SUBSTANCE ABUSE IN PATIENTS WITH FIRST ONSET CONVULSIVE SEIZURES

BY

Abdel Aziz A. Ghanem, Sameera Sh. Hamed, Rania H. Abdel-Rahman and Mohammad Abu-Hegazy*

Forensic Medicine and Clinical Toxicology & Neurology Departments, Faculty of Medicine, Mansoura University, Egypt.*

ABSTRACT

Chronic use, overdose and withdrawal are potential causes of seizures in illicit substance abusers. The aim of this work is to assess the pattern of substance abuse in patients presented with new onset seizures. Eighty patients presented to Mansoura Toxicology Unit and Neurology Department with a history of substance abuse and witnessed attack of seizure for the first time were included in the study. The mean age of patients was 25.9 ± 6.5 years and most of them were men. Substance abuse-related seizures were mostly associated (78.75%) with tramadol either alone or in combination with opiate and /or cannabis. There is a significant correlation regarding age and pattern of substance abuse-related seizures. Multi-substance abuse is more prevalent (66.25%) than single drug intake in all age groups. It could be concluded that seizures are a common serious complication in substance abusers and should not be underestimated especially with tramadol either alone or in combination with opiates and or / cannabis. Raising the awareness of general population and medical personnel regarding the seizure potential and the misconception about tramadol safety is warranted.

Keywords: *Substance abuse, seizure, tramadol, cannabis, opiates.*

INTRODUCTION

Seizures are a common toxic complication of numerous drugs and toxins. It has been estimated that 6% of new-onset seizures and up to 9% of status epilepticus are drug related (Finkelstein et al., 2013 and Reichert et al., 2014). Seizures in illicit substance abusers can occur in chronic use, overdose and withdrawal. These seizures are usually acute resulting from direct toxic effects of the abused substance on the brain, substance withdrawal or from indirect mechanisms, such as head trauma, infection and metabolic imbalance resulting from drug or alcohol abuse (Luft, 2010).

Medication-induced seizures can occur due to increased excitatory activity or suppressed inhibitory pathways, altered neurotransmitters or receptor function with resultant over activation (Chen et al., 2015).

Noteworthy, changing patterns of substance abuse and drug prescription are reflected in the incidence of substances attributable to seizures (Thundiyil et al., 2007). There are few studies regarding recreational drug use-related seizures. Hence, the aim of this work was to assess the pattern of substance abuse in patients presented first ever with seizures to Toxicology Unit and Neurology Department, Mansoura Emergency Hospital.

PATIENTS AND METHODS

The present work was carried out in the Toxicology Unit and Neurology Department in Mansoura Emergency Hospital, Egypt in the period from 15th December 2012 to 15th December 2013.

Inclusion criteria

All patients with a history of substance abuse and experiencing a new onset seizure for the first time were included in the study.

Exclusion Criteria:

Patients who had family history of epilepsy, past history of head trauma, history of prior seizure activity, infections, presence of metabolic derangement and patients taking other drugs that may induce seizures e.g. antidepressants, monoamine oxidase inhibitors (MAOIs) or selective serotonin reuptake inhibitors (SSRIs).

Methods:

a) After taking an informed consent, data was collected from conscious patients at time of admission if possible or from their relatives i.e. sociodemographic data, history of illicit drug intake, seizures and its frequency and past medical history.

b) Complete clinical examination, EEG, routine laboratory investigations e.g., arterial blood gases and random blood sugar were carried out.

c) Urine sample (10 ml) was obtained from each patient on admission for toxicological screening. After preliminary testing each sample was collected in a dry, labeled container and stored at -20°C until analysis for chromatographic confirmation.

d) Toxicological analysis:

i. Preliminary drug screen test by EMIT system (*Syva, Solaris S/N 1076 Version 3.00L. Using Emit® d.a.u. Assay*) was done for qualitative detection of cannabinoids, opiates, tramadol, benzodiazepines, barbiturates and amphetamines.

ii. Confirmatory testing of positive results by thin layer chromatography according to the methodology of George and Braithwaite (1995) and Meadway et al. (1998).

