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Investigating the frequency of seizures in patients with tramadol poisoning referred to Shahid Rahimi hospital in Khorramabad from March 2018 to March 2019

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Abstract

Background: *Tramadol is an opioid-like analgesic which causes most of drug poisonings in Iran. Considering that one of the most dangerous side effects of tramadol poisoning is seizures, the aim of this study was to investigate the frequency of seizures in patients with tramadol poisoning from March 2018 to March 2019 in Shahid Rahimi hospital in Khorramabad.*

Methods: *This cross-sectional descriptive study was performed with the retrospective review method in Shahid Rahimi hospital in Khorramabad from March 2018 to March 2019. The files of all patients referred to the emergency room and inpatient ward were examined by a questionnaire in terms of (age, gender, history of primary epilepsy, seizures, clinical signs, amount of drug used to depend on the number of tablets, previous history of tramadol consumption and tramadol poisoning,), then data were collected and analyzed by SPSS-16 software.*

Results: *Out of 123 patients, 56 (50/45%) patients had seizures which in 45(60/36%) patients, intentional use and motivation to commit suicide was reported. In this study, women were 28 people (22.80%). The average age of the patients was 22.97 ± 4.92. The youngest patient was 16 years old, and the oldest patient was 37 years old. The average of the drug used by the patients was 1500 mg and the minimum dose was 50 mg, and the maximum dose was 6000 mg.*

Conclusion: *Seizures in tramadol poisoning is common with primary epilepsy, suicide attempt, drug addiction, acute renal failure, increased creatinine phosphokinase, headache, dizziness, apnea, and intubation.*

Keywords: *seizures, tramadol, poisoning.*

Introduction

Poisonings have always been a major mental health problem in the history of societies, especially among adolescents; every year a large number of people suffer from accidental or intentional poisoning, from mild illness to hospitalization in the intensive care unit and death which imposes a heavy economic burden on oneself, one's family, and community; And the best way to deal with this dilemma is to take precautionary measures (1,3). Any substance that can cause damage or disruption to the body through chemical action is called toxin; These compounds enter the body in various ways such as oral, inhalator and injectable and induce their local and general effects (4). In general, poisonings are divided into two categories of drug poisoning and non-drug poisoning (5).

Currently, the most common poisoning in Iran is drug poisoning, so that about 25,000 people are poisoned in Tehran every year due to drug and chemical use, and 12,000 of these patients are hospitalized, 1,200 people are transferred to the intensive care unit and at least 120 people die (6). In the meantime, drug poisoning is a very high number of cases of poisoning and one of the most common cases of drug poisoning is tramadol poisoning (7).

Tramadol is one of the most widely used narcotic drugs in the world. It is an analgesic and industrial narcotic drug with central effects and is a sedative which is used for moderate to severe pains such as cancer pain, surgical pain, muscle and joint pain, and more. It is therefore weaker than morphine and pethidine and stronger than ibuprofen and acetaminophen (8-11). Most cases of tramadol poisoning are intentional and are caused by high dose consumption. Increasing the dose of tramadol is not a life-threatening condition by itself, and most deaths from tramadol poisoning are due to concomitant use with several drugs and other substances. On the other hand, long-term use of narcotics can stimulate the destruction of neuronal cells (14-15). Tramadol poisoning causes severe involvement of the nervous system. It causes dizziness, nausea, vomiting, agitation, headache, seizures, and loss of consciousness and eventually leads to coma which leads to hospitalization of about 10 percent of long-term poisoned patients in the intensive care unit (16). Various studies have examined the severity and frequency of clinical complications and signs of tramadol poisoning, but several cases, including intentional use in large numbers, usually with suicidal ideation, along with other medications and the physical condition and health of the consumer is one of the factors involved in the incidence of clinical complications and signs, as well as their severity. Suicidal ideation is one of the most common causes of tramadol poisoning (13). Severe neurological complications include seizures, respiratory arrest, and coma (16). Seizures is an

important cause of death and hospitalization in the intensive care unit (17). Most cases of seizures occur in the first 6 hours of tramadol poisoning (18-19). Due to the frequency of tramadol-related seizures and the fact that tramadol is a cause of seizures even in therapeutic doses, this study aimed to investigate the frequency of seizures in patients with tramadol poisoning at Shahid Rahimi hospital in Khorramabad from March 2018 to March 2019.

