BRIEF REPERT

Prevalence of Tramadol Consumption in First Seizure Patients; a One-Year Cross-sectional Study

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Abstract

Introduction: Previous studies have shown that there is a probability of seizure even with therapeutic doses of tramadol. Yet, no accurate data exist regarding this problem in Iran. Therefore, the present study aimed to evaluate the prevalence of tramadol consumption in patients with first seizure referred to the emergency department (ED). **Methods:** In the present retrospective one-year cross-sectional study, all patients who were referred to the ED of Poursina Hospital, Rasht, Iran, with the complaint of first seizure were evaluated. Demographic data and data regarding history of tramadol consumption, duration, total dose, last dose, and time passed from the last dose of consumption were recorded and analyzed regarding the study questions using SPSS 20. **Results:** 383 (68.9%) out of the 556 patients referred to the ED, were experiencing their first seizure (mean age 26.43 ± 6.48 years; 70.5% male). 84 (21.9%) patients had recently used tramadol. History of seizure in the family of tramadol consumers was significantly lower (3.6% compared to 11%; $p = 0.036$). Mean total tramadol consumption dose in the last 24 hours was 140.17 ± 73.53 mg (range: 50-300 mg). Duration of tramadol consumption was less than 10 days in 84.5% (df: 2; $\chi^2 = 96.1$; $p < 0.001$). In addition, 62 (73.8%) patients had seizure within 6 hours of consumption (df: 3; $\chi^2 = 29.5$; $p < 0.001$). **Conclusion:** Results of the present study showed that 21.9% of the patients with first seizure had a history of tramadol consumption. Seizure following tramadol consumption is more prevalent in the initial 10 days and within 6 hours of consumption. In addition, it seems that lower doses of tramadol may also induce seizure.

Key words: Seizures; tramadol; prevalence; epidemiology

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Introduction:

Tramadol is an opioid used for treating moderate to severe pain. It has been legally used for pain management since 1980 in some countries, and has been approved by food and drug administration of Iran since 2003. This drug is addictive and may be abused by the youth. Nausea, vomiting, central nervous system depression, tachycardia, cardiorespiratory arrest, and seizure are among the side effects of tramadol poisoning. However, there are reports that indicate the probability of seizure induction even with therapeutic doses of this drug (1-5). Tramadol abuse is increasing in Iran, (2, 6) and seizure is possible among abusers. Therefore, the present study aimed to evaluate the prevalence of tramadol abuse in patients with first seizure, who were referred to the emergency department (ED).

Methods:

In the present retrospective cross-sectional one-year study, all first seizure patients referred to the ED of Poursina Hospital, Rasht, Iran, during 2012 were evaluated. For each patient, data regarding age, sex, history of seizure in family, recent history of tramadol consumption, duration (days), total dose, last dose, and time passed from the last dose of consumption were recorded using a checklist. Data were then analyzed using SPSS 20.0. Quantitative data were reported as mean ± SD and qualitative ones as frequency and percentage. The groups with and without recent tramadol consumption were compared using independent t-test for quantitative variables and chi square or Fisher's exact test for qualitative ones. In addition, multinomial logistic regression test was used to evaluate distribution of the patients in groups regarding age, sex, duration of consumption, consumed dose in the last 24 hours, and time passed from the last dose of tramadol consumption. In all analyses, $p < 0.05$ was considered as significance level. This study

was approved by the Ethics Committee of Guilan University of Medical Sciences. The researchers adhered to the principles of Helsinki declaration.

