Egyptian Journal of Psychiatry

Vol. 45, No. 1, 2024
ISSN: 1110-1105 (print)
ISSN: 2090-2425 (online)
DOI: 10.21608/EJPSY.2024.380497

ORIGINAL ARTICLE

Sexual Dysfunction in Opiate-Dependent Male Patients

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Background Substance abuse is increasingly reported among young people, which represents a serious threat to society. This problem is more common in males. Sexual functions are seriously impaired in addicts.
The effect of substance abuse on sexual functions and sex hormones is considered as an interesting field for research.
Psychoactive drugs are commonly regarded to have an aphrodisiac effect; in fact, they affect different sexual functions negatively.
This study aims to evaluate how opioid use disorder (tramadol HCL vs. heroin) affects sexual function in men. Moreover, this study examines several important factors for prevention of sexual dysfunction in opiate abusers.

Patients and Methods All samples of the study were subjected to the following tools before and 3 months after abstinence: structural clinical interview DSM5 and addiction severity index, Arabic version (5thed). The international index of erectile function, a multidimensional scale for assessment of erectile dysfunction, Arabic version, was used.The self-seem and relationship questionnaire, Arabic version, was used. Serum levels of free testosterone were measured. Urine test for detection of opiates was done.

Results This study showed a statistically significantly higher international index of erectile function score among volunteers than the patient group (P <0.001), as well as self-esteem and relationship score. Moreover, serum free testosterone was statistically significantly higher among volunteers than the patient group (P <0.001). The previous results had improved after abstinence.
In addition, it was found that heroin addiction significantly affects sexual functions more than tramadol HCL use disorder.

Conclusions There was a significant improvement in serum testosterone and sexual dysfunction after abstinence of opioids.
Potential implications: the current results have clinical application, as they can be used for improving the understanding, prediction, and prevention of sexual dysfunction in opiate abusers.

Keywords Fertility, Heroine, Opiate abusers, Sexual dysfunction, Tramadol.
Egyptian Journal of Psychiatry 2024,

INTRODUCTION

Substance abuse is an increasing reported complaint among young individuals, which represents a serious threat to society. This problem is more common in males. Sexual functions are seriously impaired in addicts (Epstein and Mamo, 2017).

The main goal of sexual functions is preservation and continuity of the human race. The effect of substance abuse on sexual functions and sex hormones is considered an interesting field for research (Epstein and Mamo, 2017).

Psychoactive drugs are commonly thought to have an aphrodisiac effect; in fact, they affect different sexual functions negatively (Nappi and Cucinella, 2015).

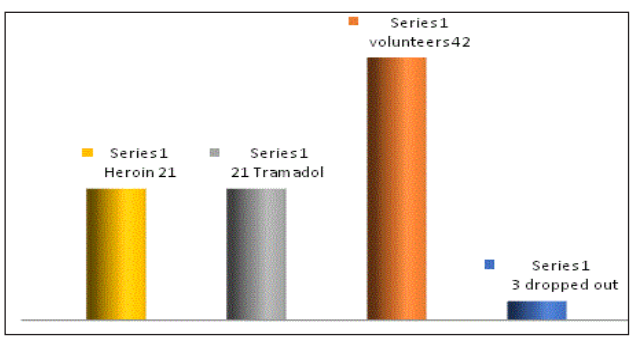
Various mechanisms are involved such as (a) inhibition of erection through affecting neurotransmitter serotonin, adrenaline, or dopamine; (b) vasoconstrictive action (cocaine); (c) affection of endothelial integrity (nicotine); and (d) inhibition of the production of luteinizing hormone (LH) (morphine) (Nappi and Cucinella, 2015).

However, it is still unknown if substance withdrawal can recover erectile function (Ghadigaonkar and Murthy, 2019). Opioids either endogenous or exogenous have the ability to bind to the opioid receptors present in the hypothalamus and the pituitary gland that control the gonadal function (Fountas *et al.,* 2018). Moreover, recent studies have reported the effect of opioids on the production of gonadotropin-releasing hormone, which subsequently negatively affects its release (Abdellatief *et al.,* 2015). Moreover, opioid-induced endocrinopathy leads to reduction in the gonadal and adrenal production of androgen (Thosani and Jimenez, 2011). In most heroin and tramadol addicts, decreased libido was present, and also erectile dysfunction was found in 40–50%, whereas delayed ejaculation was seen in more than half of those addicts (Venkatesh *et al.,* 2014). A recent case–control study reported a significant decrease in sexual acts per week in heroin addicts (Grover *et al.,* 2014).

This study aims to evaluate how opioid use disorder (tramadol HCL vs. heroin) affects sexual function in men. Moreover, this study examined several important factors for prevention of sexual dysfunction in opiate abusers.

PATIENTS AND METHODS

This quasi-experimental study included 42 male patients who were dependent on opioids (21 heroin and 21 tramadol HCL addicts) and 42 healthy volunteers, presenting to the both outpatient clinics and the inpatient ward of the Addiction Unit of Psychiatry Department, Mansoura University Hospital, from December 2019 till December 2020.



Inclusion criteria

The inclusion criteria were as follows:

(1) Age range between 18 and 45 years (to eliminate the negative influence of age on sexuality).

(2) Married males only (to be in regular sexual relationship).

Exclusion criteria

The exclusion criteria were as follows:

(1) Presence of major medical disorders.

(2) Presence of major psychiatric disorders.

(3) If they were receiving any medications.

Written informed consent was obtained from the patients to participate in the study.

All sample of the study were subjected to the following tools before and 3 months after abstinence. Three participants dropped out, and they did not come back for the second interview:

Structural clinical interview DSM5 (First *et al.,* 2015) and addiction severity index (McLellan *et al.,* 1985), Arabic version (5th ed.), were used (Qasem *et al.,* 2003).

The international index of erectile function, a multidimensional scale for assessment of erectile dysfunction (Rosen *et al.,* 1997), Arabic version, was used (Alzohiery, 2011).

The self-seem and relationship (El-Hadidy and El-Gilany, 2014) questionnaire, Arabic version, has been used (Hashim *et al.,* 2020).

Serum levels of free testosterone were measured. Urine test was done for detection of opiates.