Statistical Analysis :

All data were analyzed by using the Statistical Package for Social Scientists (SPSS) version 10.00 for windows (SPSS Inc., Chicago, IL, USA). Quantitative data were presented as mean ± standard deviation and qualitative data were presented as number and percentage. Chi square and Fischer's exact tests were done to compare between different variables. P value less than 0.05 was considered statistically significant.

RESULTS

During the study period, a total of 150 patients with a history of illicit substance intake presented to Toxicology Unit with seizure attack for the first time in life and were admitted to the Neurology Department, Mansoura Emergency Hospital. Eighty patients met the inclusion criteria and were enrolled in this research.

All patients revealed no abnormality on clinical examination. Arterial blood gases, blood sugar analysis and EEG were normal.

Table (1) illustrates the sociodemographic data of the studied patients. Male patients constituted most of the studied cases (93.75%) with male to female ratio 9:1. Their age ranged from 15-52 years (mean ± SD is 25.9 ± 6.5). The majority of cases with seizures (56.25%) were in the age group (21-30 years). Nearly half of the patients were single (51.25%), 50% had low educational level (secondary school) and most of them were from urban areas (62.5%).

Table (2) and figure (1) illustrate the results of toxicological screening and thin layer chromatographic (TLC) confirmation of urine samples in the studied patients. Combined tramadol and opiate intake constituted the highest pattern of drug abuse among the studied cases (31.25%) followed by tramadol alone or in combination with opiates and cannabis (20% and 15 % of patients respectively). TLC analysis of opiates revealed positive results for 6-monoacetyl morphine (6-MAM) and morphine metabolites. All patients' samples were negative regarding amphetamine and barbiturates.

Table (3) demonstrates the correlation between age, gender and type of substance abuse in the studied cases. The majority of tramadol abusers (60%) either alone or combined with opiates were in the age group (21-30 years). Combined

tramadol and opiate intake constituted the highest pattern of drug abuse among male patients (29.2%). There was a significant correlation regarding age and type of substance abuse (p= 0.04).

Table (1) : Sociodemographic characteristics of the studied abuser patients (n=80).

Characteristics		Number	Percentage (%)
Sex	Males Females	72 8	93.75 6.25
Age (years)	<20 20- <30 ≥ 30	18 45 17	22.5 56.25 21.25
Residence	Urban Rural	50 30	62.5 37.5
Marital status	Single Married	41 39	51.25 48.75
Educational level:	No education Secondary school (Low) High education	24 40 16	30 50 20
Occupation	Not working Government employee Private work	43 9 28	53.75 11.25 35

Table (2) : Results of toxicological screening in the studied abusing patients (n=80).

Substances of abuse	Number of cases	Percentage (%)
Tramadol+ Opiate	25	31.25%
Tramadol only	16	20%
Tramadol+ Opiate+ Cannabis	12	15%
Tramadol + Cannabis	10	12.5%
Cannabis + Opiate	6	7.5%
Cannabis only	4	5%
Opiate only	2	2.5%
Benzodiazepines	5	6.25%
Total	80	100%

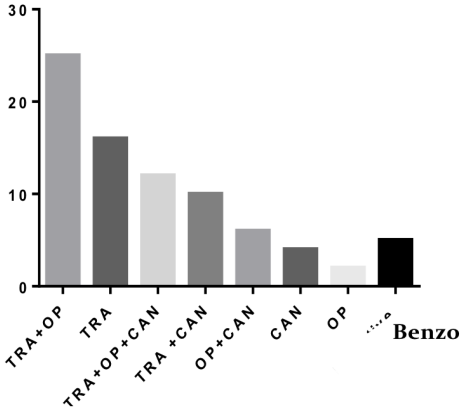

Fig. (1) : Results of thin layer chromatographic confirmation of substance abuse among studied patients (n=80). TRA: tramadol, OP: opiate, CAN: cannabis, Benzo: benzodiazepines.

Table (4) demonstrates the correlation between age, gender and pattern of substance abuse in the studied cases. Polysubstance abuse was more prevalent than single drug intake in all age groups and among males (68.1%). On the other hand, single illicit drug use was more common among females (62.5%). A significant correlation was found regarding age groups and overall prevalence of substance abuse as seen in figure 2 ($p = 0.03$). There was insignificant correlation between gender and pattern of substance abuse ($p < 0.05$).

