TRAMADOL BLOOD LEVEL AND PREDICTION OF SEIZURES IN PATIENTS WITH ACUTE TRAMADOL POISONING

BY

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ABSTRACT

Tramadol is a centrally acting synthetic opioid that is widely used for its analgesic effect. Tramadol abuse is increasing in Egypt, and seizure is possible among abusers. Hence, the aim of this study was to evaluate the characteristics of acute tramadol overdosed patients and the possibility of prediction of seizures among them. Fifty participants were recruited from acutely intoxicated tramadol patients admitted to the Poison Control Center (Emergency Hospital, Tanta University) between January, 2014 and December, 2015. For each patient history, clinical data and tramadol blood level as well as urine screen were recorded. The study showed a significant difference between different groups of age, gender, tramadol dose and period of hospital stay. The majority of cases were males, between 15 and 25 years-old, who ingested a dose ranging from 1000 to 3000 mg and stayed for less than 10 hours in the hospital. The occurrence of seizures was higher among patients exposed to a tramadol dose more than 1000 mg, those who developed hyper-reflexia and those with higher blood tramadol levels. At a cut off value >600 ng/ml, blood tramadol level had a sensitivity of 73.91%, a specificity of 74.91%, positive predictive value of 70.83% and negative predictive value of 76.92%. It could be concluded that hyper-reflexia, the amount of tramadol taken and tramadol blood concentration could be used to predict the development of seizures among tramadol overdosed patients.

Keywords: *Tramadol overdose, seizure, blood level, prognosis.*

INTRODUCTION

Tramadol is a centrally acting synthetic opioid analgesic that is widely used, and it is generally considered to be safe. The drug is generally used in moderate to severe acute and chronic pain. Its mode of action is not completely understood, but it has been postulated that tramadol achieves its analgesic activity via activation of mu opioid receptors and inhibition of norepinephrine and serotonin reuptake. Effects on G protein-coupled receptor signaling, monoamine transporters and ion

channels have been speculated (Modi et al., 2013; Minami et al., 2015).

Easy and wide availability of tramadol as an analgesic could be a basic factor of its widespread use and abuse. Tramadol rarely causes respiratory depression or physical dependence compared to other opioids. Also, its presumed role in treatment of premature ejaculation may be a major cause of increased use among youth seeking its positive impact on sexual performance (Preston et al., 1991; Houmes et al., 1992).

Tramadol intake is usually associated with nausea, dizziness, sedation, miosis, dry mouth and sweating. Respiratory depression has been observed in a small percentage of patients after intravenous tramadol administration, whereas tolerance and physical dependence can only be anticipated after long-term treatment (Leppert, 2009). Tramadol overdose has been associated with an increased rate of seizures (up to 35%), which could be associated with several complications such as rhabdomyolysis and lactic acidosis (Taghaddosinejad et al., 2011). Although incompletely understood, some research work proposed inhibition of gamma-aminobutyric acid (GABA) receptors as a possible mechanism for tramadol-induced seizure (Rehni et al., 2008).

The aim of the current study was to evaluate the characteristics of acute tramadol overdose and the possibility of prediction of seizures by the application of these findings among tramadol overdosed patients admitted to Tanta Poison Control center.

PATIENTS AND METHODS

Ethical consideration:

This study was conducted at Tanta Poison Control Center (Emergency Hospital, Tanta University) between January, 2014 and December, 2015. The study was approved by our local ethics committee. A written informed consent was obtained from each patient on initial admission. All individual information was securely protected and available to investigators only, and all the data were analyzed anonymously.

Patients:

Patients older than 18 years old, diagnosed as isolated acute tramadol overdose based on history of tramadol ingestion, clinical manifestations of tramadol overdose and positive urine tramadol screen test were included in this study. Asymptomatic patients, younger than 18 years old, with past history of epilepsy, structural brain lesion or head trauma and negative urine tramadol screen were excluded from participation in this study. Patients with exposure to other substances in addition to the tramadol were also excluded.

Management protocols:

All patients received the routine treatment including patient standard emergency and supportive care, decontamination and administration of specific antidote (naloxone) when indicated.

A complete clinical profile including the following data was recorded for each patient:

- History: age, sex, habits (smoking, alcohol consumption), dose of tramadol, time elapsed between exposure and admission to the hospital and underlying diseases.
- Examination: neurologic, respiratory, gastrointestinal and cardiovascular examination, as well as recording of vital data such as heart rate, respiratory rate, blood pressure, temperature and oxygen saturation.
- Investigations: tramadol blood level was determined by gas chromatography and urine screen was tested by multi-drugs one-step test (a rapid immunochromatographic assay for qualitative detection of tramadol in human urine).

