


Comparison of Lapse Rate in Drug Dependent Patients in 2 Methods of Methadone Maintenance Treatment and Buprenorphine Maintenance Treatment

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Substance Abuse: Research and Treatment
Volume 16: 1–5
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DOI: 10.1177/11782218221112502



ABSTRACT

BACKGROUND: Lapse has been one of the major challenges in the treatment of drug dependence sometimes leading to its relapse.

OBJECTIVES: The aim of this study was to determine the lapse rate in drug dependent patients as for the 2 methods of methadone maintenance treatment (MMT) and buprenorphine maintenance treatment (BMT) in Yazd city.

METHODS: In this cross-sectional study, 626 female and male patients who had referred to 5 SUD treatment centers in Yazd and had been treated with methadone and buprenorphine maintenance were studied. Participants were divided into 2 groups of MMT and BMT and were evaluated based on lapse within 6 months.

RESULTS: In this study, 60.9% of patients were treated with methadone but the rest were treated with buprenorphine. Overall, 33.1% of patients lapsed (35.2% for methadone and 29.8% for buprenorphine). Lapse in methadone treatment was correlated with age, occupational status, and duration of treatment ($P < .05$); it failed to correlate with any other demographic and clinical characteristics ($P > .05$). Lapse rate in buprenorphine treatment was also related to marital status and the drug used ($P < .05$). The mean dose of buprenorphine consumed showed no significant relationship with lapse ($P > .05$). The results demonstrated that given the low dose, lapse stood higher in the buprenorphine group than the methadone group; however, as to high dose, the buprenorphine group showed lower lapse than the other group.

CONCLUSIONS: In regard with the high rate of lapse, it is recommended to consider the factors related to the 2 methods of treatments, and provide counseling and training programs to lower lapse in the patients.

Ethics Committee (REC) approval code: IR.SSU.REC.1394.158.

KEYWORDS: Lapse, maintenance treatment, methadone, buprenorphine

RECEIVED: February 16, 2022. **ACCEPTED:** June 21, 2022.

TYPE: Original Research

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Introduction

Drug dependence or substance use disorder (SUD) is a chronic and recurrent disorder that threatens human health and life.¹ The disorder has long been regarded as a personal, social and even political harm and, above all, a public health issue associated with high morbidity and mortality. Given the increasing incidence and prevalence of the drug used among the youth, planning a comprehensive program around the problem of drug dependence and related behaviors seems to be urgent.² According to a 2011 UN report, Iran has the highest number of crimes related to opioid use in the world.³ In recent years, more

than 80% of the recognized drug-treatment seekers in Iran were primarily dependent on opioids.⁴ In 2015, the Iranian Drug Control Headquarters estimated that 2.8 million of 15–64-year-olds were dependent on illicit drugs.⁵ Maintenance treatment programs can provide effective therapy for patients with SUD.⁶ Maintenance treatment refers to the type of therapy in which the patient is treated with the drug from the outset. The medication is adjusted to the amount needed for the individual and prescribed for a long time on the advice of the physician to be provided to the patient. By the time the patients use this method, their desire and attraction to the drug has diminished



and even reached zero. It also enhances the quality of life function, psychiatric status, and general adaptation of patients over a long period of time.⁶ Methadone and buprenorphine are drugs used by physicians and professionals in maintenance treatment. These drugs are industrial substances that have physiological and analgesic properties similar to opiate; they, however, fail to be ecstatic.⁷ Of the major challenges in maintenance treatment are lapse and level of maintenance of the treatment.⁸ The important thing in treating a drug-dependent disorder is that the longer a patient maintains the treatment, the better his or her outcome will improve. Therefore, all treatment policies focus on keeping the patient on track and increasing strategies to increase maintenance of the treatment.⁹

In recent years, some studies have been performed on the methadone maintenance treatment.^{8,10} These studies have shown that the rate of lapse is higher in the first 6 months of the treatment; however, if the treatment persists for more than 6 months, the probability of maintenance increases.^{10,11} Regarding the importance of lapse in the treatment and its follow-up in patients consuming these drugs, this study aimed to examine lapse rate in drug dependent patients through the 2 methods of methadone maintenance treatment and buprenorphine maintenance treatment in Yazd.