Table (5) shows the correlation between residence, education, occupation and substance abuse in the studied cases. No significant correlation was found as regards any of the studied variables ($p < 0.05$).

Table (3): Correlation between age, gender and type of substance abuse in the studied patients (n=80).

Type of substance abuse	Age groups (years)			Gender	
	<20 (n=18) (% from total of age group)	20-<30 (n=45) (% from total of age group)	≥ 30 (n=17) (% from total of the age group)	Females (8) (% from total group of the female gender)	Males (72) (% from total group of the male gender)
Tramadol	0	12 (26.7%)	4 (23.5%)	4 (50%)	13 (18.1%)
Tramadol +Opiate	2 (11.1%)	15 (33.3%)	7 (41.1%)	3 (37.5%)	21 (29.2%)
Tramadol +Opiate +Cannabis	7 (38.9%)	4 (8.9%)	1 (5.9%)	0	12 (16.7%)
Tramadol + Cannabis	2 (11.1%)	7 (15.6%)	1 (5.9%)	0	10 (13.9%)
Cannabis	2 (11.1%)	3 (6.7%)	0	1 (12.5%)	3 (4.2%)
Cannabis + Opiate	2 (11.1%)	2 (4.4%)	2 (11.8%)	0	6 (8.3%)
Opiate	1 (5.6%)	1 (2.2%)	0	0	2 (2.7%)
Benzodiazepines	2 (11.1%)	1 (2.2%)	2 (11.8%)	0	5 (6.9%)
P- value	0.04*			0.28	

* Significant at p-value <0.05, n: number, %: percentage .

Table (4) : Correlation between age, gender and pattern of substance abuse in the studied cases (n=80).

Pattern of substance abuse	Age groups (years)			Gender	
	<20 (n=18) (% from total of age group)	**20-<30 (n=45) (% from total of age group)**	**≥ 30 (n=17) (% from total of the age group)**	**Females (8) (% from total group of the female gender)**	**Males (72) (% from total group of the male gender)**
Single substance	5 (27.8%)	17 (37.8%)	6 (35.3%)	5 (62.5%)	23 (31.9%)
More than one substance	13 (72.2%)	28 (62.2%)	11 (64.7%)	3 (37.5%)	49 (68.1%)
P-value	0.39			0.52	
Total tramadol	11 (61.1%)	38 (84.4)	13 (76.4%)	7 (87.5%)	56 (77.7%)
Total cannabis	11 (61.1%)	9 (20%)	3 (17.6%)	1 (12.5%)	21 (29.2%)
Total opiate	5 (27.7%)	18 (40%)	9 (52.9%)	3 (37.5%)	29 (40.2)
P-value	0.03*			0.66	

* Significant at p-value <0.05. n: number, %: percentage, Total tramadol means: all cases positive for tramadol either alone or combined with other substances, Total cannabis means: all cases positive for cannabis either alone or combined with other substances. Total opiate means: all cases positive for opiate either alone or combined with other substances.

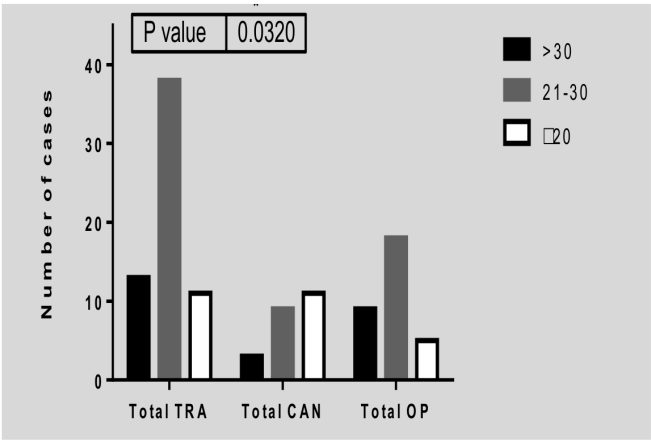

Fig. (2) : Correlation between age and overall prevalence of substance abuse in the studied cases (n=80). TRA: tramadol, OP: opiate, CAN: cannabis.

