

The assessment of sexuality and sex hormone levels in a group of synthetic opioid-dependent patients

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Background

Sexual dysfunctions are noted in chronic opiate addicts, which include reduced libido and sexual performance, erectile dysfunction, and delayed ejaculation in male population. Plasma testosterone levels have been shown to be consistently lower in opiate addicts as compared with non-substance-dependent male population.

Aim

The aim of this study was to assess the effect of synthetic opioid dependence on sexual functions of dependent patients as well as its effect on the level of sex hormone and to compare the sexuality and level of sex hormones of synthetic opioid-dependent male population with non-substance-dependent male population.

Patients and methods

Groups I and II were selected consecutively and were recruited from Kasr El-Ainy Hospital as well as private hospitals in greater Cairo during the period from November 2012 to March 2013. Group 1 included 30 substance-dependent male participants and group 2 included 30 non-substance-dependent male participants who were subjected to sexuality scale, international index of erectile function, and sex hormone levels. The addiction severity index was applied to group I only.

Results

The sociodemographic findings of the study found that 80.0% of group I participants were not working and only 20% worked, in comparison with group II in which 90% of participants were working and only 10% were not working. An overall 66.7% of group I participants were divorced and only 26.7% were married compared with group II in which no one was divorced and 86.7% of participants were married. As regards the sexuality scale, 56.6% of participants, which was more than half of group I, had intermediate level of sexual esteem, 23.3% of the group had low level of sexual esteem, and only 20% of the group had high level of sexual esteem. An overall 50%, which was half of group I had low sexual preoccupation, 30% had intermediate sexual preoccupation, and only 20% of the group had high sexual preoccupation. As regards the international index of erectile function, 26.6% had no erectile dysfunction, 36.6% had mild dysfunction, and 3.33% of men in group I had severe erectile dysfunction. An overall 6.6% of the group had no sexual desire dysfunction, 16.6% of the group had mild dysfunction, 26.6% of the group had moderate dysfunction, and 20% of group I had severe sexual desire dysfunction. An overall 10% of group I had no orgasmic dysfunction, 33.3% had mild orgasmic dysfunction, 46.6%, which was almost half of group I, had mild-to-moderate orgasmic dysfunction. According to sex hormone levels, 30% had low levels of testosterone, 50%, which was half of group I, had high prolactin levels, 3.3% had low levels, and 46.6% of the group had normal levels of prolactin, 30% of group I had high levels of luteinizing hormone, and 70% had normal levels of luteinizing hormone.

Conclusion

According to our study, it was shown that there was an effect of synthetic opioid dependency not only on the sexual functions of dependent men, including their erectile function, sexual orgasm, and desire, and their level of sexual esteem in which they experience low sexual esteem and low sexual preoccupation and high sexual depression compared with nondependent men but also on the level of their testosterone levels especially and high prolactin, which inhibit their sexual desire compared with nondependent men.

Keywords:

opiod addiction, sex hormone levels, sexual dysfunction

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Introduction

Opiates are used clinically to treat pain, the best known examples being codeine, morphine, and heroin (diacetylmorphine). These are all opiate-receptor agonists – that is, they stimulate the firing of opiate receptors to produce the effects on mood and behavior. Opiates are clearly involved at a very basic level of sexual function, from early in the evolutionary chain, with effects on endocrine (hormone) function found in human and animal studies. In humans, opiate therapy or abuse is widely associated with loss of libido (sex drive) [1].

Opiates may shift the blood circulation from genital organs to other organs and this may cause sexual disorders such as erectile dysfunction. Opiates can suppress testosterone production. More importantly, alcohol abuse or addiction inevitably has a negative effect on erectile function.

Heavy alcohol use damages the nervous system, and this can become permanent. The signals from the brain to the pelvic nerves are cut off. When this becomes irreversible, it is called alcohol-induced impotence [2].

Considerable evidence through the years have suggested that long-acting opioids used on a daily basis for more than a month can have a number of adverse effects on human endocrine function. The most common and clinically significant effects are androgen deficiencies and menstrual cycle abnormalities [3].

