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The Effect of Opium on Polysomnographic Findings in Patients with Sleep Apnea

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ABSTRACT

Background: *Many reports are available about the increasing rate of mortality due to overuse of opioids. It has been suggested that sleep apnea can be a cause of mortality because of overuse of opioids. Opium use is common in Iran. This study aimed to assess the effect of opium on polysomnographic findings in opium addicts with sleep apnea syndrome.*

Materials and Methods: *In this prospective case-control study, 50 opium addicts with sleep apnea were compared and matched for age, sex and body mass index with 50 non-addict patients with sleep apnea to determine the effect of opium on sleep disorders and polysomnographic findings. Sleep stages, apneas, hypopneas and desaturation were evaluated and recorded for participants in both groups. Data were analyzed and compared using SPSS version 15 software.*

Results: *There were significant differences between the two groups in sleep efficiency (P-value=0.00), apnea/hypopnea index (0.02), hypopnea (P-value=0.00), desaturation (P-value=0.01), sleep latency to stage 1(P-value=0.00) and central apnea (P-value=0.00) but no difference was detected for obstructive apnea (P-value=0.48).*

Conclusion: *Opium can increase central apnea, apnea- hypopnea index and desaturation in opium addicts compared with non-addicts.* ***(Tanaffos2010; 9(3): 33-36)***

Key words: *Opium, Addicts, Sleep disorders, Central apnea, Polysomnography*

INTRODUCTION

Many reports are available on the increasing rate of mortality due to overuse of opioids (1). Many of the reported mortalities due to opioid use during the recent years have been because of excessive use of methadone for pain control (2,3).Causes of these mortalities are yet to be known (4). Since opioids can increase the risk of obstructive sleep apnea (5,6), it has been suggested that sleep apnea can be a cause of mortality due to overuse of opioids .Sleep Apnea is a type of sleep breathing disorder with intermittent episodes of apnea or hypopnea which may lead to stroke, myocardial ischemia, pulmonary hypertension and heart failure (7-10).

Webster showed that 30% of patients with cancer, who used methadone for pain control, developed central sleep apnea (4). Another study reported that

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75% of methadone users developed more that 5 apneic episodes per hour of sleep (11,12).

Many studies showed that moderate opioid doses did not cause any kind of sleep breathing disorder like apnea or hypopnea in normal individuals (13-15). Kay et al. also reported that moderate intramuscular morphine injection in healthy subjects increased nocturnal awakening and omitted REM (rapid eye movements) sleep (13). Shaw et al. showed that moderate IV morphine injection reduced the amount of slow wave and REM sleep stages (15).

Walker et al. study showed that there is a dose-dependent correlation between chronic opioid use and central sleep apnea (16). Other researchers reported a 3-fold increase in mortality with increased non illicit use of methadone and oxycodone (17).

In Iran, there are two forms of opium used by subjects: Teriak (crude opium) and Shireh (refined opium). Shireh is usually made by boiling raw opium and collecting the residue. Both Teriak and Shireh can be smoked or ingested. As we searched the medical literature, no study has been done on the effect of raw opium and Shireh on polysomnographic results.

Considering the increasing rate of mortality due to overuse of opioids and based on evidences that suggest obstructive sleep apnea as a cause of opioid-induced mortality, we conducted this study as the first study on the effect of opium on polysomnographic results in opium addicts with sleep apnea compared with similar non-addict patients.

MATERIALS AND METHODS

This was a prospective case-control study. Fifty male opium addicts with sleep apnea were selected as the case group via simple sampling method among patients referred to Bamdad Sleep and Breathing Disorders Research Center in Isfahan. Case group was matched for sex, age (±5 years) and body mass index (BMI) (±5kg/m^2) with 50 non-addict men with sleep apnea.

Patients with hypertension, diabetes, obesity and hypercholesterolemia and those who were receiving ACE inhibitors, diuretics, oral hypoglycemic agents, insulin or lipid lowering agents for their conditions were also included in this study. These drugs could not be discontinued due to medical concerns.

This study was approved by the Ethics Committee of Isfahan University of Medical Sciences. Written consent was obtained from all 100 participants in both groups before the study.

All participants in both groups were interviewed by an assistant of internal medicine and a questionnaire including demographic data was completed for them. Polysomnography included central (C3/A2 and C4/A1) and occipital (O1/A2and O2/A1) electroencephalogram, right and left electrooculogram and submental electromyogram. Respiratory effort was determined by measuring chest and abdomen motions with traction bands. Nasal air flow was measured by nasal pressure transducers. Arterial oxygen saturation was measured by pulse oximeter.

