

Sleep Disorders in Methadone Maintenance Treatment Volunteers and Opium-dependent Patients

Habibolah Khazaie MD¹, Farid Najafi MD¹, Mohammad Rasoul Ghadami MD¹, Atena Azami MD¹, Marzieh Nasouri MS¹, Masoud Tahmasian MD¹, Behnam Khaledi-Paveh MSc²

Original Article

Abstract

Background: The relationship between substance use and sleep is bidirectional. Substance use directly causes sleep disturbances, and sleep problems are a critical factor in substance-use relapse.

Methods: This study evaluated sleep disorders in 65 methadone maintenance treatment (MMT) patients, and 61 opioid-dependent patients who did not receive any treatment between September 2011 and July 2012 in Kermanshah, Iran. Both groups filled out the Pittsburgh Sleep Quality Index (PSQI) and Global Sleep Assessment Questionnaire (GSAQ).

Findings: Sleep disorders were remarkably similar in both groups: 78.5% of MMT patients and 87.7% of opioid-dependent patients suffered from sleep problems. Sleep disorders in the opioid-dependent group were remarkably higher and more prominent.

Conclusion: Compared to opioid, MMT does not have as many negative effects on sleep and is more effective in mitigating sleep problems.

Keywords: Sleep disorders; Opioid dependency; Methadone maintenance treatment

Citation: Khazaie H, Najafi F, Ghadami MR, Azami A, Nasouri M, Tahmasian M, et al. **Sleep Disorders in Methadone Maintenance Treatment Volunteers and Opioid-dependent Patients.** *Addict Health* 2016; 8(2): 84-9.

Received: 11.12.2015

Accepted: 08.03.2016

Introduction

According to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR), opioid substance-related disorders are classified as psychiatric disorders.¹ Opioids have long been used by substance abusers in Iran.² With regard to the harmful physical, psychological, and social effects of opioids, it is crucial to take the treatment of these patients seriously.

In many parts of the world, methadone maintenance treatment (MMT) is one of the main methods to treat opioid dependence.³ MMT satisfies patients under treatment and can help patients more easily quit opioid and heroin.⁴ Using any sedative or narcotic substance can cause some changes in sleep; moreover, quitting and withdrawing from these substances can cause sleep disturbances.¹ The relationship between substance use and sleep is bidirectional; on the

one hand, substance use can directly cause sleep disturbances, and on the other hand, sleep problems are one of the risk factors for substance-use relapse.^{5,6} Clinically, prescribed opioids such as morphine and methadone suppress sleep during the rapid eye movement stage. Many studies have suggested the prevalence and frequency of sleep disorders among opioid users.⁷

The severity of sleep disorder symptoms in MMT patients may be related to other factors such as psychiatric symptoms, simultaneous use of other drugs, and pain.⁸ Half of MMT patients suffer from depression. Because sleep problems are widespread in depressed patients, it may be inferred that in addition to the use of opioids, sleep problems may be caused by depression disorders.⁹ Sleep problems may cause MMT to fail because the dependent person may increase their methadone dose to get rid of their sleep problems.¹⁰ Therefore, it is necessary to assess sleep problems in these individuals for management of these problems and prevent relapse.

1- Sleep Disorders Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

2- Sleep Disorders Research Center AND Department of Psychiatric Nursing, School of Nursing and Midwifery, Kermanshah University of Medical Sciences, Kermanshah, Iran

Correspondence to: Behnam Khaledi-Paveh MSc, Email: bkhaledipaveh@kums.ac.ir

The main goal of this study is to compare the frequency of sleep disorders in MMT patients and opium-dependent individuals.

Methods

This cross-sectional study was approved by the ethics committee of the Kermanshah University of Medical Sciences, Iran, and was conducted between September 2011 and July 2012 with MMT patients in Kermanshah. Written informed consent was obtained from all participants. In total, 126 persons were recruited and were divided into two groups. The inclusion criteria for the opium-dependent group were a diagnosis of opium dependency (according to DSM-IV-TR criteria), and the inclusion criteria for the MMT group were being on methadone for 2 months or longer and being on a stable dose of methadone.⁷ The exclusion criteria were having physical or psychiatric disorders that could affect sleep quality and not using any other psychoactive substances. Psychiatric evaluations were done by a psychiatrist on the basis of the DSM-IV-TR.

