

*Research Article***Sexual Dysfunctions among Male Patients with Tramadol Abuse**

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Abstract

Objectives: This study aims to assess the effect of tramadol abuse on sexual functions in males.

Methods: We recruited subjects from Hot Line Clinic of Minia Psychiatric Hospital, Minia during a 6-month period. After taking their consent, 68 subjects with a history and a positive urine analysis test of tramadol abuse were included. They were assessed clinically by international index of erectile function (IIEF). They were compared with a control group of 43 subjects with no history of drug abuse and negative urine analysis test. **Results:** All the aspects of sexual function were significantly better in the control group than the tramadol abuse group. Within the tramadol abuse group, all the parameters of sexual function were significantly better before using tramadol than during tramadol use. There was a significant correlation between the number of symptoms and the intercourse satisfaction, and erectile function; and between daily dose of tramadol and sexual desire and erectile function. **Conclusion:** Patients with tramadol abuse are more likely to have sexual dysfunctions than healthy controls.

Key Words: tramadol, abuse, sexual dysfunction

Introduction

Tramadol is a centrally-acting synthetic opioid analgesic of the aminocyclohexanol group. Although it is a synthetic analogue of codeine, it has a significantly lower affinity for opioid receptors than codeine. Additionally tramadol influences the activity of noradrenaline and serotonin processes in the central nervous system.

Tramadol causes typical opiate-like withdrawal symptoms as well as atypical withdrawal symptoms including seizures. The atypical withdrawal symptoms may be related to its effect on serotonin and norepinephrine reuptake (Choong and Ghiculesco, 2008).

An increasing alarming phenomenon of tramadol abuse has been heavily demonstrated in the Egyptian community (Salem et al., 2008). Tramadol abuse has dramatically increased in the Middle East region, especially in Egypt (Abolmaged et al., 2013). Its use is attributed to its popularity as a remedy for premature ejaculation and for extended orgasm and to increase sexual pleasure (Salem et al., 2008).

The relation between tramadol and sexual function is controversial. There is evidence that

men with premature ejaculation may benefit from using tramadol off label (Alghobary et al., 2010 and Yang et al., 2013 and Martyn- St James et al., 2015). However these patients are at risk to develop other sexual dysfunctions.

In 2010, Alghobary et al., observed that all cases with premature ejaculation showed significant less erection measured by the Arabic Index of Premature Ejaculation scores after 6 weeks and 12 weeks of using tramadol on demand compared with the baseline level.

On the other hand, in 2011 Wong et al., noticed that the incidence of erectile dysfunction among 26 opioid users and 6 controls was equally present in both groups. Men with erectile dysfunction had lower free testosterone levels regardless of whether they were on opioids.

In a study done in Egypt, tramadol was found to be associated with decreased sexual self-esteem and overall sexual relationship satisfaction as measured by the Arabic version of Self-Esteem and Relationship (SEAR) questionnaire. The study also showed significant improvement in overall sexual satisfaction 6 months after treatment compared with pretreatment assessment (El-Hadidy & El-Gilani, 2014).

Materials and Methods

The study was held in Minia Psychiatric Hospital, the official psychiatric hospital in Minia Governorate. It provides services for psychiatric patients and patients of substance abuse with a 60-bed inpatient capacity as well as a daily outpatient clinic and a Hot Line Clinic for substance abuse.

All married male clients attending Hot Line Clinic in the duration of 6 months (from July 1, 2017 to December 31, 2017) were subjected to urine screening analysis for substances of abuse. Those with a positive screening test for tramadol only were included. Additional inclusion criteria were: (1) age range: 20 to 45 years; (2) patient's consent to participate in the procedures of the study. Those with a history of major physical (such as diabetes mellitus, heart failure, renal failure, and hepatic failure) or mental (such as schizophrenia) illness were excluded. The total number of subjects finally included in the study was 68 subjects.

Another group of 43 healthy married subjects, within the same age range, were included as a control group.

A comprehensive sheet was used for evaluating the study's subjects. It included socio-demographic data, history of cigarette smoking, detailed history of tramadol use and treatment,

family history of substance use, and screening for psychiatric symptoms.

This was followed by mental state examination and general and neurological examination to exclude any major physical illness that may affect sexual functions.

Structured clinical interview for DSM-5 (SCID-5), substance use module was used for diagnosis of opioid use disorder attributed to tramadol. Then addiction severity index (ASI) was used for evaluation the severity of effect of tramadol use on different domains.

Different domains of sexual function (sexual desire, erection, ejaculation, orgasm, sexual satisfaction, sexual preoccupation, and sexual quality of life) were evaluated using international index of erectile function (IIEF).

Data analysis was done using Statistical Package for Social Sciences (SPSS) Version 19.0 for windows. Frequencies and percentages were calculated for categorical variables, whereas means and SDs were calculated for continuous variables. Descriptive statistics of the study participants were conducted. T tests were used to compare the group with tramadol use and the control group on continuous variables, whereas χ^2 tests were used in comparing the two groups on categorical variables.

