

# A Comparative Study of Maintenance Therapy Effects of Methadone, Buprenorphine and Opium Tincture on Sleep Status of Outpatients Referring to Addiction Treatment Centers in Tehran: a Prospective Study

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## ABSTRACT

**Background:** Drug abuse and dependence is one of the most important socioeconomic and health problems and is considered a crime in today's societies. Regarding the effects of maintenance therapies on addicted people's quality of life, **Aim:** To determine the effects of maintenance therapy with Methadone, Buprenorphine and Opium Tincture on the sleep status of addicted people.

**Methods:** This is a prospective cohort study conducted on 84 subjects who referred to addiction treatment centers in Tehran. The subjects were selected randomly and classified into three groups of treatment with Methadone (28 patients), Buprenorphine (28 ones) and Opium Tincture (28 ones). They were treated according to the protocol of the Ministry of Health and were followed up for 3 months.

**Results:** The mean age of the subjects was  $39.37 \pm 9.7$  years and most of them were men (67.85%). The mean Pittsburgh Sleep Quality Index (PSQI) of Methadone, Buprenorphine and Opium Tincture groups did not significantly differ at the beginning (P value = 0.528) and end of the study (P value = 0.158). The results of the treatment process in the three groups showed that the maintenance therapy with Methadone, Buprenorphine and Opium Tincture was effective on the sleep quality of the addicts (P value <0.01).

**Conclusion:** The results of this study showed that the use of maintenance drugs was associated with increased incidence of sleep disorders in those who were dependent on drugs but intended to quit, and the disorders increased during the process of quitting.

**Keywords:** maintenance therapy, sleep quality, addiction

## INTRODUCTION

Drug abuse and dependence is one of the most important socioeconomic and health problems and is considered a crime in today's societies<sup>1,2</sup>. The trend of drug dependence and abuse in less-developed and developing countries such as India, Indonesia, Malaysia, Pakistan, and Iran is increasing, so that its global burden on health has been estimated to be 0.7% in recent years<sup>3,4</sup>. In the past decades, some effective drugs have emerged for the maintenance therapy of addicted people, which help them to control drug dependence, and improve their quality of life and sexual dysfunction<sup>5,6,7</sup>. These drugs include Methadone and Buprenorphine. Methadone is an artificial opiate and a  $\mu$ -receptor agonist, which has a longer life span than other opiates (heroin), and reduces the delusional effects of other opiates without necessarily causing euphoria, relief, or lack of pain<sup>8</sup>. Methadone treatment is also one of the medical treatment methods that is internationally recognized as an effective, safe, and cost-effective intervention for drug dependents<sup>9,10</sup> and the most widely used method for the treatment of drug addicts in the United States since 1964. It is believed that in this method, Methadone not only eliminates the problems associated with quitting drugs, but also has a positive impact on the personal and social aspects of the individuals<sup>11,12,13,14</sup>. Buprenorphine is also a relative  $\mu$ -receptor agonist and a strong  $k$ -receptor antagonist, which has enough opioid agonist effects at low doses and eliminates the symptoms of quitting (15, 16). According to the studies carried out, Buprenorphine is equal to moderate Methadone doses and

reduces drug craving within 4 weeks, irrespective of its dose (17). Besides, some studies on Methadone and Buprenorphine maintenance treatments showed a reduction in the complications such as decreased sleep quality (20-18). One of the side effects of drug abuse, which is usually not considered by therapists, is sleep disorders in drug and stimulant abusers, and inadequate or undesirable sleep in these patients and its effect on memory, learning, attention, and executive functions not only affect the patient's general functioning and increase physical and psychological distress in drug abusers, but also increase the rate of treatment failure and relapse<sup>21,22,23,25</sup>.

Studies have shown that maintenance therapies not only treat addicted people and eliminate their dependence on drugs, but may also lead to a rise in their quality of life and have a positive impact on the social and personal aspects of the individuals. Clinical experiences suggest that one of the main reasons for the lack of medical cooperation and discontinuation of maintenance therapy and reuse of narcotic drugs is the symptoms of sleep disorders, the diagnosis and management of which and also the management of the problems caused by sleep disorders can lead to greater adherence to maintenance treatment (25-27). Hence, considering the effects of maintenance therapy on sleep quality of addicted individuals, this study aimed to investigate and compare the effects of maintenance therapy with Methadone, Buprenorphine and Opium Tincture on the sleep status of the outpatients referring to addiction treatment centers.