Statistical analysis:

The collected data were organized and statistically analyzed using SPSS software statistical computer package for windows version 22 (SPSS Inc., Chicago, Illinois, USA). For quantitative data, the Shapiro-Wilk test for normality was performed. For data that were not normally distributed median and interquartile range (expressed as 25^{th}-75^{th} percentiles) were calculated and Mann-Whitney U was used for comparison between groups. For normally distributed data, values were expressed as mean ± standard deviation and independent sample T test was used for comparison. For qualitative data, Pearson's Chi-square test or Fisher's exact test were calculated. Receiver–operating characteristic (ROC) curve for predicting occurrence of seizures was generated from the data. Area under ROC curve, sensitivity, specificity, positive predictive value and negative predictive value were calculated. Significance was adopted at $p<0.05$.

RESULTS

During the study period, 64 patients fulfilled the inclusion and exclusion criteria. Fourteen patients refused to participate in the study, and 50 patients accepted study participation. Socio-demographic characteristics of the study participants are illustrated in table 1. Four patients (8%) were <15 year-old, 26 patients (52%) were from 15 to 25 year-old, 14 patients (28%) were from 25 to 40 year-old and 6 patients (12%) were > 40 year-old. Male patients (38) represented 76% of the study participants. Eighteen patients (36%) re-

corded tramadol dose less than 1000 mg, 24 patients (48%) showed tramadol dose from 1000 to 3000 mg and 8 patients (16%) presented with tramadol dose more than 3000 mg. The time elapsed between exposure and admission to the hospital was less than 2 hours in 15 (30%) patients, while in 21 (42%) patients it was from 2 to 6 hours, and it was more than 6 hours in 14 (28%) patients. Regarding the period of stay, 41 (82%) patients stayed in the hospital for less than 10 hours, 6 (12%) patients stayed from 10 to 15 hours and 3 (6%) patients stayed more than 15 hours. Statistically significant differences were noticed between different age groups and different genders as well. The larger number of cases were recorded in age group 15 - 25 year-old(52%), and they were males (76%). The study showed a significant difference between different tramadol doses, where the majority of cases were recorded in tramadol dose group 1000-3000 mg. Also, a significant difference was declared in hospital stay periods with the peak noticed in the group of hospital stay period <10 hours.

Convulsions were reported in 23 (46%) patients. It was a single attack in 20 (40%) patients and recurrent in 3 patients (6%). Tramadol doses ranged between 125 and 4500 mg, and the median dose was 1000 mg. Delay time from tramadol exposure to hospital admission ranged between 1 and 15 hours with a median of 4 hours. Hospital stay time ranged from 1 to 29 hours with a median of 7 hours. Glasgow coma score (GCS) ranged between 3 and 15 with a median of 13. Headache, vomiting, agitation, constricted pupil and hyper-reflexia were registered in 19 (38%), 17 (34%), 17 (34%), 27 (54%) and 17 (34%) patients respectively. Tramadol blood level ranged from 100 to 1400 ng/ml with a mean concentration of 661 ± 365 ng/ml. The levels were less than 500 ng/ml, 500 - 1000 ng/ml and more than 1000 ng/ml in 19 (38%), 17 (34%) and 14 (28%) patients respectively. The study found a significant difference between seizing and non-seizing patients in tramadol dose, tramadol level and hyper-reflexia, but no significant differences were found between both groups in other socio-demographic or clinical data (Table 2).

Analysis of receiver operating characteristics (ROC) curve of blood tramadol level as a predictor of occurrence of seizures (Figure 1, Table 3) showed an area under the curve (AUC) equals to 0.738, with a 95% confidence interval (CI) (59.5% - 85.2%), $p<0.001$. At a cut off value >600 ng/ml, blood tramadol level had a sensitivity of 73.91% (were able to predict 73.91 of cases that developed seizures) and a specificity of 74.91%. Moreover, positive predictive value has been calculated and

was 70.83% (the probability that a patient with blood tramadol level > 600 ng/ml will develop seizures is 70.83%), while negative predictive value was 76.92%.

Table (1) : Demographic characteristics and toxicological data of the studied patients.

