

## Erectile Dysfunction in Methadone Maintenance Patients: A Cross Sectional Study in Northern Iran

Seyed Hamzeh Hosseini, MD<sup>1</sup>  
 Ali Isapour, MD<sup>2</sup>  
 Mehrdad Tavakoli, MD<sup>3</sup>  
 Mehrdad Taghipour, MD<sup>4</sup>  
 Meysam Rasuli, MD<sup>5</sup>

**1** Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Mazandaran University of Medical Sciences, Sari, Iran

**2** Department of Urology, Mazandaran University of Medical Sciences, Sari, Iran

**3** Mazandaran University of Medical Sciences, Sari, Iran

**4** Baqiatallah University of Medical Sciences, Tehran, Iran

**5** Mazandaran University of Medical Sciences, Sari, Iran

**Corresponding author:**

Mehrdad Taghipour, MD, Baqiatallah University of Medical Sciences, Tehran, Iran

**Tel:** +989113536743

**Email:** scholar1366@gmail.com

**Objective:** Erectile dysfunction affects quality of life and is a common dysfunction in drug abusers. The aim of this study was to evaluate the frequency of erectile dysfunction in drug abusers on methadone maintenance therapy to reduce this drug side effect in the future studies .

**Methods:** This cross-sectional study was conducted with two hundred addicted individuals on methadone maintenance therapy. Erectile dysfunction was surveyed using the International Index of Erectile Function (IIEF). Finally, all data were collected and analyzed by descriptive statistics such as measures of variability and central tendency and Chi-squared ( $\chi^2$ ) test using SPSS Version18.0 software .

**Results:** The amount of the total frequency of erectile dysfunction was pointed 30 or less among the two hundred patients and included the moderate and severe cases. In this study, the number of patients with erectile dysfunction was fifty three (26.5%).

**Conclusion:** The frequency of erectile dysfunction in our study was approximately 1.5 times of prevalence of the public (16.1%). In this study, all the factors related to sexual function such as erectile function, libido, orgasm, and sexual pleasure showed a decline among drug abusers.

**Key words:** *Drug Abusing, Erectile Dysfunction, Methadone*

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**E**rectile dysfunction or impotency refers to men's inability to fulfill or maintain full erection to end the coitus. This problem can be seen in all age groups, but its incidence rises with aging (1). About 18 million of the U.S men which are equal to 18.4% of the total population have this problem and 617,715 men are added to this number annually (2). As reported by the American Journal of Epidemiology, approximately 36.4% of 40-70 year old American males were diagnosed with this dysfunction in 2002 (3). The statistics show that some underlying organic factors exist in 20-50 percent of males with this dysfunction; both organic and psychogenic factors exist in some of the patients (2). The treatment of erectile dysfunction depends on its underlying factors. Typically, the treatments are limited to sex therapy which suggests limiting sexual intercourse between the couples and minimizing physical contact. Recently, surgery and some drugs like sildenafil have proven to be effective in treating erectile dysfunction (3). Opium can cause impotency

and decreases the libido. Methadone, which is widely used for opium withdrawal and relieving pain, can cause impotency. Sedatives such as methadone can decrease testosterone by blocking synthesis of releasing gonadotropin and testosterone hormones (5). Methadone, a synthetic sedative drug, is used for the treatment of opium addiction and it is also used instead of morphine and hydromorphone for patients who bear sever pain (6). Methadone has two enantiomeric forms; the rasemic form is used more frequently (7). In a study done in 2008, erectile dysfunction due to methadone therapy was 26%. Most of the prominent foreigners' sources, the prestigious pharmacological and pathological texts, sites and essays show different frequencies for erectile dysfunction; in the meantime, there is no available statistics of erectile dysfunction in patients on Methadone Maintenance Treatment (MMT) in Iran. Because a clinical trial study on persons to survey impotency due to drug abuse is not ethical, we conducted a descriptive study with a sufficient sample size to provide useful data on erectile dysfunction. The main purpose of this study was to

determine the percent of erectile dysfunction in drug abuse patients on methadone maintenance treatment to provide a useful data to help reduce this drug side effect in the future studies.