Methods

In this analytical cross-sectional study, the study population consisted of all DSM-V self-introduced substance users who were being treated in 5 SUD treatment centers in Yazd in 2016 (1 public center and 4 private centers). The study population comprised men and women undergoing maintenance treatment with methadone and buprenorphine following at least 6 months with the initial treatment. Assuming a lapse ratio of 0.32 in the methadone group and 0.16 in the buprenorphine group, with a relative risk probability of 0. Five, relative risk of 20%, and confidence interval of 95%, the sample size was calculated to be 620. The mean doses of methadone and buprenorphine drugs were 78.2 and 3.68 mg respectively. Participants were divided into 2 groups of MMT and BMT and were evaluated based on lapse within 6 months.

Data were collected using a questionnaire prepared by the Ministry of Health for use in SUD treatment centers. The study included demographic data including age, sex, occupation, education, and marital status, as well as clinical information such as duration of dependency, number of times undertaking quitting, type of the substance used, method of use, psychiatric history, family history of SUD, and type of treatment used. At the official center, the information was collected by census and at the private centers by clustering. Data were analyzed using spss20 software.

Ethical approval

The study was approved by the ethical committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.REC.1394.158). The study was conducted in accordance to

the Declaration of Helsinki written informed consent was obtained from all participants prior to data collection.

Results

The aim of this study was to investigate the lapse rate of drug dependent patients via the 2 methods of methadone maintenance therapy (MMT) and buprenorphine maintenance therapy (BMT) in Yazd.

As to MMT, Table 1 displays a significant relationship between age and lapse as well as between occupational status and lapse. No significant relationship was identified between age, education, and marital status with lapse. The mean age of the MMT group who had lapse was 34.22 ± 9.23 .

Table 1 also illustrates a significant relationship between lapse and marital status in BMT. No significant relationship could be found between gender, age, occupational status, and education with lapse given BMT.

The results of the study in Table 2 reveal an insignificant relationship between drug dose and lapse in MMT. The highest rate of lapse corresponds to the patients being on a dose of 75 to 100 mg with methadone treatment.

Moreover, a significant difference was detected between the methadone treatment dose group of 50 to 75 mg and the group of >100 mg. However, there was no significant relationship between drug dose and lapse concerning BMT. The highest lapse rate was pertinent to the patients who received buprenorphine at a 2 to 4 mg dose.

According to Table 3, of 381 patients being treated with methadone, 134 (35.2%) lapsed from the treatment but 247 (64.8%) showed no lapse. In addition, of 245 patients on buprenorphine treatment, 73 (29.8%) showed lapse whereas 172 (70.2%) others proved to be non-lapse cases. There was no significant relationship between methadone and buprenorphine treatments in regard with lapse.

Discussion

A 6-month lapse rate study of patients regarding treatment with methadone and buprenorphine revealed that in methadone maintenance treatment the greatest lapse belonged to the youth so that a statistically significant relationship was observed between age and lapse. It should be noted that most of the participants were in the age range of 25 to 35 years. In certain findings, this relationship was not significant^{12,13}; however, in the results of Mohebbi, Hosseini, and Koohestani, it proved to be significant.^{8,14,15}

Patients assume themselves to be more physically fit for SUD and its associated risks.¹⁶ Increasing age which is associated with a rise in predominantly negative experiences in the life events of substance abusers and multiple failure to abstain from substance use, as well as a change in the tendency to enjoy the transition from youth to middle age and old age and its physiological and psychological changes is one of the important factors in increasing the maintenance rate in individuals being on methadone maintenance therapy.¹⁴

In this study, gender was not associated with lapse in methadone treatment thus being in line with Koohestani and Moeeni's

Table 1. Comparison of Lapse Frequency Distribution in Drug Dependent Patients Through MMT and BMT in Terms of Demographic Characteristics.

