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Sexual Dysfunction and Sex Hormone Levels in Egyptian Opioid-Dependent Males

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ABSTRACT

Sexual dysfunctions are noted in chronic opioid addicts, including reduced libido and sexual performance, erectile dysfunction, and delayed ejaculation in males. The aim of the present study is to assess sex hormone levels and the effect of opioid dependency on sexual function in male patients compared with non-users male. The study comprises 30 male patients with opioid dependency and 30 healthy controls presenting to the inpatient addiction unit of Kasr El Aini University Hospital, Cairo, Egypt, from November 2012 to March 2013. Data were collected using the Sexuality Scale and International Index of Erectile Function (ILEF). Sex hormone levels were measured. More than half (56.6%) had an intermediate level of sexual esteem while 23.3% had a low level. Additionally, 36.6% suffered mild erectile dysfunction while 3.33 % reported severe erectile dysfunction. Furthermore, 20% had severe sexual desire dysfunction, and almost half (46.6%) had mild to moderate orgasmic dysfunction. Finally, 30% had low levels of testosterone, 50% had high prolactin levels, and 30% of the opioid-dependent group had high levels of luteinizing hormone which was statistically significant. Our findings suggest that there is a strong correlation between sexual dysfunction among male opioid dependents and high levels of luteinizing hormone.

Keywords: Opioid Dependent, Egypt, Testosterone, Luteinzing Hormone, Prolactin

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INTRODUCTION

Opioid dependency is a problem that is increasing among various populations throughout the world. In Western societies, the major source of drug abuse is heroin. Most of the research on addiction is focused on the effects of this agent on body systems. Various factors, including social, economic, and cultural factors are involved in drug use disorders and dependency[1]. Opioid dependency has increased in prevalence globally over the last few decades, particularly in the Middle East, including Egypt. The large increase in the psychiatric hospital population treated for addiction in the last four decades is due to many factors. Among these are the social and economic changes that have been gathering pace, particularly in urban areas[2]. The proportion of Egyptians aged under 20 years has increased significantly, from 30% in 1987 to 48.2% in 2006[3]. In addition, lifestyle changes due to economic growth and the re-distribution of wealth among the different social classes have contributed to the problem[3]. Among a range of potential side effects of heroin misuse and opioid agonist treatment, sexual dysfunction is common and clinically significant. This is an area often neglected and, hence, unexplored in routine clinical assessments of opioid addicts; however, it is highly clinically relevant, as it could lead to non-adherence to treatment. Opioids 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 human subjects, opioid therapy or abuse is widely associated with the loss of libido (sex drive) [4]. Sexual dysfunctions noted in chronic opioid addicts include reduced libido and sexual performance in males[5] and females, erectile dysfunction and delayed ejaculation in males[6, 7], and amenorrhea[8] and reduced fertility in females[9]. Various hypotheses have been postulated to explain the sexual dysfunctions in male opioid users. Plasma testosterone levels have been shown to be consistently lower in opioid addicts compared with controls[11, 12]. However, Cushman[13] demonstrated that patients on lower doses of heroin and methadone had higher testosterone levels. Similar findings of a negative correlation between high dose methadone and low plasma testosterone levels were also reported by Cushman and Kreek[14]. Apart from the effects of heroin and methadone on reducing testosterone levels in males, other explanations offered to explain opioid-induced sexual dysfunction include alpha-adrenergic blocking activity of opioids, which may directly influence the functioning of the accessory sex organs[15] and psychological factors, such as sedation, euphoria, and a chaotic lifestyle that impairs sexual desire and performance as these patients prefer drug-procuring behaviors to sexual encounter opportunities[16]. Early clinical studies

suggested that opioids may interfere with sex hormone secretion, resulting in acute suppression of luteinizing hormone (LH) release from the pituitary, followed by a secondary drop in plasma testosterone levels. The time course of these neuroendocrine events correlates well with the tension-reducing effects of heroin and suggests that sex drive reduction is an important component of opioid reinforcement[7]. Furthermore, opioids may shift blood circulation from the genitals to other organs, causing sexual disorders like erectile dysfunction. Furthermore, opioids can suppress testosterone production[17]. Although various studies have identified a range of hypotheses addressing the mechanism of sexual dysfunctions in male patients addicted to opioids, a prolactin sexual side effect profile has not yet been fully evaluated in opioid dependents. We investigate the sexual functioning (based on self-reports) of males using opioids and its relationship to levels of free testosterone, luteinizing hormone (LH), and prolactin hormone. Any significant change to the levels of these hormones has the propensity to induce sexual dysfunctions, thus presenting implications for prescribing opioid agonists in clinical practice.