		Number of patients (n=50)	Percentage	Chi Square Goodness of Fit Test	
				X^2	*p* value
Age (years)	<15	4	8%	23.92	<0.001*
	15-25	26	52%		
	>25-40	14	28%		
	>40	6	12%		
Gender	Female	12	24%	12.00	<0.001*
	Male	38	76%		
Tramadol dose (mg)	<1000	18	36%	7.84	0.02*
	1000-3000	24	48%		
	>3000	8	16%		
Delay time (hours)	<2	15	30%	1.72	0.423
	2-6	21	42%		
	>6	14	28%		
Hospital stay (hours)	<10	41	82%	53.56	<0.001*
	10-15	6	12%		
	>15	3	6%		

* Significant at p<0.05 .

Table (2): Comparison of demographic, toxicological, clinical and laboratory data of seizing (n=23) and non-seizing patients (n=27).

		All patients (n=50)	Non-seizing patients (n=27)	Seizing patients (n=23)	Test of significance	
					Test statistics	*p* value
Age(years)	<15	4 (8.0%)	3 (11.1%)	1 (4.3%)	X^2_{FE}= 1.758	0.703
	15-25	26 (52.0%)	14 (51.9%)	12 (52.2%)		
	25-40	14 (28.0%)	8 (29.6%)	6 (26.1%)		
	>40	6 (12.0%)	2 (7.4%)	4 (17.4%)		
Gender	Female	12 (24.0%)	8 (29.6%)	4 (17.4%)	X^2_{ChS}= 1.020	0.313
	Male	38 (76.0%)	19 (70.4%)	19 (82.6%)		
Tramadol dose (mg)	Minimum - Maximum	125-4500	125-4500	340-4500	Z_{MW}= 3.383	0.001*
	Median	1000	700	1500		
	IQR (25^{th} - 75^{th} percentile)	450-2250	340-1125	1000-3375		
Tramadol dose (mg)	<1000	18 (36.0%)	14 (51.9%)	4 (17.4%)	X^2_{FE}=9.669	0.007*
	1000-3000	24 (48.0%)	12 (44.4%)	12 (52.2%)		
	>3000	8 (16.0%)	1 (3.7%)	7 (30.4%)		
Delay time (hours)	Minimum - Maximum	1-15	1-10	1-15	Z_{MW}=0.510	0.510
	Median	4	3	4		
	IQR (25^{th} - 75^{th} percentile)	2-7	2-7	3-7		
Delay time (hours)	<2	15 (30.0%)	10 (37.0%)	5 (21.7%)	X^2_{ChS}= 2.074	0.354
	>6	14 (28.0%)	8 (29.6%)	6 (26.1%)		
	2-6	21 (42.0%)	9 (33.3%)	12 (52.2%)		
Hospital stay (hours)	Minimum - Maximum	1-29	2-18	1-29	Z_{MW}=1.295	0.195
	Median	7	6	7		
	IQR (25^{th} - 75^{th} percentile)	4-8	3-8	5-10		
Hospital stay (hours)	<10	41 (82.0%)	24 (88.9%)	17 (73.9%)	X^2_{FE}=1.887	0.454
	>15	3 (6.0%)	1 (3.7%)	2 (8.7%)		
	10-15	6 (12.0%)	2 (7.4%)	4 (17.4%)		
Glasgow coma score	Minimum - Maximum	3-15	3-15	3-15	Z_{MW}=-1.199	0.231
	Median	13	13	12		
	IQR (25^{th} - 75^{th} percentile)	9-14	9-14	4-14		
Headache	Absent	31 (62.0%)	16 (59.3%)	15 (65.2%)	X^2_{ChS}= 0.187	0.665
	Present	19 (38.0%)	11 (40.7%)	8 (34.8%)		
Nausea and vomiting	Absent	33 (66.0%)	18 (66.7%)	15 (65.2%)	X^2_{ChS}= 0.012	0.914
	Present	17 (34.0%)	9 (33.3%)	8 (34.8%)		
Agitation	Absent	33 (66.0%)	16 (59.3%)	17 (73.9%)	X^2_{ChS}= 1.188	0.276
	Present	17 (34.0%)	11 (40.7%)	6 (26.1%)		
Pupil	Dilated, reactive	1 (2.0%)	0 (0.0%)	1 (4.3%)	X^2_{FE}= 2.283	0.315
	Miotic	27 (54.0%)	13 (48.1%)	14 (60.9%)		
	Round, regular, reactive	22 (44.0%)	14 (51.9%)	8 (34.8%)		
Hyper-reflexia	Absent	33 (66.0%)	22 (81.5%)	11 (47.8%)	X^2_{ChS}= 6.269	0.012*
	Present	17 (34.0%)	5 (18.5%)	12 (52.2%)		
Tramadol level (ng/ml)	Minimum - Maximum	100-1400	100-1300	110-1400	t= -3.126	0.003*
	Mean ± S.D.	661 ± 365	524 ± 325	821 ± 348		
Tramadol level (ng/m)	<500	19 (38.0%)	13 (48.1%)	6 (26.1%)	X^2_{ChS}= 8.354	0.015*
	500-1000	17 (34.0%)	11 (40.7%)	6 (26.1%)		
	>1000	14 (28.0%)	3 (11.1%)	11 (47.8%)		

