CORRELATION BETWEEN SLEEP APNEA AND METHADONE THERAPY

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SUMMARY

Introduction: Methadone therapy is the mainstay of treatment of addict patients. The most common side effects are: dizziness, drowsiness, vomiting, sweating, dry mouth and constipation. The more serious complications that can be observed are: sleep apnea, abnormal heart rhythms, respiratory problems, euphoria, disorientation, anxiety, seizures and more.

Purpose: The purpose of this study is to determine the correlation between methadone maintenance treatment and sleep apnea in addict patients.

Materials and methods: The subject of the study are 81 methadone-treated drug-dependent patients, mean age $39 \pm 9,07$ years.

Results: The answers we received: 79% (64) of drug addicts have problems with sleep; 30.9% of them (25) reported having insomnia; 44.4% (36) experience morning fatigue; 56.8% (46) of the respondents said they were drowsy during the day and 63% of the respondents reported a change in mood; 21% (17) had a short sleep, and 26% (21) reported snoring and 18 of them have loud bothering snoring; 68% answered that they don't have problems with falling asleep and only 21% don't wake up frequently in the evening. In 83.9% nobody noticed cessation of breathing during sleep. 73.8% never nodded off or fallen asleep while driving a vehicle. 16.1% have been treated for high blood pressure, and only 2.5% have obesity.

Conclusions: Our survey found that there is a correlation between methadone therapy and sleep of patients. The key to improving the condition and reducing the risk of central sleep apnea is the monitoring of patients, as well as a combination of different types of treatment.

Keywords: Methadone, Opiate dependence, Drug addicts, Sleep apnea, Central sleep apnea, Sleep disorders,

INTRODUCTION

Methadone is an opioid used to treat chronic pain as well as supportive therapy in opioid-dependent patients. Its most common side effects are: dizziness, drowsiness, vomiting, sweating, dry mouth and constipation. [1, 2]. The more serious complications that can be observed are: sleep apnea, abnormal heart rhythms, respiratory problems, euphoria, disorientation, anxiety, seizures and more [2, 3, 4].

Addiction is a brain disorder that creates mental and/or physical dependence. It tortures millions of people around the world, which costs society a great deal in terms of medical and social problems, and immeasurable suffering for loved ones and for themselves [5]. Addiction is most commonly observed for opioid drugs. The patients we examined were addicted to heroin. There are different modes of its administration: from smoking, sniffing to oral and intravenous heroin intake [5]. Drug addicts have the highest psychoactive effect through intravenous administration, which is also the most dangerous.

Drugs are chemicals that affect a person's physical, mental and social functions by changing them in various aspects. The use and abuse of narcotic substances is common and increasing in recent years. This is a socially significant problem worldwide [6].

Methadone therapy is the mainstay of treatment of addict patients. Methadone is a synthetic opiate has a longer action than heroin and acts on the same opioid receptors. Its euphoric effect is less pronounced. Patients take it orally to treat their addiction. If injected intravenously, it will give a heroin-like intoxication. It is essential that methadone therapy is monitored by a doctor because methadone is also addictive and can have side effects. Methadone intoxication and abstinence are more powerful than heroin.

The purpose of this study is to determine the correlation between methadone maintenance treatment and sleep apnea in addict patients.

MATERIALS AND METHODS

Our survey was conducted among 81 drug addicted patients treated with methadone, 58 men (72%) and 23 women (28%). Prior to the survey, they signed informed consent and completed an anonymous survey. Most of them were treated at University Hospital "St. Marina" – Varna in the Department of Psychiatry and Medical Psychology and were monitored outpatient in the Diagnostic Consultative Center "St. Marina" – Varna, where we conducted the survey.

Patients met several including criteria: to be on methadone therapy for at least 2 months, to be addicted to opioid drugs, to complete informed consent.

All participants filled an anonymous survey in order for their sleep problems to be clarified in details. The study

consisted of 14 questions for sleep assessment. The issues of the survey refer to problems with sleep, mood swings, snoring and quality of sleep. We used the scientific literature to compare our data from a polysomnographic study for sleep apnea in methadone therapy.

RESULTS

The 81 patients we examined were $39 \pm 9,07$ years of age (mean $\pm$ SD). The proportion between men and women was unequal. There were twice as many men as women (58 versus 23). Their distribution as a percentage is given in Figure 1.

All of them are drug addicts, treated at the University Hospital "Saint Marina" and monitored at Diagnostic Consultative Center "Saint Marina" – Varna, where we conducted the polysomnographic study and the survey.