**Material and Methods**

A cross-sectional descriptive study was performed with two hundred patients who referred to a psychiatry center and underwent methadone maintenance therapy in the city of Sari between 2006 and 2009.

It should be noted that, only a small number of eligible patients were available in the clinic. Therefore, patients' data were studied first and then completed by an interview; this process was time consuming .

Patients were selected through random sampling and data were obtained by a last year medical student through an interview and filling a questionnaire. The number of samples was calculated using Krejcie and Morgan Table and review of recent studies (references). Two questionnaires were used in this study: the first was about demographic characteristics, a history of drug abuse such as opium, alcohol etc., a history of drug usage which caused erectile dysfunction, type and amount of use of methadone, a history of mental disease and a history of high risk behavior; the second questionnaires was about erectile problems. In International Index of Erectile Function (IIEF) questionnaire (33, 34), there are 15 questions that contain questions about orgasm, sexual desire, erectile function and satisfaction. Each question has 5 points and the total score is 75. The score of 30 and less presents moderate and severe cases.

**Inclusion criteria:** The patients were addicts who used MMT for withdrawal from 2006 to 2009 .

**Exclusion criteria:** Persons who had a history of erectile dysfunction and took drugs for erection such as diuretics, anti-cholinergic agents and anti-psychotics, and patients with chronic diseases like DM and ESRD were excluded. Also, the patients who had a history of artherosclerosis based cardio-vascular problems such as MI, CVA and peripheral vessels diseases were excluded from the study, because these problems can cause erectile dysfunction.

Before the study, the nature and main purpose of the study was explained to the patients. All the patients filled the consent form. They were permitted to withdraw from the study any time they desired.

Data were analyzed with descriptive statistics such as measures of variability and central tendency and also Chi-squared ( $\chi^2$ ) test using SPSS Ver.18.0 software.

**Result**

The study included two hundred addicted men with the mean age of 39.5 years (SD = 11.304). In terms of age, the most common age was 50 years (21 patients), 32 years (11 cases), 30 (9 cases) and 34 years (9 cases), respectively. Most patients (142 patients) lived in the urban and 58 (29%) lived in the rural areas. In this study, most cases were married (156 patients). In terms of education level, 86 persons (43%) had an elementary school degree, 34 cases (17%) have studied at high school, 44 (22%) had finished high school and 36 (18%) persons had higher education (Table 1). Unfortunately, due to the inappropriate response of the patients to the prepared questionnaire, some data such as the time and amount of drug abuse were not available.

The review of the history of drug abuse showed that 155 patients used opium that allocated the most statistics. Of the total patients, almost 127 cases were smoker, 80 used crack, 62 used crystals and 46 patients consumed cannabis. Most of the patients used multiple substances simultaneously. The main input substance of most patients was opium (103 cases) and crack (65 cases), respectively (Figure 1). Eighty five patients had a history of addiction treatment in recent years. Based on the findings of this study the following results were obtained in terms of risky behaviors of the subjects: 32 (16%) patients had a history of drug injection; among the total subjects, 38 (19%) had suspicious sexual relations in the past year; during the past year, 27(13.5%) patients had a history of imprisonment for at least one time; and 20(10%) patients mentioned an experience of physical beatings and conflict.

