A study of opioid dependence among Mansoura University students

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Background
The prevalence of opioid dependence is increasing in the world and in Egypt among university students, which because of many false concepts being adopted.
Objectives
This study was conducted to detect the prevalence and the effects of opioid dependence among a sample of Mansoura University students.
Participants and methods
The study was carried out on 700 male students, aged 18–25 years. All students were assessed using semistructured interview and urine drug screening. Students were divided into three groups: the first group comprised 300 students who were not drug users, the second group comprised 300 polysubstance users, and the third group comprised 100 solitary opioid users. The first and third groups were subjected to psychometric assessment using Mini Neuropsychiatric Interview for substance dependence, Arabic version. Psychometric assessment was performed with the following tools: Wisconsin Card Sorting Test, Hamilton rating scale for depression, and PANSS positive and negative symptom scale; laboratory investigations included liver function tests and kidney function test.
Results
We found that out of 100 students who were opioid users, 88 students used tramadol and 12 used heroin. Liver and renal functions were nearly normal in cases, with a high statistically significant difference between cases and controls regarding serum glutamic oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), and creatinine. Higher scores for Hamilton scale for depression and trail A and B mean values were found in cases compared with controls.
Conclusion
The prevalence of tramadol dependence among Mansoura University students is higher than heroin dependence. In addition, opioid dependence has a negative biological and psychiatric sequelae, which is contrast to the false concepts of opioid dependence.

Keywords:
Cognitive function, creatinine, depression, false concepts, liver function, opioids

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Introduction

Substance dependence is a social international problem. In Egypt, since the 1970s there has been a great increase of substance dependence (Hamdi *et al.*, 2016). According to the WHO (WHO, 2010), the prevalence of drug dependence in individuals between 15 and 64 years of age in Egypt was 0.8%. In recent studies, opioids were the substances of major problem in 44% of the substance dependence cases (tramadol tablets were the main dependence substances in 30% of the sample, heroin in 12%, and nalbuphine in 2%) (Mohamed *et al.*, 2013; Mohamed *et al.*, 2015).

In the Middle East region, tramadol dependence has increased, particularly in Iran (Nazarzadeh *et al.*, 2014) and Egypt (Abolmaged *et al.*, 2013). The prevalence of lifetime tramadol misuse among Iranian adolescents was 4.8% (Nazarzadeh *et al.*, 2014). In Egypt, it was found that 20% of Egyptian male students have used drugs (Soueif *et al.*, 1986): 5% hashish dependence, 1% opiate dependence, 2.5% tranquilizer dependence, 1.5% stimulant dependence, and 2.15% hypnotics dependence (Soueif *et al.*, 1990). The last Egyptian National Survey report shows that 8.6% of Egyptians used drugs at least once during their lives (Hamdi *et al.*, 2013). Tramadol dependence has markedly increased in Egypt since 2008 (Abolmaged *et al.*, 2013). The

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mean age of the heroin addicts' first-time use of heroin was 19.67 years. Kumar *et al.* (1996) reported that 7% of the heroin users started heroin at an age younger than 17 years, and about 83% of them began to use heroin between the ages of 16 and 24.

Drug dependence was significantly higher among individuals between 18 and 25 years of age (44%) than among those between 26 and 40 years of age (EL-Sherbiny, 2015). An Egyptian study shows that tramadol dependence starts as follows: 21% of the patients started tramadol dependence for its pleasurable effect (to improve mood), 20% of the patients for sexual purpose (prolongation of the time of intercourse), 14.1% to get more power for hard work (to delay feeling fatigue), 13% for pain relief, 12% as self-medication to relieve depression, 11% as self-medication to relive anxiety, 9.5% because of peer pressure, and 4.5% for other purposes (Mohamed *et al.*, 2015).

Chronic use of opioids leads to impairment in learning and memory because of their effect on the frontal cortex (Yang *et al.*, 2009) and the hippocampus (Lu *et al.*, 2010). Havard *et al.* (2006) reported that the prevalence of depression among opiate addicts, depending on the population, setting, and recall period, ranges between 15 and 45%.

Ilic *et al.* (2010) had reported that heroin dependence induces vesicular and fatty changes in the liver tissue. Another study showed that tramadol was found to significantly increase SGOT and SGPT among its users, and serum aminotransferase levels can be elevated in a small proportion of patients receiving tramadol at high doses (Loughrey *et al.*, 2003).

Rationale of the study

We hypothesize that opioid dependence has negative effects on psychological functions (cognitive, mood, and psychosis) and liver and/or renal functions among university students.

Participants and methods

Study design

This is a cross-sectional study and a control study.

Site of the study

This study was conducted in Mansoura University Students' Hospital.

