Original Article

Bull Emerg Trauma 2024;12(1):2-6.

Bulletin of Emergency And Trauma

Pattern of Traumatic Injuries in Patients with Tramadol Poisoning: A Cross-Sectional Study in a Tertiary Care Hospital

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Received: December 14, 2023
Revised: February 8, 2024
Accepted: March 3, 2024

ABSTRACT

Objective: This study aimed to investigate the incidence and pattern of tramadol-induced seizures and injuries in patients admitted to the hospital.
Methods: The cross-sectional study included 300 patients with alleged tramadol intoxication. Demographic information, tramadol dosage and duration of abuse, co-existing illicit drug abuse, hospital stay length, and occurrence of seizures and trauma (type and site of injuries) were collected. Different statistical tests, including the Mann-Whitney U-test, Pearson's Chi-square test, and Student's t-test, were conducted to compare the patients with and without seizures, trauma, and co-ingestion of illicit drugs. The analysis was performed using SPSS software (version 21.0). A p value of less than 0.05 was considered statistically significant.
Results: The average patient's age was 24.66±5.64 years, with males comprising 84.3% of the sample. The mean tramadol dose and duration of abuse were 1339.3±1310.2 mg and 2.43±1.35 years, respectively. Seizures were observed in 66% of patients, with men having a higher incidence (69.6% vs. 46.8%; p=0.004). Trauma was reported in 23% of patients, accounting for 35.4% of seizure cases. All trauma patients had experienced seizures, with the head and neck being the most prevalent injury sites (55.1%), typically presenting as abrasions (55.9%). Patients with seizures and trauma had an average hospital stay of 1.73±0.94 days, which was significantly longer.
Conclusion: Trauma occurs in more than one-third of tramadol-induced seizures, highlighting the need to perform physical examinations to detect and localize injuries. Tramadol-associated traumas prolonged hospitalization times and thus required prompt attention to prevent further injuries during pre-hospital handling and transferring to hospitals.

Keywords: Poisoning, Seizure, Tramadol, Wounds and injuries.

Please cite this paper as:
Mirakbari SM, Kazemifar AM, Allami A, Barikani A. Pattern of Traumatic Injuries in Patients with Tramadol Poisoning: A Cross-Sectional Study in a Tertiary Care Hospital. *Bull Emerg Trauma*. 2024;12(1):2-6. doi: 10.30476/BEAT.2024.101078.1484.

Introduction

Tramadol is a synthetic narcotic analgesic with both opioid and non-opioid properties. It is often used to treat moderate to severe pain due to its lower risk of causing respiratory depression [1, 2]. The dual analgesic effect of tramadol is achieved through its action as a μ-opioid receptor agonist and its ability to inhibit the uptake of norepinephrine and serotonin [3]. Tramadol has the potential for abuse, particularly in areas where it is easily available, prompting many individuals to seek medical assistance to address opioid addiction [4, 5]. Tramadol poisoning has emerged as a significant concern in Iranian emergency departments, resulting in serious complications, particularly among young men with mental disorders and substance abuse issues [6]. Although tramadol poisoning may not pose an immediate life-threatening risk, it can lead to serious adverse outcomes in affected patients, particularly when seizures occur [7, 8]. Seizures can cause a sudden loss of consciousness, which can lead to traumas due to falls or injuries sustained during patient restraints [7]. The impact of tramadol-induced trauma becomes particularly significant when patients with tramadol intoxication present to the emergency department with initially undiagnosed injuries [8]. More research is required into the various forms of trauma that might occur following seizures in patients admitted with tramadol ingestion. This study aimed to investigate the incidence and patterns of injuries caused by tramadol poisoning among patients who were referred to a tertiary care hospital.

Materials and Methods

A total of 300 patients with tramadol intoxication were included in this cross-sectional study, which was conducted at Bu Ali Hospital (Qazvin, Iran), from 2014 to 2017. Tramadol poisoning was defined as any clinical manifestation caused by tramadol ingestion that prompted the patients or their relatives to seek immediate medical assistance. Patients with incomplete medical records were excluded from the study.

