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The Effect of Tramadol Addiction on Convulsion and Related Factors

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Abstract

Background: *Tramadol is a drug used to control severe pain. Various side effects of this drug have been reported, one of the most important is seizures. The exact cause of tramadol-induced seizures is not known. The aim of this study was to investigate the effect of tramadol addiction on convulsion and related factors in 2018.*

Methods: *This cross-sectional study was performed on 216 patients with convulsion referred to Imam Hossain hospital of Shahroud in 2018. After reviewing and stabilizing vital signs, a questionnaire containing demographic information, medical history, medication use (especially tramadol), and drugs was completed by patients. The association between recurrent convulsion and predictors were assessed using multivariable logistic regression. Data were analyzed and compared using SPSS statistical software, version 16 and related statistical tests. The significant level was set at 0.05.*

Results: *In this study from 216 participants, 154 (71.3%) of them were male and the rest were female. The mean age of the all patients was 44.8±18.2 years (17-72 years) that was no significant difference between the two groups. Recurrent convulsion was significantly associated with history of opium use (Pvalue<0.032) and tramadol using (Pvalue<0.001) and there was no significant relationship with other variables. Tramadol using cans double your chances of having a recurrent convulsion [OR=2(95% CI: 1.752–2.689)].*

Conclusions: *The results of this study showed that taking tramadol in opium users can increase the incidence of recurrent convulsion, but more research is needed to fully confirm this.*

Keywords: Tramadol, Convulsion, Side effects
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Introduction

Tramadol is a painkiller with morphine-like properties and is used to control moderate to severe pain. It is used to treat relatively severe acute and chronic pain, can be used at different ages and in both sexes, and due to its pleasant properties, most of the required dose is used.[1,2] It has also been used as a viable alternative to drugs.[3] It is based on the replication of the molecular structure of narcissus, which is one of the alkaloids of opium. It is a central painkiller but is not chemically similar to opium compounds.[4] The mechanism of action is not fully understood, but it is likely to bind to opioid receptors and inhibit the reuptake of norepinephrine and serotonin reuptake.[4-5] The antidepressant effect of tramadol is one-tenth of that of morphine. Oral absorption of the drug is rapid and almost complete, but its bioavailability is 75%. It is mainly excreted by the liver and excreted by the kidneys (30% unchanged and 60% as metabolites).[6-8] The drug is available in various forms of tablets, capsules, drops, suppositories, and injections, but its oral form is more commonly used in humans. Severe pain in orthopedic, gynecological, burns, and chronic and incurable diseases, including cancers, is a good platform for the use of this drug and is added to its daily use.[9-10] Due to the lack of serious control over the use of this drug on the one hand and its pleasant, sedative, and accessible properties, it has been significantly abused by patients, especially addicts, and due to its uncontrolled use, the side effects of the drug it is noticeable.[11-12] The side effects of the drug are many and varied, with a long list, including general fatigue and weakness, dilation of blood vessels, anxiety, dizziness, balance disorders, nervous conditions, sleep disorders, abdominal pain, anorexia, increased bowel or constipation, skin rash, visual disturbances, frequent urination and seizures are the most important. These are the drugs,[12-14] but the most important is drug dependence (methadone addiction) and seizures. The severity of seizures in tramadol users is not exactly known, but various studies have reported between 3 and 10% in different places and in different communities.[15] The most common type of seizure seen in professional tramadol users is the generalized type and it's tonic-colonic, which is sometimes very long and dangerous and will cause irreversible side effects.[10] Tramadol-induced seizures are usually generalized and tonic-colonic, with the whole body contracting, cyanosis, biting the tongue, mydriasis, tachycardia, high blood pressure, and then jumping in different parts of the body.[10-12] The whole convulsion lasts one minute and then the post-ictal phase begins.[13] Because the use of this drug is very common, especially as an addictive substance in the community and especially among young people, and due to the lack of accurate statistics on the incidence of seizures and other important and dangerous side effects of the drug in tramadol users, the aim of this study was to investigate the effect of tramadol addiction on convulsion and related factors in patients referred to Imam Hossain hospital in Shahroud in 2018.

Materials and Methods

This cross-sectional study was performed on all patients with the first seizure who referred to Imam Hossain hospital in

Shahroud between January and December 2018, who were satisfied with participating in the above plan.

