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Sleep quality in heroin addicts under methadone maintenance treatment

Hsu W-Y, Chiu N-Y, Liu J-T, Wang C-H, Chang T-G, Liao Y-C, Kuo P-I. Sleep quality in heroin addicts under methadone maintenance treatment.

Background: Sleep disturbance is a common phenomenon among opiate addicts. The side effects of opiate addiction or opiate withdrawal might result in sleep disturbance. However, their problems might be related to sedative medication abuse, alcohol abuse or heroin relapse. Sleep is an important issue in this population.
Objective: To evaluate the prevalence of sleep disorders in heroin addicts receiving methadone maintenance treatment (MMT) and analyse the correlation between related factors, such as age at opiate exposure, opiate exposure duration, duration in MMT, methadone current dosage, methadone attendance rate and the severity of sleep disorders.
Method: We enrolled 121 heroin addicts who were receiving MMT. We collected data on the duration of insomnia, hypnotic history, Visual Analogue Scale-10 of sleep quality, Pittsburgh Sleep Quality Index (PSQI), methadone dosage, methadone history and opiate history.
Results: The mean of the PSQI was 9.1 ± 5.4, and 70.2% of patients had PSQI scores >5, indicating they were poor sleepers. We also found the PSQI scores were correlated significantly with the methadone dosage.
Conclusions: The sleep disturbance prevalence rate of opiate addicts under MMT was high in Taiwan, as shown in the previous studies, and the severity of sleep disturbance has been underestimated.

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Keywords: heroin addicts; hypnotics; methadone maintenance treatment; Pittsburgh Sleep Quality Index; sleep quality

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Significant outcomes

- About 70.2% of heroin addicts in methadone maintenance treatment had a sleep disorder in our survey.
- The severity of sleep disorder in our survey was a mean of Pittsburgh Sleep Quality Index (PSQI) 9.1 ± 5.4.
- PSQI scores were correlated significantly with the methadone dosage.

Limitations

- Lack of polysomnography to provide objective sleep evaluation.
- Limited data on the patients' abuse of hypnotics, alcohol and other substance.
- Our samples were from only one site.
- The sample size was small.

Introduction

Sleep disturbance is a common phenomenon among opiate addicts. The aetiology of sleep disturbances in the methadone maintenance treatment (MMT) population is often multifactorial and complex. Opiate withdrawal, an irregular life pattern, physical illness, comorbid psychiatric illness or other drug abuse problem might result in sleep disturbance. The

mechanisms of mu, delta and kappa receptors with regard to sleep are unclear and controversial. However, it has been noted that mu agonist significantly inhibited rapid eye movement sleep (1).

Physicians often underestimate the severity and prevalence of sleep disorders in this population. A high prevalence (84%) of sleep disorders in MMT patients was reported by Stein et al. (2). Peles et al. reported a mean PSQI score of 9 ± 4.8 in MMT patients in Israel (3). Taiwan began its methadone harm reduction program in December 2005. However, the average dosage of MMT in Taiwan is lower than that in other Western countries. The question is, does a lower methadone dosage lead to better sleep quality? But sleep disturbance and hypnotic abuse were still noted in our clinics in Taiwan. To our knowledge, there are few studies in the world relevant to this issue. The aims of this study are (a) to explore the severity of sleep quality in the MMT population, and (b) to study the relationship between sleep quality and age at opiate exposure, opiate exposure duration, duration in MMT, methadone attendance rate and methadone current dosage.

Methods

The study protocol was approved by the institutional review board of Changhua Christian Hospital. There is no commercial funding in the study. We excluded patients with schizophrenia and bipolar disorder, based on their clinical records. One hundred and twenty-one patients with a heroin addiction, including 105 males and 16 females, were enrolled from MMT clinics at the Lutung branch of Changhua Christian Hospital, which is a mental hospital located in central Taiwan. The mean age of these patients was 39.6 ± 8.6 years. The educational levels were as follows: 2 patients (1.7%) had received no education, 22 (18.2%) graduated from elementary school, 66 (54.5%) from junior high school, 29 (24.0%) from senior high school and 2 (1.7%) had graduated from college. In terms of marital status, 58 patients (47.9%) were single, 35 (28.9%) were married, 25 (20.7%) were divorced and 3 (2.5%) were widowed. Eighty-five patients (70.2%) had a job and 36 (29.8%) did not. Intravenous injection was the mode of heroin use for 113 patients (93.4%). The mean age of first use of heroin was 27.2 ± 7.4 years. The mean duration of opiate abuse was 12.4 ± 5.9 years (range, 1–24 years). The mean duration in MMT program participation was 15.7 ± 11.1 months.