The study participants filled out three questionnaires. The first questionnaire collected demographic information. The second questionnaire was the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a self-report tool whose Persian version has been used a number of studies in Iran; its validity and reliability have been ascertained previously.¹¹ The third instrument was the Global Sleep Assessment Questionnaire (GSAQ), which was used to evaluate sleep problems. The GSAQ is a simple, valid, and reliable tool for screening for potential sleep disorders, which can also distinguish between sleep disorders. This questionnaire has 11 questions with four potential forced-choice responses of never, sometimes, usually, and always. Roth et al.¹² designed the GSAQ to distinguish between the following sleep disorders: insomnia, insomnia associated with a mental disorder, obstructive sleep apnea, restless

leg syndrome, periodic limb movement disorder, parasomnias, and shift work sleep disorder. The GSAQ's reliability ranged from 0.51 to 0.92.

We compared the demographic data between the two groups using the two-sample t-test and chi-square test. The same tests were used to compare sleep disorders among patients of the two groups. To test the effects of demographic variables on the distribution of sleep disorders among the two groups, we used multivariable logistic regression. All analyses were conducted with Stata (version 11, Stata Corporation, College Station, TX, USA).

Results

During the study period, 126 men were recruited: 65 patients in the MMT group, and 61 patients in the opium-dependent group. Both groups were comparable in terms of their education, jobs, and body mass index (BMI) (Table 1). However, those who were opium dependent were younger than those in the MMT group ($P = 0.009$).

According to the PSQI, from a total of 126 patients, 104 (82.5%) had a PSQI score ≥ 5 , indicating poor sleep quality. The two groups did not significantly differ in this regard (Table 2). None of the demographic variables (age, BMI, and education level) were associated with PSQI score in the multivariable model. We compared all of the PSQI domain scores for both groups. There was a significant difference between the two groups for domain 7, daytime dysfunction. According to the results, daytime dysfunction was more severe among the opium group compared to the MMT group ($P = 0.001$) (Table 2).

The analysis of both groups for the GSAQ showed that both groups were comparable in terms of snoring, restless leg syndrome, sleep terror, sleep walking, and anxiety-related insomnia. However, opium-dependent patients were more likely to suffer from sleep-onset insomnia, morning fatigue, daytime sleepiness, daily activity impairment due to sleepiness, and periodic limb movement disorder (Table 2).

Table 1. Comparison of demographic variables between the two groups

Variables	MMT group (n = 65)	Opium-dependent group (n = 61)	P
Age (year) (mean \pm SD)	38.9 \pm 11.2	34.0 \pm 9.3	0.009
BMI (kg/m ²) (mean \pm SD)	25.2 \pm 4.1	23.9 \pm 3.2	0.050
Education [n (%)]			
Some high school	17 (26.1)	22 (36.0)	0.480
Graduated from high school	28 (43.1)	22 (36.0)	
University degree	20 (30.8)	17 (28.0)	