Materials and Methods

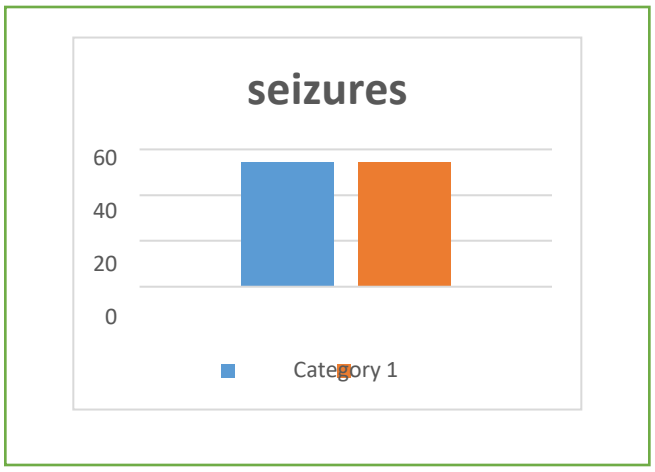
The type of study in this research is cross-sectional and is based on hospital information of patients referred to the emergency ward of Shahid Rahimi hospital in Khorramabad from March 2018 to March 2019. All patients who have knowingly and unknowingly taken tramadol and have referred to the medical educational center of Shahid Rahimi hospital in Khorramabad from March 2018 to March 2019 due to the complications caused by it and have a hospital record, entered the study. All patients in this year were about 153 people who entered this study and the census method was used in accordance with the community and all the files in the hospital were read. The criteria for excluding patients from this study included:1- receiving naloxone drug for treatment and occurrence of seizures after receiving the drug, which was considered as a deprivation syndrome.2-Incomplete information of patients files for any reason.

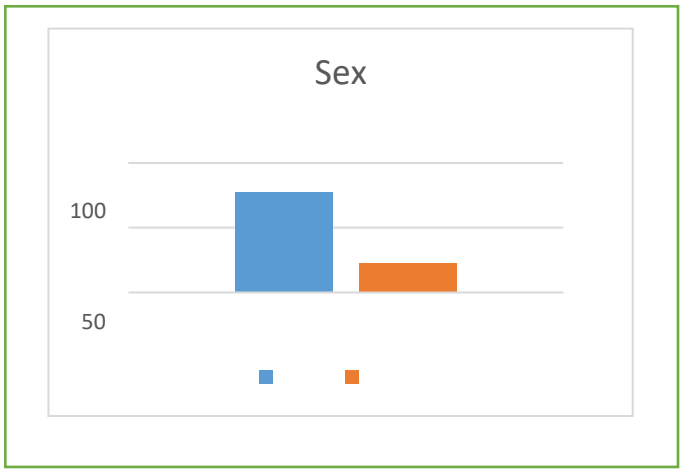
Collecting information was performed through a questionnaire of laboratory variables and the relevant procedures were extracted from the files of all patients and included in the questionnaire of laboratory variables including patient age, gender, seizures before or during hospitalization, duration of onset of symptoms until patients reference to medical centers, and duration of seizures occurrence after tramadol use, number of seizures before reference and the duration of each attack and how each attack occurred, signs accompanying or after seizures including sphincter incontinence or tongue trauma. Patient's signs on admission including headache, dizziness, drowsiness, delirium, ataxia, abdominal pain, apnea, cyanosis, chills, history of previous epilepsy, history of head trauma in the past or present, nausea, vomiting, hypertension, pulse rate on admission, number of tablets used by the patient, history of drug addiction by the patient, drug addiction in the present time, history of previous use of tramadol, level of consciousness determined for the patient by the staff of the treatment staff in the file (including the score listed on the admission form, Patient's history and report of the relevant nurse), history of concomitant use of drugs, including tricyclic antidepressants, antipsychotics, benzodiazepines, serotonin reuptake inhibitors, concomitant use of alcoholic beverages, smoking, renal function indicators including blood