We designed questionnaires, including (1) demographic variables, (2) medical history and (3) MMT-related variables, to identify the presence of insomnia, duration of insomnia, hypnotic history, Visual Analogue Scale-10 (VAS-10) of sleep quality, PSQI, methadone dosage, methadone history and opiate history. Continuous variables were analysed using the *t*-test and one-way analysis of variance. A *post hoc* correction was done when needed. Associations between sleep disorder scores and other variables were done using regression analysis. Statistical analyses were performed using the software program SPSS PC 12.0 (SPSS Inc, Chicago, IL, USA).

Chinese version of the PSQI and VAS-10 of sleep quality

The PSQI is a self-administered questionnaire used to evaluate subjective sleep quality during the previous month (4). It contains 19 self-rated questions, yielding both a global score and 7 component sub-scores: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep medication and daytime dysfunction. Each component is scored from 0 to 3, yielding a global PSQI score between 0 and 21, with higher scores indicating a lower quality of sleep. A PSQI global score greater than 5 indicates 'poor sleep' with a sensitivity of 89.6–98.7% and specificity of 84.4–86.5% (4,5). Use of the same cut-off score on the Chinese-language version of the PSQI has been shown to have a sensitivity of 98% and specificity of 55% (6), and is a reliable and valid tool for the assessment of sleep quality (4,6). The VAS-10 of sleep quality is a subjective VAS (10 cm) measuring the severity of sleep problems.

Results

Methadone use

The average daily dosage of methadone in this sample was 51.4 ± 24.9 mg. Most of the patients (88.4%) drank methadone regularly. The attendance rate for MMT in a recent month was 87.6 ± 18.9%, on average.

Sleep quality

Thirty-seven patients (30.6%) believed that they had sleep problems, including 6 females and 31 males. The mean VAS-10 sleep quality score was 6.8 ± 2.5 and the mean PSQI was 9.1 ± 5.4. The 7 PSQI sleep categories are shown in Table 1.

Management of sleep problems

Eleven patients (9.1%) took hypnotics regularly, 16 (13.2%) took hypnotics occasionally and 94 patients (77.7%) denied taking hypnotics, now; 28 patients (23.1%) would use alcohol to sleep better. Forty-five patients (38.0%) had visited clinicians due to sleep

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Table 1. PSQI categories and score distribution

PSQI categories	Scored '0'	Scored '1'	Scored '2'	Scored '3'
	N (%)			
Sleep quality	16 (13.2)	60 (49.6)	25 (20.7)	20 (16.5)
Sleep latency	14 (11.6)	21 (17.4)	10 (8.3)	76 (62.8)
Sleep duration	56 (46.3)	25 (20.7)	25 (20.7)	15 (12.4)
Sleep efficiency	69 (57.0)	21 (17.4)	12 (9.9)	19 (15.7)
Sleep disturbance	4 (3.3)	69 (57.0)	39 (32.2)	9 (7.4)
Use of sleeping medication	76 (62.8)	11 (9.1)	11 (9.1)	23 (19.0)
Daytime dysfunction	52 (43.0)	15 (12.4)	16 (13.2)	38 (31.4)

disturbance. Ten patients (8.3%) thought they would use heroin again due to sleep disturbance, and 26 (21.5%) thought they might use heroin again, for the same reason.

PSQI and gender, employment status, marital status, route of heroin use and hypnotics use

There was no significant difference in PSQI scores between males and females ($t_{(119)} = -0.641$, $p = 0.523$), between employed and unemployed ($t_{(119)} = 0.382$, $p = 0.703$), and between marital statuses ($F_{(3,117)} = 1.53$, $p = 0.21$). However, patients that injected heroin intravenously had higher PSQI scores than those that smoked heroin ($t_{(16.253)} = -3.481$, $p = 0.003$). There was a difference between educational levels and PSQI scores. Patients with a senior high school educational level had a higher PSQI score than patients with an elementary school education in the Bonfferoni *post hoc* analysis. There were also differences between hypnotics use and non-use and PSQI scores ($F_{(2,118)} = 23.58$, $p < 0.01$). PSQI scores were significantly higher in patients with regular hypnotics use or occasional hypnotics use than in patients without hypnotics in the Bonfferoni *post hoc* analysis (Fig. 1). Comparisons between mean PSQI scores and different variables are provided in Table 2.

PSQI and age at opiate exposure, opiate exposure duration, duration in MMT, methadone current dosage and methadone attendance rate

PSQI scores had no correlation with age at opiate exposure, opiate exposure duration, duration in MMT and methadone attendance rate, but PSQI scores were associated significantly with methadone dosage ($R = 0.181$, $p = 0.047$). The distribution of methadone dosages and PSQI scores, and the regression line are illustrated in Fig. 2.