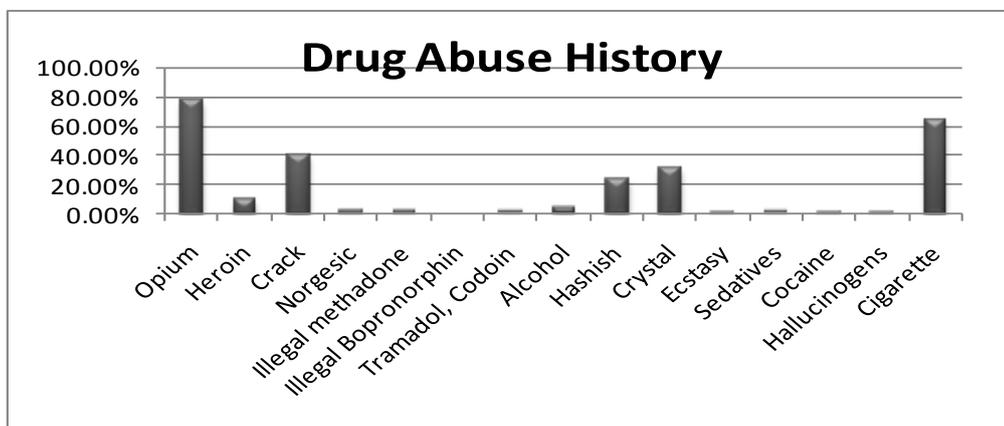


Figure 1: History of Drug Abuse in Patients

Based on the results of the interview, 43(21.5%) patients had a history of chronic disease; of whom, 40(20%) received medical treatment for their physical illness.

Associated psychiatric disorders were determined from patients' records and based on DSM-IV criterion for diagnosis: 67(33.5%) patients had depression, 63(31.5%) had anxiety, 29(14.5%) had illusion, 68(34%) had aggressive behavior, 14 (7%) had self-injuring behavior, 24 (12%) had a history of suicide and 19(9.5%) were hospitalized for their psychiatric disorders. Laboratory results of HIV and HCV tests in patients' record showed that only 2(1%) persons were HIV positive and 1(0.5%) was HCV positive. In this study, we also reviewed the occupation of the patients and we found that 66(33%) had full-time jobs, 67(33.5%) were unemployed and 49(24.5%) had part-time jobs. Also, 3 patients (1.5%) were under education and 15(7.5%) were retired. An interesting point in the results of our interviews was the rate of substance abuse in the first degree relatives; 41 patients mentioned this disturbing history in their family (Table 2). The patients who had erectile dysfunction were 36.81 years old in average, and the persons who did not have this problem were 40.34 years old in average. The illegal drugs used by the patients were recorded. Also, erectile dysfunction was studied in the drug abusers.

The results showed that among the 156 patients who used opium, 37 became impotent. In the meantime, among the patients who used heroin (6 persons), crack (26 persons), neurjizak (2 persons), teramadol, codeine and dyphnoxilate (2 persons), alcohol (17 persons), canabis (17 persons), metamphetamine (5 persons), sedatives (2 persons), cocaine (1 person), hallucination agents (2 persons) and cigarette and tobacco, 28 persons became impotent (Table 3).

Table 4 shows the distribution of different sexual problems based on IIEF which was filled by all the patients. The results showed that 19% of the patients had severe problems in erectile function, 20.5% in intercourse satisfaction, 19.5% in orgasm, 19.5% in desire and 20.5% in overall satisfaction. Moreover, the moderate, moderate to mild, mild and no dysfunction cases were studied thoroughly and their data are demonstrated in Table 5.

The overall results showed that 27 persons (13.5%) had severe erectile dysfunction, 26 (13%) had moderate problems, 66 (33%) had mild to moderate problems, 53 (26.5%) had mild problems and 28 persons (14%) had no erectile dysfunction (Table 5).

The overall prevalence of erectile dysfunction in our study was pointed 30 and less which covers the severe and moderate cases; the number of patients with erectile dysfunction was 53 (26.5%).