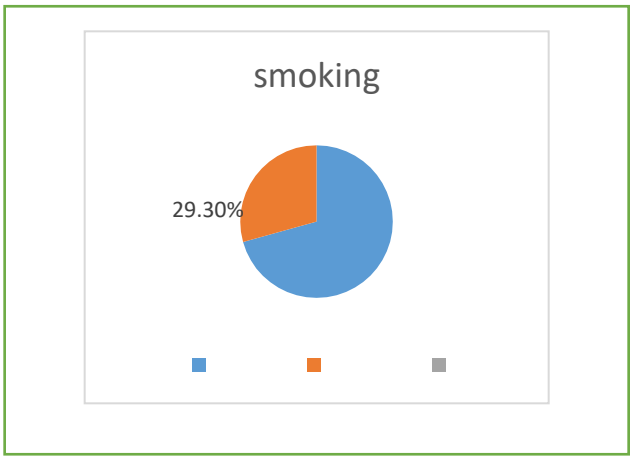
urea nitrogen levels, serum creatinine Serial measurements, Serum bicarbonate level, serum pH, blood oxygen concentration, serum carbon dioxide, urinary output, hemodialysis status of the patient , liver damage indicators including AST and ALT, serum levels of creatinine phosphokinase enzyme, lactate dehydrogenase, blood glucose levels, sodium and calcium levels of the patient on admission ,performing a consult with neurologist for diagnosis and treatment of seizures, performing a consult with psychiatrist to determine the necessary measures in patients suspected of suicide, receive or not receive naloxone on admission for treatment indications and the time of seizures occurrence according to receiving naloxone. The relevant procedures were extracted from the files of all patients and included in the questionnaire. In order to analyze the data, the calculation of frequency, average, standard deviation and statistical tests of Chi-square test, independent T test and Mann-Whitney test were used to investigate the relationship between the variables.

Results

In the present study, 153 patients with tramadol poisoning who had referred to the emergency department of Shahid Rahimi hospital in Khorramabad from March 2018 to March 2019, entered into the study.18 patients were excluded due to receiving naloxone and 12 patients were excluded due to incomplete information in their files and other 123 patients were examined. The average age of the patients was 4.92 ± 22.97 years, with the youngest being 16 years old and the oldest being 37 years old. Of the 123 patients studied, 28 patients were female (22.8) and 95 patients were male (77.2) (Table 1).