'Poor sleeper' and 'normal sleeper' groups

Among the study subjects, 70.2% had PSQI scores >5, indicating 'poor sleepers', and 29.8% had

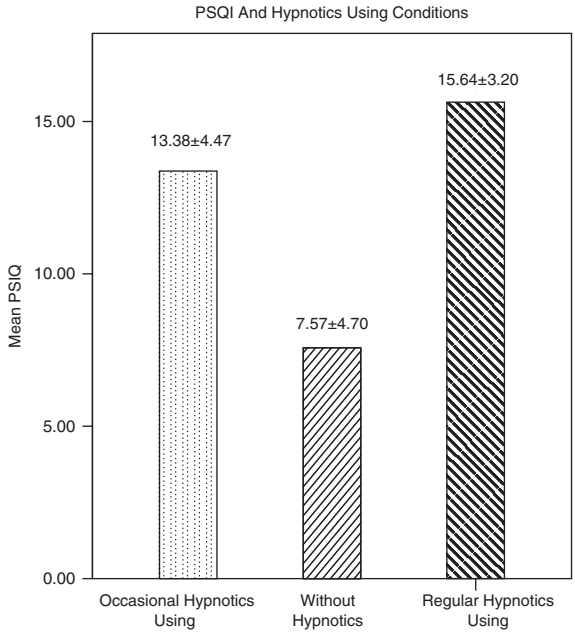

Fig. 1. PSQI scores were significantly higher in patients with regular hypnotics use or occasional hypnotics use than patients without hypnotics in Bonfferoni *post hoc* analysis (mean difference between regular hypnotic using and without hypnotics = 8.06, $p < 0.01$; mean difference between occasional hypnotic using and without hypnotics = 5.80, $p < 0.01$).

Table 2. Comparison in mean PSQI by different variables

	PSQI (mean ± SD)	*n*	*F* (df)	*p*-Values
Gender				
Male	8.95 ± 5.16	105	0.411 (1.119)	0.52
Female	9.88 ± 6.63	16		
Education				
Without education	9.00 ± 8.49	2	2.463 (4.116)	**0.049**
Elementary school	6.23 ± 4.33	22		
Junior high school	9.42 ± 5.41	66		
Senior high school	10.62 ± 5.26	29		
College	6.50 ± 4.95	2		
Marital status				
Single	9.79 ± 5.45	58	1.53 (3.117)	0.21
Married	7.46 ± 4.20	35		
Divorced	9.64 ± 6.27	25		
Widowed	9.33 ± 5.86	3		
Job				
Employed	9.36 ± 5.21	85	0.146 (1.119)	0.703
Unemployed	8.95 ± 5.44	36		
Route of using heroin				
Intravenous	9.27 ± 5.46	113	2.414 (1.119)	**0.003**
Smoking	6.25 ± 1.98	8		
Hypnotic using				
No	7.57 ± 7.70	94	23.58 (2.118)	<**0.01**
Occasional	13.38 ± 4.47	16		
Regular	15.64 ± 3.20	11		

p-Value in bold means significant difference between variables (<0.05).

PSQI scores ≤5, indicating 'normal sleepers'. These two groups were similar in age, gender, age at first exposure to opiates, duration of opiate abuse,

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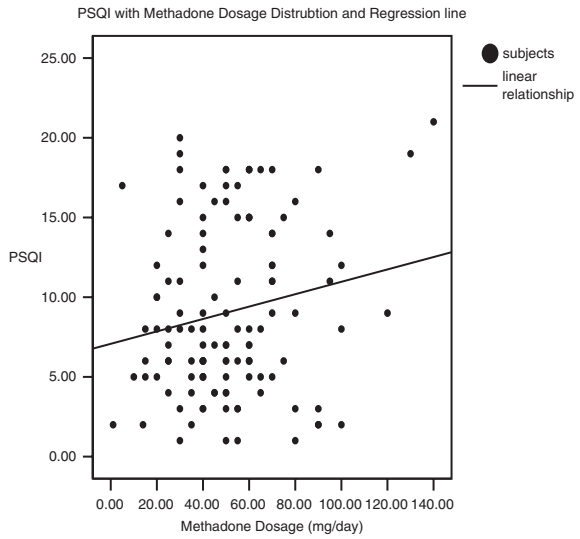

Fig. 2. Association between PSQI and methadone dosage ($R = 0.181$, $F_{(1,119} = 4.027$, $p = 0.047$).

dosage of methadone, duration of MMT and MMT attendance rate. There were significant differences in the VAS-10 of sleep quality ($t_{(105.645)} = -6.295$, $p < 0.01$).

