According to Iran's Drug Headquarters for Combating of tramadol abuse, a 26.5% is in the first row of narcotic consumption [24].

In a study in 2010 in Isfahan by Izadimood *et al.* on the consumers of tramadol, the following results were obtained. Most consumers were men with the mean age of 24 years with a history of addiction that the most common cause of hospitalization was a decrease in the level of consciousness and the subsequent symptoms were seizures, Penne bradycardia, tachycardia and increase in blood pressure, respectively. Treatments used in these patients were activated charcoal, gastric decontamination, anti-seizure drug, naloxone, tracheal intubation and artificial respiration confirmed in this patient [25].

Ahmadi *et al.* in 2010 studied the epidemiology of poisoning caused by the consumption of tramadol in Kermanshah. Poisoning at age 19 was more common in singles. The most common cause of tramadol poisoning was suicide attempt. 40% of patients had symptoms of seizures; incidence of seizure was higher in males. The amount of seizure was associated with tramadol consumption. The patient has consumed tramadol for suicide which is consistently mentioned in the study [26]. Hasanjanimoghadam *et al.* in a study in 2013 evaluated respiratory problems (Apnea) in tramadol consumers in Tehran. Respiratory problems were seen in all patients which support this study one of the main problem of our patient was dyspnea [21]. In a study by Mugunthan *et al.* in 2012, a 54 - year old woman, 2 hours after consuming 3000mg of tramadol for suicide was referred to the Emergency ward. After thirty minutes she had seizure. With GCS = 3 and blood glucose levels 52 mg, in which severe hypoglycemia was observed. Our patient with GCS = 3-4 and blood glucose levels 75 mg is had seizures, but there was not a sharp drop observed in blood sugar [27].

Loughrey *et al.* is study in 2003, entitled "Fatal liver failure after a random tramadol overdose" in which a 67-year-old man encountered a painful rib fracture. 84 tramadol 50 mg tablets were consumed daily, accidentally exceeding the recommended dose. On initial examination, he had severe dyspnea, drowsiness, central cyanosis and hypotension. In view of the results of liver function tests, hypoxia, lactic acidosis and hypoglycemia were seen. Immediately, after admission he had cardiac arrest - breathing problem and died. Acute liver failure due

to fulminant hepatic necrosis was the cause of his death. The other symptoms of this patient were drowsiness, severe dyspnea and cyanosis was confirmed [10].

N. Bekjarovski *et al.* in their study in 2012 examined the seizures after if use and abuse of tramadol. Seizures have been observed in three patients after consuming tramadol more than the permissible dose which is consistent with our study [28]. In the study of Afshari *et al.* in 2009 as seizures of wherein excessive consumption of tramadol, significant increase in CPK and acute renal failure" in which a young 19-year-old consumed 4000 mg of tramadol to commit suicide. Frequent seizures and miosis were seen. Dramatic rise was observed in CPK, LDH and creatinine in patient. The following days by prescribing fluids, NaHCO<sub>3</sub> and Chlordiazepoxide and disease management, was patient discharged without any further complications that were consistent with the findings in our study [29].

## CONCLUSIONS

Due to tramadol intoxication and abuse that leads to seizure and sometimes death and the maximum intoxication tends to occur in relatively younger ages to commit suicide, the importance to raise youth awareness, suicide prevention methods and create restriction of access and distributing this drug, particularly at young age is undeniable. Hence, additional researches are important to study the behavioral social mental health of patients.

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