Results

Table 1: Socio-demographic characteristics of the tramadol use group and the control group

Variable	Tramadol users N=68	Control N=43	Relation to tramadol	
			t test	P value*
Age (years)				
Mean ± SD	33.66±5.666	32.23±4.535		
Range	21-44	24-42	1.395	0.166
Duration of Marriage (years)				
Mean ± SD	11.19±5.502	9.79±5.031	16.405	0.180
Range	1-25	1-21		
Smoking index				
Mean ± SD	380.74±244.888	265.12±100.388	2.785	0.006*
Range	40-1200	120-520		
Occupation				
Unskilled manual worker	20 (29.4%)	5 (11.6 %)	6.039	0.110
Skilled manual worker	36 (52.9%)	26 (60.5%)		
Trade/ business	3 (4.4%)	5 (11.6 %)		
Clerk	9 (13.2%)	7 (16.3 %)		
Residence				
Rural	51 (75%)	35 (81.4 %)	0.617	0.432
Urban	17 (25%)	8 (18.6 %)		

* $P \leq 0.05$ is statistically significant

Table 2. Characteristics of tramadol use

Variables	Results
Age at onset (years)	
Mean ± SD	26.24±6.472
Range	16-41
Duration of use (years)	
Mean ± SD	7.74±3.610
Range	2-17
Average daily dose (milligrams)	
Mean ± SD	1016.53±636.539
Range	50-2700
Type of tramadol	
Illegal forms	68 (100%)
Pharmaceutical forms	0 (0%)
Route of administration	
Oral	68 (100%)
Injection and other routes	0 (0%)
Family history of substance use	
Yes	39 (57.4%)
No	29 (42.6%)
Previous treatment	
Yes	37 (54.4 %)
No	31 (45.6 %)
Inpatient	11 (29.7 %)
Outpatient	26 (70.3 %)

Table 3: Results of international index of erectile function (IIEF)

	Tramadol users N=68	Control N=43	Relation to tramadol	
			T test	P
Erectile function				
Mean ± SD	18.57±5.642	29.51±1.009	-12.56	0.000*
Range	7 to 30	26 to 30		
Intercourse satisfaction				
Mean ± SD	10.13±2.769	13.6±2.29	-6.86	0.000*
Range	3 to 15	7 to 15		
Orgasmic function				
Mean ± SD	7.44±1.731	9.88±0.391	-9.09	0.000*
Range	4 to 10	8 to 10		
Desire				
Mean ± SD	6.63±1.803	9.65±0.573	-10.63	0.000*
Range	2 to 10	8 to 10		
Overall satisfaction				
Mean ± SD	7.18±1.868	9.26±1.026	-6.68	0.000*
Range	3 to 10	6 to 10		

* $P \leq 0.05$ is statistically significant

Table 4: Correlation between sexual functions and tramadol use characteristics

	Age at first use		Duration of use		Daily dose		SCID-5	
	R	P value	R	P value	R	P value	R	P value
Erectile function	-0.217	0.076	-0.168	0.172	-0.259	0.033*	-0.440	0.000**
Intercourse satisfaction	-0.098	0.425	0.057	0.643	-0.229	0.060	-0.314	0.009**
Orgasmic function	0.206	0.091	0.040	0.743	-0.142	0.248	-0.201	0.100
Desire	-0.097	0.430	-0.196	0.109	-0.318	0.008**	-0.224	0.066
Overall satisfaction	-0.120	0.332	0.005	0.969	-0.142	0.249	-0.153	0.213

* $P \leq 0.05$ is statistically significant

As shown in (Table 1), there was no statistically significant difference between the group of tramadol users and the control group regarding socio-demographic characteristics (age, sex, residence, educational level, and working status at time of interview).

Table 2 illustrates characteristics of tramadol use among the tramadol use group. The mean age at onset of tramadol use was 26.24 ± 6.472 years. The mean duration of tramadol use was 7.74 ± 3.610 years. The average daily dose was 1016.53 ± 636.54 milligrams. All subjects reported using illegal forms and oral route of administration. 49 subjects (57.4%) reported family history of substance use. Sexual

performance and seeking pleasurable effects were the commonest factors predisposing to start of tramadol use. Most patients (60%) had moderate severity of addiction. More than half of the patients (54.4%) reported history of previous treatment. Only 29% of them reported previous hospital admission for treatment of addiction.

Table 3 shows that there was a statistically significant difference between the tramadol users and control group regarding erectile function, sexual desire, orgasm, intercourse satisfaction and overall satisfaction as measured by IIEF.