Patients and methods

Patients

This research was prospectively conducted as case-control study and comprised a sample of 60 individuals. The case group consisted of 30 patients recruited from Kasr El-Ainy Hospital as well as private hospitals in greater Cairo during the period from November 2012 to March 2013 who were previously diagnosed with opioid addiction according to *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed., with no intoxication or withdrawal symptoms for at least 1 month, hospitalized for at least 2 weeks, and no previous history of psychotropic medications for at least 1 month before the study. The control group had no individual history of substance abuse, was free from any medical condition that affects the sexual functions, and had no previous history of psychotropic medications for at least 1 month before the

study. The control group was age-matched and sex-matched to case group individuals.

Ethical aspects of the study were approved by the institutional ethics committee and all participants signed an informed consent form before undergoing any study procedure.

Procedures

Participants provided information on their age, sex, marital status, education, and profession. The sexuality scale [4] was used. It is an instrument designed to measure three aspects of human sexuality, which included evaluation of sexual esteem, sexual depression, and sexual preoccupation. Participants were also subjected to the international index of erectile function (IIEF) [5].

It is a brief 15-item, self-administered questionnaire that was developed as a measure to detect treatment-related erectile function in patients in cross-cultural settings, including erectile function (six items), orgasmic function (two items), sexual desire (two items), intercourse satisfaction (three items), and overall satisfaction (two items). Participants were subjected to evaluation of free testosterone level, luteinizing hormone (LH), and prolactin hormone using ELISA test. They were also subjected to evaluation of blood glucose level and urine sampling using drug screening strips applied to groups I and II. Only participants of group I were subjected to the addiction severity index [6]. It is a semistructured interview designed to provide a multidimensional assessment of problems presented by patients with substance use disorders to guide initial treatment planning and to allow monitoring of patient's progress over time. It is designed for use in inpatient and outpatient alcohol and drug abuse treatment settings.

Results

The results of the study showed that the majority of participants in group I (80.0%) were not working and only 20% were working; in comparison, in group II the majority of the group was working. An overall 66.7% of participants in group I were divorced and only 26.7% were married compared with group II in which 0% of participants were divorced and 86.7% ($n = 26$) were married. An overall 93.3% ($n = 28$) of participants in group I had a history of divorce and only 6.7% had no history of divorce compared with group II in which 93.3% had no history of divorce and only 6.7% were divorced (Table 1).

Table 1 Sociodemographic results as regards both groups

	Age (years) [n (%)] (mean)	Occupation [n (%)]		Education	Marital status [n (%)]			History of divorce [n (%)]	
		Not working	Working		Divorced	Married	Single	None	Present
Group I	14 (46.6) (30.20)	24 (80)	6 (20)	30 (100)	20 (66.7)	8 (26.7)	2 (6.7)	2 (6.7)	28 (93.3)
Group II	16 (53.3) (25.73)	10 (27)	27 (90)		0 (0)	26 (86.7)	4 (13.3)	28 (93.3)	2 (6.7)
		$\chi^2 = 29.6$ $P = 0.00$ (<0.05) (significant)			$\chi^2 = 30.19$ $P = 0.00$ (<0.05) (significant)			$\chi^2 = 45.06$ $P = 0.00$ (<0.05) (significant)	

Group I suffered medical problems ranging from moderate degree in 46.7% to severe degree in 20% due to opioid dependence. Almost half of the group (56.7%) had severe occupational deterioration due to opioid dependence, and 36.7% had moderate deterioration. The majority of participants in group I (96.7%) had severe alcohol and drug use. Group I suffered legal problems due to opioid dependence ranging from mild degree (53.3%) to moderate degree, and 26.7% suffered moderate degree legal problems. The majority of participants in group I (80%) suffered severe social relationship problems due to substance dependence and 20% suffered moderate problems. The majority of the group had psychological problems due to their opioid dependence ranging from severe degree (76.7%) to moderate degree (23.3%) (Table 2).