During the interview, we collected urine samples from the participants. These samples were collected in a sterile container with each participant name labeled on it. The urine samples were assessed by a multidrug one-step test, which is a test used for the qualitative detection of tramadol, heroin, cocaine, amphetamine, cannabis, benzodiazepine, and barbiturates. This test does not measure quantity. Blood was withdrawn by venipuncture and hemolyzed, icteric, and lipemic serum was ruled out. Serum was stored in duplicate aliquots in deep freezer at -20ºC. Storage of kit was done at 2–8ºC. Opened standard was valid for 6 months at 2–8ºC. Laboratory analysis for free testosterone: before assay procedure, all patients' samples were allowed to thaw at room temperature and inverted several times to ensure proper mixing (samples were thawed once as repeated thawing and freezing was not allowed). All reagents especially standards were left at room temperature for 30min. Reagent preparation was follows: ×20 wash buffer prepare ×1 wash buffer by adding the content of the bottle (25ml, ×20) to 475ml of distilled or deionized water and kept at room temperature (18–26ºC).

Free testosterone was measured by ELISA technique (Calbiotech Inc., Spring Valley, California, USA).

RESULTS

Table 1 shows a statistically significantly higher international index of erectile function score among volunteers than the patient group (P <0.001) as well as self-esteem and relationship score. Moreover, serum free testosterone was statistically significantly higher among volunteer than the patient group (P <0.001).

Table 2 shows that the international index of erectile function score and self-esteem and relationship score were statistically significantly higher among patients after abstinence than among them during drug abuse (P <0.001). Moreover, serum free testosterone was statistically significantly higher among patients after abstinence than among them during drug abuse (P <0.001).

Table 3 shows that there was a statistically significantly higher international index of erectile function score among tramadol patients than heroin patients during abuse (P <0.05). Moreover, tramadol patients had statistically significantly higher international index of erectile function score than heroin patients after abstinence (P <0.05). Except intercourse satisfaction, there was a statistically insignificant difference among tramadol patients and heroin patients after abstinence (P= 0.05). Concerning the effect of abstinence, the international index of erectile function scores were statistically significantly higher among persons after abstinence from tramadol than among them during abuse (P <0.05). Similar to heroin group, the international index of erectile function scores were statistically significantly higher among persons after abstinence from heroin than among them during heroin abuse (P <0.05).

There was a statistically significantly higher self-esteem and relationship questionnaire score among tramadol patients than heroin patients during abuse (P= 0.024). Moreover, there was a statistically insignificant difference between tramadol patients and heroin patients regarding self-esteem and overall relation (P >0.05). Regarding self-esteem and relationship score parameters after abstinence, there was a statistically insignificant difference between tramadol patients and heroin patients (P >0.05). Concerning self-esteem and relationship questionnaire parameters, the scores were statistically significantly higher among persons after abstinence from tramadol than among them during tramadol abuse (P <0.05). The same finding observed in the heroin group. Self-esteem and relationship questionnaire parameter scores were statistically significant higher among persons after abstinence than during abuse (P <0.05).

In addition, there was a statistically significantly higher serum free testosterone level among tramadol patients than heroin patients during abuse (P= 0.002) and after abstinence (P= 0.004). Regarding tramadol group and heroin group, there was a statistically significant higher serum free testosterone level among persons after abstinence than among them during drug abuse (P= 0.0001).

Table 4 reveals a statistically significant positive correlation between duration of tramadol abuse per years and patient age. There was a statistically significant negative correlation between duration of tramadol abuse per year and international index of erectile function, self-esteem, and relationship score among person during the tramadol abuse. However, there was a statistically significant positive correlation between serum free testosterone during drug abuse and all parameters of international index of erectile function and sexual relation during tramadol abuse (P <0.05).

Table 5 demonstrates that there was a statistically significant positive correlation (P <0.05) between serum free testosterone after treatment and all parameters of international index of erectile function and sexual relation after treatment tramadol abuse.

Table 6 shows that there was a statistically significant negative correlation between duration heroin abuse per year and heroin dose per mg. There was a statistically significant negative correlation between duration heroin abuse per year and erectile function, orgasm function, overall satisfaction, and also self-esteem, relationship, and total scores among person during the heroin abuse. However, there was a statistically significant positive correlation between serum free testosterone and all parameters of international index of erectile function, self-esteem, and relation questionnaire score during heroin abuse (P <0.05). On the contrary, a negative correlation between duration of heroin abuse per years and serum free testosterone.

Table 7 shows that there was a statistically significant negative correlation between duration heroin abuse per year and serum free testosterone after treatment heroin abuse (P= 0.004). However, there was a statistically significant positive correlation between serum free testosterone after treatment and all parameters of international index of erectile function and sexual relation after heroin abuse treatment (P <0.05) (Figs 1–7).

Statistical analysis

All data were analyzed using SPSS 20.0 for Windows (2011; SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean±SD. Qualitative data were expressed as absolute frequencies (number) and relative frequencies (percentage). P value less than 0.05 was considered statistically significant.

Table 1: Comparison between, patient group (before abstinence) and volunteer group regarding international index of erectile function, self-esteem and relationship, and serum free testosterone:

	Studied groups			
	Patient group (*N*=42)	**Volunteer group (N=42)**	***t***	***P* value**
International index of erectile function				
Erectile function	17.6±5.6	4.3±24.86	6.6	<0.001
Orgasm function	5.52±1.75	1.1±8.14	8.2	<0.001
Sexual desire	5.79±1.6	1.1±8.71	9.6	<0.001
Intercourse satisfaction	9.29±2.1	1.5±12.76	8.7	<0.001
Overall satisfaction	5.64±1.6	1.2±8.36	8.9	<0.001
Self-esteem and relationship				
Sexual relationship	52.9±20.2	15.1±80.58	U=5.7	<0.001
Self-esteem	50.74±20.4	13.2±80.21	U=6.1	<0.001
Overall relationship	52.1±18.9	13.2±79.91	U=6	<0.001
Total score	51.72±18.62.	13.19±79.42	U=6.05	<0.001
Serum free testosterone	7.97±3.8	4.8±16.65	U=6.6	<0.001

Data expressed as mean±SD; *t*: Student *t* test; *U*: Mann–Whitney *U* test; Significant *P* value more than 0.05.

