

Methadone Treatment in Iranian Opiate Addicts: A Preliminary Report

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Abstract

Background: This study aimed to investigate the initial dosage of methadone and factors affecting it in maintenance therapy.

Methods: This cross-sectional, descriptive-analytic study was conducted on 157 individuals referring to a methadone maintenance therapy (MMT) clinic. The initial dosage of methadone was 20-45 mg which was adjusted during the treatment based on each patient's evaluation. Three groups were formed according to methadone dosage (less than 30 mg, between 30-50 mg, and more than 50 mg).

Findings: Significant relations were observed between increased methadone dosage in the initial phase and marital status ($P = 0.03$), injection ($P = 0.03$), medical comorbidity ($P = 0.009$), and borderline personality disorder ($P < 0.001$).

Conclusion: Further studies with larger sample size and including the history of previous detoxification, substance abuse, omission of self-recording, evaluation of women's addiction and MMT program performance with counseling support should be performed.

Keywords: Addiction, Methadone, Personality disorder.

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Introduction

Opioid dependency is a chronic and often recurrent disorder that causes several medical problems such as AIDS, hepatitis, and social problems. Due to its chronicity, longtime, or even sometimes lifelong, treatment with substitution of opioids, such as methadone, is necessary for decreasing physical and psychosocial problems.

Considering how different psychosocial dimensions of problems associated with drug abuse affect the family of the addict, the huge number of Iranian people involved with addiction becomes obvious.¹⁻⁶

Due to its strategic situation in the Middle East and its young population, Iran is at a high risk of opium consumption.^{2,3} However; it differs from other countries in terms of type and style of opioid use. In addition, statistics show higher unsuccessful opioid withdrawal in the country. Although there are several kinds of treatment methods, most drug addicts do not achieve permanent abstinence and obtain a life-long habit of using opium.^{2,3}

Opioid addiction might be treated through detoxification or maintenance therapy. Several guidelines are suggested and followed for detoxification ranging from treatment of symptoms with sedative and hypnotic drugs in outpatient centers to ultra rapid detoxification. Outpatient detoxification has not been very successful since it highly depends on the active attendance of the patients in self-helping groups after the detoxification.^{2,3}

Methadone maintenance treatment (MMT) is one of the treatments which not only prevents relapse, but also causes improvement in physical and psychosocial health of the patient. In addition to bringing stability into the patient's life, MMT decreases the risk of transmission of infectious diseases such as HIV/AIDS, hepatitis C viral infection (HCV), hepatitis B viral infection (HBV), and tuberculosis, along with the risk of committing a crime, and illegal use of drugs.^{3,5,7-9}

Maintenance therapy is used with addicted subjects who have not been successful in opioid withdrawal. MMT is more successful than short time methadone therapy in prevention of relapse.⁹⁻¹¹ However, a drawback of MMT is that the patients should at least be 18 and need to have been addicted for at least one year duration.^{9,10}

The dose of methadone is determined based on the kind and amount of the substance used,

age, gender, psychosocial condition, and medical and psychiatric comorbidities. The comorbidity of substance related disorders is more in men than in women. In addition, not only depression is very prevalent among drug addicts, but also antisocial personality disorder is four times more common in them than in the general population.

Based on Iran National Research Center for Addiction, MMT is started with an initial dose of 20-30 mg methadone per day. During treatment, especially the first weeks, methadone dose is adjusted based on the patient's evaluation until he becomes stable.^{5,8}

In 1999, the U.S federal rules allowed not only the clinics but also the offices to perform MMT for drug addicts which enabled primary care practitioners to use methadone therapy in their private offices.

Treatment aims to prevent withdrawal syndrome, i.e. it involves lowering craving to opioids and blocking euphoric and sedative effects of illegal use of opioid.