The findings of the study showed that 56.6%, which was more than half of group I, had intermediate sexual esteem and only 20% had high sexual esteem compared with group II in which the majority of the group (83.3%) had high sexual esteem and 16.6% of the group had intermediate sexual esteem, and no participant in the group had low sexual esteem. An overall 40% of group I had intermediate sexual depression and 30% had low sexual depression compared with group II in which 80%, which was the majority of group II, had low sexual depression and only 20% of the group had intermediate sexual depression. An overall 50%, which was half of group I, had low sexual pre occupation and only 20% of the group had high sexual preoccupation compared with group II in which 66.6%, which was more than half of group II, had high sexual preoccupation and 33.2% of the group had sexual preoccupation ranging from low to intermediate (Table 3).

The findings of the study showed that 3.33% of group I had severe erectile dysfunction, 69.8%, which was more than half of the group, had dysfunction ranging from mild to moderate compared with group II in which 93.3% of group II had no erectile dysfunction and only 6.6% had mild erectile dysfunction, and no participant in group II

had mild-to-moderate dysfunction. An overall 10% of participants in group I had severe orgasmic dysfunction, 46.6%, which was almost half of group I, had mild-to-moderate orgasmic dysfunction compared with group II in which 93.3%, which was the majority of group II, had no orgasmic dysfunction and only 6.6% of group II had mild orgasmic dysfunction, and no participant in the group had severe orgasmic dysfunction. An overall 20% of participants in group I had severe sexual desire dysfunction, 26.6% of the group had moderate dysfunction, 30% had mild-to-moderate dysfunction, 16.6% of the group had mild dysfunction, and only 6.6% of the group had no sexual desire dysfunction compared with group II in which all members in group II (100%) had no sexual desire dysfunction (Table 4).

An overall 70% of participants in group I had normal levels of testosterone and 30% had low levels of testosterone compared with group II in which all members of group II had normal testosterone level and no participant in group II had low levels of testosterone. An overall 50%, which was half of group I, had high prolactin levels, 3.3% had low levels, and 46.6% of the group had normal level of prolactin compared with group II in which all members of the group have normal level of prolactin. An overall 30% of men in group I had high levels of LH and 70% had normal levels of LH compared with group II in which all members of group II had normal levels of LH (Table 5).

Discussion

As regards the sociodemographic data, the findings of our study are consistent with the study by United Nations Office On Drugs And Crime report in 2015, which stated that individuals between 15 and 64 years of age had used an illicit drug in 2013. That represents an increase of three million over the previous year, but because of the increase in the global population, illicit drug use has in fact remained stable. The magnitude of the world drug problem becomes more apparent when considering that more than one out of 10 drug users is a problem drug user,

Table 2 Distribution of group I as regards the addiction severity index

Addiction severity index	Mild [n (%)]	Moderate [n (%)]	Severe [n (%)]	Total [n (%)]
Medical status	10 (33.3)	14 (46.7)	6 (20)	30 (100)
Occupational deterioration	2 (6.7)	11 (36.7)	17 (56.7)	30 (100)
Alcohol and drug use	0 (0)	1 (3.3)	29 (96.7)	30 (100)
Legal state	16 (53.3)	8 (26.7)	6 (20)	30 (100)
Family history of drug use	20 (66.7)	8 (26.7)	2 (6.7)	30 (100)
Social relationship problems	0 (0)	6 (20)	24 (80)	30 (100)
Psychiatric state	0 (0)	7 (23.3)	23 (76.7)	30 (100)