Participants and Procedure

This research was conducted prospectively as a case-control study comprising a sample of 60 individuals. Male patients aged between 18 and 55 years, with DSM IV diagnosis of opioid dependence syndrome, were included in the study. From November 2012 to March 2013, all patients hospitalized for at least two weeks were recruited prospectively until a sample size of 30 in each of the two groups (opioid dependent and drug-free) was reached. All research activities were conducted at Kasr El Aini University Hospital. The control group, which had no individual history of substance abuse, was age-matched to case group individuals. Subjects were excluded from the study if they had any of the following conditions: co-morbid alcohol dependence, chronic physical disorders (e.g., diabetes mellitus), hypertension, chronic pain, rheumatoid arthritis, endocrine disorders, urological disorders, a history of pelvic trauma or history of psychotropic medications within one month prior to the study. The nature and scope of the study were discussed with each patient and written informed consent was obtained from all patients prior to the interview. This study was reviewed and approved by the Kasr El Aini Hospital Ethics Committee. All eligible subjects (based on self-reports of drug use) were tested for psychoactive substances by urinalysis to confirm their use of opioids and exclude concurrent use of other psychoactive substances. The interviews were conducted in a quiet, comfortable setting and each interview lasted about one hour.

Measures

A pro-forma data collection sheet was used to record socio-demographic information and to detail the participants' clinical and drug use histories. The Sexuality scale[18] was employed to assess aspects of participants' sexual functioning. This instrument measures three aspects of human sexuality: sexual-esteem, sexual-depression, and sexual-preoccupation. Participants also completed the International Index of Erectile Function (ILEF) survey[19], which isa15-item, self-administered questionnaire to detect treatment-related erectile function in patients in cross-cultural settings. The question topics are erectile function (6 items); orgasmic function (2 items); sexual desire (2 items);intercourse satisfaction (3 items); and overall satisfaction (2 items). All participants' levels of free testosterone, luteinizing hormone (LH), and prolactin hormone were measured using ELISA and blood glucose levels and drug screening was done using urine samples. Participants in group I only were evaluated using the addiction severity index (ASI) [20], a semi-structured interview designed to provide a multidimensional assessment of problems associated with substance use disorders to guide initial treatment planning and to allow monitoring of a patient's progress over time. The ASI is designed for use in inpatient and outpatient alcohol and drug abuse treatment settings.

Analysis

Descriptive statistics of the demographic and clinical variables (means and standard deviations, as appropriate) were calculated. The chi-square test was used to compare the frequencies of sexual dysfunction between the two groups. The data are presented as means and ranges. Two-tailed tests were used and a *p* value of 0.05 or less was regarded as significant. Data analysis was performed using SPSS, Version 15.0. To study the relationship between two variables, Pearson's and/or Spearman's correlation coefficients were calculated.

RESULTS AND DISCUSSION

Study Sample Description

The mean age of the sample was 30.2 years. The majority of group I was unemployed (80 %), whereas the majority of group II (90%) was employed (Table 1).

Clinical Characteristics of Concurrent Substance Use and its Consequences by Patient Group

More than half (16, 53.3%) of group I used heroin and 14patients (46.7%) used tramadol as their main substance of dependency. The maximum duration of drug use by group I was17 years and the minimum duration was 1 year (mean = 7.5 years, SD=4.99). Half of group I had experienced depressive symptoms within the 30 days prior to entering treatment. Other symptoms included:

hallucinations (10, 33.3 %); anxiety (20, 66.6 %); difficulty concentrating (25, 83.3%); aggression (26, 86.6%); suicidal thoughts (5, 16.6%); and suicidal attempts (4, 13.3%). According to the Addiction Severity Index (ASI), Group I suffered medical problems ranging from moderate (14, 46.7 %) to severe (6, 20%). Almost half the group (17, 56.7 %) had severe occupational deterioration and (11, 36.7%) had moderate deterioration. The majority of group I (29, 96.7%) had severe drug use. Group I suffered legal problems ranging from mild (16, 53.3%) to moderate (8, 26.7%). The majority of group I (24, 80%) suffered severe social relationship problems and (6, 20 %) suffered moderate problems. The majority of group I had psychological problems ranging from severe (23, 76.7%) to moderate (7, 23.3%).