In the first phase of methadone treatment, the patient will become ready for a steady state in which he usually takes a dose of 20 to 30 mg (with a maximum of 45 mg) of methadone. Methadone will be prescribed until the satisfactory dose is determined. Then, the patient would be examined for other chronic medical or psychiatric disorders. MMT is continued until the patient is proved to be ready for successful detoxification.⁹

During the maintenance phase, a dose 80 to 120 mg (or even higher) is required. In addition, longtime treatment is more effective than short time treatment in preventing relapse.^{4,5}

Based on the results of a recent review of notes of methadone clinics, urinalysis of patients who had received methadone for at least 6 months revealed that 22% of them experienced illegal use of opioids. This report indicated that in 4 methadone clinics in Philadelphia 23% of illegal use of opioids is more than 10 days during a month. Overall, one-year commitment to methadone programs with doses over 80 mg per day was more than programs employing lower doses.

It's impotent to increase the dose of methadone in MMT due to tolerance; otherwise the patients will be tempted to use illegal drugs.^{7,8}

Since, to our knowledge, no exact relation between initial dose of methadone and factors affecting this dose has been determined which in

most cases necessitates correction, we tried to recognize the factors affecting initial dose for having better conditions during the process of opioid withdrawal.

Methods

This analytic prospective study was conducted on 157 opiate dependents referred to an MMT clinic. Since the only source of information about drug abuse was the participants themselves, they were first asked about demographics, amount and type of drugs they used, duration of use, and simultaneous use of other medicines. Then, the obtained data was recorded in files. Patients were evaluated and visited by a psychiatrist as soon as starting this treatment. Methadone was started with a minimal dose of 20 mg and maximum dose of 45 mg per day based on the type and amount of the drug used, as well as physical and psychiatric disorders. During the treatment, appropriate decisions were taken considering the evaluations each patient made. The dose of methadone was increased to a maximum of 125 mg during the first 2 weeks which was continued if necessary.

The dose of methadone was determined based on the amount of opium used. Patients who used more than 4.5 g of opium or 1 g heroin were prescribed with 30 mg methadone. If the patient was addicted to heroin with injection, dose of methadone was raised by 50%. If the patient was taking opium vapor, methadone dose was decreased 5 to 10 mg. In case of opium smoking or opium residue usage, the dose of methadone was increased for 5-10 mg (based on the adsorbed morphine).

Patients were divided into three groups based on methadone dose. The first group received less than 30 mg methadone, the second group 30 to 50 mg methadone, and the third group over 50 mg methadone.

According to our data, the patients with comorbid physical and psychiatric disorders or those using drugs such as benzodiazepines were more likely to require higher doses of methadone.

After describing the variables, first, the differences in a group were evaluated using t-test and ANOVA. Then, the most exact logistic regression model determining the required dose of methadone was tried to be formed based on all the studied variables. The precision of the

regression model was investigated using R-adjusted.

Results

Totally, 157 patients participated in this study including 145 (92.4%) males and 12 (7.6%) females. In addition, 53.4% were married, 32.1% were single, and 14% were widowers or divorcees.

The majority of participants had a high school diploma or a higher degree (50%). However, some only finished junior high school (23.1%), were high school dropouts (18%), or elementary school graduates (8.9%). Among those who had a job, 33.1% worked full-time and 16.6% part-time. In addition, 57.9% were self-employed. It took 62.6% of them less than 30 minutes to get to the treatment center. Moreover, while 49.7% lived with their own family, 42.7% were living with their parents.

Opium, sap, and heroin were used by 51.6%, 40.1%, and 37.6% of the participants, respectively. Subjects used different methods of using drugs including eating (55.4%), smoking (54.1%), injection (15.9%), and snuffing (5.1%) (Table 1).

Opium was used mainly with cigarettes (90.7%), anticholinergics (38.9%), alcohol 21.1%), cannabis (18.5%), tramadol (15.3%), benzodiazepines (6.4%). Among all, 26.3% had an experience of injection and 21.3% had been in jail. While 7.6% of the subjects had more than 10 sex partners, each of HIV, HCV, HBV infections were seen in 2.4% of the participants (Table 1).

A psychiatrist interviewed the patients to investigate the probability of axis I/II psychiatric disorders (based on DSM-IV-TR), other physical diseases, as well as abuse of other drugs. A significant correlation was found between increased dose of methadone and having borderline personality disorder or physical illnesses (Table 2).

