



Quality of Sleep and Related Factors in Individuals Undergoing Methadone Maintenance Treatment

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Abstract

Background: Poor sleep quality and its relationship with other sleep disorders and medical and psychiatric disorders have been noted in many individuals who use methadone as a maintenance treatment for drug abuse. This study aimed to investigate the quality of sleep and its related factors in people undergoing methadone maintenance treatment.

Methods: This study was conducted on 80 individuals who were undergoing methadone maintenance treatment (MMT) in MMT clinics selected by the convenience sampling method. The researcher-made data collection form, the Pittsburgh Sleep Quality Index questionnaire, and the Depression, Anxiety, and Stress Scale questionnaire were completed by the participants. Kendall's tau-b correlation coefficient, chi-square, Mann-Whitney *U*, or Kruskal-Wallis tests were used for analyses.

Findings: In the present study, 80 participants undergoing maintenance treatment (86.25% male) were studied. Most individuals (75%) had good sleep quality (average questionnaire score of 4.31). In addition, the majority of participants had anxiety (63.75%; average score of 6.2), depression (66.25%; average score of 7.45), and stress at a normal level (91.25%; average score of 6.25). Women had significantly lower sleep quality than men ($P=0.009$). The level of education ($P=0.036$) and the frequency of alcohol consumption influenced sleep quality ($P=0.018$). However, marital status, employment status, smoking, methamphetamine use, or use of drugs other than methadone were not significantly associated with sleep quality. The average score of sleep quality was significantly influenced by the level of anxiety ($P<0.001$), depression ($P<0.001$), and stress ($P=0.008$). The age of starting methadone had a weak negative but significant correlation with the sleep quality score ($r=-0.2$ and $P=0.01$). The daily methadone dose had a weak but significant positive correlation with poorer sleep quality. ($r=0.173$ and $P=0.049$).

Conclusion: Considering the significant relationship found between the severity of anxiety, depression, and stress and the quality of sleep in the participants of this study, it is recommended to screen these disorders more carefully in this group of people so that the necessary interventions can be carried out to improve their conditions. In addition, patients should be warned about consuming alcohol and increasing the daily dose of methadone.

Keywords: Sleep disorders, Methadone maintenance treatment, Anxiety disorders, Depressive disorders, Stress disorders

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Introduction

Opioid use disorder (OUD) remains an epidemic challenge worldwide. Three million US citizens and 16 million people worldwide suffer from opioid use disorder.^{1,2}

According to the report of the World Health Organization (WHO), Iran has the highest level of opium and opioid use globally, and the consumption of these substances in Iran is three times the global average.³ Statistics show that about 2 million people in Iran use drugs daily, which is approximately 2.7% of the country's population.⁴ Estimates suggest that about 2.3% of adults in Iran struggle with opium addiction, with some rural regions showing an even higher prevalence of up to 22%.⁵

Opioids bind to central and peripheral nervous system receptors (primarily delta, kappa, and mu). Acting on

these receptors produces euphoria, which can lead many individuals to continue using opioids in an attempt to recreate their initial experience of euphoria.⁶

Dr. Robert Halliday introduced Opioid Agonist Therapy (OAT) for addiction treatment at the Drug Dependency Foundation in British Columbia.⁷ During that period in the United States, Marie Nyswander and Vincent Dole conducted research on methadone, marking it the first maintenance treatment for opioid use disorder (OUD).⁸ Currently, OAT is widely considered the gold standard treatment for OUD.^{9,10} Opioid agonist therapy reduces the use of illegal opioids and the risk of death from excessive use of these substances.¹¹ This approach can positively influence individuals, families, and communities by decreasing substance use, promoting family stability,



reducing crime rates, boosting mental and physical health, and elevating overall quality of life.^{8,12} Long-term participation in OAT can lead to fewer adverse outcomes and lower mortality rates. It also significantly enhances the quality of life for individuals looking to reduce or stop their opioid use.^{13,14}

Although the benefits of methadone for individuals with OUD are clear, most people receiving methadone for OAT experience poor sleep quality, both subjectively and objectively.¹⁵ Additionally, this disrupted sleep during treatment may persist rather than normalize over time, increasing the possibility that the medication itself may be contributing to or exacerbating pre-existing conditions.¹⁶ Furthermore, treatment with methadone has been associated with central sleep apnea and obstructive sleep apnea in individuals.¹⁷

The worse the quality of sleep in these individuals, the less they can engage in daily activities. Numerous studies have shown that sleep disorders in individuals undergoing OAT are also associated with higher unemployment rates (16.2% of individuals with sleep disorders were unemployed compared to only 5.5% of individuals without sleep disorders).^{18,19} This study investigated sleep quality in individuals undergoing methadone maintenance treatment, looking at factors like demographics, age of drug use onset, methadone dosage, and concurrent substance use. Poor sleep can significantly impact financial, emotional, and occupational health benefits.