## MATERIALS AND METHODS

This is a prospective cohort study carried out on all the people referring to Tehran addiction treatment centers in 2018. After obtaining their informed consent, the subjects were enrolled in the study on the basis of the inclusion and exclusion criteria. All the individuals who referred to the addiction treatment centers for opioid dependence treatment and had the criteria for entering maintenance therapy with Methadone, Buprenorphine and Opium Tincture according to the protocol of the Ministry of Health, and were also willing to participate in this study were considered to have the inclusion criteria. The exclusion criteria included serious medical or psychiatric illnesses that led to hospitalization or long-term treatment with drugs. In addition, those who were using hypnotic drugs, sedatives, alcohol, and stimulant medications were excluded from the study process. In general, 84 subjects under maintenance therapy in the three groups of Methadone, Buprenorphine and Opium Tincture who had the inclusion criteria were randomly selected (28 subjects from each group) and entered into the study. The individuals in each treatment group (Methadone, Buprenorphine and Opium Tincture) who were under maintenance therapy were followed up within 12 weeks. The dosage of all maintenance drugs was fixed throughout the study and was based on the Iranian Ministry of Health's protocol in authorized addiction treatment centers, and was prescribed by psychiatrists and nurses.

The Pittsburgh Sleep Quality Index (PSQI) was used to assess the sleep quality of the subjects in each group treated with Methadone, Buprenorphine and Opium Tincture. The sleep quality was assessed at the beginning and the end of the study (12<sup>th</sup> week). The PSQI measures the people's sleep status, including delay in falling asleep, waking up during sleep, etc. within the past 4 weeks. The questionnaire consists of 7 questions which are scored based on the Likert scale and the increase in severity. Obtaining 6 or a higher score shows the patient's poor sleep quality. The validity and reliability of the questionnaire were well documented in domestic and foreign studies (28, 29). The Cronbach's alpha of the Persian version of PSQI was about 0.77, indicating a good reliability of this questionnaire.

## STATISTICAL METHODS

The descriptive statistics such as mean and standard deviation were used to describe the data in each of the study groups including Methadone, Buprenorphine and Opium Tincture. The

paired t-test was also used to assess the sleep quality in each treatment group. We used the independent T-test and ANOVA to compare the groups in terms of quantitative variables at each time interval. Furthermore, the Chi2 test was used to examine the difference in the frequency of the qualitative variables in the studied groups. The statistical analysis was carried out using SPSS software (version 16, Chicago, IL, USA), and the significance level was considered lower than 0.05.

## RESULTS

A total of 84 patients were studied in three treatment groups including Methadone (28 patients), Buprenorphine (28 ones) and Opium Tincture (28 cases). The mean age of the participants in this study was  $39.37 \pm 9.7$  years. Most of the subjects (57 ones) were men (67.85%), which did not show a significant difference in terms of sex distribution among the treatment groups (P value = 0.99). Also, examining the subjects' characteristics at the beginning of the study, as shown in Table 1, indicated that there was no significant difference between the type of drug used, the number of quitting, the way of drug abuse, and the subjects' occupation in the treatment groups (Methadone, Buprenorphine and Opium Tincture) before the study (P value > 0.05).

The mean sleep quality scores (PSQI) at baseline in the treatment groups with Methadone, ( $7.75 \pm 1.1$ ), Buprenorphine ( $7.7 \pm 1.05$ ) and Opium Tincture ( $0.8 \pm 8$ ) are observed in Table 2. The maintenance treatment groups had no significant difference in terms of the quality of sleep and the same effect was found on the quality of sleep in the subjects at the beginning and the end of the study (P value > 0.05). However, the results of studying the quality of sleep in the subjects undergoing any maintenance treatment (with Methadone, Buprenorphine and Opium Tincture) within the beginning and the end of the study showed a significant difference in the PSQI scores of the three groups, indicating the effect of maintenance therapies on the quality of sleep of the people under treatment.

A comparison of the three groups treated with Methadone, Buprenorphine and Opium Tincture in terms of the mean difference in sleep quality score (Figure 1) showed that there was no significant difference between the PSQI scores of the treatment groups at the end of the study (P value > 0.05). However, it was found out at the end of the study that Opium Tincture had not significantly affected the sleep status of the patients compared to other maintenance treatments.