Table 2: Comparison between, patient group regarding international index of erectile function, self-esteem and relationship questionnaire and serum free testosterone during drug abuse and after abstinence:

	Patient group			
	During abuse (*N*=39)	**After treatment (*N*=39)**	**Paired *t***	***P* value**
International index of erectile function				
Erectile function	5.4±17.05	5.6±19.56	5.4	<0.001
Orgasm function	1.7±5.36	1.7±6.21	5.08	<0.001
Sexual desire	1.5±5.62	1.6±6.72	6.5	<0.001
Intercourse satisfaction	2.1±9.1	2±10.64	7.8	<0.001
Overall satisfaction	1.6±5.49	1.6±6.62	6.8	<0.001
Self-esteem and relationship				
Sexual relationship	19.1±50.64	19.5±59.7	W=4.6	<0.001
Self-esteem	19.7±48.71	18.5±59.77	W=4.5	<0.001
Overall relationship	17.7.±49.83	18.±61.7	W=4.6	<0.001
Total score	18.62±51.72	17.78±60.62	W=5.3	>0.001
Serum free testosterone	3.8±7.74	4.4±9.49	W=5.1	<0.001

Data expressed as mean±SD; *t*: Student *t* test; *W*: Wilcoxon signed ranks test; Significant *P* value more than 0.05.

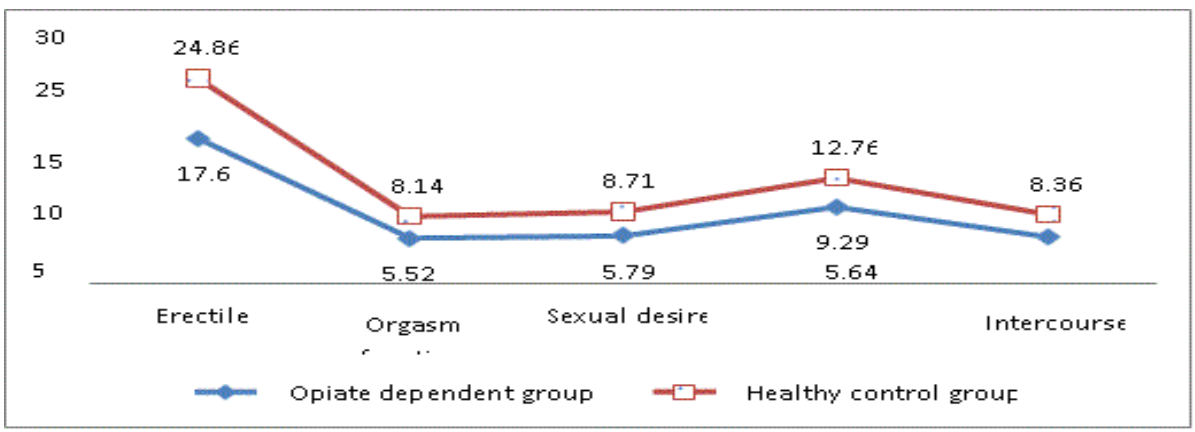


Figure 1: Mean of international index of erectile function score for patients group during drug abuse and volunteers group.

Table 3: Comparison between tramadol group and heroine group regarding international index of erectile function, self-esteem and relationship questionnaire and serum testosterone during abuse and after abstinence:

	Tramadol group		Heroin group		*P* value^	
International index of erectile function	**During**	**After**	**During**	**After**	**During**	**After**
Erectile function (mean±SD)	19.5±4.9	5.1±21.4	14.47±4.8	5.5±17.63	0.003	0.03
	P= 0.002*		*P*= 0.001*			
Orgasm function (mean±SD)	1.7±6.1	1.5±6.8	1.4±4.58	1.8±5.58	0.004	0.029
	P= 0.002*		*P*= 0.002*			
Sexual desire (mean±SD)	1.4±6.25	1.4±7.25	1.3±4.95	1.5±6.16	0.006	0.026
	P= 0.0001*		*P*= 0.0001*			
Intercourse satisfaction (mean±SD)	1.9±9.9	1.9±11.25	2±8.26	2±10	0.013	0.05
	P= 0.0001*		*P*= 0.0001*			
Overall satisfaction (mean±SD)	1.4±6.15	1.4±7.2	1.4±4.79	1.6±6	0.005	0.017
	P= 0.0001*		*P*= 0.0001*			
Self-esteem and relationship						
Sexual relation (mean±SD)	19±57.5	19.2±63.59	16.8±43.42	19.5±55.6	0.024	0.21
	P= 0.002**		*P*= 0.001**			
Self-esteem (mean±SD)	21.4±54.05	18.3±64.69	16.4±43.09	17.8±54.59	063.	072.
	P= 0.001**		*P*= 0.001**			
Overall relation (mean±SD)	18.9±54.68	18.3±65.94	15.2±44.74	16.9±57.24	094.	0.16
	P= 0.001**		*P*= 0.002**			
Total score (mean±SD)	17.85±54.66	18.12±64.75	15±43.94	16.79±56.28	0.065	0.14
	P <0.001**		*P* <0.001**			
Serum free testosterone (mean±SD)	3.8±9.58	4.2±11.49	2.9±5.81	3.5±7.39	0.002	0.004
	P= 0.0001**		*P*= 0.0001**			

U: Mann–Whitney *U* test; *Paired *t* test, significant; ^*P* value less than 0.05, Student *t* test; ***P*: Wilcoxon signed-rank test.

Table 4: Correlating of the dose of tramadol, duration of the use, and serum free testosterone with international index of erectile function, self-esteem, and relationship among person during the tramadol abuse:

	Tramadol group during abuse					
	Dose		**Duration of tramadol abuse years**		**Testosterone during drug abuse**	
Parameters	***r***	***P***	***r***	***P***	***r***	***P***
Age	−0.129	0.588	0.512*	0.021	−0.295	0.207
Dose (mg)	1	0	−0.304	0.193	−0.232	0.326
Duration	−0.304	0.193	1	0	−0.402	0.079
Erectile function during	−0.121	0.611	−0.702**	0.001	0.578**	0.008
Orgasm function during	−0.253	0.282	−0.647**	0.002	0.633**	0.003
Sexual desire during	−0.15	0.527	−0.629**	0.003	0.500*	0.025
Intercourse satisfaction during	−0.186	0.433	−0.696**	0.001	0.594**	0.006
Overall satisfaction during	−0.141	0.555	−0.615**	0.004	0.568**	0.009
Sexual relation during	−0.15	0.527	−0.685**	0.001	0.513*	0.021
Self-esteem during	−0.28	0.219	−0.559*	0.01	0.39	0.089
Overall relation during	−0.195	0.409	−0.558*	0.011	0.429	0.059
Total score	−0.25	0.273	−0.607**	0.004	0.418**	0.059

r: correlation coefficient; *Statistically significant; ***P* value more than 0.05 statistically significant less than 0.01.

