

Suicidal behaviors among patients with tramadol dependence in a sample of Egyptian population

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Background

Suicidal behaviors are a major health problem in opioid-dependent patients. Tramadol is one of the most abused substance in Egypt, presenting a public burden and associated with higher morbidity and mortality. This study aimed to look for suicidal ideation, suicidal attempts, and nonsuicidal self-injurious behavior among patients with tramadol dependence.

Patients, methods, and results

This study included 120 participants (60 for patient with tramadol dependence and 60 for comparative group). Participants were assessed using the Structured Clinical Interview (SCID-I), (SCID-II) according to the Diagnostic and Statistical Manual, fourth edition; Addiction Severity Index; and Columbia-Suicide Severity Rating Scale. Suicidal ideation was detected in 38.3% of tramadol cases and 13.3% in comparative group ($P=0.001$). Suicidal behaviors were reported in 26.6% of cases and 6.6% in comparative group ($P=0.003$).

Conclusions

Suicide is common in patients with tramadol dependence and is associated with severity of addiction.

Keywords:

dependence, Egypt, suicidal behavior, suicide, tramadol

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Background

Substance dependence is considered a social problem in Egypt; the lifetime prevalence of substance use disorder was 9.6% (Hamdi *et al.*, 2013). Approximately 20–40% of people with substance use disorder used tramadol in Egypt (Abbas *et al.*, 2013). Approximately 83% of Egyptian school students with substance use disorder used tramadol at least once in their lifetime (Bassiony *et al.*, 2015). Tramadol is a centrally acting synthetic opioid analgesic that consists of two enantiomers; both of them contribute to its analgesic activity by different mechanisms. Tramadol and its metabolite desmethyltramadol act as agonists on μ -opioid receptors, and also tramadol enhances presynaptic release of serotonin, inhibits reuptake of serotonin, and inhibits reuptake of norepinephrine (Keskinbora and Aydinli, 2006). Tramadol has become very popular owing to its availability and low price, so thousands of people are developing tramadol dependence. They use it as a self-medication to relieve headache, abdominal pain, depression, and anxiety (Progler, 2010). In Egypt, there is misconception that opioids enhance cognitive and sexual performances and delay physical exhaustion (El-gilany and El-hadidy, 2014). Hence, tramadol abuse has become very popular, especially among young people and middle aged groups, as a self-medication for their sexual problems such as premature ejaculation (Salem *et al.*, 2008). Several studies have

found that the prevalence of suicidal ideation and suicidal attempts are linked with severity and frequency of substance use (Garlow, 2002). Suicidal behaviors are a major health problem in opioid-dependent patients. The mortality ratio for suicide in opioid-dependent patients is 14 times that of their matched peers (Fabien *et al.*, 2008) Suicidality is defined as the act of intentionally ending one's own life. Nonfatal suicidal behaviors are suicidal ideation, suicidal plan, and suicidal attempt (Nock *et al.*, 2006). In Egypt, there is no data bank about suicide leading to underestimation of the suicide problem, and also there is minimal information regarding the suicide risk associated with particular substance use. This lack of data diminishes the ability to evaluate the extent to which risk varies across different types of substance use disorders owing to differences in populations, study designs, and measures between studies (Bohnert *et al.*, 2017). The need for this study comes from observation of high prevalence of suicide among substance-dependent participants. Tramadol is the most abused substance in Egypt, presenting a public burden, and is associated with higher morbidity and mortality among

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young population. To our knowledge, there is no study done to detect suicidality in tramadol-dependent patients. Most studies on suicide-related risks among opioid users have focused on users of heroin (Darke and Ross, 2002).

This study aimed to assess suicidal thoughts, intensity, and behavior among patients with tramadol dependence versus comparative group using Columbia-Suicide Severity Rating Scale.