Sexual dysfunctions across the two groups

The sexual functioning of patients was assessed using both the Sexuality Scale (18) (Table 2) and the International Index of Erectile Function (ILEF)(19) (Table3). The findings showed that more than half of group I (56.6%) had intermediate sexual esteem, whereas 83.3 % of group II had high sexual esteem (Table 2).

Furthermore, the findings showed that 3.33% of group I had severe erectile dysfunction, with 69.8% suffering dysfunction ranging from mild to moderate. Meanwhile, 93.3 % of group II had no erectile dysfunction and the remainder had mild erectile dysfunction (Table 3).

Table 1: Socio-Demographic Results Regarding both Groups

	Age(years in age)		Occupation				Education		Marital status						History of divorce			
			Not working		Working				Divorced		Married		single		None		present	
	No	%	No	%	no	%	no	%	No	%	no	%	No	%	no	%	no	%
Group I	14	46.6%	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%	10	27%	27	90%			0	0%	26	86.7%	4	13.3%	28	93.3%	2	6.7%
	Mean(30.20)	25.73	χ^2=29.6, p <0.05)				High education		χ^2=30.19, p <0.05						χ^2=45.06, p <0.05			

Table 2: Distribution of the Studied Groups According to the Sexuality Scale

		Sexual esteem			Sexual depression			Sexual Preoccupation			Total
		High	Intermediate	Low	High	Intermediate	Low	High	Intermediate	Low	
Group I	No	6	17	7	9	12	9	6	9	15	30
	%	20.0%	56.6%	23.3%	30.0%	40.0%	30.0%	20.0%	30.0%	50.0%	100%
Group II	No	25	5	0	0	6	24	20	5	5	30
	%	83.3%	16.6%	0.0%	0.0%	20.0%	80.0%	66.6%	16.6%	16.6%	100%
Total	No	31	22	7	9	18	33	26	14	20	60
χ^2=25.19, P <0.05					χ^2=17.8, P <0.05			χ^2=13.68, P<0.05			

Table 3: Distribution of the studied groups according to ILEF

		Erectile function					Orgasmic function					Sexual desire					Intercourse satisfaction				
		No dysfunction	Mild	Mild-moderate	Moderate	Severe	No dysfunction	Mild	Mild to moderate	moderate	severe	No dysfunction	Mild	Mild to moderate	moderate	Severe	No dysfunction	mild	Mild to moderate	moderate	severe
	%	26.66%	36.66%	16.66%	16.66%	3.33%	10.0%	33.33%	23.33%	23.33%	10.0%	6.66%	16.6%	30.0%	26.66%	20.0%	9	14	4	2	1
Group II	No	28	2	0	0	0	28	2	0	0	0	30	0	0	0	0	30.0%	46.6%	13.3%	10.0%	3.33%
	%	93.33%	6.66%	0.0%	0.0%	0.0%	93.33%	6.66%	0.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%	28	2	0	0	0
χ^2 ==28.342, p< 0.000							χ^2 =42.49, p< 0.000					χ^2=52.5, p< 0.000					χ^2 =25.7, P<0.000				

Table 4: Distribution of the Studied Groups Regarding the Sex Hormone Levels

		Free testosterone level		Prolactin level			Luteinizing hormone		Total
		Low	Normal	Low	normal	High	Normal	High	
Group I	No	9	21	1	14	15	21	9	30
	%	30.0%	70.0%	3.3%	46.6%	50.0%	70.0%	30.0%	100%
Group II	No	0	30	0	30	0	30	0	30
	%	0.0%	100.0%	0.0%	100.0%	0.0%	100.0%	0.0%	100%
Total	No	9	51	1	44	15	51	9	60
	%	15.0%	85.0%	1.6%	73.3%	25.0%	85%	15%	100%
χ^2 =10.588, p<0.001				χ^2 =21.818, p<0.00			χ^2 =10.588, p<0.01		

Table 5: Distribution of Group I Regarding Sexual Depression in Relation to Sex Hormone Levels