Discussion

Effect of opioids on sleep

The mechanism of opioid medication and opiates in relation to sleep might be unclear. However, clinical studies have shown the effects of opioid medications and methadone. Dimsdale found that single doses of oral opioid medications can significantly affect sleep architecture in healthy adults; decreased deep sleep and increased stage two sleep were noted (7). In Xiao's study, patients in early MMT had poor sleep quality and abnormal sleep architecture, including lower sleep efficiency, shorter total sleep time, more awakenings and shorter slow wave sleep (8).

Sleep disorders prevalence and severity

In our study, we found that the sleep disorder prevalence rate was high (70.2%) in heroin addicts under MMT. The prevalence of insomnia was 39.4% in the general Chinese population (9). The mean PSQI in our subjects was 9.1 ± 5.4. Stein et al. reported 84% of subjects had PSQI scores of 6 or higher, and found a mean PSQI of 10.64 ± 4.9 (2). In Pele's study, 75.2% of subjects had PSQI scores of 6 or higher, and a mean PSQI (9 ± 4.8) was shown (3). We found a prevalence and severity of sleep disorder similar to these studies. Sleep disorder is a serious problem in these patients, with at least 70% experiencing it.

Relative factors analyses

We also found that patients injecting heroin intravenously had higher PSQI scores than patients that smoked heroin. Severity of opiate dependence could be a factor related to this phenomenon. However, we did not find a significant difference between poor sleep and normal sleep in terms of age at first exposure to opiates, duration of opiate abuse, dosage of methadone, duration of MMT and MMT attendance rate.

PSQI and methadone dosage

We found a linear correlation between PSQI scores and methadone dosage. Patients with a higher methadone daily dosage had a higher PSQI score. This result correlated with the results of Stein's and Pele's studies (2,3). Although the association between PSQI and methadone dosage is significant, the effect size (i.e. $R = 0.181$) of this study is between small and moderate (10). The sample size enhanced the statistical power of this study. In other words, the association is not strong, which may imply that the sleep quality is influenced by other potential antecedents as well as methadone dosage in our sample. On the other hand, a large effect size ($R = 0.48$) of the association between methadone dosage and PQSI was reported by Peles et al. Underlying factors moderating this association remain to be investigated.

Hypnotics prevalence

The current prevalence rate of hypnotics use was 22.3% in our sample. However, several studies reported a high prevalence rate of hypnotics use. Psychiatric comorbidity was associated with a more severe substance use disorder among treatment-seeking opioid abusers (11). In Gelkopf's study, a lifetime and current prevalence of benzodiazepines (BZD) abuse were found in 66.3 and 50.8% patients in MMT (12). The prevalence of hypnotics use in our sample was not as high as in Gelkopf's study. The self-report questionnaire on hypnotics use in our study might have resulted in a lower prevalence. Also, we found that 29.8% of our patients might relapse due to sleep disturbance; therefore, sleep disturbance could be a risk factor for heroin relapse. Brands et al. reported ongoing BZD users were more likely to have opioid-positive and cocaine-positive urine screens during MMT (13). In another recent study, baseline BZD use correlated with lower retention rates, and ongoing BZD use correlated with poorer outcomes in heroin-assisted treatment and MMT (14). Concomitant consumption of BZD and opioids is a major problem in patients with opioid dependence. It may have a substantial impact on

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morbidity, mortality and the clinical course. BZD use by MMT patients is associated with a more complex clinical picture and may negatively influence treatment outcomes (15). Paying more attention to this issue may yield better maintenance outcomes.

Limitations

There are still several limitations to our study. The first was the lack of polysomnography to provide objective sleep evaluation. Sharkey et al. reported objective sleep measures confirmed subjective measures in MMT patients with disturbed sleep. And, both objective and subjective measures are useful in research and clinical settings to assess sleep in opioid-dependent patients (15). The second is the limited data on the patients' abuse of hypnotics, alcohol and other substance. The third is that our samples were from only one site. There might be some differentness in different sites. The fourth is the small sample size. A larger sample would give the analysis of differences between each variable more power.

Clinical implications

Patients with heroin addiction might have sleep problems. The severity of their sleep problem was serious in our survey. Clinicians should routinely assess their sleep and differential diagnosis. Sleep quality questionnaires, sleep diaries, polysomnography and home polysomnography are useful in assessment. In addition, clinicians also should be aware of hypnotics use or abuse in this population. Education on sleep hygiene, lifestyle resetting and the risk of drug interactions might be helpful.

Conclusion

The sleep disturbance prevalence rate in opiate addicts in MMT was high in this survey, and the severity of these sleep problems was underestimated. This study highlighted the serious problem in this population. Further studies with objective sleep examinations are needed. Clinicians should pay more attention to sleep problems in opiate addicts in MMT, especially those receiving a high dosage of methadone.

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