n: number, S.D.: Standard deviation, IQR: Interquartile range, X^2FE: Fisher's Exact test, X^2 ChS: Pearson's Chi square test, t: Independent samples T test, ZMW: Z test of Mann Whitney. * Significant at p<0.05

Table (3) : Best cutoff, sensitivity, specificity and area under the curve values of blood tramadol level for predicting the occurrence of seizures.

Area under the ROC curve (95% CI)	0.738 (0.595 to 0.852)
Z statistic	3.237
p value	0.001*
Best cut off value	>600
Sensitivity	73.91 %
Specificity	74.91 %
Positive predictive value	70.83%
Negative predictive value	76.92%

ROC: Receiver operating characteristics, CI: Confidence interval, * Significant at p<0.05

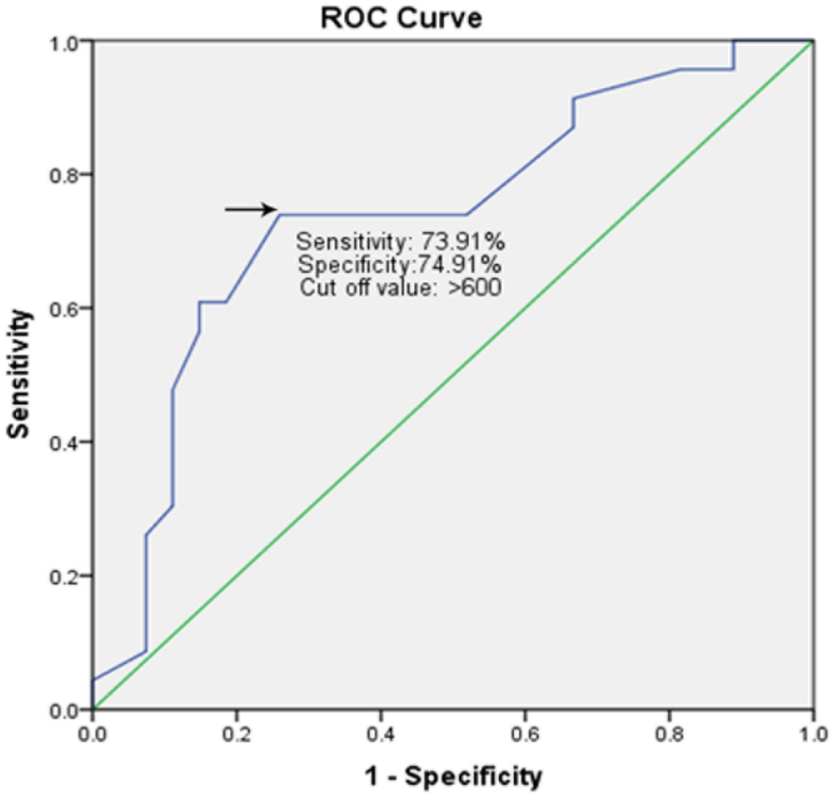

Fig. (1) : Receiver operating characteristics (ROC)curve analysis of blood tramadol level as predictor of occurrence of seizures. Area under the curve = 0.738, p<0.001*, sensitivity 73.91% and specificity 74.91% at cut off value >600 ng/ml.

DISCUSSION

Tramadol is a commonly used centrally acting analgesic. Its use is associated with seizures and suspected to cause serotonin syndrome in overdose (Ryan and Isbister, 2015). The aim of the current study was to evaluate prevalence of tramadol overdose and to predict occurrence of seizures among patients admitted to Tanta Poison Control Center with acute tramadol overdose.