Participants

All students (n=700) who came to the psychiatric clinic of Mansoura University Students' Hospital in 6 months duration were subjected to urine screening for drugs. Out of 700 screened students, 43% (n=301) were negative for drug use, 42.8% (n=299) were multidrug addicts, 12.2% (n=86) were tramadoladdicts, and 2% (n=14) were heroin addicts. A total of 100 students fulfilling the criteria for diagnosis of solitary opioid dependence matched with 100 healthy control individuals as regards age and sex. Informed written consent was obtained from all subjects after explanation of the procedures.

Inclusion criteria for the patient group

Patients were recruited from the outpatient clinic of Psychiatry Department at Mansoura University Students' Hospital, according to the criteria of opioid dependence of DSM-IV-TR. Male individuals were aged from 18 to 25 years old.

Exclusion criteria

Exclusion criteria included other drug use or polysubstance use, cases that have any hepatic or renal illness before the use of drugs or because of any other causes (viral hepatitis), or cases taking any other drugs that affect renal or hepatic function.

Inclusion criteria for controls: Controls were recruited from the attendants coming to medicine clinics at Mansoura University Students' Hospital (for medical fitness before they could join certain sports or gym). Cases with no history of psychiatric or neurological diseases and those who do not have any hepatic or renal diseases were included in the study. Controls included people of both sexes and same age range between 18 and 25 years. All were subjected to the same scales and tools of the case group.

Assessment tools

(1) *Clinical assessment of the patients*: A semistructured interview was conducted, which included the following – detailed history taking and thorough clinical examination using Mansoura University Hospital psychiatric sheet and Mini Neuro-psychiatric Interview for substance dependence Arabic version (Sheehan *et al.*, 1998), and complete thorough physical and neurological examinations.

(2) *Psychometric assessment*: This included Wisconsin Card Sorting Test (WCST) (Heaton *et al.*, 1993), trail making cognitive test (Reitan, 1958), Hamilton rating scale for depression (Hamilton, 1960), and PANSS positive and negative syndrome scale (Kay *et al.*, 1987).

(3) Laboratory: Laboratory investigations included liver function tests (SGOT) and (SGPT) levels, as well as renal function test.

All data were collected, tabulated, and statistically analyzed using SPSS 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

This study was approved by Ethical Committee at Mansoura University, Faculty of Medicine.

Results

Table 1 shows that the studied groups were matched regarding age and sex, with a mean age of 22.29 and 22 years, respectively, for cases and control. All participants were male. Opioid dependence was more frequent in rural areas than in urban areas.

Table 2 shows that there was a high statistically significant difference between cases and controls regarding SGOT, SGPT, and creatinine, with higher mean values in cases than in controls (38.8, 38.03, and 0.79 for cases vs. 36.8, 37.4, and 0.65 for controls). In spite of this difference, very few cases showed an abnormal level of SGOT and SGPT without a statistically significant difference between cases and controls.

Table 3 shows that there was a high statistically significant difference between cases and controls regarding mean Hamilton scale for depression score and its grouping, with higher mean score in cases than in controls (11.92 and 8.32, respectively). Mild depression was higher among controls, whereas moderate depression presented in cases.

Table 4 shows a statistically significant weak positive correlation between trail making test, PANSS scores, and Hamilton scale for depression score in cases, whereas Wisconsin card sorting score shows a statistically significant weak negative correlation with Hamilton scale for depression score in the control group.

Table 5 shows that the Hamilton scale for depression score, PANSS test positive and negative symptom scores, trail A, trail B, and preservative response were statistically significant predictors for cases, with the total percentage predicted to be 99.5%.

Discussion

As the international society is striving to increase the social awareness about dependence – especially opioid dependence – this study was conducted to highlight the problem of opioid dependence being a great social and international concern in an alarming phenomenon, especially the use of tramadol with a lot of wrong concepts about its effects. In our search, we focused on the effects of opioid dependence (tramadol and

Table 1 Sociodemographic data of the whole sample

Group characteristics	Cases (*N*=100) [*N* (%)]	Control (*N*=100) [*N* (%)]	Significance	OR (95% CI)
Age (years) (mean±SD)	22.29±2.1	22±1.4	t=1.004P=0.32	
Sex				
Male	100 (100)	100 (100)		
Residence				
Rural (r)	58 (58)	54 (54)	χ^2=0.33P=0.56	1.176 (0.673–2.06)
Urban	42 (42)	46 (46)		
Family history	25 (100)	0		

CI, confidence interval; OR, odds ratio.