VARIABLE		LAPSE IN MMT			LAPSE IN BMT		
		YES	NO	P VALUE	YES	NO	P VALUE
		N (%)	N (%)		N (%)	N (%)	
Gender	Female	4 (3.0)	11 (4.5)	.482	3 (4.1)	10 (5.8)	.586
	Male	130 (97.0)	23 (695.5)		70 (95.9)	162 (94.2)	
Age	25>	21 (15.7)	20 (8.1)	.027	4 (5.5)	10 (5.8)	.946
	35-25	66 (49.3)	104 (42.0)		30 (41.4)	66 (38.4)	
	45-35	26 (19.4)	73 (29.6)		17 (23.3)	38 (22.1)	
	55-45	16 (11.9)	32 (13.0)		15 (20.5)	35 (20.3)	
	55<	5 (3.7)	18 (7.3)		7 (9.6)	23 (13.4)	
Job status	Unemployed	9 (6.7)	30 (12.2)	.004	1 (1.4)	8 (4.7)	.605
	Employed	121 (90.3)	186 (75.3)		59 (80.8)	135 (78.4)	
	Retired	1 (0.7)	16 (6.5)		10 (13.7)	19 (0.11)	
	Disabled	0 (0)	7 (2.8)		0 (0)	2 (1.2)	
	housewife	3 (2.3)	8 (3.2)		3 (4.1)	8 (4.7)	
Education	Illiterate	11 (8.2)	8 (3.2)	.069	4 (5.5)	7 (4.1)	.164
	primary school	31 (23.2)	58 (23.5)		16 (21.9)	37 (21.5)	
	First-level high school	42 (31.3)	76 (30.8)		21 (28.8)	49 (28.5)	
	Second-level high school	43 (32.1)	75 (30.4)		27 (0.37)	47 (27.3)	
	higher education	7 (5.2)	30 (12.1)		5 (6.8)	32 (18.6)	
marital status	Single	28 (20.9)	72 (29.1)	.198	6 (8.2)	38 (22.1)	.031
	Married	102 (76.1)	170 (68.8)		65 (89.1)	128 (74.4)	
	Others (widow/divorced, etc.)	4 (0.3)	5 (2.1)		2 (2.7)	6 (3.5)	

Bold denotes that the *P* value <.05.

findings.^{12,15} It should be noted that in all the 3 studies, the males captured the highest rate of cases.

Asserting that employment has a protective effect on most mental disorders,¹⁴ a significant relationship was detected between occupational status and lapse in methadone treatment. For example, results revealed a significant relationship between employed and retired patients. In Mohebbi's findings, job status was also effective in maintaining the treatment so that the retired, full-time job holders, students, and soldiers better kept on the treatment respectively¹⁴ thus not being consistent with Koohestani et al's¹⁵ results. This difference may be due to differences in the population under study, the number of samples probed, as well as social and cultural discrepancies. In addition, education level was not correlated with lapse in methadone treatment, hence being consistent with Koohestani and Moeeni's result^{12,15} but contradicting that of Mohebbi¹⁴; of course, there are differences in sample size between the 2 studies. Most of the patients in Mohebbi's

study were first-level graduates of high school whereas in this study they were second-level graduates.

Marital status had also no significant relationship with lapse in methadone treatment, which was similar to Koohestani, Mohebbi, and Moeeni's results^{12,14,15}; however, Riahi et al¹³ considers it to be effective in the treatment failure and Hosseini reports a significant relationship between marriage and maintenance of the treatment.⁸ Perhaps this difference is a reflection of some cultural diversities such as patriarchy or, in other words, husband's dominance, which is a characteristic of the traditional context and lack of women's influence on the behavior and performance of their husbands in the study area.¹⁴

In buprenorphine treatment, there was a significant relationship only between marital status and lapse, but there no significant relationship was identified between any other demographic characteristics and lapse. The results demonstrated a significant relationship between single and married cases. Due to the lack of research conducted either in Iran or

Table 2. Comparison of Lapse Frequency Distribution in Drug Dependent Patients Through MMT and BMT on the Basis of Daily Drug Dose.

VARIABLE		LAPSE		P VALUE
		N (%)	N (%)	
Maintenance treatment dose with methadone (mg)	25>	7 (5.2)	7 (8.2)	.067
	50-25	25 (18.7)	48 (4.19)	
	75-50	43 (1.32)	58 (6.23)	
	100-75	45 (6.33)	84 (1.34)	
	100<	14 (4.10)	50 (2.20)	
Maintenance treatment dose with buprenorphine (mg)	2>	20 (4.27)	53 (8.30)	.785
	4-2	33 (2.45)	74 (43)	
	6-4	18 (6.24)	35 (3.20)	
	8-6	1 (4.1)	4 (3.2)	
	8<	1 (4.1)	6 (5.3)	

Table 3. Comparison of Lapse Frequency Distribution in Drug Dependent Patients Through MMT and BMT.