Patients and methods

Study design and setting

This was a cross-sectional comparative study conducted at Psychiatry Department in Mansoura University Hospital over 6 months. The research work was approved by the local ethical committee of Mansoura University, and all participants gave an informed written consent to participate in the study. Patients' data were secured and coded in a personal computer of the principal investigator from each participating center. The calculated sample size of the study was 60 for patient group and 60 for comparative group according to the nearest paper to our study (Ghaffari-Nejad *et al.*, 2012). Inclusion criteria of the patient group were as follows: (a) age: 18–60 years old, (b) sex: males and females, (c) participants fulfilled the text revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria of tramadol hydrochloride dependence, (d) urine toxicology screen is positive only for tramadol, and (e) regular use of tramadol for at least 1 year. Exclusion criteria of the patient group were as follows: (a) age below 18 years or above 60 years, (b) patients with comorbid axis I diagnosis as verified by Structured Clinical Interviewing using DSM-IV (SCID-I), (c) patients with comorbid medical disorders, (d) patients in acute intoxication or disturbed conscious level, (e) patients with polysubstance abuse, and (f) patients who refuse to share or did not complete the study. Criteria of the comparative group were as follows: (a) matched with patient group for age and sex, (b) never used substances except for nicotine, and (c) have no psychiatric or medical disorder.

Tools

Participants were subjected to the followings: (a) sociodemographic data; (b) medical and neurological history and examination; (c) SCID, which is used to diagnose opioid abuse or dependence and exclude other axis I diagnosis according to DSM-IV-TR classification. Its Arabic version was previously used and validated (Hatata *et al.*, 2004); (d) the SCID-II disorders, which is designed to assess the personality

disorders according to DSM IV. The study used the Arabic version of the SCID-II personality disorders (Hatata *et al.*, 2004); (e) urine samples were collected from the participants to perform urine drug screen by using Abon Biopharm Multi-Drug Screen kits. The screen was for the opioids, tramadol, cannabis, and benzodiazepines to confirm the intake of tramadol and exclude the intake of other addictive substances; (f) assessment of the severity of addiction by Addiction Severity Index, which covers potential problem areas in substance-abusing patients: medical status, employment and support, drug use, legal status, family/social status, and psychiatric status; and (g) the Columbia-Suicide Severity Rating Scale, which is a questionnaire used for assessment of suicidality developed by many institutions, including Columbia University. It is used to assess actual suicidal attempts, nonsuicidal self-injurious behavior, interrupted attempts, aborted attempts, preparatory acts or behaviors, five types of suicidal ideation, intensity of suicidal ideations, and also risk and protective factors of suicide. The study used the Arabic version (Posner *et al.*, 2011). The severity of suicidal ideation was rated on a five-point ordinal scale. The intensity of suicidal ideation was measured depending on five items: frequency, duration, controllability, deterrents, and reasons for suicidal ideation. All items were rated using a five-point scale, where higher points indicate higher intensity. The total intensity scores range from 0 to 25. suicidal behavior was rated categorically as yes/no. The lethality rating for actual suicide attempts was taken directly from the Columbia scale (Nilsson *et al.*, 2013).

Statistical analysis

Calculations were done with the statistical package of SPSS for Windows, version 20.0. Data were expressed as means±SD, frequencies (number of cases), and relative frequencies (percentages). Comparisons of quantitative variables between the study groups were done using Student *t* test. Categorical variables were compared using χ^2 test and Fisher exact test (when more than 20% of cells have count <5). The odds ratios, 95% confidence intervals, and significances were calculated. For all tests, values of *P* value less than 0.05 were considered statistically significant.

Results

The mean age of tramadol group was 29.63±7.4 years and comparative group was 27.62±7.4 years, which had no statistically significant difference. The two groups were matched regarding sex, and the majority of tramadol patients were males. The mean age of

onset of tramadol use was 25.45 ± 7.3 years. The mean number of tramadol tablets was 5.28 ± 2.9 . Approximately 53.3% of cases had previous trials to stop tramadol intake. Approximately 43.3% of tramadol patients used other substances before focusing on tramadol only. Approximately 18.3% of cases had family history of substance abuse, and 6.6% had family history of psychiatric illness. The lifetime suicidal ideation was detected in 38.3% of tramadol use patients, whereas in comparative group was 13.3%, which is statistically significant ($P=0.0017$), as shown in Tables 1 and 2. The lifetime suicidal behaviors were reported in 26.6% of tramadol patients and 6.6% in comparative group, which is statistically significant ($P=0.003$). The mean number of total suicidal attempt among cases was 1.69 ± 1.4 , whereas in control group was 1.25 ± 0.5 , which is not statistically significant. Nonsuicidal self-injurious behavior was found in 16.6% of cases and 3.3% of control group, which is statistically significant ($P=0.014$), as shown in Table 2. There is a

statistically significant correlation between interviewer severity rating of addiction severity index (drug subscale), suicidal ideation score, and intensity score of suicidal ideation. Regression analysis revealed that previous use of other substance and residence were significant predictors for suicidal ideation among patients, whereas age of first use of tramadol, duration of use, employment, and residence were significant predictors for suicidal behavior, as shown in Tables 3 and 4.