Table 2 Comparison of laboratory results between cases and control

Group (laboratory results)	Cases (*N*=100)	Control (*N*=100)	Significance
SGOT (U/l) (mean±SD)	38.8±2.5	36.8±1.4	t=7.01P<0.001*
SGPT (U/l) (mean±SD)	38.03±1.7	37.4±1.7	t=2.62P=0.01*
Creatinine (mg/dl) (mean±SD)	0.79±0.16	0.65±0.16	t=6.12P<0.001*
SGOT (U/l)			
Abnormal	5 (5)	0	Fischer exact, P=0.06
Normal	95 (95)	100 (100)	
SGPT (U/l)			
Abnormal	(1)	0	Fischer exact, P=1
Normal	99 (99)	100 (100)	
Creatinine (mg/dl)			
Normal	100	100	–

*Significant P value below 0.05.

Table 3 Comparison of Hamilton score between cases and control

Groups (Hamilton)	Cases (*N*=100)	Control (*N*=100)	Significance
Mean±SD	11.92±2.2	8.32±0.91	t=15.15P<0.001*
Hamilton scale [*N* (%)]			
Normal	0	20 (20)	χ^2=45.16P<0.001*
Mild depression	75 (75)	80 (80)	
Moderate depression	25 (25)	0	

*Significant P value below 0.05.

Table 4 Correlation of Hamilton score with age, PANSS, trail making test, and Wisconsin Card Sorting Test scores

Group parameters	Cases (*n*=100)	Control (*n*=100)
Age	*r*=0.165	*r*=−0.204
	P=0.102	*P*=0.042
PANSS	*r*=0.2	*r*=0.224
	P=0.046*	*P*=0.025
Trail test	*r*=0.29	*r*=0.09
	P=0.003*	*P*=0.37
Wisconsin test	*r*=0.167	*r*=−0.23
	P=0.096	*P*=0.025*

*Significant *P* value below 0.05.

Table 5 Logistic regression for prediction of cases of dependence

Predictors	β	*P* value	OR	95% CI of odds ratio
Hamilton	2.88	0.001*	17.9	3.18–100.2
PANSS	−2.88	0.027*	0.06	0.004–0.724
Trail A	0.45	0.016*	1.57	109–2.26
Trail B	0.17	0.017*	1.19	1.03–1.36
PR	0.42	0.002*	1.52	1.16–1.98

Constant=−89.58; model χ^2=258.14; percent predicted=99.5%. CI, confidence interval; OR, odds ratio; PR, preservative response. *P<0.001.

heroin), as they have great social, physical, and neuropsychological consequences (Gruber Staci *et al.*, 2007). Therefore, this study was conducted to reveal the effects of opioid dependence on the cognitive functions, psychiatric effects, and physical effects (liver and renal functions), as well as to know about the prevalence of opioid dependence among university students and to have a comparison between tramadol and heroin dependence in a sample of university students.

We found that 43% of cases were positive for multidrug and other drug use, 12% were positive for tramadol use, and 2% were positive for heroin use. This result is in agreement with another study, which reported that about 43.94% (*n*=145) of the patients were under polysubstance use, whereas the percentages of patients who used one substance were as follows: tramadol, 30.30% (*n*=100); and heroin, 11.52% (*n*=38) (Mohamed *et al.*, 2015). In contrast to our study (Bassiony *et al.*, 2015), another study stated that tramadol dependence is more prevalent than other drugs, and this may be because of the different age range. From these results, we found that tramadol is more addictive than heroin, and these results were supported by the study by Fawzy (2010) who reported that tramadol is associated with an increased probability of being addicted, as it is more accessible and cheaper than heroin, its price is lower, its availability without prescription makes it easy to obtain, and also because of the false concept about tramadol as they consider it as a treatment for premature ejaculation and to increase sexual orgasm, and as it lowers depressive criteria in relation to stresses, such as headaches and relieve back aches to increase the productivity. It was stated by epidemiological reports that tramadol dependence has increased in the USA, and recently in (Dare *et al.*, 2011) Iran (Nazarzadeh *et al.*, 2014) and Egypt (Abolmaged *et al.*, 2013).

The sociodemographic data of the two groups (opioid dependences and control) showed that the studied groups were matched regarding age and sex, with a mean age of 22 years. Other studies are in harmony with our results showing that the mean age of the heroin addicts' first-time use of heroin was 22±4 years old (Mohamed Mosad Salama *et al.*, 2015).

In agreement with our study, a study reported the highest prevalence of substance abuse among persons to be between 18 and 25 years of age (Hamdi *et al.*, 2013).

Cases were more frequent in rural areas than in urban areas, without a statistically significant difference between cases and controls. In contrast, one study suggested (Hamdi *et al.*, 2013) that opioid abuse is less prevalent in rural areas. This difference may be because the university students attending to the psychiatric clinic in university student's hospital are from rural areas and cannot go to private clinics, and the urban students prefer going to private clinics.