The results of the current study revealed significant difference between different genders and different age groups presenting with acute tramadol overdose. The majority of cases was males and was reported in age group 15 to 25 year-old. Such results could be explained in light of increasing drug abuse among Egyptian youth to overcome stresses of financial and social problems in the Egyptian community (Fawzi, 2011). Prevalence among males could be due to its alleged enhancement of sexual performance. Tramadol may prolong sexual act through mechanisms related to its serotonin reuptake inhibiting effect (Salem et al., 2008; Giuliano, 2012). Worldwide and over time several studies revealed comparable results (Shadnia et al., 2012; Rahimi et al., 2014).

High frequency of seizure (46%) in the present study is remarkably different from other studies (Gardner et al., 2000; Gasse et al., 2000) in which the patients received tramadol at therapeutic doses. Nevertheless, many authors have reported that 54.4% and 46% of cases experienced seizures (Jovanovic-Cupic et al., 2006; Talaie et al., 2009). Large doses of tramadol and alcohol ingestion were considered as predisposing factors that may have been involved in the high incidence of seizures (Gasse et al., 2000). However, information on alcohol consumption was not easily obtainable from the current study participants because alcoholic beverages are prohibited and alcohol drinking is considered a social stigma in Egypt.

Single seizure was recorded in 40% of total cases (86.9% of seizing patients) while multiple seizures were noticed in 6% of total cases (13.1% of seizing patients), which is more or less comparable to other research work (Epstein et al., 2006; Taghaddosinejad et al., 2011; Shadnia et al., 2012). In contrast, one study have noted that 45% of seizing patients suffered from single seizures and 55% suffered from repeated attacks (Jovanovic-Cupic et al., 2006).

The current study did not report significant difference between seizing and non-seizing patients in each of age, gender, delay time to presentation and hospital stay period. In the same direction some authors found that seizure was not gender related, and the previously proposed rela-

tion to younger ages was questionable (Taghaddosinejad et al., 2011). These observations are inconsistent with some earlier reports (Gardner et al., 2000; Jovanovic-Cupic et al., 2006).

The present study showed a wide range of intake of tramadol doses starting from 125 mg up to 4500 mg. The majority of cases was recorded in tramadol dose group 1000-3000 mg, which could be explained by purity and concentration of active ingredients in tramadol preparations available in the Egyptian market. Other studies reported higher ranges of tramadol overdose exposure. Shadnia et al. (2008) reported tramadol dose between 100 and 14000 mg with an average of 1650 mg. Meanwhile, Tashakori and Afshari (2010) observed doses between 150 to 9375 mg. Such dose variation in different countries might be attributed to differences in financial and social classes abusing tramadol in these countries. The lowest dose associated with seizures in the present study was 340 mg compared to 500 mg recorded by Spiller et al. (1997). On the other hand, Talaie et al. (2009) reported 100 mg as minimum dose of tramadol-associated seizure. It has been documented in two other studies that 200 mg is the minimum dose to induce seizures (Marquardt et al., 2005; Jovanovic-Cupic et al., 2006). Mechanisms of tramadol induced seizures appear to be complex, and much of the neurological toxicity in tramadol overdose could be attributed to monoamine uptake inhibition rather than opiate-related effects (Spiller et al., 1997). This study found a significant difference between seizing and non-seizing patients regarding tramadol dose. This was consistent with reports from previous studies (Potschka et al., 2000; Taghaddosinejad et al., 2011) that showed increased seizures frequency with higher doses, which suggests seizure as a dose-dependent characteristic of tramadol overdose. As a result, the doses reported in case of acute tramadol overdose seem to be a good indicator to predict seizure.

The clinical manifestations of tramadol toxicity included headache, vomiting, coma, agitation, constricted pupil and hyper-reflexia. These manifestations can vary from person to person, and this depends on several factors including how an individual's body responds to the drug, how much was taken and whether it was taken in combination with any other substances or not (Fouad et al., 2015). This study reported a statistically significant difference between seizing and non-seizing patients regarding hyper-reflexia and tramadol blood level. Reports from previous research work considered the significance of tramadol blood level evaluation (Galer and Krzyzanowski, 2004; Tjaderborn et al., 2007; Taghaddosinejad et al., 2011). Analysis of receiver operating characteristics (ROC) curve of blood tramadol level as a predictor of occurrence of

seizures revealed that at a cut off value > 600 ng/ml, blood tramadol level was able to predict 73.91% of cases that developed convulsions. Moreover, the probability that a patient with blood tramadol level > 600 ng/ml will develop seizures is 70.83%.