Table (5) : Correlation between residence, education, occupation and pattern of substance abuse in the studied cases (n=80).

Pattern of substance abuse	Education			Residence		Occupation		
	No (n=24)	Low (n=40)	High (n=16)	Urban (n=50)	Rural (n=30)	No work (n=43)	Governmental (n=9)	Private (n=28)
Tramadol	3 (12.6 %)	14 (35%)	1 (6.25%)	9 (18%)	8 (26.7%)	8 (18.6%)	3 (33.3%)	5 (17.9%)
Opiates	2 (8.3%)	0	0	2 (4%)	0	2 (4.7%)	0	0
Tramadol + Opiates + Cannabis	2 (8.3%)	6 (15%)	4 (25%)	8 (16%)	4 (13.3%)	8 (18.6%)	1 (11.1%)	3 (10.7%)
Cannabis	0	2 (5%)	2 (12.5%)	3 (6%)	1 (3.3%)	3 (7%)	0	1 (3.6%)
Tramadol + Cannabis	3 (12.6%)	4 (10%)	2 (12.5%)	4 (8%)	3 (10%)	5 (11.6%)	2 (22.3%)	3 (10.7%)
Tramadol + Opiates	10 (41.6%)	10 (25%)	4 (25%)	14 (28%)	11 (36.7%)	9 (20.9%)	3 (33.3%)	13 (46.4%)
Cannabis+ Opiates	2 (8.3%)	2 (5%)	2 (12.5%)	7 (14%)	2 (6.7%)	4 (9.3%)	0	2 (7.1%)
Benzodiazpines	2 (8.3%)	2 (5%)	1 (6.25%)	3 (6%)	1 (3.3%)	4 (9.3%)	0	1 (3.6%)
P- value	0.21			0.78		0.68		
Total tramadol	18 (75%)	34 (85%)	11 (68.75%)	35 (70%)	26 (86.6%)	30 (69.7%)	9 (100%)	24 (85.7%)
Total cannabis	4 (16.6%)	10 (25%)	8 (50%)	18 (36%)	7 (23.3%)	15 (34.8%)	1 (11%)	6 (21.4%)
Total opiates	14 (58.3%)	12 (30%)	6 (37.5%)	23 (46%)	13 (34.3%)	15 (34.8%)	3 (33.3%)	15 (53.5%)

* Significant at p-value <0.05. n: number, %: percentage. Total tramadol means: all cases positive for tramadol either alone or combined with other substances, Total cannabis means: all cases positive for cannabis either alone or combined with other substances, Total opiate means: all cases positive for opiate either alone or combined with other substances.

DISCUSSION

The present work was carried out to assess the pattern of illicit drug use among patients presented with new-onset seizures. More than half of the studied patients (65.25%) were in the age group (20- < 30 years) and most of them were males (93.75%).

More or less similar, Behnoush et al. (2012) studied 143 patients presented with drug-induced seizures in Baharloo Hospital, Iran. Their age was mainly between 20-30 years with 53.3% male. Fawzi (2011) studied 640 Egyptian abusers most of

them were males (77.2). In another study, Tashakori and Afshari (2010) and Shadnia et al. (2012), stated that seizure is more common in young males (22-39.5 years). However, Farajidana et al. (2012) reported non significant difference in the frequency of seizure between different genders.

In contrast, Talaie et al. (2009) reported that 26.5% of the patients who developed seizure after tramadol poisoning were females while Eizadi-Mood et al. (2009) and Jovanovic-Cupic et al. (2006) mentioned that the frequency of seizures in females was 47.6% and 16.1% respectively.

No definite conclusion could be made in the present study, about gender distribution among patients with substance abuse-induced seizures because of the small number of cases. However, men and young adults aged 18 to 25 years are reported to be at a higher risk of substance dependence (Delker et al., 2015) and this may explain the higher incidence of seizures among this group.