SD: Standard deviation; MMT: Methadone maintenance treatment

Table 2. Sleep abnormalities among the two groups

Sleep abnormalities	MMT group (n = 65)	Opium-dependent group (n = 61)	P
	[n (%)]	[n (%)]	
PSQI $\geq 5^*$	51 (78.5)	53 (86.9)	0.210
Subjective sleep quality	3 (4.6)	6 (9.8)	0.270
Sleep latency	22 (33.9)	23 (37.7)	0.810
Sleep duration	14 (21.5)	9 (14.8)	0.330
Habitual sleep efficiency	12 (18.5)	14 (53.8)	0.930
Sleep disturbance	3 (4.6)	4 (6.6)	0.930
Use of sleep medication	15 (23.1)	7 (11.5)	0.060
Daytime dysfunction	2 (3.1)	17 (27.9)	0.001
GSAQ			
Insomnia			
Sleep-onset insomnia	11 (16.9)	19 (31.2)	0.060
Sleepiness			
Morning fatigue	27 (41.5)	40 (65.6)	0.007
Daytime sleepiness	16 (24.6)	39 (63.9)	< 0.001
Daily activity impairment due to sleepiness	14 (21.5)	28 (45.9)	0.004
Snoring	13 (20.0)	16 (26.2)	0.410
Restless leg syndrome	8 (12.3)	14 (23.0)	0.110
Periodic limb movement disorder	13 (20.0)	22 (36.1)	0.040
Sleep terror	13 (20.0)	15 (24.6)	0.530
Sleep walking	4 (6.2)	5 (8.2)	0.650
Secondary sleep disorders			
Anxiety-related insomnia	9 (13.9)	10 (16.4)	0.690
Depression-related insomnia	19 (29.2)	30 (49.2)	0.020

*Values show the negative extreme on the Likert scale (score = 3) except for sleep latency (score = 2).

MMT: Methadone maintenance treatment; PSQI: Pittsburgh Sleep Quality Index; GSAQ: Global Sleep Assessment Questionnaire

Using a logistic multivariable regression model that compared each GSAQ item to demographic variables, we found that periodic leg movement disorder was associated with age [odds ratio (OR) = 0.92, 95% confidence interval (CI): 0.87-0.98]. Other demographic variables were not associated with any of the sleep disorders diagnosable with the GSAQ.

Discussion

This study's results show that 78.5% of MMT patients and 87.7% of opium-dependent patients suffer from poor sleep quality. No meaningful difference in PSQI scores was observed between groups. According to the results of the GSAQ, the severity of sleep disorders including sleep walking, periodic limb movement, snoring, sleepiness, and secondary insomnia are higher in the opium-dependent group rather than MMT group.

Peles et al.¹⁰ conducted a study on the sleep quality of 101 MMT patients, which found a mean PSQI score of 9.0 ± 4.8 , and 75.2% had PSQI scores > 5, indicating sleep disturbances. Stein et al.¹³ assessed the relationship between sleep disorders and demographic characteristics,

mental health, drug use, and other factors in 225 MMT patients. According to PSQI results, 84% of MMT patients had serious sleep problems. Compared to our study, the prevalence of sleep disturbance in Stein et al.¹³ is greater. This difference may be due to differences in the number of people sampled and with the evaluation of mental health.

In a study conducted on 44 opium-dependent patients, Peles et al.¹⁴ showed that a large number of MMT patients had poor sleep quality. They emphasized that sleep disorders among MMT patients are not only dose-dependent but may also be due to other patient issues. Mahfoud et al.¹⁵ assessed sleep disorders in 30 active substance abusers. The results of their study showed that sleep abnormalities in substance abusers are 5-10 times greater than in the general population. The findings of Mahfoud et al.¹⁵ support our findings.

Wang et al.¹⁶ conducted a study, in which 50 MMT patients and 20 control subjects were included. They were tested using polysomnography (PSG), blood toxicology, the Epworth sleepiness scale (ESS), the functional

outcome of sleep questionnaire, and the Beck depression inventory (BDI). Compared to the control subjects, MMT patients had a significantly worse daytime function, were more depressed, and had more daytime sleepiness. However, the daytime sleepiness index in MMT patients was still in the normal range.¹⁶ In our study, we compared MMT patients with opium-dependent individuals, whereas in Wang et al.¹⁶ MMT patients and normal subjects were compared. Moreover, in Wang et al.'s study, more procedures were tested including PSG, blood toxicology, and BDI.¹⁶

In a study on 62 MMT patients, Sharkey et al.¹⁷ measured sleep disturbances using week-long daily sleep diaries, one night of home PSG, a questionnaire completed the morning after the PSG, and the PSQI, as well as demographic and drug use measures. Average diary sleep time, subjective ratings of feeling rested, and PSG sleep efficiency were significantly related to the PSQI scores. This means that the subjective findings confirmed the objective findings of sleep disorders in MMT patients, which reflect pathology rather than sleep misperception.