Methods

In this cross-sectional descriptive-analytical study, individuals undergoing methadone maintenance treatment (MMT) who were referred to MMT clinics in Kerman City, Iran, in 2022 were investigated. Three MMT clinics from three different regions of the city were randomly selected, and 80 individuals were included in the study.

According to the study by Li et al considering the 95% confidence level and 80% test power and based on the sample size formula ($n = z^2 p(1-p) / d^2$), with a 10% drop in the sample size of 77 patients, 70 people were determined as the minimum sample size.²⁰

The study's inclusion criteria required participants to be at least 18 years old, able to give informed verbal consent, and capable of understanding and communicating in Persian. They also needed to regularly attend the MMT clinic and be under MMT.

The exclusion criteria included having a major psychiatric disorder (e.g., mood, anxiety, or psychotic disorders), intellectual disability, a history of significant trauma, and chronic medical conditions that could affect sleep (e.g., cancers, multiple sclerosis, rheumatoid arthritis, respiratory illnesses, or kidney failure). Additionally, individuals consuming high levels of

caffeine (more than 3 cups of coffee or 6 cups of tea daily) were excluded. Participants who were unwilling to continue and provided incomplete information were also excluded from the study.

Subsequently, individuals were asked to carefully complete the validated Persian versions of the Pittsburgh Sleep Quality Index (PSQI) questionnaire,²¹ the Depression, Anxiety, and Stress Scale (DASS-21) questionnaire,²² and a researcher-made data collection form containing demographic information and information related to methadone and other substance use.

In the PSQI assessment, each component is scored from 0 (indicating no issues) to 3 (indicating a severe problem). The scores for all components are summed to produce a total score that ranges from 0 to 21. Higher scores in individual components or the overall total suggest poor sleep quality, with a score of 6 or more indicating poor sleep quality. The Persian version of the questionnaire has demonstrated validity and reliability, achieving a Cronbach's alpha of 0.83.²¹

The DASS-21 questionnaire has three subscales: depression, anxiety, and stress, each with seven questions. Scores range from 0 (not true) to 3 (completely true), and the final scores are doubled for standardization. The Persian version has the test-retest reliability of 0.80 for depression, 0.76 for anxiety, and 0.77 for stress, with Cronbach's alpha at 0.81, 0.74, and 0.78, respectively.²²

Statistical Analysis

Data were analyzed using SPSS version 27, with qualitative variables described by frequency and percentage and quantitative variables by mean and standard deviation (normal distribution) or mean and standard error (non-normal distribution). Kendall's tau-b, chi-square, *t*-test, or Kruskal-Wallis test were used for inferential analysis, considering a *P* value of less than 0.05 as statistically significant.

Results

The study involved 80 participants (86.25% male, 78.75% married) undergoing methadone maintenance treatment, with a mean age of 45.03 ± 10.92 years. Sleep quality was assessed based on demographic and personal variables (Table 1). Women had significantly lower sleep quality than men ($P=0.009$). Education level also impacted sleep quality ($P=0.036$), with illiterate individuals reporting better sleep than those with high school diplomas ($P=0.03$). Additionally, non-drinkers had better sleep quality than occasional drinkers ($P=0.018$). Marital status ($P=0.274$), employment status ($P=0.253$), smoking ($P=0.645$), methamphetamine use ($P=0.826$), and use of other drugs ($P=0.085$) showed no significant association with sleep quality (Table 1).

Most individuals had good sleep quality (75%).