With respect to other sociodemographic data reported in the current research, about two thirds of substance abusers presented with new-onset seizures were from urban areas (62.5%). Half of the studied patients had low educational level (secondary school) (51.25%) were single and (53.75%) were not working. There was no significant correlation between pattern of illicit drug abuse and any of the previous data.

Most of addicts are unemployed, have low socioeconomic level, from suburban areas with minimal educational status according to the study published by Fawzi (2011).

All the current cases presented with single episode of new-onset seizure. Toxicological analysis of their urine samples revealed that overall tramadol positive screen was the most frequent (78.75%) either alone or combined with other recreational drugs. A significant correlation was found between substance abuse and age either single or as an overall pattern. In particular, total tramadol and opiate intake was prevalent in youth in the age group (21-30 years) while cannabis abuse was more prominent in the adolescent age <20 years.

Likewise, Fawzi (2011) reported a high prevalence of tramadol abuse among their studied population sample (67.9%). It was reported that seizure is one of the most important life-threatening clinical presentation of tramadol in therapeutic and toxic doses. Most of the patients experience only one episode of seizure within 24 hours after tramadol use (Hassanian-Moghaddam et al., 2013; Rahimi et al., 2014; Mehrpour et al., 2015 and Ryan and Isbister, 2015).

In Egypt, along the past five years, there was an alarming increased abuse of tramadol especially among youth and middle aged population. Popularity of tramadol is attributed to its easy accessibility, illegal smuggling, low price, presumption that tramadol is a safe medication for pain management and that it could treat premature ejaculation, extend orgasm and heighten sexual pleasure. Another factor is misconception about its safety and beneficial effects promoted by irresponsible social media and internet drug sales (Salem et al., 2008 and Fawzi, 2011).

Findings of this study regarding the occurrence of seizures in abusers of a single or polysubstance use showed that (66.25%) of patients first ever presented with seizures were abusing more than one substance. Tramadol was consumed alone in 20% of cases, combined with opiates (31.25%) or associated with opiates and / or cannabis abuse (27.5%).

Shadnia et al. (2008) stated that seizures could not be due to tramadol agonistic action on the opioid receptor since administration of an opioid antagonist seems to aggravate seizures. The mechanism by which tramadol induces seizures is suggested by Hassanian-Moghaddam et al. (2013) to be due to suppression of gamma aminobutyric acid (GABA) receptors and inhibition of GABA pathways. Some individuals are more sensitive to seizures induced by tramadol as they are poor metabolizers because of a genetic polymorphism of CYP2D6 (Gardner et al., 2000).

Concerning the other substance abuse-related seizures in the current work, (7.5%) of patients exhibited positive cannabis and opiates urine drug screen, while cannabis only was positive in (5%) of patients. Five cases (6.25%) were positive for benzodiazepines only. Opiates only was positive in (2.5%) of patients. TLC analysis of opiates revealed positive results for heroin metabolites "6-monoacetyl morphine (6-MAM) and morphine".

Likewise, seizures were observed in 8.63% of abusing patients (12.5% are due to opioid abuse). They occurred during withdrawal from heroin (Mattoo et al., 2009). Furthermore, Warner-Smith et al. (2002) reported new-onset seizures in 2% of heroin-overdosed patients which may be attributed to heroin itself or to epileptogenic adulterants present in commercial street heroin.

On the contrary, it is stated that seizures are uncommon during opioid withdrawal; and if they exist, this suggests either concomitant use of another drug or central nervous system infection, especially with intravenous drug abuse (Chaila and Delanty, 2010).

On the other hand, Gholami and Saboory (2013) stated that morphine abuse can alter seizure threshold. Further, Shafaroodi et al. (2007) and Zhang and Ko (2009) postulated that morphine can modulate seizure susceptibility in a biphasic contrasting manner and cause dose-dependent anticonvulsant and proconvulsant effects.

Seizures related to opiates alone are uncommon due to their inhibitory actions on the brain resulting in decreased neuronal excitability (Saboory et al., 2007). Hence, other causes should be explored. In this case series, no other causes or risk factors (e.g. stroke, infection, metabolic derangement frequently seen in addicts) could explain the new-onset seizures. So, it may be due to direct toxic effects of adulterants as suggested by Luft (2010).