**Table 1: General Characteristics of Methadone in Patients**

Factors		Characteristics <sup>a</sup>	MET <sup>b</sup>
Basic Demographics	Age	Mean	39.5
	Residency	Urban	142(71)
		Rural	58(29)
	Marriage	Married	156(78)
		Single	40(20)
		Armistice	1(0.5)
		Died wife	0
		Divorced	1(0.5)
	Education	Elementary school	86(43)
		High school	34(17)
Finished high school		44(22)	
Higher diploma		36(18)	
Treatment History		85	
Risky Behaviors	Injection experience	32(16)	
	Suspicious sexual relations	38(19)	
	Imprisonment	27(13.5)	
	Physical beatings and conflict	20(10)	
Family and Social Status	Family history of addiction		41(20.5)
		Job	
	Full-time jobs	66(33)	
	Unemployed	67(33.5)	
	Under education	3(1.5)	
	Part-time job	49(24.5)	
	Retired	15(7.5)	

<sup>a</sup> Absolute frequencies are accompanied by percentages (in parenthesis). For continuous variables, mean (standard deviation) or median (range) are reported, as specified in the "Characteristics" column.

<sup>b</sup> Methadone

Table 2: Psychiatric and Medical Status

Factor	MET <sup>a</sup>
History of chronic disease	43(21.5)
Medical treatment for physical disorders	40(20)
Psychiatric Status	
Depression	67(33.5)
Anxiety	63(31.5)
Illusion	29(14.5)
Aggressive behavior	63(34)
Self injuring	14(7)
History of suicide	24(12)
Hospitalization experience	19(9.5)
HIV <sup>b</sup> Negative	76(38)
Positive	2(1)
Unknown	122(61)
Serology for infectious diseases	
HCV <sup>c</sup> Negative	76(38)
Positive	1(0.5)
Unknown	123(61.5)

Absolute frequency is accompanied by percentages (in parenthesis).

<sup>a</sup> Methadone

<sup>b</sup> Human Immunodeficiency Virus.

<sup>c</sup> Hepatitis C Virus

**Table 3: The Average Age of Addicted Individuals with and without Erectile Dysfunction and the Number and Percentage of Patients in Methadone Maintenance Treatment with Erectile Dysfunction Associated with Drug Abuse**

Variables	No ED group(Percent)	ED group(Percent)	P-Value
Mean Age	(40.34)	(36.81)	0.50
Opium	119 (76.29)	37(23.71)	0.31
Heroin	14(70)	6(30)	0.43
Crack	(67.5)54	26(32.5)	0.22
Norjisak <sup>*</sup>	3(60)	2(40)	-
Tamzijak (Bupronorphin) <sup>*</sup>	0	0	-
Other (Tramadole, Codeine, iphenoxylate,)	1(33.4)	2(66.6)	-
Alcohol	45(72.59)	17(27.41)	0.44
Cannabis	31(67.4)	15(32.6)	0.11
Methamphetamine (Ice) <sup>*</sup>	3(37.5)	5(62.5)	-
Ecstasy	1(100)	0	-
Relaxants ( BZN, Barbitorates) <sup>*</sup>	1(33.4)	2(66.6)	-
Cocaine	1(50)	1(50)	-
Hallucinators (LSD...) <sup>*</sup>	0	2(100)	-
Cigarette and Tobacco	99(77.96)	28(22.04)	0.16

\* P-value was not mentioned for some cases because of the small number of patients and its non-meaningfulness.

**Table 4: Number and Percentage of Addicted Individuals in Methadone Maintenance Treatment with Sexual Dysfunction Based on the Severity of Dysfunction**

	Severe dysfunction (Percent)	Moderate dysfunction (Percent)	Mild to moderate dysfunction (Percent)	Mild dysfunction (Percent)	No dysfunction (Percent)
Erectile Function	37(19%)	27(13.5%)	62(31)	32 (16)	41(20.5)
Intercourse	41(20.5)	33(16.5)	63(31.5)	36(18)	27(13.5)
Satisfaction	39(19.5)	28(14)	78(39)	27(13.5)	28(14)
Orgasm	39(19.5)	20(10)	80(40)	40(20)	21(10.5)
Overall satisfaction	41(20.5)	33(16.5)	63 (31.5)	36(18)	27(13.5)