Table 1. The demographic, personal, and sleep quality (PSQI) characteristics of individuals undergoing maintenance treatment with methadone

Variable	(N=80)	n (%)	Sleep quality score mean (standard deviation)	P value
Gender	Female	11 (13.75%)	6.64 (1.28)	0.009*
	Male	69 (86.25%)	3.94 (0.27)	
Marital status	Single	15 (18.75%)	4.6 (0.8)	0.274
	Married	63 (78.75%)	4.17 (0.34)	
	Divorced	2 (2.5%)	6.5 (0.5)	
Education	Illiterate	3 (3.75%)	2 (0.58)	0.036*
	Below high school diploma	31 (38.75%)	3.65 (0.37)	
	High school diploma	27 (33.75%)	5.04 (0.48)	
	University degree	19 (23.75%)	4.74 (0.87)	
Occupation	Unemployed	12 (15%)	6.25 (1.3)	0.253
	Self-employed	52 (65%)	3.98 (0.29)	
	Governmental	16 (20%)	3.94 (0.64)	
Cigarette consumption	Non-smoker	21 (26.25%)	3.62 (0.43)	0.645
	Occasionally	25 (31.25%)	4.88 (0.7)	
	Everyday	34 (42.5%)	4.32 (0.42)	
Alcohol consumption	Non-drinker	63 (78.75%)	4 (0.34)	0.018*
	Occasionally	17 (21.25%)	5.47 (0.66)	
	Everyday	0 (0%)	-	
Methamphetamine consumption	Negative	79 (98.75%)	4.32 (0.31)	0.826
	Positive	1 (1.25%)	4 (0)	
Injectable narcotics	Negative	80 (100%)	--	--
	Positive	0 (0%)	--	
Consumption of other drugs besides methadone	Negative	69 (86.25%)	4.14 (0.26)	0.085
	Opium syrup	3 (3.75%)	4 (1)	
	Benzodiazepine	2 (2.5%)	9 (1)	
	Other	6 (7.5%)	4.83 (2.66)	
Age (years)	---	Mean $\pm$ SD 45.03 $\pm$ 10.92	---	---
Age of starting substance Use	---	25.28 $\pm$ 0.96	---	---
Age of starting methadone	---	39.19 $\pm$ 1.21	---	---
Duration methadone use	---	5.52 $\pm$ 0.45	---	---
Daily dose	---	81.56 $\pm$ 2	---	---

* Significant at $p \leq 0.05$ level, ** Significant at $p \leq 0.01$ level.

Additionally, most participants had normal levels of anxiety (63.75% with an average score of 6.2), depression (66.25% with an average score of 7.45), and stress (91.25% with an average score of 6.25) (Table 2).

Additionally, the sleep quality scores of individuals undergoing MMT were examined based on the levels of anxiety, depression, and stress. The mean sleep quality was significantly related to the level of anxiety (qualitatively) ($P < 0.001$), to the extent that individuals with normal anxiety levels had significantly better sleep quality than those with mild ($P < 0.01$), moderate ($P < 0.01$), severe ($P < 0.01$), and very severe ($P < 0.01$) anxiety levels. Moreover, individuals with very severe anxiety had significantly worse sleep quality than those with mild ($P = 0.019$), moderate ($P = 0.03$), and severe ($P = 0.049$)

anxiety levels (Table 2).

The level of depression also had a significant relationship with sleep quality ($P < 0.001$), to the extent that individuals with normal levels of depression had significantly better sleep quality than those with moderate ($P < 0.001$) and very severe ($P = 0.015$) levels of depression. Additionally, individuals with mild depression had significantly better sleep quality than those with moderate ($P = 0.004$) and very severe ($P = 0.02$) levels of depression. Moreover, individuals with moderate depression had significantly better sleep quality than those with very severe depression ($P = 0.039$). However, the other groups did not differ significantly regarding sleep quality (Table 2).

The level of stress also had a significant relationship with sleep quality ($P = 0.008$), to the extent that individuals

Table 2. The distribution of scores for sleep quality (PSQI) in individuals undergoing methadone maintenance treatment according to the levels of anxiety, depression, and stress (measured by the DASS-2011 subscales)