VARIABLE	N(%)	P VALUE
Lapse in MMT	Yes	134 (2.35)
	No	247 (8.64)
Lapse in BMT	Yes	73 (8.29)
	No	172 (2.70)

other countries on demographic characteristics of patients undergoing the treatment, it is not possible to compare the results with others.

The mean dose of methadone was 78.2 mg. The results demonstrated a significant difference between the drug dose group 50 and 75 mg and the group >100 mg in methadone treatment. According to Moeeni, Riahi, and Mohebbi's results, certain dose of methadone can affect maintenance of treatment; maintenance is greater with a higher dose¹²⁻¹⁴ thus being in line with the results of ours. Riahi et al¹³ reports that increment of methadone likely reduces temptation for its use thus increasing the chances of success in treatment.

The mean dose of buprenorphine was 3.69 mg and had no significant relationship with lapse; however, at low dose of buprenorphine (less than 2 mg), lapse was greater than the high dose (more than 8 mg). In Ling et al¹⁷ report on the maintenance of opioid-dependent subjects, retention rates were 61%, 52%, 51%, and 40% at buprenorphine doses of 16, 8, 4, and 1 mg, respectively but the difference was not significant. In Fareed et al¹⁸ meta-analysis based on 21 randomized clinical trials, there was Strong evidence that the higher

buprenorphine dose (16-32) may improve retention in buprenorphine maintenance treatment, despite the fact that the mean daily buprenorphine dose in our study was markedly lower. At high dose of buprenorphine (6-8 mg) it was significantly lower than a high dose of methadone (100-140 mg), which in some respects is similar to Ahmadi's results.¹⁹ In his study, the maintenance of treatment increased remarkably with high-dose buprenorphine compared with a low-dose. Also, maintenance in high-dose methadone was higher than in low-dose buprenorphine. But at high doses, there was no significant difference between the 2 drugs.¹⁹ In Hser et al study in 1267 patients, treatment retention rates of methadone and buprenorphine showed a higher retention rate with methadone than with buprenorphine (74% vs 46%); retention increased to 80% in the methadone group when the maximum dose reached or exceeded 60 mg/day. With buprenorphine, the completion rate increased linearly with higher doses, reaching 60% with doses of 30 to 32 mg/day.²⁰ In Simon's study, better results were obtained via high-dose treatment with both methadone and buprenorphine. A low dose of methadone, that is, 20 mg is less effective than buprenorphine at 2 to 8 mg, and higher doses of methadone (50-65 mg) are slightly more effective than buprenorphine (2-8 mg).²¹ The differences of the results appear to be due to variances in drug dose in different studies. It should be noted that heroin is the drug used in most countries and this may be the reason for different drug dosage employed in various studies.

Non-lapse during the 6-month study through methadone treatment was 64.8%. Maintenance in different studies came to the following results; Krinsky 78.1%, Kaplan 52%, Moebie 35.4%, Hosseini 68.2%, and Fakhraie and Babayance 69%.^{8,10,14,22,23} Maintenance of buprenorphine treatment was only studied by Krinsky and proved to be 57.7%²² and in the present study, non-lapse leveled at 70.2%.

The efficacy of buprenorphine as maintenance therapy has been demonstrated in a number of clinical studies. In some, buprenorphine has been compared with placebo and in several others it has been compared with methadone or levo-acetylmethyl. According to these inquiries, a daily dose of 8 to 16 mg of buprenorphine is as effective as 60 mg of methadone.²⁴ In general, one of the reasons for the differences in the results seems to be the number of samples in each of the cases. In addition, the impact of social, cultural, and geographical conditions, the ease and availability of the drug at the study setting cannot be ignored.¹⁴ Moreover, owing to the fact that except for the patient's medication and biographical information, other information tips are based on the patients' own statements, this limitation should be taken into account when interpreting the results. Our attempts to find similar findings revealed very limited number of investigations on buprenorphine in Iran, so it is necessary to conduct extensive research regarding the results of using the drug and compare it with methadone so as to find better results as for SUD treatment.

Acknowledgements

The authors acknowledge the patients who patiently assisted us in conducting this study.

Author Contributions

Study conception and design: MV and HZ. Data collection: SM and HZ. Data analysis and interpretation: AD and MS. Wrote the original draft of the manuscript: SM and MDT. Manuscript review and editing: MDT and MS. All authors reviewed the manuscript and provided final approval of the version to be published.

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