From the results of the current study, it could be concluded that tramadol overdose is connected with high risk of developing seizures. Seizures were more frequent in patients reporting intake of high tramadol doses, suggesting seizure as a dose-dependent characteristic of tramadol overdose. Hyper-reflexia was a clinical manifestation with high tendency in seizing patients, but tramadol blood concentration showed a limited correlation with seizure in these patients. An obvious limitation of the current study was the limited sample size as only 50 subjects agreed to participate in this study. Furthermore, assessment of the amount ingested was based on patient self-reporting, which is obviously subjective.

REFERENCES

Epstein, D. H., Preston, K. L., and Jasinski, D. R. (2006): "Abuse liability, behavioral pharmacology, and physical-dependence potential of opioids in humans and laboratory animals: lessons from tramadol". Biol. Psychol., 73 (1): 90-99.

Fawzi, M. M. (2011): "Some medicolegal aspects concerning tramadol abuse: The new Middle East youth plague 2010. An Egyptian overview". Egy. J. Forensic Sci., 1(2): 99-102.

Fouad, S., Hassan, N., Nassief, N., et al. (2015): "Critical score as a predictor for Progression of tramadol intoxication". J. Clin. Toxicol., 5 (3): 249.

Galer, K., and Krzyzanowski, M. (2004): "Death attributed to toxic interaction of tramadol and other drugs". Arch Med. Sadowej. Kryminol., 54(1): 73-78.

Gardner, J. S., Blough, D., Drinkard, C. R., et al. (2000): "Tramadol and seizures: a surveillance study in a managed care population". Pharmacotherapy, 20(12): 1423-1431.

Gasse, C., Derby, L., Vasilakis-Scaramozza, C., and Jick, H. (2000): "Incidence of first-time idiopathic seizures in users of tramadol". Pharmacotherapy, 20 (6): 629-634.

Giuliano, F. A. (2012): "Tramadol for the treatment of premature ejaculation". Eur. Urol., 61(4): 744-745.

Houmes, R. J., Voets, M. A., Verkaaik, A., et al. (1992): "Efficacy and safety of tramadol versus morphine for moderate and severe postoperative pain with special

regard to respiratory depression". Anesth. Analg., 74(4): 510-514.

Jovanovic-Cupic, V., Martinovic, Z., and Nesic, N. (2006): "Seizures associated with intoxication and abuse of tramadol". Clin. Toxicol. (Phila.), 44(2): 143-146.

Leppert, W. (2009): "Tramadol as an analgesic for mild to moderate cancer pain". Pharmacol. Rep., 61(6): 978-992.

Marquardt, K. A., Alsop, J. A., and Albertson, T. E. (2005): "Tramadol exposures reported to statewide poison control system". Ann. Pharmacother., 39 (6): 1039-1044.

Minami, K., Ogata, J., and Uezono, Y. (2015): "What is the main mechanism of tramadol"? Naunyn. Schmiedebergs Arch. Pharmacol., 388 (10): 999-1007.

Modi, H., Mazumdar, B., and Bhatt, J. (2013): "Study of interaction of tramadol with amlodipine in mice". Indian J. Pharmacol., 45(1): 76-79.

Potschka, H., Friderichs, E., and Loscher, W. (2000): "Anticonvulsant and proconvulsant effects of tramadol, its enantiomers and its M1 metabolite in the rat kindling model of epilepsy". Br. J. Pharmacol., 131(2): 203-212.

Preston, K. L., Jasinski, D. R., and Testa, M. (1991): "Abuse potential and pharmacological comparison of tramadol and morphine". Drug Alcohol Depend., 27 (1): 7-17.

Rahimi, H. R., Soltaninejad, K., and Shadnia, S. (2014): "Acute tramadol poisoning and its clinical and laboratory findings". J. Res. Med. Sci., 19(9): 855-859.

Rehni, A. K., Singh, I., and Kumar, M. (2008): "Tramadol-induced seizurogenic effect: a possible role of opioid-dependent gamma-aminobutyric acid inhibitory pathway". Basic Clin. Pharmacol. Toxicol., 103(3): 262-266.

Ryan, N. M., and Isbister, G. K. (2015): "Tramadol overdose causes seizures and respiratory depression but serotonin toxicity appears unlikely". Clin. Toxicol. (Phila.), 53` (6): 545-550.