According to our findings, there were not any significant relations between the required methadone dose in the first 10 days and sex, age, education, source of income, the distance between the living place and the clinic, and the living situation.

There was a negative correlation between marital status and employment with the dose of methadone in the first 10 days of treatment, i.e. those who were married or had a full-time job

needed lower doses of methadone.

Moreover, while heroin had a positive correlation with methadone dosage, opium abuse and methadone usage were not significantly related. In addition, the way of abuse did not have a significant relation with methadone dose. Although simultaneous use of the drug with alcohol, benzodiazepines, tramadol, anticholinergic, and cannabis, led to the need for higher doses of methadone, the only

significant increase in required dose of methadone was observed in case of antiparkinsonian anticholinergics (Table 1).

There was a significant correlation between experiences of risky behaviors, such as injection and being in prison, and the required dose of methadone. However, no significant relations could be found between the dose of methadone and having more than 10 sex partners and HIV, HCV, and HBV infections (Table 1).

Table 1. The relation between the initial methadone dose and type of substance, additional drugs, and history of high risk behaviors

		Numbers of methadone pills (5mg) during the first 10 days								P-value
		< 6		6-10		> 10		Total		
		%	f	%	f	%	f	%	f	
Substance										
Heroin	No	82.4	14	67.8	61	46.0	23	62.4	98	0.008
	Yes	17.6	3	32.2	29	54.0	27	37.6	59	
Other drugs										
Anticholinergics	No	88.2	15	67.8	61	40.0	20	61.1	96	0.0001
	Yes	11.8	2	32.2	29	60.0	30	38.9	61	
High risk behavior										
Injection	No	78.6	11	84.3	75	53.1	26	73.7	112	0.001
	Yes	21.4	3	15.7	14	46.9	23	26.3	40	
Jail experience	No	86.7	13	88.9	80	58.7	29	78.7	112	0.001

Table 2. The relation between the initial methadone dosage and comorbid physical and psychiatric disorders

		Numbers of methadone pills (5mg) during the first 10 days								P-value
		< 6		6-10		> 10		Total		
		%	f	%	f	%	f	%	f	
Axis I										
None		11.8	2	80.9	8	4	2	7.6	12	0.24
MDD (Major depressive disorder)		23.5	4	20	15	24	12	21.7	34	
Bipolar		5.9	1	1.1	1	10	5	4.5	7	0.0001
Anxiety		5.9	1	2.2	2	0.0	0	1.9	3	
Others		52.9	9	67.8	61	62	31	64.3	101	
Axis II										
None		17.6	3	8.9	8	2	1	7.6	12	0.0001
BPD (borderline personality disorder)		0.0	0	7.8	7	22	11	11.5	18	
APD (antisocial personality disorder)		5.9	1	12.2	11	46	23	22.3	35	0.06
Others		76.5	13	71.1	64	30	15	58.6	92	
Physical diseases										
No		46.9	23	71.3	62	46.9	23	63.8	97	0.01
Yes		53.1	26	28.7	25	53.1	26	36.2	55	
Other drug abuse										
No		90.9	10	90.2	55	71.9	23	84.6	88	0.06
Yes		9.1	1	9.8	6	28.1	9	15.4	16	

Table 3. Ordinary multivariable logistic regression model of factors affecting the initial methadone dosage

Variable	OR	95% CI
Marital status		
Single	1	-
Married	0.19	0.05-0.69
Others	0.23	0.04-1.37
Age groups (Linear effect)	0.71	0.43-1.17
Heroin use	0.41	0.13-1.32
Injection	5.9	1.14-30.5
Comorbid physical illnesses	4.5	1.46-13.9
Bipolar Disorder	13.7	3.2-58.6