**Table 5: The Number and Percentage of Drug Addicts in Methadone Maintenance Treatment Suffering from Erectile Dysfunction in Terms of Severity of Dysfunction**

Erectile Dysfunction	(Percent)
Severe dysfunction	27(13.5%)
Moderate dysfunction	26(13%)
Mild to moderate dysfunction	66(33%)
Mild dysfunction	53(26.5%)
No dysfunction	28(14%)

## Discussion

Erectile Dysfunction, as a public health problem, affects the quality life of the families. The prevalence of erectile dysfunction in the general population is about 16.1% or more (8, 9), and in diabetic population and ESRD is reported to be up to 90%. Psychotropic drugs show their adverse effect through central inhibitory neuroendocrine mechanisms and local neuromuscular junction, and they also affect the hormone system (10, 11). The relationship between drugs and erectile dysfunction is not always direct, but depends on social, cultural and other peripheral factors. Therefore, this theorem can rationalize the differences between the prevalence of this dysfunction in different studies. Just a few studies have been done on the synergism effects of different drugs on erectile dysfunction; this problem has led us to study all the drugs in this paper thoroughly. In this paper, the impact of each drug and prevalence of erectile dysfunction have been studied and the mechanism of this dysfunction has been reported. The results of this study show that erectile dysfunction, as a side effect of MMT in drug abusers, can be of concern. This subject has been certified in different studies (12).

It should be noted that the direct relationship between methadone usage and erectile dysfunction was not evaluated in this study .

Hallinan. R et al. (2009) conducted some studies about the side effects of MMT. They conducted a study in pursuit of finding the etiology of hypogonadism caused by methadone. They chose 103 addicted males and found that the amount of free testosterone in the males under MMT decreased. In our paper, erectile dysfunction due to each drug and their total prevalence in the society on the basis of IIEF were studied, but the mechanism of dysfunction was not. In a study done by Brown et al. (13, 14), age was found to be a very important risk factor for erectile dysfunction with MMT. The age range of the subjects in our study was 18 to 55 with the average of 39.5; of the total subjects in this study, 26.5% had erectile dysfunction, whereas in study of Gianluca Quaglini (15) the subjects were 18 to 47 with the average of 31 and 42% of them had this problem. Besides, in a study (2000) conducted on Italian males aged 18 to 39 years of age, this number was 2% (16). The differences between the result of our study and that of others may be due to the existence of some factors like sample size, social condition and different human populations .

The mean age of the patients with ED were lower than those of non-infected patients and this difference could be due to sexual activity in the younger patients.

In this study, the number of sample was two hundred, while S.M Giacomuzzi et al. used 60 patients in their study which definitely could not be representative of the majority of the population. In our paper, those drugs that caused erectile dysfunction were studied. Most of the patients had a history of opium misuse; of whom, 37 patients (23.71%) had erectile dysfunction.

In another study performed by Venkat Chekuri et al. this number was about 16.9%. Long duration of opium addiction can block the gonadotropin releasing hormone and therefore decreases the testosterone and ultimately decreases sexual desire in males. In contrast to other countries where opium derivations are used most frequently, in Iran opium is used directly; and unfortunately, the specialists and physicians do not pay enough attention to the side effects of MMT. Therefore, we can see a rise in erectile dysfunction in these people nowadays. Unfortunately, no specific statistics in this field is available. Heroin causes testicular function decline and blocks LH release.