In this study, eligible patients were selected by simple census method to complete the sample size, based on having or not having a history of tramadol using, they were divided into exposed and unexposed groups and compared in the study. The exposed group included those who already using or had a history of tramadol using. Tramadol use or positive history of tramadol use means that patient had used one or two tablets or ampoules of tramadol continuously and at least daily for the past six months, and this use had continued until for at least two weeks before the start of the study. The unexposed group was included people without using tramadol in the past six months. Then patients in both groups were asked about clinical and demographic information including age, sex, convulsion times, duration of convulsion, history of specific and long-term drug use, alcohol, and opium use, history of the underlying disease, and educational level and were recorded in a special sheet. Then the patients were monitored for one month and all those who suffered from recurrent seizures during this period. The relationship between recurrent convulsion and history of using tramadol and all other predictors including Moore's factors were assessed using a multivariable regression model.

Descriptive statistics including mean and standard deviation, as well as relative frequency were used to describe the data. To examine the relationships and comparisons between the two groups, was used the chi-square test and multivariate logistic regression were used to evaluate the odds of each of the variables. All analyzes were performed using SPSS software version 16 and the significant level was set at 0.05. Sample size using Epi info 7.2 at a significant level of 5% and a power of 80%, equal to 108 people in each group and a total of 216 people.

This study has an ethics code number (IR.SHMU.REC.1397.166) from the research deputy of Shahroud university of medical sciences. The essential information and the objectives of the study were explained to the patients, and written consent was obtained for participation in the plan.

Results

In this study from 216 participants (those who have seizures for the first time), 154 (71.3%) of them were male and the rest were female. The mean age of all patients was 44.8±18.2 years (17-72 years) that was no significant difference between the two groups. The mean BMI of all patients was 24.1±3.5 kg/m^2 that there was no significant difference between the two groups. Also in the tramadol group the average time for using tramadol was 14.15±8.28 months and the average dosage tramadol used was 37.25±29.75 mg/day. The demographic, clinical, and laboratory data of the two groups are listed in table 1.

In this study, independent variables related to convulsion were investigated in multivariate regression model. As shown in table 2, recurrent convulsion as a dichotomous response variable was significantly associated with a history of opium use (Pvalue<0.032) and tramadol use (Pvalue<0.001) and there was no significant relationship with other variables. The results of this study also showed that using tramadol can double the chances of convulsion [OR=2(95% CI: 1.752–2.689)]. The results of the multivariate logistic regression model are presented in table 2.

Table 1. The demographic, clinical and lab information of patients with convulsion in beginning of study

Demographic & clinical information	Tramadol used group Mean±SD/Number (%)	No tramadol used group Mean±SD/Number (%)	Total Mean±SD/Number (%)	Pvalue
Age (year)	46.3±20.9	42.9±17.3	44.8±18.2	0.088
Age category				
– < 20 years	14(12.9)	12(11.0)	26(12.0)	
– 20- 40 years	22(20.4)	25(23.2)	47(21.7)	
– 40-60 years	47(43.5)	46(42.6)	93(43.1)	0.095
– > 60 years	25(23.2)	25(23.2)	50(23.2)	
Sex				
– Male	74(68.5)	80(74.1)	154(71.3)	0.059
– Female	34(31.5)	28(25.9)	62(28.7)	
BMI (kg/m^2)	24.3±3.5	23.9±3.4	24.1±3.5	0.213
History of sedative use				
– Positive	38(35.2)	35(32.4)	73(33.8)	0.109
– Negative	70(64.8)	73(67.6)	143(66.2)	
History of opium use				
– Positive	21(19.4)	18(16.7)	39(18.1)	0.081
– Negative	87(80.6)	90(85.3)	177(81.9)	
History of alcohol use				
– Positive	11(10.2)	12(11.1)	23(10.6)	0.141
– Negative	97(89.8)	96(88.9)	193(89.4)	
BS (mg/dl)	85.1±18.5	92.8±16.7	88.6±17.3	0.095
Calcium serum (mg/dl)	9.1±1.7	8.8±2.1	8.9±1.9	0.103
BUN (mg/dl)	67.4±25.6	65.9±26.4	66.3±25.9	0. 091
Hemoglobin (g/dl)	12.7±1.9	13.1±2.1	12.9±1.9	0.184
EKG				
– Normal	94(87.1)	97(89.8)	191(88.4)	0.092
– Abnormal	14(12.9)	11(10.2)	25(11.6)	

