Original Article

Respiratory Apnea in Patients with Acute Poisoning by Tramadol (Two Years Study)

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ABSTRACT

Background: Tramadol is an analgesic drug being abused today a lot. Excessive ingestion will lead to hazardous complications such as convulsion and occasionally respiratory apnea. The aim of this study based on frequency respiratory apnea in patients with acute tramadol poisoning hospitalized in Farshchian Hospital of Hamadan, Iran from Jan 2014 to Dec 2015.

Methods: All patients with tramadol poisoning who hospitalized and treated at poisoning ward were enrolled into the study. Their demographic data including age, gender, drug ingestion dose, and respiratory apnea leading to taking naloxone or intubation collected and analyzed statistically by SPSS software.

Results: Overall, 350 patients aged between 14 to 68 yr old were investigated. About 75% of them were male and among them, 81.14% had deliberate self-poisoning. 4.86% developed apnea whose average tramadol consumption was 4158.83 mg. In patients who had not apnea, the average tramadol consumption was 122.38 mg, that was statistically significant difference (P<0.001).

Conclusion: Although apnea development frequency in patients with excessive tramadol ingestion is rare, it is significant as a potentially life-threatening risk, occasionally ignored.

Keywords: Apnea, Iran, Poisoning, Tramadol.

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INTRODUCTION

Tramadol ingestion has been one of the main reasons of drug poisoning in Iran during recent years and deliberate self-poisoning has been reported as the major reason [1]. Tramadol is an opioid-like analgesic used for the treatment of moderate to severe pains. At the first glance, the most common and obvious side effects due to tramadol usage or abusement are independent convulsion to this drug [2-6]. However, particularly in cases with excessive ingestion, it leads to bradycardia, apnea, headache, dysphoria, and even coma in addition to convulsion [7-9].

Tramadol can develop convulsion and some other side effects even with pharmaceutical doses, with increase in ingestion, side effects appear more [10, 11]. One of the main complications caused by tramadol poisoning is apnea. Despite, vast majority of specialists' belief, tramadol can cause apnea and consequently death [12]. The main reason of death in patients with more than 5 gr tramadol ingestion is cardiorespiratory arrest. This study aimed to investigate the frequency of respiratory apnea due to tramadol ingestion and take special notice to this life-threatening side effect frequently ignored by medical doctors compared with more common disorders like convulsion easily treated by enough doses of naloxone or tracheal intubation. Therefore, it is required to pay more attention to it than past.

MATERIALS AND METHODS

In this prospective cross-sectional study, all patients purely poisoned by tramadol, hospitalized at poisoning ward of Farshchian Hospital in Hamadan, Iran, from Jan 2014 to Dec 2015 were included.

Ethics Committee of Hamadan University of Medical Sciences approved the study. Informed consent was taken from the patients.

Demographic data including age, gender, poisoning sort (intentional and unintentional), drug ingestion dose and respiratory apnea leading to

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taking naloxone or intubation was registered. Based on the exclusion criteria, all patients with history or evidence of respiratory diseases or those taken any other drug in addition to tramadol were eliminated.

The collected data were analyzed by SPSS software (ver. 16, Chicago, IL, USA), Mann-Whitney, Chi-square, and *t*-tests. The *P*-value <0.05 was considered statistically significant.

RESULTS

Overall, 350 patients referred to Farshchian Hospital during 2014-2015 and were qualified to enter into the study. The mean age was 25.53 yr with the mean ingestion dose of 1365 mg. Results of statistical tests of Shapiro-Wilk W and Shapiro - Francia demonstrated that age and the mean dose of ingestion variables did not follow the normal distribution, therefore non-parametric tests were used to examine the assumption. 75.14% of patients (263 patients) were male. Totally, 284 patients (81.14%) had deliberate self-poisoning and 66 patients (18.86%) had taken it unintentionally. Eventually, 17 patients (4.86%) developed apnea. The Chi-square test results showed that apnea development in both genders was the same and this difference was not statistically significant (Table 1).