Discussion

In this study, participants were divided into 3 groups based on the initial dose of methadone. The first group (less than 30 mg) included 17 subjects, while the second (between 30 to 50 mg) and thirds (more than 50 mg) groups included 90 and 50 participants, respectively. In the first group, while opium and cigarette consumption were the most frequent, heroin and opium inhalation and eating, along with using alcohol, cannabis, tramadol, anticholinergic, and benzodiazepine were the least frequent. Among all groups, the second group had the highest percentile of opium use, and lowest percentage of injection, cigarette smoking, history of imprisonment, and infection to HIV, HCV or HBV. Although the third group had the highest frequency of using heroin, alcohol, cannabis, anticholinergics, benzodiazepine, and tramadol, the differences were only significant in case of heroin ($P = 0.008$) and anticholinergics ($P = 0.0001$). Members of the third group also had the highest rate of inhalation, consumption, injection, and imprisonment, and the lowest rate of smoking, opium use, and having more than 10 sex partners.

Like Behdani et al.,¹² we found a significant difference between the proportion of men and women since women do not tend to attend clinics for treatment. However, an exact estimation of sex proportion was not available (this could be highlighted by further studies investigating this proportion in different clinics and various regions). It seems the required dose of methadone is more in men than in women.

The percentile of subjects aging less than 31 rose from the first to the 3rd group. Subjects aging 36-54 had the highest percentage, and also the highest frequency in the 1st group in comparison

to others. In a study in Mashhad,¹² most subjects aged 18-30 which would be logical since the city is near Afghanistan. However, the fact that the age of addiction is dropping needs attention. While in Kermanshah most drug addicts aged 25-29, substance abuse was most common in adults aging 30-34 in Tehran and Mazandaran. Most married individuals needed the lowest doses of methadone in contrast with single subjects ($P = 0.01$).

In addition, the participants living in areas less than 30 minutes from the clinic needed lower doses. Similar to a previous national study in Kermanshah, Mashhad, Isfahan, and other cities, we found that more than half of the subjects had a high school diploma or higher, while the lowest frequency was associated with primary school education. More than half of the participants were married and 60% were financially independent. As it was suggested by Behdani et al.¹² and national researches,¹³ spouse and family support had a significant role in motivating the addicts for withdrawal. They also found that methadone treatment caused an improvement in daily activities which made the patient able to keep his independent financial source and full-time job.

It took 63% of the participants less than 30 minutes to get to the clinic. Moreover, 50% lived with their families. In Washington, Deck and Carlson believed that availability barriers including simultaneous abuse of several substances, referral from legal system, living in team houses, and not having a financial source or a shelter, had significant relations with MMT. On the other hand, factors enhancing the access to methadone use were pregnancy and self referral treatments. Based on their findings, those living far from methadone clinics were more interested in referral.¹⁴

The experience of injection was more common

in the 3rd group, and those patients needed higher doses of methadone. Gill et al. claimed that although there were not any significant relations between antisocial personality disorders, risky sexual behaviors, infection to HIV, infusion, and methadone treatment, patients with antisocial personality disorder were more likely to become interested in the use of shared injection equipments, infection to HIV, and appearance of antisocial behaviors after the treatment cycle.⁷

In contrast to the opium users, the percentile of heroin users rose from the 1st to the 3rd group. This was different from what Banta-Green et al. had found. They conducted a retrospective study to compare methadone maintenance doses between 2 user groups (prescription-type opioid primary (PTOP) and heroin abusers). They also investigated the type of substance used during the 12 month MMT period. In addition, they surveyed opiate use in the last 30 days, and heroin or any other substance used for the first time without heroin. After homogenizing demographic information, use of other kinds of substances, type of general support, and considering medical, psychiatric, social, legal, and family factors, no significant relation was observed between the differences in maintenance phase of treatment and the type of substance.¹⁵ In this study, while eating or inhalation of the substance increased the initial dose of methadone, smoking the drug decreased it. Moreover, although using alcohol, cannabis, anticholinergics, benzodiazepine, and tramadol increased the initial dose of methadone, the only significant relation was seen in case of anticholinergics ($P = 0.0001$). Cigarette smoking was most common in the first group (In fact, all participants this group were cigarette smokers). Epstein and Preston performed a retrospective clinical trial and announced that the use of cannabis was not effective on methadone dosage in heroin abusers.¹⁶

The number of participant with depression and bipolar disorder increased from the second group to the third and it caused an increase in the initial dose of methadone. On the contrary, the percentile of having anxiety disorder had an inverse relation with the initial dose of methadone. Having borderline and antisocial personality disorders and physical illnesses, during the period of substance abuse increased the initial dose of methadone.