The sample size was determined based on a prevalence of 15%, an α error of 5%, and an accuracy of 5%, resulting in a calculated sample size of 220 participants. Anticipating a 20% loss to follow-up, 300 patients were ultimately enrolled. A convenient sampling method was used to include patients who met the criteria. Following explaining the objectives of the study to eligible patients, written informed consent was obtained from them.

A checklist was utilized to collect the patient's information, which included demographic information, such as age and sex), history and duration of tramadol abuse, alleged dose of ingested tramadol, co-ingestion of other illicit drugs, such as heroin, opium, and methamphetamine, length of hospital stay (LOS), occurrence of seizure and trauma, as well as the site and type of injury.

The collected data was analyzed using SPSS software, version 21.0 (IBM Statistics, Chicago, USA). A comparative analysis was conducted between patients with and without seizures, trauma, and co-ingestion of illicit drugs in relation to their demographic characteristics (sex and age), tramadol ingested dosage, duration of tramadol abuse, and LOS using the Mann-Whitney U-test, Pearson's Chi-square, and Student's t-test. A p value of <0.05 was considered statistically significant.

Results

A total of 300 patients were admitted to hospital with tramadol poisoning. The demographic and clinical characteristics of the patients are summarized in Table 1. The average age of the patients was 24.66±5.64 years, ranging from 14 to 52 years, and 84.3% were men (n=253). The mean LOS was 1.73±0.94 days, with no in-hospital mortality. Out of the total, 44 patients(14.7%) had concurrently abused another illicit drug. The mean tramadol ingested dose was 1339.3±1310.2 mg, and the mean duration of tramadol abuse was 2.43±1.35 years. Patients who used other illicit drugs had a higher mean tramadol ingested dose (p=0.006) and were hospitalized for a longer period (p=0.004).

Table 2 presents the frequency of seizures based on demographic variables (age and sex), tramadol ingested dose, duration of tramadol abuse, and LOS. It shows that 66% of the patients experienced seizures, with men having a higher incidence than women (69.6% vs. 46.8%; p=0.004). Patients with seizures had a higher mean tramadol dose (1524.7±1395.9 vs. 1028.5±1006.6 mg; p=0.002) and a longer LOS (1.81±0.97 vs. 1.57±0.66 days; p=0.02) than those without seizures.

Table 1. Demographic and clinical attributes of the patients with tramadol poisoning

Variables		Patients n (%) N=300
Sex	Male	253 (84.3)
	Female	47 (15.7)
Age		24.66±5.64
Tramadol dose (mg)		1339.3±1310.2
Duration of tramadol abuse (year)		2.43±1.35
Length of hospital stay (day)		1.73±0.94

Table 2. The frequency of seizure based on the demographic variables (age and sex), tramadol ingested dose, duration of tramadol abuse, and length of hospital stay

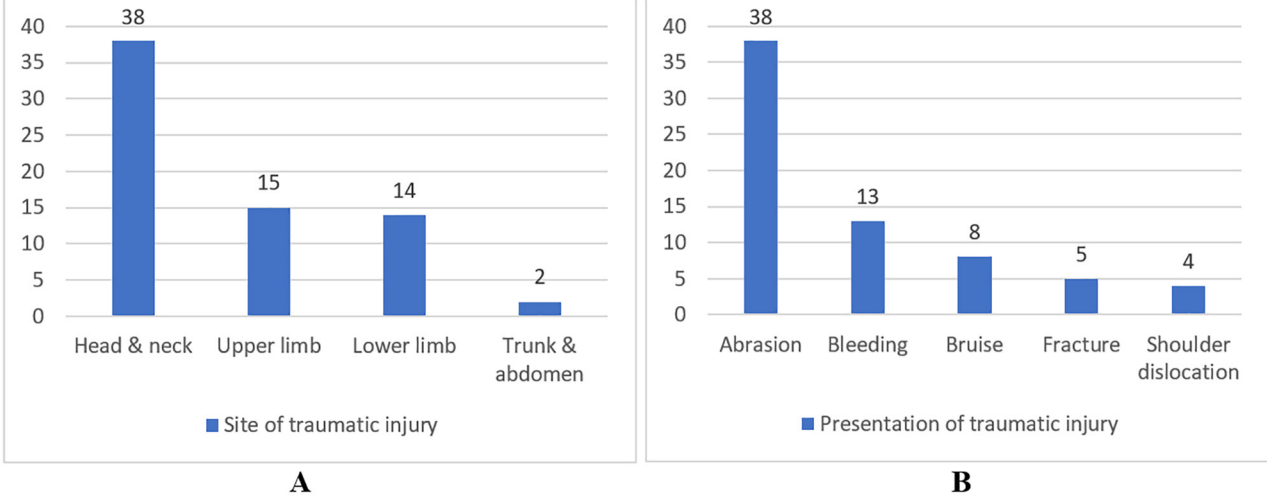
Variables		Seizure		*p* value
		Yes (n=198)	No (n=102)	
Sex	Male	176 (88.9)	77 (75.5)	0.004[a]
	Female	22 (11.1)	25 (24.5)	
Age		24.81±5.44	24.38±6.03	0.532[b]
Tramadol dose (mg)		1482.1±1763.2	1192.7±1413.1	0.002[c]
Duration of tramadol abuse (year)		2.44±1.35	2.41±1.4	0.88[b]
Length of hospital stay (day)		1.81±0.97	1.57±0.66	0.02[b]