Table 5: Correlating between serum free testosterone with age, dose of tramadol, duration of the use, tramadol, international index of erectile function, self-esteem and relationship among person after treatment from the tramadol abuse:

	Tramadol group after treatment	
	Serum free testosterone after treatment	
Parameters	***r***	***P***
Age	−0.244	0.301
Dose (mg)	−0.248	0.292
Duration	−0.348	0.132
Erectile function after	0.448*	0.048
Orgasm function after	0.517*	0.02
Sexual desire after	0.481*	0.032
Intercourse satisfaction after	0.472*	0.035
Overall satisfaction after	0.456*	0.043
Sexual relation after	0.468*	0.037
Self-esteem after	0.423	0.063
Overall relation after	0.41	0.072
Total score	0.474*	0.035

r: correlation coefficient; *: Statistically significant with *P* value less than 0.05.

Table 7: Correlating between the, serum free testosterone with age, dose of heroine, duration per years, international index of erectile function, self-esteem and relationship among person after treatment from heroin abuse:

	Person after treatment from heroin	
	Testosterone after	
Parameters	***r***	***P***
Age	−0.345	0.148
Dose (mg)	0.347	0.146
Duration	−0.632**	0.004
International index of erectile function after	0.890**	0.0001
Orgasm function after	0.882**	0.0001
Sexual desire after	0.767**	0.0001
Intercourse satisfaction after	0.893**	0.0001
Overall satisfaction after	0.918**	0.0001
Sexual relation after	0.909**	0.0001
Self-esteem after	0.885**	0.0001
Overall relation after	0.898**	0.0001
Total score after	0.89**	0.0001

r: correlation coefficient; **: Statistically significant with *P* value less than 0.01.

Table 6: Correlating between the dose of heroin, duration of the use, serum free testosterone with international index of erectile function, self-esteem and relationship among person during heroin abuse:

	Patient during the heroin abuse					
	Dose		Duration years		Testosterone during	
Parameters	***r***	***P***	***r***	***P***	***r***	***P***
Age	0.159	0.515	0.14	0.567	−0.405	0.085
Dose per mg	1	–	−0.519*	0.023	0.186	0.445
Duration	−0.519*	0.023	1	–	−0.539*	0.017
Erectile function during	0.151	0.537	−0.622**	0.004	0.832**	0.0001
Orgasm function during	0.099	0.686	−0.468*	0.043	0.761**	0.0001
Sexual desire during	−0.208	0.393	−0.403	0.087	0.636**	0.003
Intercourse satisfaction during	0.165	0.5	−0.454	0.051	0.856**	0.0001
Overall satisfaction during	0.088	0.721	−0.507*	0.027	0.876**	0.0001
Sexual relation during	0.161	0.509	−0.465*	0.045	0.775**	0.0001
Self-Esteem during	0.238	0.327	−0.587**	0.008	0.768**	0.0001
Overall relation during	0.06	0.809	−0.472*	0.041	0.847**	0.0001
Total score	0.11	0.628	−0.505	0.02	0.85	0.0001

r: correlation coefficient; *Statistically significant; ***P* value more than 0.05 statistically significant less than 0.01.

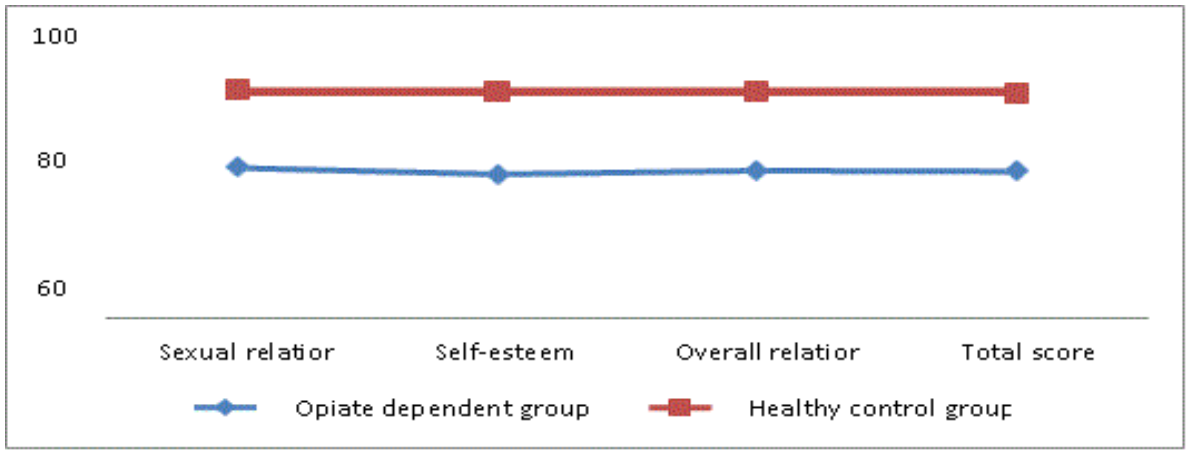


Figure 2: Mean of self-esteem and relationship score for patients group during drug abuse and volunteers group.

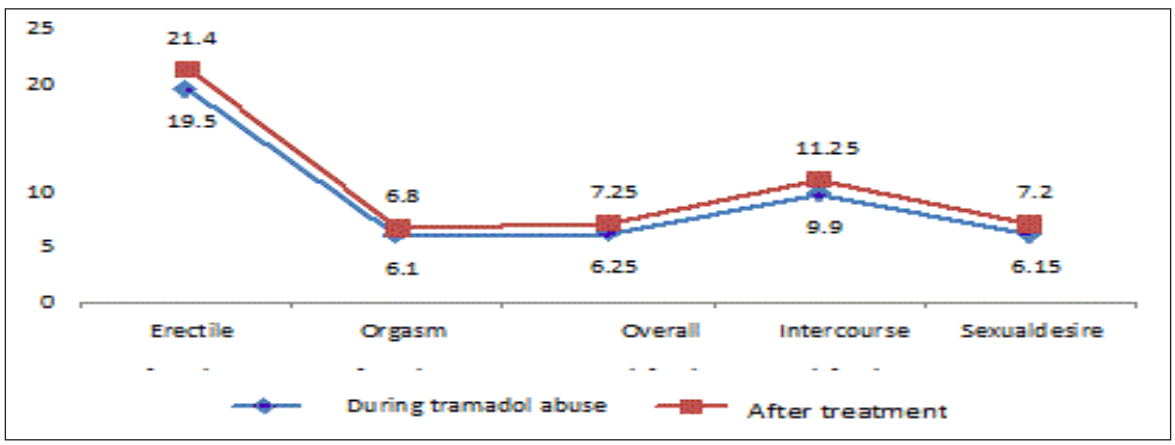


Figure 3: Mean international index of erectile function score during tramadol abuse group and after treatment.