Polysomnography (Somnomedics- Germany) was performed for all subjects in both case and control groups. Polysomnographic findings, sleep stages and respiratory events were analyzed manually by an expert pulmonologist using 2007 guidelines of American Academy of Sleep Medicine (18).

Data were analyzed and compared using t-test and SPSS version 15 software.

RESULTS

Descriptive statistics, comparison of demographic characteristics, polysomnographic findings and sleep characteristics between opium addicts and non - addicts are shown in Table1.

Significant differences were seen between case and control groups in latency to stage 1(P-value=0.00), apnea/ hypopnea index (P-value= 0.00), central apnea (P-value=0.00), hypopnea index (P-value=0.00) and desaturation index (P-value=0.00).

Table 1. Comparison of demographic characteristics, polysomnographic findings and sleep characteristics between opium addicts (inhalation routes) and non- addicts

Characteristics	Opium addicts (inhalation route)	Non-addicts	P-value
Demographic Characteristics			
Age(year)	(No=50) 52.84±10	(No=50) 52.76±11	0.64
Height(m)	(No=50) 1.73±0.06	(No=50) 1.71±0.06	0.45
Weight (Kg)	(No=50) 90.41±16	(No=50) 88.34±19	0.25
BMI (Kg/m^2)	(No=50) 29.9±5	(No=50) 30.01±5	0.76
Sleep Characteristics			
Total sleep time(hour)	(No=50) 3.12±85	(No=50) 3.07±80	0.94
Sleep efficiency (%)	(No=50) 72.94±15	(No=50) 70.23±16	0.96
Number of awakenings (time)	(No=50) 22.82±16	(No=50) 24.36±14	0.56
Sleep latency (min)			
Latency to stage 1	(No=47) 39.73±48	(No=50) 71.56±39	0.00
Latency to stage 2	(No=50) 48.64±39	(No=50) 32.78±31	0.06
REM latency	(No=44) 1.87±98	(No=42) 1.45±93	0.61
Apnea / hypopnea index (No./h)	(No=50) 33.66±31	(No=50) 19.30±19	0.00
Obstructive apnea index	(No=46) 6.92±11	(No=48) 5.26±10	0.48
Central apnea index (No./h)	(No=45) 7.21±11	(No=42) 1.14±3	0.00
Mixed apnea index (No./h)	(No=42) 1.08±2	(No=39) 0.72±1	0.44
Hypopnea index (No./h)	(No=50) 19.99±19	(No=49) 11.48±9	0.00
O_2 desaturation (%)	(No=49) 34.25±31	(No=50) 19.47±19	0.00

DISCUSSION

Results of this study showed that opium addiction can increase frequency of desaturation, central apnea and hypopnea. Our results showed no significant difference between opium addicts compared with non-addicts in sleep characteristics except for sleep latency to stage 1.

Webster showed that 30% of patients with cancer who used methadone for pain control, developed central sleep apnea (4). Another study reported that 75% of methadone users developed more that 5 apneic episodes per hour of sleep (11-12). Our study results were in accord with those of above mentioned studies.

On the contrary, Kay et al., Bernards et al. and Shaw et al. reported that moderate opioid doses did not cause any kind of sleep breathing disorder like apnea or hypopnea in normal individuals (13-15). Kay et al. reported that moderate intramuscular morphine injection in healthy subjects increases nocturnal awakening (13). However, in our study no significant difference was seen in sleep pattern between opium addicts (inhalation route) and non - addicts except for sleep latency to stage 1.

These differences between our study and those of above-mentioned studies (13-15) may be due to different route of opium use by our understudy subjects (inhalation) and probably higher doses of opium use in our case group. Also, it should be mentioned that in our study the opioid used was pure opium but in other studies opium derivatives were used and this can cause differences in results.

Walker et al. study showed that there is a dose-dependent correlation between chronic opioid use and central sleep apnea (16). Another researchers reported a 3-fold increase in mortality with an increased rate of non-illicit use of methadone and oxycodone (17).

Although we showed that chronic opium use can worsen central apnea, we did not measure the dose of

opium in our subjects. It was difficult to assess the exact dose and time intervals of opium abuse. Therefore, we could not suggest any correlation between the dose of opium and the severity of central apnea and this is a limitation of our study.

Another limitation of this study was including patients who used other medications as well which may affect the results of final analysis.

Our study concluded that chronic opium use can worsen desaturation and increase central apnea, hypopnea and sleep latency to stage 1. Since this study was the first conducted on the effect of opium on sleep disorders, more studies are necessary to evaluate the effect of exact dose of opium and its underlying mechanisms on polysomnographic findings in a normal individual.

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