Discussion

Suicidal behavior is a continuum which starts with suicidal ideation and may extend further to planning, attempts, and completion (Yuodelis-Flores and Ries, 2015). Several studies found that the prevalence of suicidal ideation and suicidal attempts are linked with severity and frequency of substance use (Garlow, 2002). In viewing the sociodemographic characteristics of our sample, it was predominantly formed of male adults,

Table 1 Demographic characteristics of tramadol and comparative groups

	Tramadol group (N=60)	Comparative group (N=60)	P value
Age (years)			
Mean \pm SD	29.63 \pm 7.4	27.62 \pm 7.4	$P=0.10$
Sex [n (%)]			
Male	58 (96.7)	58 (96.7)	
Female	2 (3.3)	2 (3.3)	
Education			
Elementary and secondary	56 (93.3)	21 (35.0)	$P<0.001^*$
College	4 (6.7)	39 (65.0)	
Occupation			
Unemployed	9 (15.0)	10 (16.7)	$P=0.80$
Employed	51 (85.0)	50 (83.3)	
Marital status			
Currently unmarried	22 (36.7)	39 (65.0)	$P=0.003^*$
Currently married	38 (63.3)	21 (35.0)	
Residence			
Rural	40 (66.7)	29 (48.3)	$P=0.042^*$
Urban	20 (33.3)	31 (51.7)	
Income			
Low	20 (33.3)	7 (11.7)	
Moderate and high	40 (66.7)	53 (88.3)	$P=0.007^*$
Smoking			
Non-smoker	7 (11.7)	51 (85.0)	$P<0.001^*$
smoker	53 (88.3)	9 (15)	

Table 2 Comparison between tramadol and comparative groups regarding lifetime suicidal ideation and behavior

Suicide	Tramadol group (N=60) [n (%)]	Comparative group (N=60) [n (%)]	P value
Any suicidal ideation	23 (38.3)	8 (13.3)	0017^*
Suicidal ideation score [median (range)]	0.0 (0.0–5.0)	0.0 (0.0–4.0)	0.001^*
Suicidal ideation intensity score [median (range)]	0.0 (0.0–18.0)	0.0 (0.0–7.0)	0.001^*
Any suicidal behavior	16 (26.6)	4 (6.6)	0.003^*
Total number of attempts (mean \pm SD)	1.69 ± 1.4	1.25 ± 0.5	0.82
Nonsuicidal self-injurious behavior	10 (16.6)	2 (3.3)	0.014^*

Table 3 Regression analysis to detect suicidal ideation among tramadol cases

Predictors of ideation	β	<i>P</i>	Odds ratio (95% CI)
Previous use other substances	2.13	0.019*	8.42 (1.41–10.87)
Employment			
Not working	3.4	0.06	11.33 (2.34–24.56)
Working			Reference
Residence			
Rural	10.87	0.03*	4.5 (3.45–16.78)
Urban			Reference

Overall % predicted=85.0%. CI, confidence interval.

Table 4 Regression analysis to detect suicidal behavior among tramadol cases

Predictors of suicidal attempts	β	<i>P</i>	Odds ratio (95% CI)
Age at first presentation (years)	-0.437	0.02*	0.65 (0.41–0.87)
Duration of use	0.60	0.013*	3.83 (1.84–7.02)
Previous use other substances	4.01	0.17	55.1 (0.18–172.0)
Employment			
Not working	9.98	0.04*	20.34 (1.45–100.6)
Working			<i>r</i>
Residence			
Rural	4.54	0.02*	16.78 (5.6–25.82)
Urban			<i>r</i>