Table 1: Demographic and background characteristics of the subjects under maintenance treatment

| Group                 |           | Methadone<br>Mean±SD/n (%) | Buprenorphine<br>Mean±SD/n (%) | Opium Tincture<br>Mean±SD/n (%) | P value |
|-----------------------|-----------|----------------------------|--------------------------------|---------------------------------|---------|
| Age (year)            |           | 37.03±10.4                 | 38.78±9.4                      | 42.21±9.6                       | 0.62    |
| Gender                | Male      | 16(%57.15)                 | 14(%50)                        | 17(%60.72)                      | 0.99    |
|                       | Female    | 12(%42.85)                 | 14(%50)                        | 11(%39.28)                      |         |
| Number of<br>quitting | 1         | 9(%32.15)                  | 11(%39.28)                     | 10(%35.71)                      | 0.58    |
|                       | 2         | 12(%42.85)                 | 13(%46.43)                     | 10(%35.71)                      |         |
|                       | 3 or more | 7(%25)                     | 4(%14.29)                      | 8(%28.58)                       |         |
| Type of<br>drug used  | Opium     | 12(%42.85)                 | 14(%50)                        | 8(%28.58)                       | 0.53    |
|                       | Heroin    | 10(%35.71)                 | 10(%35.71)                     | 13(%46.43)                      |         |

|              |                             |            |            |            |      |
|--------------|-----------------------------|------------|------------|------------|------|
|              | Tramadol and narcotic pills | 6(%21.44)  | 4(%14.29)  | 7(%25)     |      |
| Abuse method | Inhalation                  | 12(%42.85) | 12(%42.85) | 12(%42.85) | 0.43 |
|              | Oral                        | 11(%39.28) | 14(%50)    | 10(%35.71) |      |
|              | Injection                   | 5(%17.85)  | 2(%7.14)   | 6(%21.44)  |      |
| Occupation   | Employed                    | 10(%35.71) | 15(%53.57) | 9(%32.14)  | 0.41 |
|              | Unemployed                  | 18(%64.29) | 13(%46.43) | 19(67.86)  |      |

Table 2: The mean PSQI scores in the maintenance treatment groups at the beginning and the end of the study

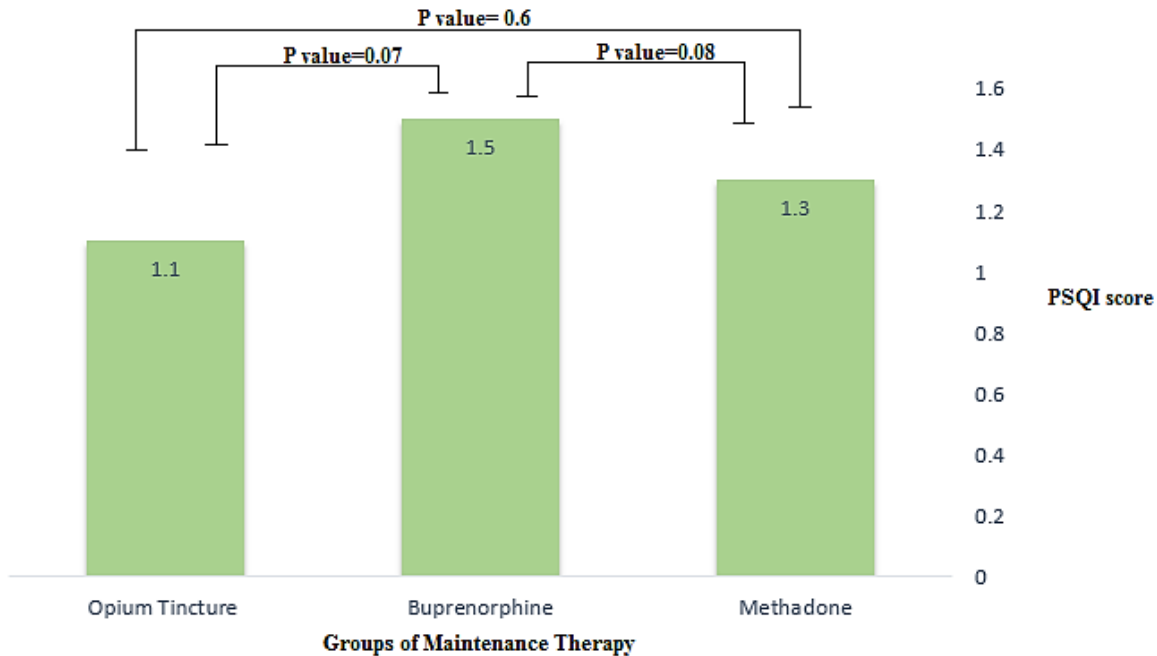
| Group     |                | Methodone | Buprenorphine | Opium Tincture | P value† |
|-----------|----------------|-----------|---------------|----------------|----------|
| PSQI      | Onset of study | 1.1±7.57  | 1.05±7.7      | 0.8±8          | 0.528    |
|           | 3 months later | 1.3±10.89 | 1.5±13.96     | 1.1±14.03      | 0.158    |
| P value†† |                | 0.01*     | 0.01*         | 0.01*          |          |