The prevalence of erectile dysfunction due to heroin addiction was 30% in our study which is close to other studies that have found it to be 39 to 48 percent. Cigarette smoking can affect sexual function by nicotine as a vasoconstrictive agent. Nicotine rises in blood after smoking and increases the sympathetic tone in penis and interacts with relaxation of smooth muscles in corpus cavernous (21, 22). Wolf and Shalman (23) concluded that changes in relaxing factors derived from endothelium, No, Prostaglandin, Prostacyclin and tromboxan are important in cigarette related erectile dysfunction. In their study, the prevalence of erectile dysfunction in cigarette smokers was about 22.7%; in this study, it was 22.04%. Getting everyone to quit smoking should be seen as a goal to reduce erectile dysfunction. Also, alcoholism may atrophies testicle by blocking testosterone and spermatogenesis. Survey on alcoholic males showed that amount, frequency and duration of alcohol use are related to erectile dysfunction and libido (24). In our study, the prevalence of erectile dysfunction due to alcoholism was 27.41, while O'Farrell reported the minimum prevalence of alcoholism in these people to be 25%. Amphetamines increase the CNS function by stimulating, releasing or inhibiting uptake of norepinephrine and dopamine. Long duration of amphetamine drugs use can cause erectile dysfunction and delay ejaculation. Long duration of using these drugs causes a condition called Crystal Dick, with strong libido, high energy and decrease in sexual blockage, but the person cannot reach to full erection (26, 27). Bang-Ping (20) and colleagues have reported the prevalence of erectile dysfunction to be 34.5%. The effect of MDMA (ecstasy) is due to releasing serotonin and inhibiting dopamine uptake. Dopamine stimulates sexual function while serotonin inhibits it (19). Zemishlany(28) reported that these substances have about 40% negative and 40% positive effect on erectile function. Indeed, there are just few studies done about sexual effects of crack misuse. Cocaine causes erection malfunctions through hyperprolactinemia and negative feedback of hypothalamic dopamine receptors (29, 30). McDuland (31) reported that 66% of patients who used cocaine for more than one year became impotent. In a very vast study done about canaboids (marijuana, hashish) it was reported that 70% of males who used these substances showed increase in sexual satisfaction

(32). The impacts of long duration of these drugs are still ambiguous (24).

In our study, according to the IEFF questionnaire, moderate and severe data were considered as erectile dysfunction. In terms of sexual desire, 29.5% of the patients had problems; this number was lower than what was found in the study of Venkat Chekuri et al. (38.4%) (18). Also, in this study, 33.5% of the patients had an orgasm dysfunction that was roughly similar to the study of Quaglio et al. (15).

In our study, 13.5% of the patients had severe and 13% had moderate dysfunction; while these problems in Hallinan R (4) study were 53% and 26%, respectively. The frequency of erectile dysfunction in our study was 26.5% which was more than the result of Brown R et al. study (14%), and slightly less than Hallinan R. results (26%) (4).

Statistical differences between the result of our study and that of others may be due to the differences in the number of samples and the diagnostic tools. There was no simultaneous access to all patients, so this limitation resulted in prolonged duration of the study.

The limitations of this study were as follows: Some abused drugs had low range of usage in the patients; therefore, it was not possible to make comparisons between groups.

A noticeable part of this survey was the large sample size and studying erectile dysfunction caused by each drug. However, one of the limitations of this study was sampling of people coming to only one of the MMT centers in Sari. The followings are highly recommended for the future studies: Larger sample size, conducting studies in multiple centers in the province, and even in all parts of the country. Also, a very extensive cohort study should be conducted to investigate the erectile dysfunction and evaluate the hormones, neurotransmitters, some blood substances changes and morphologic and physiologic changes in testis and penis in persons using illegal drugs.

## Conclusion

In this study, all the factors related to sexual function such as erectile function, sexual desire, orgasm, sexual and overall satisfaction have decreased considerably. This study proved that erectile dysfunction and other sexual dysfunctions have a high prevalence in drug abuser males. This issue has not drawn enough attention yet and is still unknown in the public health. This problem has its own effects on patients' health and worsens the prognosis of drug abuse. Addiction withdrawal centers are connected to this aspect of patients' health. Therefore, they should be warned about the side effects and dysfunctions caused by the medications used at these centers. Moreover, this issue should be recognized as a protective factor to prevent addiction in the future.

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