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

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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 opium-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 opium-dependent patients suffered from sleep problems. Sleep disorders in the opium-dependent group were remarkably higher and more prominent.

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

Keywords: Sleep disorders, Opium dependency, Methadone maintenance treatment


Received: 11.12.2015

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 opium 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 opium 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.

Notes:

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http://ahj.kmu.ac.ir, 3 April
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. 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. 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. 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

<table>
<thead>
<tr>
<th>Variables</th>
<th>MMT group (n = 65)</th>
<th>Opium-dependent group (n = 61)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year) (mean ± SD)</td>
<td>38.9 ± 11.2</td>
<td>34.0 ± 9.3</td>
<td>0.009</td>
</tr>
<tr>
<td>BMI (kg/m²) (mean ± SD)</td>
<td>25.2 ± 4.1</td>
<td>23.9 ± 3.2</td>
<td>0.050</td>
</tr>
<tr>
<td>Education [n (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some high school</td>
<td>17 (26.1)</td>
<td>22 (36.0)</td>
<td>0.480</td>
</tr>
<tr>
<td>Graduated from high school</td>
<td>28 (43.1)</td>
<td>22 (36.0)</td>
<td></td>
</tr>
<tr>
<td>University degree</td>
<td>20 (30.8)</td>
<td>17 (28.0)</td>
<td></td>
</tr>
</tbody>
</table>

SD: Standard deviation; MMT: Methadone maintenance treatment
### Table 2. Sleep abnormalities among the two groups

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

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. In our study, we compared MMT patients with opium-dependent individuals, whereas in Wang et al. MMT patients and normal subjects were compared. Moreover, in Wang et al.’s study, more procedures were tested including PSG, blood toxicology, and BDI.

In a study on 62 MMT patients, Sharkey et al. 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. 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 (≥ 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**

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چکیده
مقدمه: اختلالات خواب بین مواد و خواب، یک رابطه دوست‌توجه است. اختلالات خواب باعث اختلال در خواب شده و یک عاملی از عوامل اصلی اختلال در خواب می‌گردد. همچنین، مشکلات خواب می‌تواند یکی از عوامل عوارض اختلال در خواب محسوب شود.

روش‌ها: مطالعه حاضر اختلالات خواب را بر روی ۶۵ بیمار تحت درمان نگهدارنده با متوان (Methadone maintenance treatment) یا MMT و ۶۱ بیمار واکنش به درمان که درمان دیگری را دریافت نکرده بودند، طی بازی زمانی شهری سال ۱۳۹۱ تا ۱۳۹۲ در شهر کرمانشاه بررسی شد. برای بررسی کیفیت خواب از سوالی Pittsburg Sleep Quality Index (PSQI) و بررسی کیفیت خواب از Global Sleep Assessment Questionnaire (GSAQ) استفاده شد.

یافته‌ها: اختلالات خواب به طور قابل مشاهده در دو گروه مشاهده شد. درصد از بیماران تحت درمان نگهدارنده با متوان و واکنش به درمان مشاهده شد.

نتیجه‌گیری: اختلالات خواب در افراد تحت درمان نگهدارنده با متوان و واکنش به درمان تریاک بهتر از افراد تحت درمان نگهدارنده با متوان و واکنش به درمان نگهدارنده با MMT مشاهده شد.

واژگان کلیدی: اختلالات خواب، تریاک، درمان نگهدارنده با متوان

ارجاع: خلیلی خ، نجفی فرید. قدمی محمد رسول، اعتصامی آنا. نمودار مرضیه، طلایی مسعود، خالدی پاوه پاوه. اختلالات خواب در افراد تحت درمان نگهدارنده با متوان و واکنش به درمان. مجله اعتیاد و سلامت، ۱۳۹۵، ۹۱ (۱): ۸-۲۸.

تاریخ دریافت: ۱۳۹۴/۹/۲۰
تاریخ پذیرش: ۱۳۹۴/۱۲/۱۸

مقاله پژوهشی

نوع پژوهش: پژوهشی

کیفیت خواب، اختلالات خواب، درمان نگهدارنده با متوان، درمان نگهدارنده با متوان (Methadone maintenance treatment)