Peles et al.¹⁸ studied 23 opioid-dependent patients who had been on methadone for 6-12 months. They assessed the patients' sleep using PSQI and PSG. Their findings showed that MMT does not have any negative effects on the objective findings of sleep. However, extensive

weight gain in a minority of patients ($\geq 25\%$ of their entry weight) was associated with obstructive sleep apnea.

The main limitation of our study was that participants refused to participate in objective assessments of sleep disturbances such as PSG and actigraphy. Therefore, it is highly recommended that objective procedures be employed in future studies.

Conclusion

In summary, the findings of this study are similar to those of the previous studies. Compared to opium, MMT has fewer negative effects on the sleep and is more effective in mitigating sleep problems. However, because of the high prevalence of sleep problems in MMT patients, we believe that sleep problems could impair continuation of treatment which could lead to relapse or continued drug use. The clinical use of our findings is that symptoms of sleep problems in MMT patients are important to investigation and treatment.

Conflict of Interests

The Authors have no conflict of interest.

Acknowledgements

The others thank all personnel of MMT centers for their kind cooperation.

References

1. Sadock BJ. Kaplan and Sadock's comprehensive textbook of psychiatry. 9th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2012.
2. Nissaramanesh B, Trace M, Robert M. The rise of harm reduction in the Islamic republic of Iran [Online]. [cited 2005 Jul]; Available from: URL: http://www.beckleyfoundation.org/pdf/paper_08.pdf
3. Watson B, Lingford-Hughes A. Pharmacological treatment of addiction. *Psychiatry* 2007; 6(7): 309-12.
4. Havard A, Teesson M, Darke S, Ross J. Depression among heroin users: 12-Month outcomes from the Australian Treatment Outcome Study (ATOS). *J Subst Abuse Treat* 2006; 30(4): 355-62.
5. Hasler BP, Smith LJ, Cousins JC, Bootzin RR. Circadian rhythms, sleep, and substance abuse. *Sleep Med Rev* 2012; 16(1): 67-81.
6. Kurth ME, Sharkey KM, Millman RP, Corso RP, Stein MD. Insomnia among methadone-maintained individuals: the feasibility of collecting home polysomnographic recordings. *J Addict Dis* 2009; 28(3): 219-25.
7. Wang D, Teichtahl H. Opioids, sleep architecture and sleep-disordered breathing. *Sleep Med Rev* 2007; 11(1): 35-46.
8. Sharkey KM, Kurth ME, Anderson BJ, Corso RP, Millman RP, Stein MD. Obstructive sleep apnea is more common than central sleep apnea in methadone maintenance patients with subjective sleep complaints. *Drug Alcohol Depend* 2010; 108(1-2): 77-83.
9. Peles E, Schreiber S, Naumovsky Y, Adelson M. Depression in methadone maintenance treatment patients: rate and risk factors. *J Affect Disord* 2007; 99(1-3): 213-20.
10. Peles E, Schreiber S, Adelson M. Variables associated with perceived sleep disorders in methadone maintenance treatment (MMT) patients. *Drug Alcohol Depend* 2006; 82(2): 103-10.

11. Farrahi MJ, Nakhaee N, Sheibani V, Garrusi B, Amirkafi A. Reliability and validity of the Persian version of the Pittsburgh Sleep Quality Index (PSQI-P). *Sleep Breath* 2012; 16(1): 79-82.
12. Roth T, Zammit G, Kushida C, Doghramji K, Mathias SD, Wong JM, et al. A new questionnaire to detect sleep disorders. *Sleep Med* 2002; 3(2): 99-108.
13. Stein MD, Herman DS, Bishop S, Lessor JA, Weinstock M, Anthony J, et al. Sleep disturbances among methadone maintained patients. *J Subst Abuse Treat* 2004; 26(3): 175-80.
14. Peles E, Schreiber S, Adelson M. Documented poor sleep among methadone-maintained patients is associated with chronic pain and benzodiazepine abuse, but not with methadone dose. *Eur Neuropsychopharmacol* 2009; 19(8): 581-8.
15. Mahfoud Y, Talih F, Streem D, Budur K. Sleep disorders in substance abusers: how common are they? *Psychiatry (Edgmont)* 2009; 6(9): 38-42.
16. Wang D, Teichtahl H, Goodman C, Drummer O, Grunstein RR, Kronborg I. Subjective daytime sleepiness and daytime function in patients on stable methadone maintenance treatment: Possible Mechanisms. *J Clin Sleep Med* 2008; 4(6): 557-62.
17. Sharkey KM, Kurth ME, Anderson BJ, Corso RP, Millman RP, Stein MD. Assessing sleep in opioid dependence: A comparison of subjective ratings, sleep diaries, and home polysomnography in methadone maintenance patients. *Drug Alcohol Depend* 2011; 113(2-3): 245-8.
18. Peles E, Schreiber S, Hamburger RB, Adelson M. No change of sleep after 6 and 12 months of methadone maintenance treatment. *J Addict Med* 2011; 5(2): 141-7.