Sexual depression	Sex Hormone Levels	Free testosterone		Prolactin			Luteinizing Hormone	
		Low	Normal	High	Normal	Low	High	normal
High	No	3	6	4	5	0	5	4
	%	33.3%	66.7%	4.44%	55.6%	0%	55.6%	44.4%
Intermediate	No	3	9	5	6	1	4	8
	%	25%	75%	41.7%	50%	8.3%	33.3%	66.7%
Low	No	3	6	6	3	0	0	9
	%	33.3%	66.7%	66.7%	33.3%	0%	0%	100%
Total	No	9	21	15	14	1	9	21
	%	30%	70%	50%	46.7%	3.3%	30%	70%
	Total: 100%			Total: 100%			Total:100%	
	χ^2 ==0.238, p<0.88			χ^2 ==2.74, p<0.60			χ^2 ==6.7, p<0.035	

Sex hormone levels and their relationships to sexual depression

Only 30% of group I had low levels of free testosterone compared with group II, in which all members had normal testosterone levels. Half of group I had high prolactin levels, 3.3% had low levels, and 46.6% of the group had normal levels of prolactin, whereas all group II members had normal prolactin levels. In addition, 30% of group I had high levels of luteinizing hormone; whereas all group II members had normal levels of luteinizing hormone (Table 5). Of group I members with high luteinizing hormone levels, 16.6% suffered high sexual depression and 13.3% suffered intermediate sexual depression. There is a significant statistical relationship between sexual depression and LH levels in opioid-dependent patients, indicating that higher levels of luteinizing hormone trigger more severe sexual depression (Table 5).

The findings in this study indicate that higher levels of luteinizing hormone result in more severe sexual depression. Our results are consistent with those of other researchers studying sex hormone problems in opioid dependency[21]. Yen and colleagues[21] found that the testicles of men who were dependent on opioids lose their ability to produce testosterone, no matter how much LH is produced. This type of testosterone deficiency is diagnosed when blood tests show high levels of LH and low levels of testosterone. In other words, the pituitary gland is telling the testicles (by secreting LH) to produce testosterone, but the testicles have lost their functional ability, so the pituitary gland vainly continues to secrete LH because there is not enough testosterone in the blood to provide a feedback mechanism to shut down the pituitary. In other cases, the hypothalamus or pituitary gland fails to produce sufficient amounts of LH, thus preventing healthy testicles from secreting testosterone. This decline in testosterone plays an important role in a series of signs and symptoms, such as a decline in virility, libido, sexual activity, muscle mass, strength, and bone mass (osteoporosis) as well as an increase in abdominal fat. A decrease in the feeling of general well-being sometimes manifests as depression, a common psychological complication of hormonal imbalance[21]. In our study, there were a very high percentage of patients suffering erectile dysfunction ranging from mild to severe. This finding is consistent with other studies in that chronic opioid dependency is strongly associated with sexual dysfunctions, including reduced libido, erectile dysfunction, and delayed ejaculation in males[7, 22–25]. These study findings also show that divorce rates are higher among opioid-dependent men. This finding is consistent with studies that show opioid dependency creates significant costs to society through unemployment, homelessness, family disruption, loss of economic productivity, social instability, and criminal activities[26]. A possible explanation is that substance abuse can affect overall marital satisfaction and quality. According to Skinner et al.[27],

marital distress is reported more frequently among spouses suffering from or dealing with a spouse battling alcoholism. Distress and anger were also associated with high levels of drug abuse in a marriage. Opiate use can increase negative and hostile communication and lead to less warmth and unity in the relationship. With the breakdown of communication, marital distress and other troubles affect the marriage and result in greater marital dissatisfaction and divorce[27]. One of the limitations of this study was the limited sample size. The inclusion of only inpatients and exclusion of females could potentially limit the validity and generalizability of these findings. Other limitations include the failure to obtain objective measures of erectile function, such as plethysmography. In conclusion, nearly fifty percent of the users used heroin as their main substance of dependence and the rest used tramadol, emphasizing the prevalence and the wide spread use of tramadol in Egypt due its cheap price, its availability and the belief by our culture that it gives more power and energy and increasing the sexual performance. There was a significant difference between the groups in erectile dysfunctions. This study reveals that there is a significant statistical relationship between sexual depression and LH levels in opioid-dependent male inpatients. Furthermore, opioid-dependent inpatients had lower levels of free testosterone compared with non-users. In addition, half the opioid-dependent inpatients had high prolactin levels. A large prospective, randomized, controlled study is warranted based on these data.

Conflict of Interest

The authors declare no conflict of interest.

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