Table 3 Distribution of the studied groups according to the sexuality scale

	Sexual esteem [n (%)]			Sexual depression [n (%)]			Sexual preoccupation [n (%)]			Total
	High	Intermediate	Low	High	Intermediate	Low	High	Intermediate	Low	
Group I	6 (20.0)	17 (56.6)	7 (23.3)	9 (30.0)	12 (40.0)	9 (30.0)	6 (20.0)	9 (30.0)	15 (50.0)	30 (100)
Group II	25 (83.3)	5 (16.6)	0 (0.0)	0 (0.0)	6 (20.0)	24 (80.0)	20 (66.6)	5 (16.6)	5 (16.6)	30 (100)
Total (N)	31	22	7	9	18	33	26	14	20	60
	P=0.00 (<0.05) (significant) $\chi^2=25.19$			P=0.00 (<0.05) (significant) $\chi^2=17.8$			P=0.01 (<0.05) (significant) $\chi^2=13.68$			

Table 5 Distribution of the studied groups as regards the sex hormone levels

	Free testosterone level [n (%)]		Prolactin level [n (%)]			Luteinizing hormone [n (%)]		Total
	Low	Normal	Low [n (%)]	Normal	High	Normal	High	
Group I	9 (30.0)	21 (70.0)	1 (3.3)	14 (46.6)	15 (50.0)	21 (70.0)	9 (30.0)	30 (100)
Group II	0 (0.0)	30 (100.0)	0 (0.0)	30 (100.0)	0 (0.0)	30 (100.0)	0 (0.0)	30 (100)
Total	9 (15.0)	51 (85.0)	1 (1.6)	44 (73.3)	15 (25.0)	51 (85)	9 (15)	60 (100)
	$P=0.001 (<0.05)$ (significant)		$P=0.00 (<0.05)$ (significant)			$P=0.01 (<0.05)$ (significant)		
	$\chi^2=10.588$		$\chi^2=21.818$			$\chi^2=10.588$		

predominantly reported erectile dysfunction and retarded ejaculation. Both heroin and methadone have been found to increase these conditions. A higher incidence of erectile dysfunction (20.3%) and premature ejaculation (37.5%) was found in a substance-misusing population, before their substance misuse. They hypothesized that sexual problems or conviction that one has a sexual difficulty is a risk factor for opioid abuse in men [11].

As regards the sexuality scale, the findings of our study are consistent with the study by Laurie and Green [12] in a sample of pain-management patients receiving opioid analgesic therapy; it had been reported that decreased libido and impotency were present in 23 of 24 men and in 22 of 32 men receiving opioids, respectively.

The findings of the study are consistent with the study by Kalyani *et al.* [13], who showed that there was considerable evidence through the years, which had suggested that long-acting opioids used on a daily basis for more than a month can have a number of adverse effects on human endocrine function. The most common and clinically significant effects are androgen deficiencies and the hypogonadal and androgen-inhibiting effects, which are a 'class effect' of all opioids to some extent, and can lead to sexual dysfunctions in men and cause depressive symptoms [13].

The findings of the study are consistent with the study by Weckbecker *et al.* [14], who stated that in most drug addicts, mainly opioid addicts, it can be almost impossible for them to maintain intimate relationships. This is because these opioids would become their obsession, and there would be no room for anyone else. As the individual falls further into opioid addiction they may even lose interest in sex completely. Opiate addiction drives the individual into a world of delusion and selfish action. It will not be possible for another human to trust them fully, and this will prove to be a barrier to intimacy. The addict is still likely to have people who love them, but there will be a sense of wariness mixed in with the affection. The person who is abusing opioids may feel almost incapable of feeling true affection for other people; they are too self-obsessed with the drug to think beyond their own sexual needs unlike nondependent men [14].

As regards the ILEF, the findings of our study are consistent with the study by Bang and Kim [15], which stated that regular heroin users experienced erectile dysfunction, which was present in 39–48% of cases and delayed ejaculation was present in over 50% of the opioid addicts.

Numerous studies have been conducted on heroin use and methadone treatment, and many have found that sexual dysfunction, including hypoactive sexual desire disorder, erectile dysfunction, and orgasmic dysfunction, is common in heroin users and individuals being treated for heroin addiction. In a recent meta-analysis, the meta-analytical pooled prevalence for sexual dysfunction among methadone users was 52% (95% confidence interval, 0.39–0.65). Hypoactive sexual desire disorder and low libido were the most prevalent sexual dysfunctions, accounting for 51% of cases. Although reduction in the dose or discontinuation of methadone would be expected to improve sexual function, conflicting results have been obtained in previous studies [16].