Table 2. Relationship between independent variables with recurrent convulsion in multivariate logistic regression model

Independent variables	Odds ratio	95% Confidence	Pvalue
Age category (year)			
– <20	1.000		
– 20 to 40	1.016	0.085-1.142	0.093
– 40 to 60	1.077	0.088-1.238	0.075
– >60	1.161	0.091-1.351	0.053
Sex			
– Female	1.000		
– Male	1.125	0.815-1.213	0.069
Body mass index (kg/m^2)			
– 18-25	1.000		
– <18	1.323	0.996-1.385	0.059
– >25	0.881	0.612-1.105	0.085
History of sedative use			
– Negative	1.000		
– Positive	1.151	0.871-1.323	0.103
History of opium use			
– Negative	1.000		
– Positive	1.496	1.109-1.842	0.032
History of alcohol use			
– Negative	1.000		
– Positive	1.179	0.891-1.367	0.096
BS(mg/dl)			
– >70	1.000		
– <70	1.289	1.016-1.363	0.071
Calcium serum (mg/dl)			
– >8.5	1.000		
– <8.5	1.228	0.968-1.382	0.079
BUN (mg/dl)			
– <40	1.000		
– >40	1.028	0.857-1.282	0.079
Hemoglobin (g/dl)			
– <11	1.000		
– >11	1.147	0.869-1.377	0.101
EKG			
– Normal	1.000		
– Abnormal	1.081	0.855-1.218	0.088
Tramadol using			
– Negative	1.000		
– Positive	2.089	1.752-2.689	0.001

Discussion

The results of this study showed that taking tramadol could significantly increase the chances of recurrent convulsion (OR=2). It has also been shown that a history of opium use can significantly increase the chances of recurrent convulsion. This finding is fully consistent with the results of Rehni, Sansone, and Talaie and is largely consistent with the findings of Afshari and Katz.[16-20]

Complications of medications, especially tramadol, are one of the major problems for all people in Iran and other developing countries. Identifying the cause and amount of consumption is very important and vital and is the key to treating this problem. Due to the variety of causes, it is important to know the dangerous side effects of controlling the disease.[21-22]

Tramadol is one of the most widely used addictive drugs in developing countries and one of the most important etiological factors of drug abuse in Iran, especially among young people.[23]

In the present study, it was found that in patients with seizures, addiction to sedatives with 33.8% and then opium addiction with 18.1%, the use of these drugs was much higher in patients of tramadol group. This is somewhat different from the results of Thundiyil study, which found that opium and alcohol use were the most common in patients with convulsion.[24] The reason for this difference may be related to the choice of study groups, sample size, geographical area, social and cultural status and time of patients' visit to medical centers, but by studying other researchers such as Moreno-Izco and Jovanović-Cupić is quite compatible.[25-26]

The results of this study also showed that a history of opium significant, which may be due to inexperience and excessive tramadol use by adolescents. Although these findings are different from studies conducted in European countries, they are in good agreement with studies conducted in developing countries.[29-30]

Because taking tramadol can play a role in many problems, especially seizures, and this disorder is the cause of a chronic and debilitating disease, we expect to see a reduction in these problems with timely control.[31] Therefore, information about the incidence of tramadol-induced seizures, sources and methods of occurrence and exacerbation of risk factors for tramadol-induced complications,[32] control and management of drug use among patients and especially young people are important and due to the abundance and availability Tramadol,

more extensive studies and the use of stronger and more consistent rules to control the use of this drug, especially in Iran, can be considered.[33-34]

The results of this study showed that taking tramadol can increase the incidence of recurrent convulsion and this increase will increase more in opium users. But more research is needed to fully confirm this. Therefore, all patients with convulsion, especially recurrent convulsion, and young people should be screened for tramadol using and, if identified, monitored as soon as possible.

One of the limitations of the present study is the type of study (cross-sectional) which can limit the possibility of examining all the factors affecting the occurrence of seizures in tramadol consumers and also the patients' self-expression for taking tramadol.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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