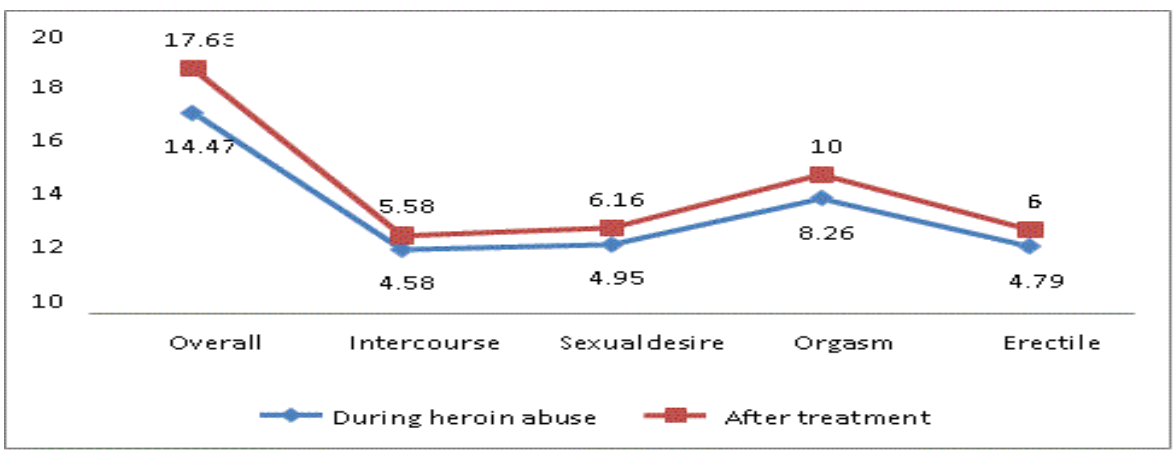


Figure 4: Mean international index of erectile function score during heroin abuse group and after treatment.

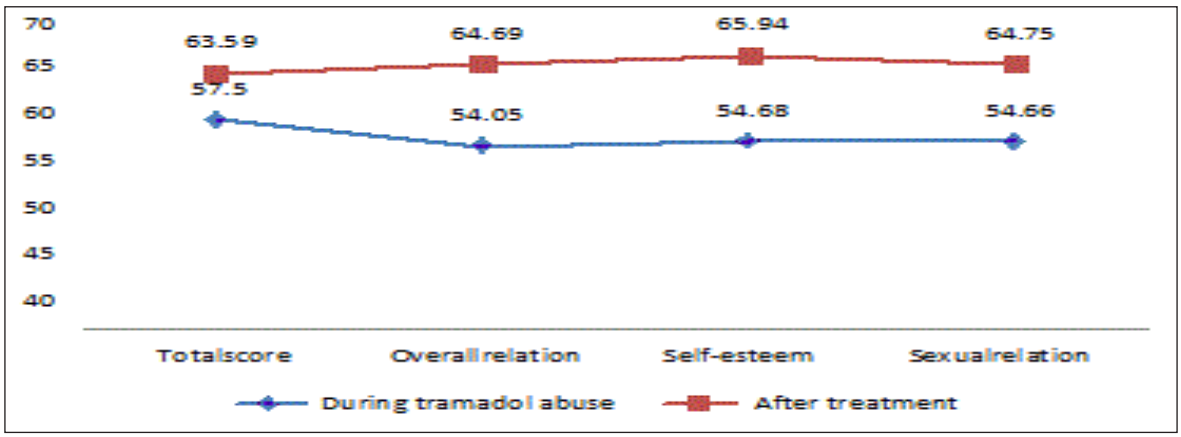


Figure 5: Sexual relation, self-esteem, overall relationship and total score during tramadol abuse group and after treatment.

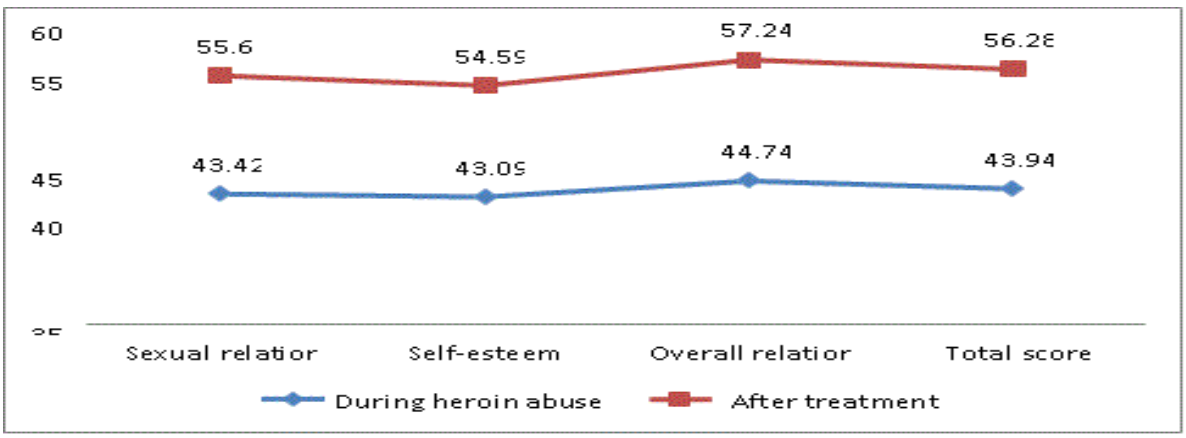


Figure 6: Mean sexual relation self-esteem overall relationship and total score during heroin abuse group and after treatment.