The renal and liver functions were within normal ranges in the two groups but significantly higher in cases than in controls (high normal). These results were supported by a recent study in rats, which reported a significant increase in the levels of liver functions enzymes and creatinine as a result of chronic use of opioids, and these findings suggest the possible hepatotoxic effects of opioids (morphine and tramadol) in the long term (Atici *et al.*, 2005). A more recent study by El-Hadidy and Helaly (2015) in humans documented that the liver function enzymes were within normal limits; however, a

slight nonsignificant rise in liver enzymes was reported in some cases.

The current study showed that a higher mean score of Hamilton scale of depression was found in cases than in the control group, with a high statistically significant difference. Moderate depression was more frequent among heroin addicts and mild depression was more frequent among tramadol addicts. This is in agreement with that found by El-Hadidy and Helaly (2015), who reported that depression scores were higher with a statistically significant difference after stopping tramadol use than before the treatment, as tramadol has a mechanism of action by which it increases serotonin, norepinephrine, and 5/HT2-C antagonist receptors and this results in improvement in the depressive symptoms. Another study supports our results, reporting that depression is more prevalent in heroin users and is higher than in the general population (Havard *et al.*, 2006).

Moreover, in this study, the severity of depressive symptoms assessed with the Hamilton scale of depression was one of the predictors of opioid dependence. This result is consistent with another study (Boscarino *et al.*, 2010). The other important predictor for opioid dependence was PANSS scores (positive and negative symptoms scores). Many contradictory studies have been established related to this issue. For example, one study (Dervaux *et al.*, 2001) reported no relationships between the severity of symptoms and substance dependence, whereas Pencer and Addington (2003) reported that substance use was associated with more severe positive symptoms. After that Talamo *et al.* (2006) adopted the hypothesis that cases with comorbid disorders had more positive versus negative symptoms than cases with no comorbidity, and both studies are in agreement with our current study.

A great number of models were proven to explain the association between substance dependence and psychotic symptoms, and the most agreed one is self-medication hypothesis (Khantzian, 1997), which states that substance abuse disorder is an extension of psychotic disorder to decrease their symptoms, especially opioids, as opioids have an antipsychotic effect. Besides, there are models that suggest that schizophrenia (Gottesman and Shields, 1976) and substance use disorder (Rhee *et al.*, 2003) stem from the same genetic load.

In the current study, we found group differences regarding neurocognitive assessments by using WCST and trail test. The psychometric properties of WCST were examined using factor analytic techniques by several studies. By applying these factors to our results, we found that there was poor performance across the parameters of factors 1 and 3 in cases (indicating deficits in concept formation, flexibility, memory, and attention). Better performance was found in factor 2, which represents problem-solving. This comes with what was reported by another study (Soyka *et al.*, 2011), which states that chronic opiate abuse, such as heroin and morphine, is found to harm cognitive function. Other studies suggested that chronic opiate dependence has effects on brain points related to learning and memory, such as the frontal cortex (Yang *et al.*, 2009) and the hippocampus (Lu *et al.*, 2010). On the contrary, other studies (Guerra *et al.*, 1987) found that there was no difference between heroin dependences and controls with regard to neuropsychological measures. This may be explained by the dose and duration of the opioid dependence in this study and different methodological tools. Some studies have found that the performance in heroin dependence was the same as the control group (Rohlinga *et al.*, 2002), or that some areas of cognitive function are spared relative to others.

This study also reveals that the cognitive function is negatively correlated with depressive symptoms and age, and this was in agreement with many studies, one of which was the study by Gould Thomas (2010), who stated that depressed mood was associated with decreased performance on measures of memory. Moreover, this study found that cognitive function is a good predictor for substance dependence in general, and opioid dependence. We found that there was a positive correlation between trail making test part A and B scores and opioid dependence, which means that cognitive dysfunction predicts opioid dependence, and this is in agreement with the study by Gould Thomas (2010).

Conclusion

We found that polysubstance dependence is more prevalent in university students. Tramadol dependence is more prevalent among students than heroin dependence. Opiate dependence was associated with severe depression and deterioration of cognitive function. Depressive symptoms and cognitive dysfunction can predict opioid dependence.

Limitations of the study

This study is limited by the small sample size. Consequently, the participants might not be

representative of Mansoura University students. In addition, the denial of students in this study decreases our chances of detecting the prevalence of dependences. Besides, the young age of the case group decreased our chance to detect sexual effects of opioid dependence, as they are not married.

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Conflicts of interest
There are no conflicts of interest.

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