Variable	(N=80)	n (%)	(mean and SD)	P value
PSQI score (Pittsburgh Sleep Quality Index)		Mean (SD) 4.31 (0.31)	--	--
Sleep quality	Good	N (%) 60 (75%)	--	--
	Insufficient	20 (25%)	--	--
Anxiety score		Mean (SD) 6.2 (0.65)	--	--
Level of anxiety		N (%)		
	Normal	51 (63.75%)	3.24 (0.22)	
	Mild	13 (16.25%)	5.08 (0.57)	
	Moderate	10 (12.5%)	5.4 (0.75)	
	Severe	4 (5%)	7.75 (0.75)	
	Very severe	2 (2.5%)	14.5 (3.5)	
Depression score		Mean (SD) 7.45 (0.84)		
Level of depression		N (%)		
	Normal	53 (66.25%)	3.53 (0.27)	
	Mild	15 (18.75%)	4.27 (0.49)	
	Moderate	7 (8.75%)	7.14 (0.51)	
	Severe	3 (3.75%)	5 (1)	
	Very severe	2 (2.5%)	14.5 (3.5)	
Stress score		Mean (SD) 6.25 (0.69)		
Level of stress		N (%)		
	Normal	73 (91.25%)	3.89 (0.24)	
	Mild	4 (5%)	6.25 (0.85)	
	Moderate	1 (1.25%)	7 (0)	
	Severe	2 (2.5%)	14.5 (3.5)	
	Very severe	0 (0%)	--	

* Significant at $P \leq 0.05$ level, ** Significant at $P \leq 0.01$ level.

with normal levels of stress had significantly better sleep quality than those with mild ($P=0.031$) and severe ($P=0.014$) levels of stress. However, the other groups did not differ significantly regarding sleep quality (Table 2).

The study examined the correlation between sleep quality scores and quantitative variables. The results revealed a weak but significant negative correlation between the age of methadone initiation and sleep quality score ($r=-0.2$, $P=0.01$). Conversely, the daily dose of methadone showed a weak but significant positive correlation with sleep quality score ($r=0.173$, $P=0.049$). Additionally, anxiety ($r=0.454$, $P<0.001$), depression ($r=0.449$, $P<0.001$), and stress ($r=0.468$, $P<0.001$) all exhibited significant moderate positive correlations with sleep quality scores.

However, the correlation between age ($P=0.14$), age of substance use initiation ($P=0.66$), and duration of methadone use initiation ($P=0.17$) was not statistically significant (Table 3).

Discussion

Poor sleep quality is a major concern for those on

Table 3. The correlation between the overall score of sleep quality and quantitative variables

Variable	The coefficient of correlation	P value
Age	0.12	0.14
Age of substance use initiation	-0.04	0.66
Age of methadone use initiation	0.200	0.01
Duration of methadone use	0.11	0.17
Daily dose	0.173	0.049
Anxiety score	0.454	<0.001
Depression score	0.449	<0.001
Stress score	-0.04	<0.001

methadone treatment, impacting their well-being and limiting access to financial, emotional, and occupational benefits. These sleep issues arise from various factors, not just methadone treatment. The present study explored this further.

The results showed that individuals undergoing maintenance therapy had generally good sleep quality, with most experiencing normal levels of anxiety, depression, and stress. However, poorer sleep quality was linked to being female, having higher education (not statistically significant), and using alcohol. Additionally, initiation of methadone use at younger ages, higher daily doses, and increased anxiety, depression, and stress were associated with reduced sleep quality. Factors like age, marital status, employment status, smoking, age of drug use initiation, and duration of use of methadone and other drugs did not influence sleep quality.

The participants in the present study had fewer complaints of decreased sleep quality, with a prevalence of 25% and an average PSQI score of about 4.3. This reflects much lower rates of sleep disorders compared to those reported in previous studies, where over 50% to 85% reported sleep issues.²³ This finding suggests that sleep disorders may be less affected by methadone due to similar dosage and duration in this and other studies. Factors such as gender distribution, anxiety disorder prevalence, and post-opioid behavioral habits also play a role. Moreover, many individuals had sleep disorders before starting methadone use, and some even before addiction, which significantly influenced the results of earlier studies.²⁴⁻²⁶

In the present study, women had lower sleep quality compared to men. This finding is consistent with similar studies, indicating a significant effect of the female gender on the sleep quality of individuals under maintenance treatment.^{23,27,28} However, we should not overlook the fact that, in general, women also have a higher prevalence of anxiety and mood disorders, which can also be influenced by confounding factors.²⁹ Nevertheless, based on the results of this study, clinical practitioners and individuals involved in the process of quitting opioid drugs are recommended to pay closer attention to the women in

their care, and also, pay more attention to their sleep disorders.