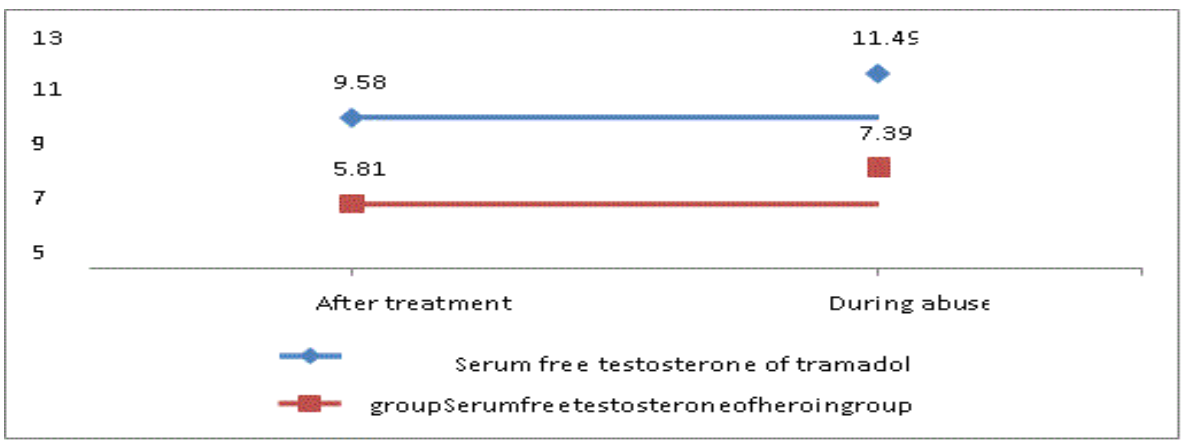


Figure 7: Mean serum free testosterone level during abuse and after treatment for both tramadol group and heroin group.

DISCUSSION

On comparing patients and volunteers' sociodemographic characteristics, no statistically significant differences were found between the studied groups. This was compatible with Hashim *et al.,* (2020) who did not find statistically significant differences regarding age on comparing the studied groups.

Regarding mean free testosterone level, it was found that heroin use patients showed the lowest levels compared

with tramadol HCL patients. Mean free testosterone levels were less than those of healthy volunteers, who showed the highest levels of hormone. The difference between heroin dependents and volunteers was highly significant and much higher than the significant difference between tramadol HCL group and volunteers. Moreover, there was significant improvement in testosterone level after treatment. This is similar to a meta-analysis, which stated that testosterone is reduced by nearly half, with significant improvement in testosterone level after treatment (Bawor *et al.,* 2015).

Cepeda *et al.,* (2015) agreed with the current findings, who conducted a study on a sample of US residents with exposure to oral prescription opioids [the types of oral opioids used were hydrocodone (38.5%), oxycodone (23.6%), tramadol (14.8%) and others]. Despite this heterogeneity in oral opioid substances, individuals using oral opioids in their study were likely to have decreased levels of testosterone compared with individuals who are not using opioids. Hashim *et al.,* (2020) found that testosterone level was reduced, significantly, when comparing healthy and diseased groups. Comparing patients using heroin and tramadol, tramadol abusers testosterone level is higher than heroin. On the contrary, studies on animals found that tramadol significantly reduced testosterone level when compared with controls (El-Gaafarawi, 2006; Ahmed and Kurkar, 2014; Abdellatief *et al.,* 2015; Youssef and Zidan, 2016). However, the current results are contradictory to Abdelazim *et al.,* (2015), where only 30% of opioid use disorder patients had low levels of free testosterone and high levels of LH, in comparison with the healthy controls. It had a different study design, and also the effects of opioids were assessed as one class.

In summary, patients using heroin had significantly lower levels of free testosterone than those using tramadol. Some nonopioid actions of tramadol could have affected testosterone levels, such as inhibition of reuptake of norepinephrine, which may have a reducing effect on the level of testosterone than heroin, which affects via stimulation of opioid receptors only. Testosterone may play an important role in a series symptoms, such as a sexual activity, muscle mass, and bone mass osteoporosis (Abdelazim *et al.,* 2015).

Regarding erectile function, most heroin-dependent patients had erectile dysfunctions. In comparison, the tramadol-dependent group scored less in the erectile dysfunction variable. In contrast, most of the volunteer group showed no erectile dysfunction. This difference was highly significant. Comparing the mean scores, it was found that the heroin group showed the lowest mean scores compared with the tramadol HCL group, whereas the volunteer group showed the highest mean scores. These differences were striking and highly significant statistically. Regarding the orgasm, the sexual desire, intercourse satisfaction, and the overall satisfaction and comparing the means, it was found that the heroin group showed lower mean scores compared with the tramadol HCL group, whereas the volunteer group showed the highest means. These differences were statistically significant between both patients groups and between opioid dependents and volunteers. Moreover, there was significant improvement in international index of erectile function after treatment. This came in agreement with Goodyear-Smith *et al.,* (2008) who stated that erectile dysfunction was improved by decreasing the given dose. To summarize, the finding of SD in opioid use disorder patients (both groups) compared with healthy volunteers indicates that opioids abuse is associated with significant SD. These results are important in our country regarding that, the belief that opioid consumption increases sexual activity. Moreover, in the present study, there was a significant increased postabstinence self-esteem and relationship score compared with preabstinence score. This came in agreement with El-Hadidy and El-Gilany (2014) who found that there was significant increase after treatment compared with before treatment.

Studies on heroin use disorder patients had comparable results to the current study. For example, in the study by Zhang *et al.,* (2014), all five international index of erectile function-15 domains were strongly associated with use of heroin. However, the results of Babakhanian *et al.,* (2012) were moderately prevalent among participants, which was comparable to our results (slightly higher). In an Indian study (Aggarwal *et al.,* 2016), the difference between the SD presence among opioid dependents (without specifying opiate type) and control group was highly significant. Another study stated that sexual dysfunctions are common results of chronic opium use (Van Ahlen *et al.,* 1995). Hashim *et al.,* (2020), found that SD was highly prevalent in opioid use disorder patients, especially, heroin, when compared with healthy controls. Heroin addicts have higher rates than general population, regarding SD (Colameco and Coren, 2009; Venkatesh *et al.,* 2014), with erectile problems, premature ejaculation, orgasmic dysfunction, and decreased libido being mostly affected (Jiann, 2008; Grover *et al.,* 2014).

Opioids affect sexual function peripherally and centrally (Subirán *et al.,* 2011). Centrally, there is inhibition of the hypothalamic–pituitary–gonadal axis (Colameco and Coren, 2009). This is a result of LH suppression, leading to androgen deficiency (Smith and Elliott, 2012; Moselhy *et al.,* 2015). Regarding testicles, opioids lead to lower secretion of testicular interstitial fluid (Katz and Mazer, 2009). Regarding body tissues, they lower activation of testosterone to its active form (Aloisi *et al.,* 2010; Smith and Elliott, 2012; Abdel-Hamid *et al.,* 2016). Tramadol abusers' self-esteem was improved after ceasing substance, with good sexual performance without drug abuse (Zhang *et al.,* 2014). Research on tramadol sexual risks is still limited (Andersson, 2011). Tramadol enhances penile erection, via increasing dopamine release and reduce erection via

inhibiting serotonin reuptake. Tramadol, which act through norepinephrine reuptake inhibition, may relax or alleviate its effect on level of testosterone in comparison with opioids, which work only via opioid receptors (Andersson, 2011; Eichenbaum *et al.,* 2015).