Results:

383 (68.9%) out of the 556 patients who were referred to the ED with chief complaint of seizure throughout the course of the study, were experiencing their first seizure. Mean age of first seizure patients was 26.43 ± 6.48 years (range: 16-55 years; 70.5% male). 84 (21.9%) patients out of the 383 first seizures had recent history of tramadol consumption. 69 (82.1%) of tramadol consumers and 201 (67.2%) of other patients were male (p = 0.005). 48.8% of the tramadol consuming patients and 59.9% of other patients were 20-30 years old (p = 0.016). History of seizure in the family of tramadol consumers was significantly lower (3.6% compared to 11%; p = 0.036). Table 1 shows baseline characteristics of the tramadol consumers. Mean total tramadol consumption dose in the last 24 hours was 140.17 ± 73.53 mg (range: 50-300 mg). Duration of consumption was less than 10 days in 84.5% of the patients, 11-20 days in 10.7%, and more than 20 days in 4.8%. Incidence of seizure following ingestion was higher in patients who had recently started consumption (df: 2; $\chi^2 = 96.1$; $p < 0.001$). Yet, no correlation was detected between tramadol dosage and seizure incidence (df: 3; $\chi 2 = 1.2$; $p = 0.1$). Seizure had occurred within 6 hours of consumption in 62 (73.8%) patients (df: 3; $\chi^2 = 29.5$; $p < 0.001$).

Discussion:

Findings of the present study showed that 68.9% of the patients referred to Poursina Hospital, Rasht, Iran, were experiencing their first seizure, 21.9% of which had recent history of tramadol consumption. Seizure following tramadol consumption was more prevalent in the initial 10 days and within 6 hours of consumption. Previous studies show that about 86% of neurologic side effects manifest within 6 hours of consumption (7, 8). The present study showed that 73.8% of seizures due to tramadol consumption also happened in this time. Based on the existing standards, to prevent side effects such as seizure, daily dose of tramadol should not exceed 400 mg (1, 2, 9). In this cross-section, mean total tramadol consumption dose in 24 hours was 140.17 ± 73.53 mg. In a study by Shadnia et al. (2), this dose was 1650 mg while, in a study by Pedramfar et al. (5), total dose in the 12 hours pre-seizure was 363.2 ± 303.1 mg (50 -1500). Mean consumption dose in the participants of this study was significantly lower than the mentioned studies. This may be due to the patients not revealing their real consumption dose, genetic differences in the studied populations, different pharmaceutical companies making the drugs and other unknown reasons. Therefore, we should note that tramadol might also be able to induce seizure in lower doses. One of the limitations of this study was being retrospective, which led to limited access to some

Table 1: Baseline characteristics of tramadol consuming patients

Characteristics	Number (%)	P value
Sex		
Male	69 (82.1)	ref
Female	15 (17.9)	<0.001
Age (Year)		
< 20	19 (22.7)	0.006
20-30	41 (48.8)	ref
31-40	18 (21.4)	0.004
> 40	6 (7.1)	<0.001
Consumption duration (Day)		
< 10	71 (84.5)	ref
11-20	9 (10.7)	<0.001
> 20	4 (4.8)	<0.001
Dose in the last 24 hours (mg)		
50	16 (19.0)	ref
50-100	27 (32.1)	0.1
100-200	29 (34.5)	0.06
> 200	12 (14.3)	0.45
Time passed since the last dose (Hour)		
< 3 hours	32 (38.1)	ref
3-6 hours	30 (35.7)	0.8
6-12 hours	18 (21.4)	0.049
> 12 hours	4 (4.8)	<0.001

of the required data. Moreover, serum tramadol level was not evaluated and therefore its correlation with seizure incidence could not be determined.

Conclusion:

Results of the present study showed that 21.9% of the patients with first seizure had a history of tramadol consumption. Seizure following tramadol consumption is more prevalent in the initial 10 days and within 6 hours of consumption. Although the maximum recommended therapeutic dose of tramadol is 400 mg/day, mean consumption dose among the participants of this study was 140.17 ± 53.73 mg. Therefore, we might be able to conclude that lower doses of tramadol may also induce seizure.

Conflict of interest:

None

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Authors' contributions:

All authors passed four criteria for authorship contribution based on recommendations of the International Committee of Medical Journal Editors.

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