†P value between groups (ANOVA),

††P value Trend (Paired T test),

\* Statistical significant ate the level <0.01

Fig. 1: Comparison of the mean sleep quality (PSQI) in the maintenance treatment groups at the end of the study



**DISCUSSION**

The results of this study, which aimed to evaluate and compare the maintenance therapies with Methadone, Buprenorphine and Opium Tincture to improve the patients' sleep status, showed that the maintenance therapies with these drugs influenced the sleep status and life quality of the patients referring to the addiction treatment clinics due to their dependence on drug. However, there was no significant difference between the sleep quality scores of the three groups treated with Methadone, Buprenorphine and Opium Tincture at the beginning and end of the study. It seems that these drugs had the same effect on improving the sleep status of the addicted people. However, the subjects treated with Opium Tincture had better sleep status at the end of the 3-month follow up. Also, the comparison between the three groups showed that there was no significant difference between the maintenance treatment groups.

Studies have shown the effectiveness of maintenance therapy with Methadone, Buprenorphine and Opium Tincture to improve mental and physical health, social performance and quality of life (13, 14). Similarly, using these maintenance

medications, opioid dependent persons can have access to an alternative of a fixed dose of the authorized drugs. As a result, the individuals under treatment will temporarily get rid of the permanent stress of using unauthorized opioid that is associated with criminal and sexual behaviors and dangerous injections. Using this type of treatment will allow the individuals to achieve a relatively stable mood instead of the constant experience of mood swings (30-32). Studies have shown that Opium Tincture is used in developed countries such as the United Kingdom and the United States to treat and control diarrhea, pain and symptoms in newborns of addicted and opioid-dependent mothers (33-35). In their study, Nikoo et al. (33) clearly found that Opium Tincture was effective in improving the quality of sleep in drug-dependent individuals and even improving their nutritional and sexual status, which is consistent with the results of the present study on improving sleep status, although there was no difference between Opium Tincture and other drugs. Dunn (36) also found that maintenance treatment with Methadone and Buprenorphine was accompanied by increased sleep disorders and reduced quality of life, which is somewhat consistent with the results of our study.

The occurrence of sleep disorders in people undergoing Buprenorphine treatment was higher than treatment with Methadone and Opium Tincture. Tabassomi (37) stated that sleep disorders were among the most common complications in people using Opium Tincture, and the use of maintenance medications in drug-dependent individuals was associated with an increase in the incidence of sleep disorders, which is consistent with the results of this study in which the incidence of sleep disorders in Opium Tincture users was not significantly lower than those treated with Buprenorphine. Parvaresh et al. (38) also showed that addicted people under Methadone maintenance treatment had poor sleep quality while in our study, sleep quality was moderate. They also showed that Methadone maintenance treatment within 6 months of follow-up increased the incidence of sleep and sexual disorders in addicts, which is consistent with the results of the present study in which the sleep quality of the people undergoing Methadone treatment decreased within 3 months of follow-up. Peles (39) stated in his study that during the 12 months of follow-up, no change was observed in the sleep quality of the people undergoing Methadone treatment, which is different from the results of our study. Rouhani et al. (40) concluded that Methadone maintenance therapy increased the quality of life of the addicts, which is not consistent with the results of the present study. Other findings of this study also indicated that most people covered by maintenance therapies were male. Although drug abuse is more prevalent among men around the world, the women studied in this research were far less likely to abuse drug than the women worldwide. This inconsistency was also observed in other studies conducted in Iran, and generally suggests that there is very limited information about the addiction of women in the country (38, 40). Furthermore, the mean age of drug addicts was 36 years, which is close to the mean age stated in other studies (41). One of the limitations of this study was the small sample size of the groups treated with maintenance medications. Besides, a longer follow-up of the treatment groups and the evaluation of various doses of maintenance medications in the onset of sleep disorders could help achieve more favorable outcomes.

## CONCLUSION

In general, the results of this study showed that the use of maintenance medications such as Methadone, Buprenorphine and Opium Tincture was associated with an increased incidence of sleep disorders in drug-dependent people who intended to quit, and these disorders increased during the quitting process. It was also shown that the use of Opium Tincture along with other maintenance medications could help to improve the sleep disorders.

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