On comparing the current findings with an Egyptian study (Abdelazim *et al.,* 2015), the difference between the patients and healthy control groups was still highly significant in this study, which is comparable to our findings. In contradictory to Wong and Malde (2013), Wu *et al.,* (2012), Eassa and El-Shazly (2013), tramadol shows promise as a drug, causing delayed ejaculation. When used on demand, not with regular use for more than 1 year. To the best of our knowledge, only few studies have assessed tramadol's sexual effects. In Egypt, the results of El-Hadidy and El-Gilany (2014) were compatible with the current results. In conclusion, current research results counter the belief that tramadol enhances sexual and physical activity. There was a significant correlation between the hormonal profile and sexual functions. In disagreement with our study, Isidori *et al.,* (2005) found that endocrinal causes were responsible for a few cases of SD in the general population. Our results came in agreement with El-Hadidy and El-Gilany (2014), who found that opiates may impair secretion of sexual hormones. In disagreement with our study, Zhang *et al.,* (2014) stated that testosterone lower level was not the main cause of SD in heroin abusers. Hashim *et al.,* (2020) stated that there was no correlation between sexual function domains and the levels of sexual hormones, in opiate abuse patients. In fact, there was no consistent correlation of erectile function with testosterone levels (Smith and Elliott, 2012). Moreover, taking into consideration the anhedonic effect (not depression) resulting from chronic use of opiate, this can explain the idea of decreasing the sexual drive in the presence of good hormonal function, which is attributed to the resetting of the reward center as described in the study by Wang (2019).

Regarding heroin and tramadol use disorder patients, there was a negative correlation between use of heroin and tramadol duration and erectile, orgasmic function, and overall satisfaction, whereas there was no correlation between testosterone and duration of use. In disagreement with our study, Hejazian *et al.,* (2007) demonstrated that serum testosterone lowering was directly proportional to opium use duration. Hashim *et al.,* (2020) stated that there was a significant negative correlation between the free testosterone level and duration of substance use. Moreover, in contrast to the current findings, an Indian study Aggarwal *et al.,* (2016) stated that there is no association between the duration of opioid dependence and the SD. Venkatesh *et al.,* (2014) support them in this regard. This difference could be attributed to other substance use and sample selection.

Regarding opiate use patients, no significant correlation was found between the daily dose and the sex hormone levels or sexual functions scores in our study. In agreement with our observation, Al-Gommer *et al.,* (2007) stated that testosterone level varies according to the time of last dose, as it markedly declines in the first 4h after administration and this was difficult to be controlled due to the different presentation time of the patients to the OPC and admission. Moreover, Hashim *et al.,* (2020) found the same. These findings come in contrast with some studies, which have found a relationship between testosterone level and heroin dose (Cushman, 1973).

Before we conclude, we would like to discuss the limitations of this study: self-report tools without sexual partners may underestimated the actual size of the problem. Nicotine dose-controlling difficulty among patients and volunteers may have affected sexual function scores. Short duration and single-center design with a small sample size must be taken into consideration.

CONCLUSION

In contrast to traditional myth that tramadol promotes sexual abilities, the scientific results of research including our study show that tramadol and other opioids have a significant negative effect on all stages of sexual cycle. Public awareness of this fact can actually have a protective effect against tramadol addiction.

Potential implications: these results can be applied clinically for improving the understanding, prediction, and prevention of sexual dysfunction in opiate abusers.

ACKNOWLEDGEMENTS

The authors are appreciative of all participants in this study.

Authors' contributions: M.A.A.: preparing of the study design, conducting the psychiatric evaluation, writing primary draft, and data collection. Y.S.: preparing of the study design, conducting the psychiatric evaluation, analysis and interpretation of data, and manuscript drafting and revising. I.H.R.E.: preparing of the study methods, conducting the psychiatric evaluation, analysis and interpretation of data, and manuscript drafting and revising. M.A.E.H.: preparing of the study methods, conducting the psychiatric evaluation, analysis and interpretation of data, and manuscript drafting and revising.

FINANCIAL SUPPORT AND SPONSORSHIP

Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest.

REFERENCE

Abdel-Hamid IA., Andersson KE., Waldinger MD., Anis TH. (2016). Tramadol abuse and sexual function. Sex Med Rev 4:235–246.

Abdelazim S., Abolmagd SF., Abdalla H., Enaba DA., Elsheikh SM., Moselhy HF. (2015). Sexual dysfunction and sex hormone levels in Egyptian opioid-dependent males. Am J. Pharm Health Res 3:81–91.

Abdellatief RB., Elgamal D., Mohamed AA. (2015). Effects of chronic tramadol administration on testicular tissue in rats: an experimental study. Andrologia 47:674–679.

Aggarwal N., Kherada S., Gocher S. (2016). A study of assessment of sexual dysfunction in male subjects with opioid dependence. Mahesh Sohu Asian J. Psychiatry 23:17–23.

Ahmed MA., Kurkar A. (2014). Effects of opioid (tramadol) treatment on testicular functions in adult male rats: the role of nitric oxide and oxidative stress. Clin Exp Pharmacol Physiol 41:317–323.

Al-Gommer O., George S., Haque WS. (2007). Sexual dysfunctions in male opiate users: a comparative study of heroin, methadone, and buprenorphine. Addict Disord Treat 6:137–143.

Aloisi AM., Ceccarelli I., Fiorenzani P., Maddalena M., Rossi A., Tomei V. (2010). Aromatase and 5-alpha reductase gene expression: modulation by pain andmorphine treatment in male rats. Mol Pain 6:69.

Alzohiery AM. (2011). Reliability and validity of the Arabic version of the international index of erectile function-15 (IIEF-15) in Egyptian population [MSc thesis, in andrology, sexology and sexually transmitted diseases]. Cairo, Egypt: Faculty of Medicine, Ain-Shams University.

Andersson KE. (2011). Mechanisms of penile erection and basis for pharmacological treatment of erectile dysfunction. Pharmacol Rev 63:811–859.