Overall % predicted=98.3%. CI, confidence interval.

smokers, and living in rural areas. Most of them used tramadol in an attempt to control premature ejaculation and enhance sexual performance, tolerate their difficult psychosocial problems, elevate their mood, escape pain, and enhance their work power, especially in the difficult political and economic situations in Egypt. Lifetime suicidal ideation was observed in 38.3% of the patient group, whereas in comparative group was 13.3%, which was statistically significant, and suicidal behavior was reported in 26.6% of patient group and 6.6% in control group. This finding was statistically significant. Our findings were in agreement with a study on heroin-dependent participants, which found that suicidal ideations were ranging between 34 and 60% (Darke *et al.*, 2004). In another study on cocaine users, suicidal ideation was reported in 40.5% (Garlow *et al.*, 2003). Our results were lower than those recorded in a study on heroin-dependent patients in Lebanon, where they found that 65.6% of patients were suicidal ideators (Kazour *et al.*, 2016). Concerning the results of suicidal behavior, our results were lower than the results of a Norwegian study, which reported attempts in 58% of patients with polysubstance use (Landheim *et al.*, 2006). In another study of opiate addicts, the lifetime prevalence of suicidal behavior was 49% (Oyefeso *et al.*, 2008), and also in a study done on 160 opioid-dependent patients, 48% of participants reported suicidal behavior (Trémeau *et al.*, 2008). In a study on cocaine-dependent participants seeking substance abuse treatment, it was demonstrated

that 39.2% of participants reported suicide attempts (Roy and Segal, 2001). Similar results were reported in a study by Roy (2009); they found that 43.5% of abstinent cocaine-dependent participants had attempted suicide. Our results were higher than those recorded in a Turkish study, which denoted that 23% of students (aged 13–18 years) had suicidal ideations during their lifetime (Eskin *et al.*, 2007). Moreover, our results were higher than those recorded in a study done by Guo *et al.* (2019) to assess the association between opioids and suicide among Chinese students. They observed that 16.1% students had suicidal ideation, and 3.1% of them had suicidal attempts (Guo *et al.*, 2019). Notably, the prevalence of suicide is highly variable; this may be owing to many factors, such as sample characteristics, the used scales, and study designs. The possible explanations of association between tramadol abuse and suicide in our study may be owing to the pharmacological properties of tramadol itself; social factors associated with tramadol abuse such as low education, low income, and rural residence; the characteristics of the individuals; and psychological factors, such as hopelessness, helplessness, increased frustration, and personality factors such as high impulsivity. All these factors may interact in ways that lead certain individuals to become prone to engage in health-damaging behavior. Another explanation of such association is the negative effect of tramadol use on cognitive functions, leading to poor judgment, which increases the risk of impulsive suicide

and self-induced injurious behavior, especially when taken in high doses (most of our cases took a large number of tramadol tablets). It has been found that prolonged opioid use can induce an over-response to painful stimuli (Chu *et al.*, 2008); this increased sensitivity to pain may explain the association between opioid use and suicidal behaviors (Olié *et al.*, 2013). The direct association between opioid use and suicide can be explained by the disinhibition effects of opioids, which could increase the likelihood that individuals with suicidal thoughts or plans could act on these impulses (Conner *et al.*, 2011). Moreover, opioid use may represent a coping strategy to reduce despair created from pain, emotional problems, sleep disturbance, heightened arousal, and agitation (Fink *et al.*, 2014), each of which are also associated with suicide (Borges and Loera, 2010).

Strengths of the study

The strength of this study is that it is one of the earliest studies done to measure the association between tramadol dependence and suicide.

Limitations of the study

This study has some limitations: (a) cases were from a single location and were of limited number, so generalization of our results cannot be done, (b) no follow-up was done for cases, as the study was conducted on their first visit to outpatient clinic, and (c) the cross-sectional design did not allow establishing an evidence-based relationship or a temporal sequence between tramadol dependence and suicidal ideations or plans.

Conclusions

Tramadol dependence is a major health problem in Egypt, particularly in the working years of life. Tramadol-dependent participants have higher rates of suicidal ideation and attempts compared with general population, which is associated with the severity of tramadol dependence.

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Conflicts of interest

There are no conflicts of interest.

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