Salem, E. A., Wilson, S. K., Bissada, N. K., et al. (2008): "Tramadol HCL has promise in on-demand use to treat premature ejaculation". J. Sex. Med., 5(1): 188-193.

Shadnia, S., Brent, J., Mousavi-Fatemi, K., et al. (2012): "Recurrent seizures in tramadol intoxication: implications for therapy based on 100 patients". Basic Clin. Pharmacol. Toxicol., 111(2): 133-136.

Shadnia, S., Soltaninejad, K., Heydari, K., et al. (2008): "Tramadol intoxication: a review of 114 cases". Hum. Exp. Toxicol., 27(3): 201-205.

Spiller, H. A., Gorman, S. E., Villalobos, D., et al. (1997): "Prospective multicenter evaluation of tramadol exposure". J. Toxicol. Clin. Toxicol., 35(4): 361-364.

Taghaddosinejad, F., Mehrpour, O., Afshari, R., et al. (2011): "Factors related to seizure in tramadol poisoning and its blood concentration". J. Med. Toxicol., 7 (3): 183-188.

Talaie, H., Panahandeh, R., Fayaznouri, M., et al. (2009): "Dose-independent occurrence of seizure with tramadol". J. Med. Toxicol., 5(2): 63-67.

Tashakori, A., and Afshari, R. (2010): "Tramadol overdose as a cause of serotonin syndrome: a case series". Clin. Toxicol. (Phila.), 48(4): 337-341.

Tjaderborn, M., Jonsson, A. K., Hagg, S., and Ahlner, J. (2007): "Fatal unintentional intoxications with tramadol during 1995-2005". Forensic Sci. Int., 173(2-3): 107-111.

مستوى الترامادول بالدم والتنبؤ بالتشنجات في المرضى الذين يعانون من التسمم الحاد بالترامادول

المشتركون فى البحث

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الترامادول هو نوع من الأفيونات الاصطناعية الذي يعمل مركزيا ويتم استخدامه على نطاق واسع لتأثيره المسكن.إن تعاطي الترامادول يتزايد في مصر، وحدوث التشنجات وارد بين متعاطيه، لذا كان الهدف من هذه الدراسة هو تقييم خصائص المرضى الذين يتناولون جرعات زائدة من الترامادول وإمكانية التنبؤ بالتشنجات فيهم.

تم اختيار خمسين مشاركا من مرضى التسمم الحاد بالترامادول الذين تم إدخالهم إلى مركز علاج التسمم (مستشفى الطوارئ، جامعة طنطا) بين يناير ٢٠١٤ وديسمبر ٢٠١٥، ولقد تم تسجيل البيانات الآتية لكل مريض: التاريخ المرضي، الفحص السريري، مستوى الترامادول بالدم وكذلك فحص عينة البول.

أظهرت الدراسة وجود فرق ذي دلالة إحصائية بين مختلف المجموعات حسب فئات العمر والجنس وجرعة الترامادول وفترة الإقامة في المستشفى، وكانت معظم الحالات من الذكور، الذين تتراوح أعمارهم بين ١٥ و ٢٥سنة، والذين تناولوا جرعة من الترامادول تتراوح بين ١٠٠٠ و ٣٠٠٠ ملجم، واستمر وجودهم لمدة أقل من ١٠ساعات في المستشفى، وكان وقوع التشنجات أعلى بين المرضى الذين تعرضوا لجرعة ترامادول أكثر من ١٠٠٠ ملجم، وأولئك الذين حدث لهم فرط الأفعال المنعكسة، والذين أظهروا ارتفاعا في مستوى الترامادول بالدم،وعند المستوى الحدي ٦٠٠ نانوجرام/مل كان مستوى الترامادول بالدم له حساسية بنسبة ٧٣,٩١٪ وخصوصية بنسبة ٧٤,٩١٪ وقيمة تنبؤية إيجابية بنسبة ٧٠,٨٣٪ وقيمة تنبؤية سلبية بنسبة ٧٦,٩٢٪ .

يمكن أن نخلص من هذه الدراسة إلى أن فرط الأفعال المنعكسة وكمية الترامادول المتناولة وتركيز الترامادول بالدم يمكن أن يستخدموا للتنبؤ بحدوث التشنجات بين المرضى الذين تناولوا جرعة زائدة من الترامادول.