However, the significant relations were only observed between the increased initial dose of methadone and physical disorders ($P = 0.01$) and borderline personality disorder ($P = 0.001$). In contrast, Gill et al. could not find this significant relation in their study.⁷

Ahmadi suggested that since general health practitioners were interested in substance abusers, they could focus on risky individual behaviors or social factors to lower the risks.⁶ In an investigation in Australia, Haig reported that substance abuse and injection decreased after MMT. He suggested that like social programs, methadone programs should be spread and used in prisons, too.¹⁷

Totally, as was shown by Krambeer et al., MMT was effective in lowering the use of injection and shared syringes. In addition, while daily doses of more than 80 mg of methadone led to better outputs, doses less than 40 mg per day were not enough or effective.⁸ However, the period for which MMT remains effective is affected by the type of the program, methadone dose and duration of treatment, and the time allocated to supporting services in the withdrawal program. It seemed that bigger numbers of volunteers in the withdrawal group, the longer duration of treatment, and available supporting and counseling services from the beginning of the programs or even after finishing the treatment all caused better outcomes and saved more money.⁵ It is proven that MMT in substance dependents decreased illegal substance abuse, risk of infection and transmission of HIV, tuberculosis, hepatitis, and crimes.⁵ Access to appropriate supporting treatments lowered the risky behaviors. For instance, Avants et al. showed that supportive services from harm reduction groups promoted patients' self-control against sexual behaviors and drug abuse and therefore, increased the effectiveness of methadone therapy. Although MMT with group therapy seems expensive, it is considered as a method of withdrawal since similar programs have been successful in changing views towards HIV.¹¹

Furthermore, gathering information and getting feedback from patients behaviors by program developers can reduce crime rates and increase social rapport in volunteer groups.^{18,19}

Finally, apart from aforementioned elements

in this study, MMT should be investigated in combination with non pharmacological interventions such as group therapy and supportive counseling.

Conflict of Interest: The Authors have no conflict of interest.

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تجربه درمان با متادون در معتادین به تریاک: یک گزارش مقدماتی

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چکیده

مقدمه: این مطالعه با هدف تعیین دوز اولیه متادون در درمان نگهدارنده و شناسایی عوامل مؤثر بر این دوز انجام شد.

روش‌ها: مطالعه به صورت مقطعی، از نوع توصیفی- تحلیلی با ۱۵۷ مراجعه کننده به کلینیک MMT (Methadone maintenance therapy) انجام شد. متادون با دوز حداقل ۲۰ میلی‌گرم و حداکثر ۴۵ میلی‌گرم، شروع و دوز مورد نیاز هر فرد در طی دوره درمان با ارزیابی بیمار تنظیم شد. سه گروه با دوزهای کمتر از ۳۰، بین ۳۰ تا ۵۰ و بیش از ۵۰ میلی‌گرم تشکیل گردید.

یافته‌ها: وضعیت تأهل ($P = ۰/۰۳$)، مصرف تزریقی ($P = ۰/۰۳$)، وجود بیماری‌های جسمی ($P = ۰/۰۰۹$) و اختلال شخصیت مرزی ($P < ۰/۰۰۱$) با افزایش دوز متادون مصرفی در فاز اولیه ارتباط معنی‌داری داشتند.

نتیجه‌گیری: توصیه می‌شود جهت تأیید نتایج این مطالعه، علاوه بر جامعه آماری بزرگ‌تر، سابقه ترک‌های قبلی، مصرف غیر مجاز مواد، حذف خود گزارش دهی، بررسی اعتیاد زنان و انجام طرح MMT با حمایت مشاوره‌ای مورد بررسی قرار گیرند.

واژگان کلیدی: اختلال شخصیت، اعتیاد، متادون.

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