The dysfunction noticed in our study on the international index among the opioid dependents could be attributed to the fact that opiates reduce testosterone levels in men, which the adrenergic blocking activity of opiates may directly influence the functioning of accessory sex organs and the psychological factors such as sedation, euphoria, and a chaotic lifestyle in addicts, thus impairing sexual desire and performance and these patients preferring drug-procuring behaviors to sexual encounter opportunities. Moreover, opiates shift the blood circulation from the genital organs to other organs and this may cause sexual disorders such as erectile dysfunction, and decreased sexual desire and orgasmic dysfunction, which consequently affect the sexual intercourse satisfaction and the overall satisfaction.

The findings of our study are consistent with the study by Daniell [17], which stated that long-term use of opioids can bind to opioid receptors primarily in the hypothalamus, in the pituitary, and the testes, to modulate gonadal function. Decreased release, or interference with the normal pulsatility of release of gonadotropin-releasing hormone at the level of the hypothalamus, had been documented, with consequently decreased release of LH and follicle-stimulating hormone from the pituitary. Direct effects of opioids on the testes, including decreased secretion of testosterone and testicular interstitial fluid, have been documented. Moreover, increased pituitary release of prolactin in preclinical studies, with secondary effects of decreasing testosterone secretion have also been documented [17].

This could be attributed to the fact that the long-term use of opioid by opioid-dependent patients leads to decreased testosterone levels, which in turn affects their erectile function and consequently causes low sexual confidence and esteem in their sexual performance due

to the erectile dysfunction and accordingly affect their mood and may lead to depression due to this dysfunction.

Statistics

The results were analyzed using the statistical package of social science (SPSS) computer software program, version 10, 1 (SPSS Inc., Chicago, Illinois, USA).

Qualitative data are presented as a mean SD for normally distributed data as medians and percentiles for skewed data. Qualitative data were presented in the form of frequencies and percentages.

For normally distributed parameters, differences among groups were tested using Student's test and the one-way analysis of variance with post-hoc test, whereas for skewed data the Mann-Whitney rank sum test and Kruskal-Wallis analysis of variance were used. For qualitative data, differences among groups were tested using Pearson's (χ^2) and Fischer's exact test.

Conclusion

The mean age of group I (opioid-dependent men) was 30 years with a SD of 6.08, whereas the mean age of group II (nondependent men) was 25 years with a SD of 4.15.

An overall 80.0% ($n = 24$) of men in group I (opioid-dependent men) were not working and only 20% were working compared with group II in which 90% ($n = 27$) were working and only 10% ($n = 3$) were not working. This showed the extent to which opioid dependence caused them occupational deterioration and losses. An overall 66.7% ($n = 20$) of men in group I were divorced and only 26.7% ($n = 8$) were married compared with group II in which no one was divorced and 86.7% ($n = 26$) were married.

An overall 53.3% ($n = 16$) of men in group I used heroin as their main substance of dependence and 46.7% ($n = 14$) used tramadol as their main substance of dependence, emphasizing the prevalence and the widespread use of tramadol in Egypt due its cheap price, its availability, and the belief in our culture that it gives more power and energy and increases sexual performance.

On comparing the sexuality scale of both groups, there was a significant difference between the groups. An overall 56.6%, which was more than half of group I, had intermediate level of sexual esteem, 23.3% of men in the group had low level of sexual esteem, and only 20% of the group had high level of sexual esteem; 40% of men in group I had intermediate level of sexual depression, 30% had low sexual depression, and 30% had high sexual depression. An overall 50%, which is half of group I, had low sexual preoccupation, 30% ($n = 9$) had intermediate sexual preoccupation, and only 20% of the group had high sexual preoccupation. In group II 83.3% ($n = 25$), which is the majority of group II, had high level of sexual esteem, 80% ($n = 24$), which is the majority of group I, had low sexual depression, and 66.6% ($n = 20$), which is more than half of group II, had high sexual preoccupation.