[a]Pearson's Chi-square, [b]Independent samples t-test, [c]Mann-Whitney U test

Table 3. The frequency of traumatic Injuries based on the demographic variables (age and sex), tramadol ingested dose, duration of tramadol abuse, and length of hospital stay

Variables		Trauma		*p* value
		Yes (n=70)	No (n=230)	
Sex	Male	59 (84.3)	194 (84.3)	0.861[a]
	Female	11 (15.7)	36 (15.7)	
Age		24.86±5.79	24.61±5.62	0.74[b]
Tramadol dose (mg)		1680.1±1782.5	1302.1±1347.1	0.067[c]
Duration of tramadol abuse (years)		2.69±1.31	2.33±1.37	0.13[b]
Length of hospital stay (day)		2.14±1.26	1.61±0.7	0.001[b]

[a]Pearson's Chi-square, [b]Independent samples t-test, [c]Mann-Whitney U test



A **B**

Fig. 1. Site (A) and presentation (B) of traumatic injury among patients with tramadol poisoning and incidence of trauma

Table 3 outlines the prevalence of traumatic injury based on demographic variables, tramadol ingested dose, duration of tramadol abuse, and LOS. It indicates that 23% of the patients experienced trauma, which accounted for 34.8% of the patients with seizures, all of whom had seizures. As shown in Figure 1, the most common sites of trauma in patients with tramadol poisoning were the head and neck (55.1%), followed by the upper extremities (21.7%), and trunk (20.4%). The most prevalent types of injury were abrasions (55.9%), bleeding (19.1%), and fractures (15.5%). Patients with trauma had a longer LOS than those without (2.14±1.26 vs. 1.61±0.7 days; p=0.001). However, the mean tramadol ingested dose and ingestion duration did not differ between patients with or without trauma (p=0.067 and p=0.13, respectively).

Discussion

The findings of the present study revealed that seizure and trauma were frequent and serious complications of tramadol poisoning, associated with higher tramadol doses and longer duration of abuse, leading to extended LOS. Among the admitted patients with tramadol intoxication, 66% experienced seizures, which outnumbered other opioid toxicities [9]. A review of 51 articles with a total sample size of 101,770 patients reported that seizures occurred in 30% to 52.5% of tramadol abusers [10], which was similar to the findings of the present study. The pooled incidence (17%) reported in this meta-analysis was lower than that of the present study, most likely due to the inclusion of therapeutic doses, while our study focused only

on drug poisoning.

The present study also found trauma in 23% of admitted tramadol cases, with all traumatic cases associated with seizure occurrences. More than one-third (35.4%) of seizure cases in the present study resulted in traumatic injury. Tramadol-intoxicated patients experienced generalized tonic-clonic seizures without any warning, which resulted in falls and subsequent injuries [11].