Table 4 illustrates that there was a statistically significant negative correlation between average daily dose of tramadol and erectile function and sexual desire. Also, there was a statistically significant negative correlation between number of symptoms according to SCID-5 and intercourse satisfaction and erectile function. Age at onset of tramadol use and duration of tramadol use showed no statistically significant correlations with any of the assessed domains of sexual function.

Discussion

Similar to our study, many previous Egyptian studies of tramadol addiction were carried out in outpatient addiction clinics (El-Hadidy & El-Gilani, 2014; El-Hadidy & El-Helaly, 2015; El-Sayed et al., 2015; Bassiony et al., 2016 & 2017).

The inclusion of subjects in the study provided that they were *married*, was for insuring that patients have regular sexual intercourse. This is similar to a previous study by El-Hadidi & El-Gilani (2014). However, this is difference from Abdelazim et al. (2015) who included divorced and single subjects in his study.

Only subjects in the *age range from 20 to 45 years* were included; this helps avoiding as much as possible the effect of old age on sexual functions. Other studies put comparable age restrictions for the same purpose (El-Hammadi et al., 2014 and Abdelazim et al., 2015). El-Hadid & El-Gilani (2014) didn't state a maximum age for inclusion, however there was no subjects in their sample above 49 years.

The selection of subjects with *pure tramadol abuse* and exclusion of polysubstance abusers (on the bases of history and urine screen tests for substances of abuse) was decided on the grounds of avoiding the effects of other substances on the sexual functions as well as the interactions between tramadol and the other substance as a cause for sexual dysfunctions. This coincides with one previous study (El-Hadid & El-Gilani, 2014), but it was not the case in other studies; Farag et al. (2018) included not only patients with pure tramadol use, but also patients with predominantly tramadol use.

The average *daily dose* was $1,016.53 \pm 636.539$ milligrams, ranging from 50 to 2,700 milligrams. This high dose can be explained by the phenomenon of tolerance. These findings are consistent with previous Egyptian studies (El-Hadidy and El-Helaly, 2015; Shalaby et al., 2015; Rizk et al., 2016; Abou El-Magd et al., 2018 and El-Wasify et al., 2018) who found approximately similar results. However, there was one study found much lower average daily dose around 650 milligrams daily (Farag et al., 2018).

Our study found a statistically very significant difference between the tramadol use group and control group regarding use of medications for erectile dysfunction. All the 57 subjects started use of ED medications after the onset of tramadol use. This is in consistent with two previous studies which found increase in use of medications for erectile dysfunction among those using opioid analgesics for long durations (Deyo et al., 2013 and Chou et al., 2015). These findings indicate the bad effect of long-term tramadol use on the erectile function, which is confirmed by other tools in our study and in previous studies on sexual functions in tramadol users (Daniell, 2002; Al-Gommer et al., 2007; Bang, 2007; Palha & Steves, 2008; Bhasin et al., 2010; Zhang et al., 2014; Abdelazim et al., 2015; Ferrer et al., 2015 and Abd El-Qader, 2017).

Also, the two groups showed a statistically significant difference in erectile function. This is in consistent with many previous studies including Daniell, 2002; Al-Gommer et al., 2007; Palha & Steves, 2008; Zhang et al., 2014 and Abdelazim et al., 2015. This can be explained by the inhibitory effect of tramadol on sex hormones (Abdelazim et al., 2015; Abo El-Soud, 2016; Abd El-Qader et al., 2017 and Fahim, 2018).

Regarding sexual desire, our study found a statistically significant difference between the two groups. This is in agreement with other previous studies (Mirin et al., 1908; Al-Gommer et al., 2007; Abdelazim et al., 2015 and Aggarwal et al., 2016).

There was a statistically significant difference between the two groups in orgasmic function. This in agreement with other previous studies (Goldsmith et al., 1984; Zhang et al., 2014 and Abdelazim et al., 2015).

Intercourse satisfaction and overall satisfaction showed a statistically significant difference between the two groups. This is in consistence with other findings in our study that is the poor scores of all other domains of sexual functions which subsequently lead to poor sexual satisfaction; and also in agreement with previous studies (El-Hadidy & El-Gilani, 2014 and Abdelazim et al., 2015).

Our study found a statistically significant negative correlation between daily dose of tramadol and both *erectile function* and *sexual desire*. This is in consistent with Cushman (1973) who found a significant inverse correlation between opiates dose and serum testosterone level and hence sexual functions. However, this is in contrast with Al-Gommer et al., (2007) and Abd El-Qader (2017) who failed to demonstrate any significant relationship between dose of heroin or tramadol and any of sexual functions or sex hormone levels. This can be explained by the relatively smaller number of subjects and lower average of daily dose of tramadol in their study than ours.

Conclusions

- (1) Long term tramadol use has a statistically significant negative effect on all domains of male sexual functions.
- (2) Average daily dose and severity of addiction are significantly correlated to sexual dysfunctions in patients with tramadol abuse.

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