Controversies are observed in the literature regarding cannabis-related seizures. Hoyte et al. (2012) found that 3.8% of patients who require medical care for synthetic cannabinoids intoxication present with seizures. Also, de Havenon et al. (2011) and Hamerle et al. (2014) reported four cases with no prior history of neurological disease that experienced their first generalized tonic–clonic seizure after smoking cannabis (Spice).

In contrast, Devinsky et al. (2014) and Maa and Figi (2014) stated that seizures are not commonly seen with marijuana use and it is claimed to be protective against new-onset seizures and epilepsy. However, the epidemiological data and case reports suggest that, at least in some patients, cannabis may not affect epilepsy at all or may even exacerbate seizures (Szaflarski and Bebin, 2014; dos Santos et al., 2015 and Kersten and McLaughlin, 2015).

The mechanism behind the possible proconvulsant effect of synthetic cannabinoids is not known, but it may be due to their effects at the cannabinoid receptor CB1 (Schep et al., 2015).

The current finding of benzodiazepines-related seizure in five patients may be due to withdrawal. This is in agreement with O'Connor et al. (2004) and Ashton (2005) who reported that benzodiazepine withdrawal syndrome occurs following trials to withdraw even from therapeutic doses with an incidence of 30-100%. Symptoms range from sleep disorders, anxiety, panic attacks and muscle spasms to excitability, convulsions, psychosis and hallucinations (Lader, 2014; Liebrenz et al., 2015).

Also, Albiero et al. (2012) described two patients developed seizures during benzodiazepine detoxification. There is no previous history of seizures or evidence of intracerebral lesions. A diffuse decrease in

the seizure threshold due to generalized excitatory rebound is the probable cause of seizures (Chaila and Delanty, 2010).

In summary, drug abuse is an important risk factor for new-onset seizures. Tramadol is the most frequent drug encountered followed by opiates and cannabis. More larger scale studies should be targeted towards the potential risk of seizures associated with tramadol, its mechanism and susceptibility in different populations especially when combined with other medications.

REFERENCES

Albiero, A.; Brigo, F.; Faccini, M.; et al. (2012): "Focal non-convulsive seizures during detoxification for benzodiazepine abuse". Epilepsy and Behavior, 23: 168-170.

Ashton, H. (2005): "The diagnosis and management of benzodiazepine dependence". Curr. Opin. Psychiatry, 18(3): 249-255.

Behnoush, B.; Taghadosinejad, F.; Arefi, M.; et al. (2012):"Prevalence and complications of drug-induced seizures in Baharloo Hospital, Tehran, Iran". Iranian Journal of Toxicology, 6 (16):588-593.

Chaila, E. and Delanty, N. (2010): Alcohol and illicit drug abuse associated with epileptic seizures. In: Atlas of Epilepsies, Panayiotopoulos, C.P. (ed.), Springer-Verlag London Limited., Ch. 22, P.P. 165-170.

Chen, H.Y.; Albertson, T.E. and Olson, K.R. (2015): "Treatment of drug-induced seizures".Br. J. Clin. Pharmacol., 1-8.

de Havenon, A.; Chin, B.; Thomas, K.C. and Afra, P. (2011): "The secret "Spice": An undetectable toxic cause of seizure". The Neurohospitalist, 1(4): 182-186.

Delker, E; Brown, Q. and Hasin, D. (2015): "Epidemiological studies of substance dependence and abuse in adults". Curr. Behav. Neurosci. Rep., 2(1):15-22.

Devinsky, O.; Cilio, M.R.; Cross, H.; et al. (2014): "Cannabidiol: pharmacology and potential therapeutic role in epilepsy and other neuropsychiatric disorders". Epilepsia, 55:791-802.

dos Santos, R. G.; Hallak, J. E.; Leite, J. P.; et al. (2015): "Phytocannabinoids and epilepsy". J. Clin. Pharm. Therap., 40, 135-143.