The present study found that higher education levels, particularly having a high school diploma versus being illiterate, were associated with decreased sleep quality in individuals under methadone maintenance treatment. No other studies have explored the effect of education on sleep quality in this context, so further investigation is recommended. Higher education levels may lead to a better understanding of drug dependence, resulting in increased psychological involvement and, consequently, poorer sleep quality.³⁰

The study found that higher education levels, especially having a high school diploma versus being illiterate, were associated with lower sleep quality in individuals undergoing methadone maintenance treatment. The effect of education on sleep has not been studied before, so further research is recommended. Higher education may lead to a greater awareness of drug dependence, an increase in psychological stress, and a negative impact on sleep quality.³¹ Furthermore, even consuming relatively small amounts of alcohol before sleep can increase sleep fragmentation and disrupt REM sleep.³² Therefore, individuals undergoing OAT treatment are recommended to avoid alcohol consumption, even in small amounts, to enhance sleep quality. Encouraging patients to refrain from alcohol consumption during their treatment can help reduce sleep disorders.

Age, marital status, employment status, smoking, methamphetamine use, and use of other drugs had no significant impact on sleep quality. This study mainly involved middle-aged participants, while previous research on OAT treatment and sleep disorders focused on those aged over 65 years. This age distribution difference limits the generalizability of past findings to the current population.^{33,34} Also, it is noteworthy that aging leads to a decrease in sleep quality in individuals.³⁵ Therefore, age cannot be considered an effective factor in sleep quality during OAT treatment, especially in young and middle-aged age groups. Previous studies have emphasized the negative impact of smoking (especially in cases of heavy smoking) on sleep quality.^{27,36} However, sudden smoking cessation is also associated with a decrease in sleep quality.³⁷ Therefore, it is better not to insist on sudden smoking cessation in individuals undergoing OAT treatment to avoid affecting their sleep quality. Regarding other mentioned factors, including behavioral and therapeutic factors, the number of individuals with these factors was not sufficient to confidently confirm or reject their effects.

Increased anxiety was linked to a further decline in sleep quality, with those experiencing severe anxiety reporting the poorest sleep. Similarly, higher levels of depression also correlated with decreased sleep quality. Additionally, participant stress negatively impacted sleep

quality. Research has indicated that mood and anxiety disorders are associated with lower sleep quality, and in many cases, this decline serves as a key indicator of these disorders.^{38,39} The participants in this study were not officially diagnosed with mood or anxiety disorders by a psychiatrist; instead, their diagnoses were based solely on the completed questionnaires. This reliance on self-reported data highlights a limitation of the study, as participants did not receive definitive diagnoses. However, the findings still indicate that levels of stress, anxiety, and depression are significantly associated with sleep quality among individuals undergoing Opioid Agonist Treatment (OAT). This aligns with the results from previous research.¹⁶ It is recommended to monitor not just methadone dosage and sleep symptoms but also levels of stress and depression in these individuals to improve sleep quality. Those who started methadone use at younger ages experienced worse sleep quality despite the absence of a correlation with the age of drug use initiation or duration of methadone use. Additionally, higher daily doses of methadone were linked to poorer sleep quality. These findings align with the results of prior research.⁴⁰ It has been mentioned that the risk of central sleep apnea in the context of chronic exposure to opioid substances is very important, and this issue is also dose-dependent, which is consistent with the results of the present study.⁴⁰ It can be argued that longer exposure to methadone and its higher doses can put individuals at higher risk of methadone-related side effects resulting from the activity of the body's opioid receptors (especially kappa and mu receptors), which can also increase the prevalence of sleep disorders in these individuals.⁴¹

Conclusion

In conclusion, it is recommended to pay more attention to the mental health of individuals undergoing methadone maintenance treatment to improve their mood and anxiety disorders, as well as to reduce risky behaviors such as alcohol consumption. This can significantly improve their sleep quality and, consequently, their occupational and social quality of life. Additionally, efforts should be made to minimize the duration of methadone maintenance treatment and the dosage used to better control sleep quality.

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Competing Interests

The authors have no conflict of interest.

Ethical Approval

The study received ethical approval from Kerman University of Medical Sciences (IR.KMU.AH.REC.1400.282). Informed verbal consent was obtained from the participants before the study, and confidentiality and privacy were maintained throughout all stages of the research.

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