A cohort study on seizure-related traumas in adult and pediatric patients with epilepsy (age ≥ 7 years) indicated that out of 200 patients, 86 individuals (43% of the group) suffered injuries while experiencing their typical seizures [12]. The inclusion of children with epilepsy in this study may contribute to a higher incidence of trauma in seizure events. Willems *et al.* investigated 292 adult patients with epilepsy (range 18-86 years) and found that 14.0% suffered from epilepsy-related injuries [13].

Regarding the effect of dose on seizures, the findings of the present study indicated that the mean tramadol dose was higher in patients who experienced seizures. The effect of tramadol dose on the incidence of seizures was controversial. Some studies suggested that seizures were dose-dependent and more frequent in higher doses, especially those with recurrent seizures who had consumed double doses than those with single seizures [14, 15], while others suggested that seizures might occur at any dose, even at therapeutic doses or minor overdose [16, 17].

The present study showed a higher incidence of tramadol poisoning in men. A meta-analysis of 18 studies also showed a pooled odds ratio of 2.24 for seizure incidence in men [10], which was in line with the results of the present study. This is while other Iranian studies have rejected the association of seizure with the age or sex of the patients [16-18]. The study on the U.S.A. registry also showed no association between age and seizure after tramadol poisoning [19]. These results were inconsistent with the results of the present study. This difference might be related to the difference in other factors, which could influence the incidence of seizures in patients with tramadol poisoning, such as having a history of epilepsy or having more than one episode of seizure [20]. In the current study, the mean duration of tramadol abuse was 2.43 years, higher in those who had seizures. Furthermore, patients, who used concurrently other illicit drugs, consumed higher doses of tramadol and abused it for a longer period of time. Others have also reported that patients with tramadol poisoning also ingested benzodiazepines, naloxone, and illicit agents (opium, heroin, and cannabis) in patients with tramadol poisoning [9, 16]. Medical comorbidities and concomitant use of proconvulsant serotonergic cytochrome P-450 inhibitors were identified as risk factors for serotonin toxicity and seizures [21].

According to the findings of the present study, trauma was another important injury that was observed after tramadol poisoning. As provided in the results, about one-fourth (23%) of the admitted patients had trauma after tramadol poisoning, mainly in the head and neck, and upper and lower extremities. In a study by Farajidana *et al.,* 24.6% of patients had trauma to the face, shoulder, head, trunk, and upper extremities. Trauma is considered an important consequence, especially in the head and neck, which might worsen patients with loss of consciousness and unrecognized injuries [7].

The present study recommended a physical examination to determine the type and site of injuries, as many injuries would be mild and may remain undetected. Tramadol-associated trauma complicates patients with prolonged hospitalization and requires prompt detection to prevent further injuries during patients' pre-hospital handling and transfer to the hospital. It is essential to weigh the risk-benefit ratio of using tramadol for pain management and consider alternative therapies in vulnerable individuals. Caution must be exercised when prescribing opioid medications to patients, as these drugs have the potential to induce side effects such as seizures or prolonged QTc intervals [22].

The present study had several strengths. First, the findings of this study provided valuable insights into the types and severity of injuries associated with tramadol-related admissions, allowing healthcare professionals to better identify and manage these cases. Second, the key strength of this study was its large sample size. Several limitations required to be noted regarding the present study. The responses relating to co-existing illicit drug abuse were subjective and thus prone to recall bias. This study provided no report of mortality because it lacked pre-hospital and post-discharge follow-up mortality statistics.

Declaration

Ethics approval and consent to participate: The protocol of the study was approved by the Ethics Committee of Qazvin University of Medical Sciences (code: IR.QUMS.REC.1397.286).

Consent for publication: The authors expressed their consent to the publication of this article.

Conflict of Interest: The authors declared no conflict of interest.

Funding: None.

Authors' Contribution: Study concept, study design, and supervision: SM. M.; acquisition of data: SM. M., AM. K.; analysis and interpretation of data, drafting of the manuscript, technical and material support: SM. M, A. A., A. B.

Acknowledgments: The authors acknowledge Iman Ashoorzadeh for assisting the research team, as well as the staff and nurses of the Emergency Department of Bu Ali Hospital, in Qazvin province, who assisted us in conducting the study.

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