On comparing the ILEF, there was a significant difference between the groups; 26.6% ($n = 8$) had no erectile dysfunction, 36.6% ($n = 11$) had mild dysfunction, 33.2% ($n = 10$) had mild-to-moderate erectile dysfunction, and 3.33% ($n = 1$) of group I had severe erectile dysfunction, whereas 93.3% ($n = 28$) of group II had no erectile dysfunction.

An overall 10% ($n = 3$) of men in group I had no orgasmic dysfunction, 33.3% ($n = 10$) had mild orgasmic dysfunction, 46.6% ($n = 14$), which is almost half of group I, had mild-to-moderate orgasmic dysfunction. However, 93.3% ($n = 28$), which was the majority of group II, had no orgasmic dysfunction. An overall, 6.6% ($n = 2$) of men in the group had no sexual desire dysfunction, 16.6% ($n = 5$) of the group had mild dysfunction, 30% ($n = 9$) had mild-to-moderate dysfunction, 26.6% ($n = 8$) of the group had moderate dysfunction, and 20% ($n = 6$) of men in group I had severe sexual desire dysfunction, whereas no member of group II (100%) ($n = 30$) had sexual desire dysfunction. An overall 30% ($n = 9$) of men in group I had no intercourse dysfunction, 46.6% ($n = 14$) had mild intercourse satisfaction dysfunction, 13.3% ($n = 4$) had mild-to-moderate intercourse satisfaction dysfunction, 10% ($n = 2$) of the group had moderate satisfaction, and 3.3% ($n = 1$) had severe intercourse satisfaction; however, 93.3% ($n = 28$) of men group II had no intercourse satisfaction dysfunction.

There is a relation between the sexual esteem and the erectile function in opioid-dependent men; the more the presence of erectile dysfunction, the lower the sexual esteem of men as 14.3% ($n = 1$) of men who had severe erectile dysfunction had low sexual esteem.

The more the degree of erectile dysfunction in opioid-dependent men, the more the degree of sexual depression compared with nondependent men; 33.3% ($n = 3$) of men who had moderate erectile dysfunction had high sexual depression, 22.2% ($n = 2$) who had no erectile dysfunction had high depression, 11.1% ($n = 1$) who had severe erectile dysfunction had high depression, 22.2% ($n = 2$) who had mild-to-moderate erectile dysfunction had high depression, and 11.1% ($n = 1$) who had mild erectile dysfunction had high sexual depression.

Clinical implications

Further studies and research are needed to address the prevalence and epidemiology of tramadol use in Egypt and the concept of the community about tramadol use and improving the sexual performance. Further awareness campaigns and education about tramadol dependence in school and college students are recommended to modify the belief about tramadol use as a stimulant to give more energy and concentration for academic achievement by addressing the different consequences of tramadol abuse.

Epidemiological studies are needed to address the relation between the sexual dysfunction and opioid dependence and how it affects their sex hormone levels and how it can be one of the causes of future hypogonadism and infertility. Further researches are needed to assess the relation between opioid dependence and endocrine function. Investigations are needed to

assess opioid-dependent men during early treatment, not only by means of routine laboratory investigations but also by evaluating sex hormone levels (testosterone/prolactin/LH) to exclude any sign of hypogonadism and to see whether or not testosterone therapy is needed. Serum calcium evaluation is significant in assessing osteoporosis.

Dual diagnosis is often associated with severe illness course, poor treatment outcome, poor compliance, frequent relapses, and high service utilization. Thus, it is important for the treating doctors to recognize the psychiatry comorbidity in managing their opioid-dependent patients.

There is a need for routine screening and understanding of psychiatric symptoms in relation to addictive disorders in order to provide accurate assessment and appropriate services.

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Conflicts of interest

There are no conflicts of interest.

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