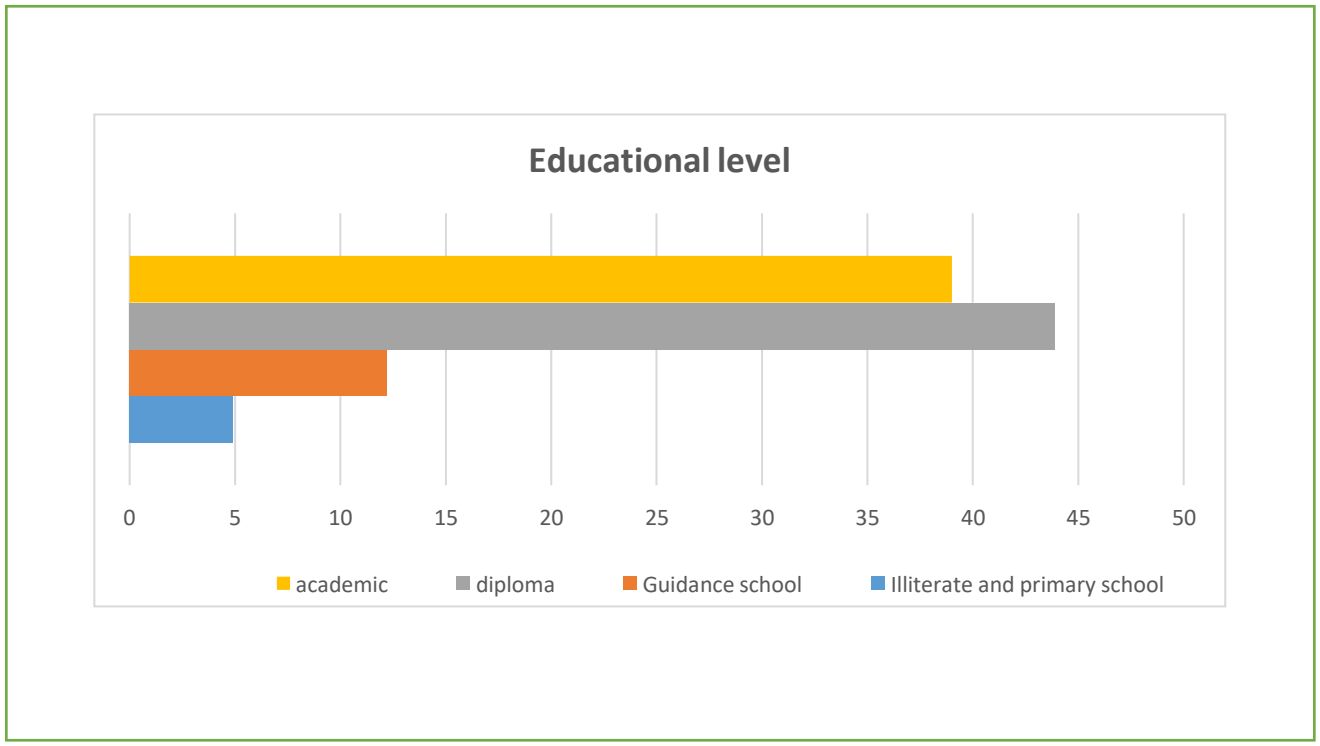


Table (1) Absolute and percentage distribution of the studied units according to the individual and social characteristics of the studied units

p-value	Total frequency	Female	Male	gender seizures
0.235 0	56 (45.5%)	10 (8.1 %)	46 (37.4 %)	positive
	67 (54.5%)	18 (14.6%)	49 (39.8%)	negative
	123 (100%)	28 (22.8%)	95 (77.2%)	Total

Table (2): The frequency of hospitalized patients in Shahid Rahimi hospital in Khorramabad due to tramadol poisoning according to gender and seizures status.

According to the results of this study, out of all patients with seizures, 40 patients (32.5%) had generalized seizures and 8 patients (6.5%) had focal seizures and 7 patients (5.6%) had persistent epileptic seizures and 1 patient (0.8) diagnosed with absence seizures. Based on p= 0.05, there was a significant statistically relationship between seizures and type of attack (Table 3).

p-value	Frequency	Without seizures	absence	Persistent seizures	Focal	Generalized	**Type of seizures**
							seizures
0.05%	**56** **45.5%**	0 0.00%	1 0.8%	7 5.7%	8 6.5%	40 32.5%	**positive**
	67 **54.5%**	65 52.8%	0 0.00%	0 0.00%	2 1.6%	0 0.00%	**negative**
	123 **100%**	65 52.8%	1 0.8%	7 5.7%	10 8.1%	40 32.5%	**Total**

Table 3: The frequency of hospitalized patients in Shahid Rahimi Hospital in Khorramabad due to tramadol poisoning according to the type of seizures and seizures status.