Eiza-dimood, N.; Yaraghi, A.; Gheshlaghi, F. and Mojiri, R. (2009): "Causes, treatments and outcome of seizure in drugs and toxins- intoxicated patients". Journal of Tehran University of Medical Sciences, 66 (3): 214-220.

Farajidana, H.; Hassanian-Moghaddam, H.; Zamani, N. and Sanaei-Zadeh, H. (2012): "Tramadol-induced seizures and trauma". Eur. Rev. Med. Pharmacol. Sci., 16(1):34-37.

Fawzi, M.M. (2011): "Medicolegal aspects concerning tramadol abuse. The new middle East youth plague: An Egyptian overview 2010". J. Forensic Res., 2(5):1-3.

Finkelstein, Y.; Hutson, J.R.; Freedman, S.B.; et al. (2013): " Drug-induced seizures in children and adolescents presenting for emergency care: current and emerging trends". Clin.Toxicol., 51: 761-766.

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.

George, S. and Braithwaite, R.A. (1995): "A preliminary evaluation of five rapid detection kits for on site drugs of abuse screening". Addiction, 90:227-232.

Gholami, M. and Saboory, E. (2013): "Morphine exposure induces age-dependent alterations in pentyl enetetrazole-induced epileptic behaviors in prepubertal rats". Dev. Psychobiol., 55:881-887.

Hamerle, M.; Ghaeni, L.; Kowski, A.; et al. (2014): "Cannabis and other illicit drug use in epilepsy patients". Europ. J. Neurology, 21: 167-170.

Hassanian_Moghaddam, H.; Farajidana, H.; Sarjami, S. and Owliaey, H. (2013): "Tramadol_induced apnea". Am. J. Emerg. Med., 31:26_31.

Hoyte, C.O.; Jacob, J.; Monte, A.A.; et al. (2012): "A characterization of synthetic cannabinoid exposures reported to the National poison data system in 2010". Ann. Emerg. Med., 60: 435-438.

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

Kersten, B.P. and McLaughlin M. E. (2015): "Toxicology and management of novel psychoactive drugs". Journal of Pharmacy Practice, 28(1): 50-65.

Lader, M. (2014): "Benzodiazepine harm: How can it be reduced?" Br. J. Clin. Pharmacol., 77 (2):295-301.

Liebrenz, M.; Gehring , M.T.; Buadze, A. and Caflisch, C. (2015): "High-dose benzodiazepine dependence: a qualitative study of patients' perception on cessation and withdrawal". BMC Psychiatry, 15:116-126.

Luft, A.R. (2010): Critical care seizures related to illicit drugs and toxins. In: Seizures in Critical Care: A Guide to Diagnosis and Therapeutics: Current Clinical Neurology, Varelas, P. (Ed.), Second Edition, Humana Press, Ch. 14, P.P. 341-354.

Maa, E. and Figi, P. (2014): "The case for medical marijuana in epilepsy". Epilepsia, 55: 783-786.

Mattoo, S.K.; Singh, S.M.; Bhardwaj, R.; et al. (2009): "Prevalence and correlates of epileptic seizure in substance-abusing subjects". Psychiatry and Clinical Neurosciences; 63: 580-582.

Meadway, C., George, S. and Braithwaite, R. (1998): "Opiate concentrations following the ingestion of poppy seed products-evidence for `the poppy seed defense". Forens. Sci. Int., 96 (1): 29-38.

Mehrpour, O.; Sharifi, M. and Zamani, N. (2015): Tramadol poisoning. In: Toxicology Studies-Cells, Drugs and Environment. INTECH. Ch. 5, P.P. 101-126.

O'Connor, K.P.; Marchand, A.; Belanger, L.; et al. (2004): "Psychological distress and adaptational problems associated with benzodiazepine withdrawal and outcome: a replication". Addict. Behav. 29 (3):583-593.

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

Reichert, C.; Reichert, P.; Monnet-Tschudi, F.; et al. (2014): "Seizures after single-agent overdose with pharmaceutical drugs: Analysis of cases reported to a poison center". Clin. Toxicol., 52(6): 629-634.

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

Saboory, E.; Derchansky, M.; Ismaili, M.; et al. (2007): "Mechanisms of morphine enhancement of spontaneous seizure activity". Anesth. Analg., 105:1729-1735.