Table 1. Apnea development frequency based on to gender.

	Apnea			
Gender	**No**	**Yes**	**Total**	***P*-value**
Male	253 (96.20)	10(3.80)	263	
Female	80 (91.95)	7 (8.05)	87	
Total	**333 (95.14)**	**17(4.86)**	**350 (100)**	**0.11**

The mean age of patients who developed apnea was 32.48 yr and patients without apnea development were 25.18 yr; so Mann-Whitney test demonstrated that this difference was statistically significant. In other words, apnea development was more among patients with higher mean age. The most frequency was observed in 20-30 yr-old patients which were statistically significant (*P* <0.05) (Table 2).

Table 2. Apnea development frequency according to age group.

Age group (yr)	*Apnea*	
	No	**Yes**
14-20	72 (21.62)	2 (11.76)
20-30	131 (39.34)	6 (35.29)
30-40	117 (35.14)	4 (23.53)
40<	13 (3.90)	5 (29.41)
Total	**333**	**17**

The mean dose of tramadol ingestion among patients who developed apnea was 4158.83 mg, however, among patients without apnea development was 1222.38 mg. The Mann-Whitney test turned out that this difference was statistically significant (*P*=0.00001) (Table 3).

Table 3. The comparison of the mean dose of ingested tramadol in patients with and without apnea development.

Side effects	*Mean*	*SD*	*P*-value
Without apnea	1222.38	736.59	
With apnea	**1307.69**	**4158.83**	**0.00001**

Among patients with apnea development, 4 people (23.52%) were required to take intubation and others were treated by naloxone. Eventually, only one patient (0.29%) died due to tramadol poisoning during the two-yr study.

DISCUSSION

A number of patients developed apnea. The mean age of under-studying patients was 25.53 yr, which demonstrate young people are more in danger of developing tramadol poisoning. In a study, the mean age of patients was 22.5 yr [13] and 23.29 in another study [14]. About 80% of people referred to drugstores to get tramadol were under 18 yr old [15].

In the current study, most patients were male [14,15]. The risk of tramadol poisoning is more among males rather than females, which may be due to easier access to tramadol by males or less report of its ingestion among females since it is considered unacceptable [16]. Ten male and 7 female patients developed apnea that no statistically significant difference was observed from gender aspect. In this study, most patients had deliberate self-poisoning and the other patients had claimed their ingestion unintentional. Deliberate self-poisoning was more than our study's statistics [13].

Current study demonstrated that 17 patients (4.86%) out of 350 under-studying patients developed apnea. Four patients were treated by intubation and 13 patients by naloxone injection. Only nine patients (3.6%) out of 525 poisoned patients due to tramadol ingestion developed apnea [12] whose results went well with our study that demonstrates the scarcity of this disorder. The mean tramadol ingestion dose in patients with apnea development was more than patients not developed that disorder. The mean tramadol ingestion dose among those patients developed apnea was 4158.83 mg and among those without apnea, development

was 1222.38 mg. This difference was statistically significant. The mean tramadol ingestion dose has been 2500 mg in patients with apnea development and 1000 mg in patients who did not develop apnea [17] and in our study, the mean ingestion dose was 4000 mg among those who developed apnea and 1200 mg for those who did not. The mean tramadol ingestion dose in males was 1434.23 mg and in females was 115.75 mg that was statistically significant. The mean ingestion dose in males and females were reported 2413 and 1706 mg, respectively, which went well with our study's results [5]. During two-yr study, only one patient (0.29%) out of completely poisoned patients died eventually which was less than some other studies [18-20].

CONCLUSION

Although respiratory apnea is less frequent compared with other more common disorders due to excessive tramadol ingestion; it has been the potentially life-threatening risk. Due to vast majority of specialists' recommendation, so as not to prescribe naloxone to prevent probable convulsion, this significant issue can be ignored and the result in irremediable implications for the patients. Therefore, specialists must not ignore it.

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