According to the relationship between the time elapsed from drug use and seizures, of the total number of patients with seizures, 18 patients (14.6%) in less than an hour, 27 patients (22%) in the period between 1 to 6 hours, six patients (4.9%) between 6- and 24-hours hours and 5 patients (4.06%) after at least 24 hours were referred to treatment centers. According to P= 0.349, there was a significant relationship between the time elapsed from drug use to referring to the first medical centers and seizures (Table 4).

p-value	Total	After 1 day	Less than 24 hours	Less than6 hours	Less than1 hour	Time of reference to hospital seizures
0.349	56 (45.5 %)	5 4 %	6 4.9 %	27 22 %	18 14.6 %	positive
	67 (54.5 %)	5 4.1 %	15 12.2 %	31 25.2 %	16 13 %	negative
	123 (100 %)	10 8.2 %	21 17.1 %	58 47.2%	34 27.6 %	Total

Table 4: The frequency of hospitalized patients in Shahid Rahimi hospital in Khorramabad due to tramadol poisoning according to the time of reference to hospital and seizures status.

Discussion

The overall goal of this study was to determine the frequency of ss in patients with tramadol poisoning. The use of tramadol in Iran is increasing due to the analgesic and relative agonist effects of the μ receptor and its quasi-narcotic effects, which is due to the low price and accessibility. Currently, patients who complain of tramadol use are monitored in the emergency room for several hours due to the patient's clinical history and concomitant use of other drugs, and then the patient is discharged if there is no seizures and the clinical condition is stable.

In the Marquardt study, 55% of patients were female. While in this study, women made up 22.80% of the study population. The average age of the patients in this study was 22.97 ± 4.92, with the youngest being 16 years old and the oldest being 37 years old; Which is different with the study of Taleborne and his colleagues in Sweden, whose average age was 44 years. On the other hand, it is consistent with Abbasi's

study conducted in Iran and the average age of patients was 23.93 years which indicates an increase in the use of tobacco and tramadol in adolescents and young people in the community, which should be considered as an important issue for adolescent and young health. On the other hand, smoking was positive in 87 patients (70.70%) and only in 17 patients (13.80%) alcohol consumption was chronic and concomitant with tramadol. This study shows the high prevalence of smoking in the study population; However, there was no significant relationship between smoking and ss, as well as alcohol and seizures. There was no relationship between education level and seizures and 54 patients (43.9%) had diploma and 48 patients (39%) had university degree. Also, seizures in this study was 45.5% (56 patients compared to Rashidi et al.'s study, which accounted for 31% of seizures, and Yazdi et al.'s study, which accounted for 25%, and Marquardt's study, which reported 13.7% seizures., Was much more.

However, it was less than the study of Abbasi et al., Which was performed on 150 patients and 69.3% of patients had seizures. In this study the average drug use by patients was calculated to be 1500 mg and the minimum dose used by patients was recorded as 50 mg and the maximum dose of the drug was recorded as 6000 mg. Also in this study, the time elapsed from drug use to the onset of the first seizures attack and reference to hospital was assessed, the highest seizures rate after tramadol poisoning in the first 6 hours was 75.86% (44 patients) and half of this amount (37.9%) occurred less than an hour after taking the drug; In this regard ,it was consistent with the study of Marcos et al., Which was 84.60% in the first 6 hours, as well as the study of Rashidi, which was 98% in the first 6 hours.

According to P = 0.349, there was no significant statistical relationship between the time elapsed from drug use to the onset of the first seizures attack and reference to the hospital.

Conclusion

According to the results of the study, 75% of seizures occur in less than the first 6 hours. Supportive measures such as airway establishment and seizures control can be effective in reducing more serious complications and reducing hospital stay and treatment costs. Also, due to the fact that no minimal embroidery is agreed upon to begin treatment for the effects of poisoning, it is recommended that similar studies be performed at a larger sample size and with monitoring of therapeutic results.

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