Babakhanian M., Mehrjerdi AZ., Shenaiy Y. (2012). Sexual dysfunction in male crystalline heroin dependents before and after MMT: a pilot study. Arch Iran Med 15:751–755.

Bawor M., Bami H., Dennis BB., Plater C., Worster A., Varenbut M. (2015). Testosterone suppression in opioid users: a systematic review and meta-analysis. Drug Alcohol Depend 149:1–9.

Cepeda MS., Zhu V., Vorsanger G., Eichenbaum G. (2015). Effect of opioids on testosterone levels: cross-sectional study using NHANES. Pain Med 16:2235–2242.

Colameco S., Coren JS. (2009). Opioid-induced endocrinopathy. J. Am Osteopath Assoc 109:20–25.

Cushman P Jr. (1973). Plasma testosterone in narcotic addiction. Am J. Med 55:452–458.

Eassa BI., El-Shazly MA. (2013). Safety and efficacy of tramadol hydrochloride on treatment of premature ejaculation. Asian J. Androl 15:138–142.

Eichenbaum G., Gohler H., Etropolski M. (2015). Does tapentadol affect sex hormone concentrations differently from morphine and oxycodone? An initial assessment and possible implications for OPIATES. J. Opioid Manag 11:211–227.

El-Gaafarawi II. (2006). Biochemical toxicity induced by tramadol administration in male rats. Egypt J. Hosp Med 23:353–362.

El-Hadidy MA., El-Gilany AH. (2014). Physical and sexual wellbeingduring and after tramadol dependence. Middle East Curr Psychiatry 21:148–151.

Epstein S., Mamo L. (2017). The proliferation of sexual health: diverse social problems and the legitimation of sexuality. Soc Sci Med 188:176–190.

First MB., Williams JBW., Karg RS., Spitzer RL. (2015). Structured clinical interview for DSM-5 – research version (SCID-5 for DSM-5, research version; SCID-5-RV, Version 1.0.0. Arlington, VA: American Psychiatric Association.

Fountas A., Chai ST., Kourkouti C., Karavitaki N. (2018). Mechanisms of endocrinology: endocrinology of opioids. Eur J. Endocrinol 179:183–196.

Ghadigaonkar DS, Murthy P. (2019). Sexual Dysfunction in Persons With Substance Use Disorders. Journal of Psychosexual Health. 1(2):117-121. doi:10.1177/2631831819849365.

Goodyear-Smith F., Gohns A., Butler R., Sheridan J., Wheeler A. (2008). Metha-done maintenance treatment: barriers to, and incentives for, the transfer of opioid dependent people from secondary care to primary health care. Drug Alcohol Rev 27:178–184.

Grover S., Mattoo SK., Pendharkar S., Kandappan V. (2014). Sexual dysfunctionin patients with alcohol and opioid dependence. Indian J. Psychol 36:355–365.

Hashim MA., el Rasheed AH., Ismail GA., Awaad MI., El Habiby MM., Ibrahim NM. (2020). Sexual dysfunction in tramadol hydrochloride use disorder male patients: a case-control study. Int Clin Psychopharmacol 35:42–48.

Hejazian SH., Dashti MH., Rafati A. (2007). The effect of opium on serum LH, FSH and testosterone concentration in addicted men. Iran J. Reprod Med 1:35–38.

Isidori AM., Giannetta E., Gianfrilli D. (2005). Effects of testosterone on sexual function in men: results of a meta-analysis. Clin (Oxford) 63: 381–394.

Jiann BP. (2008). Erectile dysfunction associated with psychoactive substances. Chonnam Med J 44:117–124.

Katz N., Mazer NA. (2009). The impact of opioids on the endocrine system. Clin J. Pain 25:170–175.

McLellan AT., Luborsky L., Cacciola J., Griffith J., Evans F., BarrHL., O'Brien CP. (1985). New data from the Addiction Severity Index. Reliability and validity in three centers. J. Nerv Ment Dis 173:412–423.

Moselhy HF., Abdelazim S., Abolmagd SF., Abdalla H., Enaba DA., Elsheikh SM. (2015). Sexual dysfunction and sex hormone levels in Egyptian opioiddependent males. Am J. Pharm Health Res 3:2321–3647.

Nappi RE., Cucinella L. (2015). Advances in pharmacotherapy for treating female sexual dysfunction. Expert Opin Pharmacother 16:875-887.

Qasem T., Beshry Z., Asaad T., Omar, A., Abdel Mawgoud M. (2003). Profiles of neuropsychological dysfunction in chronic heroin users [MD degree thesis]. Cairo, Egypt: Faculty of Medicine, Ain Shams University.

Rosen RC., Riley A., Wagner G., Osterloh IH., Kirkpatrick J., Mishra A. (1997). The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology 49:822–830.

Smith HS., Elliott JA. (2012). Opioid-induced androgen deficiency (OPIAD). Pain Physician 15:145–156.

Subirán N., Casis L., Irazusta J. (2011). Regulation of male fertility by the opioid system. Mol Med 17:846–853.

Thosani S., Jimenez C. (2011). Opioid-induced biochemical alterations of the neuroendocrine axis. Exp Rev Endocrinol Metab 6:705–713.

Van Ahlen H., Piechota HJ., Kias HJ. (1995). Opiate antagonists in erectile dysfunction: a possible new treatment option? Results of a pilot study with naltrexone. Eur Urol 28:246–250.

Venkatesh K., Mattoo SK., Grover S. (2014). Sexual dysfunction in men seeking treatment for opioid dependence: a study from India. J. Sex Med 11:2055–2064.

Wang S. (2019). Historical review: opiate addiction and opioid receptors. Cell Transplant 28:233–238.

Wong BL., Malde S. (2013). The use of tramadol 'on-demand' for premature ejaculation: a systematic review. Urology 81:98–103.

Wu T., Yue X., Duan X., Luo D., Cheng Y., Tian Y., *et al.* Efficacy and safety of tramadol for premature ejaculation: a systematic review and meta-analysis. Urology 2012; 80:618–624.

Youssef SH., Zidan AH. (2016). Histopathological and biochemical effects of acute and chronic tramadol drug toxicity on liver, kidney and testicular function in adult male albino rats. J. Med Toxicol Clin Forensic Med 1:40–45.

Zhang M., Zhang H., Shi CX., McGoogan JM., Zhang B., Zhao L. (2014). Sexual dysfunction improved in heroin-dependent men after methadone maintenance treatment in Tianjin, China. PLoS ONE 9:1–7.