اختلالات خواب در افراد تحت درمان نگهدارنده با متادون و وابستگان به تریاک

دکتر حبیب‌اله خزایی^۱، دکتر فرید نجفی^۱، دکتر محمد رسول قدمی^۱، دکتر آتنا اعظمی^۱، مرضیه نصوری^۱،
دکتر مسعود طهماسیان^۱، بهنام خالدی پاوه^۲

مقاله پژوهشی

چکیده

مقدمه: ارتباط بین مواد و خواب، یک رابطه دوسویه است. مصرف مواد مخدر به طور مستقیم باعث اختلال در خواب می‌گردد. همچنین، مشکلات خواب می‌تواند یکی از عوامل عود مصرف مواد محسوب شود.

روش‌ها: مطالعه حاضر اختلالات خواب را بر روی ۶۵ بیمار تحت درمان نگهدارنده با متادون (Methadone maintenance treatment) یا (MMT) و ۶۱ بیمار وابسته به تریاک که درمان دیگری را دریافت نکرده بودند، طی بازه زمانی شهریور سال ۱۳۹۱ تا تیر سال ۱۳۹۲ در شهر کرمانشاه بررسی نمود. هر دو گروه پرسش‌نامه کیفیت خواب Pittsburgh (Pittsburgh Sleep Quality Index یا PSQI) و پرسش‌نامه بررسی کلی خواب (Global Sleep Assessment Questionnaire یا GSAQ) را تکمیل کردند.

یافته‌ها: اختلالات خواب به طور قابل ملاحظه‌ای در دو گروه مشاهده شد. ۷۸/۵ درصد از بیماران تحت درمان نگهدارنده با متادون و ۸۷/۷ درصد از وابستگان به تریاک، مشکل خواب داشتند. اختلالات خواب در مصرف‌کنندگان تریاک بیشتر مشاهده شد.

نتیجه‌گیری: درمان نگهدارنده با متادون در مقایسه با اپیوم، اثرات منفی بر خواب وابستگان به تریاک ندارد و دارای اثربخشی مناسبی برای کاهش مشکلات خواب آن‌ها می‌باشد.

واژگان کلیدی: اختلالات خواب، وابستگی به تریاک، درمان نگهدارنده با متادون

ارجاع: خزایی حبیب‌اله، نجفی فرید، قدمی محمد رسول، اعظمی آتنا، نصوری مرضیه، طهماسیان مسعود، خالدی پاوه بهنام. اختلالات خواب در افراد تحت درمان نگهدارنده با متادون و وابستگان به تریاک. مجله اعتیاد و سلامت ۱۳۹۵؛ ۸(۲): ۸۹-۸۴.

تاریخ پذیرش: ۹۴/۱۲/۱۸

تاریخ دریافت: ۹۴/۹/۲۰

۱- مرکز تحقیقات اختلالات خواب، دانشگاه علوم پزشکی کرمانشاه، کرمانشاه، ایران

۲- مرکز تحقیقات اختلالات خواب و گروه روان‌پرستاری، دانشکده پرستاری و مامایی، دانشگاه علوم پزشکی کرمانشاه، کرمانشاه، ایران