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: 188-193.

Schep, L.J.; Slaughter, R.J.; Hudson, S.; et al. (2015): "Delayed seizure-like activity following analytically confirmed use of previously unreported synthetic cannabinoid analogues". Hum. Exp. Toxicol., 34 (5): 557-560.

Shadnia, S.; Soltaninejad, K.; Heydari,

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

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

Shafaroodi, H.; Asadi, S.; Sadeghipour, H.; et al. (2007): "Role of ATP-sensitive potassium channels in the biphasic effects of morphine on pentylenetetrazole-induced seizure threshold in mice". Epilepsy Res., 75:63-69.

Szaflarski, J. P. and Bebin E. M. (2014): "Cannabis, cannabidiol, and epilepsy-From receptors to clinical response". Epilepsy and Behavior, 41: 277-282.

Talaie, H.; Panahandeh, R.; Fayaznouri, M.R.; 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". Clinical Toxicology, 48(4):337-341.

Thundiyil, J.G.; Kearney, T.E. and Olson, K.R. (2007): "The evolving epidemiology of drug induced seizures reported to a poison control center system". J. Med. Toxicol. 3(1):15-19.

Warner-Smith, M.; Darke, S. and Day, C. (2002): "Morbidity associated with non-fatal heroin overdose". Addiction, 97:963.

Zhang, H.N. and Ko, M.C. (2009): "Seizure activity involved in the up-regulation of BDNF mRNA expression by activation of centralmu opioid receptors". Neuroscience, 161:301-310.

تعاطى المخدرات فى المرضى الذين يعانون من نوبات التشنج للمرة الأولى

المشتركون فى البحث

أ.د. عبد العزيز أبو الفتوح غانم د. سميرة شعبان
د. رانيا حامد عبد الرحمن د. محمد أبو حجازى*

من أقسام الطب الشرعى والسموم الإكلينيكية والعصبية* - كلية الطب - جامعة المنصورة

يعد الإستخدام المزمن والجرعة الزائدة والانسحاب من الأسباب المحتملة لنوبات التشنج في متعاطى المخدرات. لذلك هدفت هذه الدراسة إلى تقييم نمط تعاطي المخدرات في المرضى الذين يعانون للمرة الأولى من نوبات التشنج. وقد شمل هذا البحث ثمانين من المرضى الذين يعانون من نوبات التشنج للمرة الأولى وتم عرضهم على وحدة السموم وقسم الأعصاب بمستشفى الطوارئ بجامعة المنصورة. وتم أخذ تاريخ مرضى كامل من متعاطي المخدرات وبيانات عن تناول المواد والأدوية الغير مشروعة. وقد أجري فحص إكلينيكى شامل وعمل تحاليل للمخدرات فى عينات البول.

وقد أظهرت النتائج ما يلي : كان متوسط عمر المرضى ٢٥,٩ ± ٦,٥ عام ومعظمهم من الذكور. وقد ارتبطت هذه النوبات في الغالب بتعاطى الترامادول (٧٨,٧٥٪) سواء كان منفردا أو بالاشتراك مع المواد الأفيونية ومخلفاتها / أوالقنب أو كلاهما. وهناك ارتباط ذو دلالة احصائية بين العمر و نمط تعاطي المخدرات في المرضى الذين يعانون للمرة الأولى من نوبات التشنج. ووجد أن تعاطي مواد متعددة من المخدرات هو الأكثر انتشارا من تناول مادة واحدة في جميع الفئات العمرية وبين الذكور (٦٦,٢٥٪) ويمكن أن نخلص إلى أن نوبات التشنج من المضاعفات الخطيرة والشائعة في متعاطي المخدرات، وينبغي عدم الاستهانة بها خصوصا مع الترامادول سواء بمفرده أو مع المخدرات الأخرى. كما يجب رفع مستوى الوعي لدى عامة الناس والعاملين في المجال الطبي بشأن إمكانية حدوث تلك النوبات والاعتقاد الخاطئ بأن الترامادول آمن ولا يتوقع أي أخطار أو أعراض جانبية منه .