Fig. 1. Percentage of examined patients

We prepared a special questionnaire for patients. After they filled it, we summarized the received answers by calculating the percentage of answers with "Yes" or "No", respectively, and the results are shown in Figures 2 to 11, 14 and 15. Two of the questions had multiple choice, they are shown in Figures 12 and 13.

The first question was about sleeping problems - whether or not patients had them. We found that 79% said they had (fig.2). Each patient reported a different sleep problem.

On the following questions, the received answers are shown as a percentage:

- "Do you suffer from insomnia?" 25 (30,9%) responded positively
- "Do you have morning fatigue?" - 44,4% (36) said they experience morning fatigue
- "Do you feel sleepy during the day?" 56,8% (46) answered negatively
- 63% of patients reported "mood swings during the day"
- To the questions "Is your dream short?" and "Do you snore?" patients who answered "yes" were respectively 21% (17) and 26% (21)
- From patients who answered yes on previous question (21pts), 18 answered that their snoring bothered other people
- 26 (32%) patients had difficulty falling asleep.
- 21% (17) of the respondents do not wake up often in the evening

- "Has anyone noticed that you quit breathing during your sleep?" - Nearly every day (0 pts); 3–4 times a week (2 pts, 2.5%); 1–2 times a week (3 pts, 3.7%); 1–2 times a month (8 pts, 9.9%); Never or nearly never (68 pts, 83.9%)

- On the question "Have you ever nodded off or fallen asleep while driving a vehicle?" - 1 patient (1.2%) answered "nearly every day"; 3 patients (3.7%) - 3–4 times a week; 5 patients (6.2%) - 1–2 times a week; 1–2 times a month (13 pts, 16.1%); and "never or nearly never" - 59 pts (72.8%)

- Do you have or are you being treated for high blood pressure? - 13 patients (16.1%) have

- BMI ≥ 35 kg/m²? - only 2 patients (2.5%) answered positively

Fig. 2. The share of pts with the sleep problem

Fig. 3. The share of pts with insomnia

Fig. 4. The share of pts with morning fatigue

Fig. 5. The share of pts feeling sleepy during the day

Fig. 6. The share of pts with mood swing

Fig. 7. The share of pts with a short dream

Fig. 8. The share of pts with snoring

Fig. 9. The share of pts whose snoring bothers others

Fig. 10. The share of pts who have hard falling asleep

Fig. 11. The share of pts who often wake up

Fig. 12. The share of pts whos partner noticed cessation of breathing

Fig. 13. The share of pts whoever noddod off or fallen asleep while driving a vehicle

Fig. 14. The share of pts who are /have been treated for high blood pressure

Fig. 15. The share of pts with BMI ≥ 35 kg/m²

DISCUSSION

The relationship between drugs use and sleep is two-way. On the one hand, opioid use causes sleep disorders, and on the other, sleep problems affect recurrent opiate abuse [7].

Central sleep apnea (CSA) is characterized by a lack of airflow for ≥ 10 seconds with no effort of breathing, and

an apnea-hypopnea index (AHI) of more than 5 per hour is considered significant [8].

For the diagnosis of central sleep apnea in opioid-dependent patients, there are 3 clinical symptoms that may be present both individually and together: 1) the respiratory pattern - ataxia or irregularly; 2) interruption of breathing - apnea or hypopnea 3) gas exchange - hypoxia and hypercapnia. Central apnea may have different morphology: irregular intervals with ataxic respiration or periodic with cluster respiration [8].

Polysomnographic examination is the gold standard for diagnosing OSA, but it is a time-consuming and costly procedure. To address this problem, many studies use developed screening questionnaires to help identify patients with OSA. The survey method is a proven useful, simple and alternative approach used to diagnose sleep apnea by asking patients to report their symptoms [9,10]. Our questionnaire is a self-administered screening tool, which combines questions about the risk factors for sleep apnea. In this way, the risk can be determined.

Breathing disorders during sleep (sleep disordered breathing) in patients using opiates are extremely high. According to the study of Correa D et al., they range from 42% to 85%, and the incidence of central sleep apnea is many times higher than in the general population (24%) [8].

After taking opioids, breathing becomes shallow and irregular, leading to hypercapnia and hypoxia. The specific one observed by Randerath WJ and George S (2012) in opioid-induced sleep apnea patients is daytime drowsiness, dizziness, and impaired concentration [11].

For the most accurate diagnosis of central sleep apnea, a polysomnographic study should be used as well as a multidisciplinary team. Two abnormal breathing patterns are observed in diagnosed patients - reduced effort to inhale during an obstructive event and longer than expected respiration pauses [14]. In a polysomnographic study done by Sharkey, K, and a team of 71 methadone patients, 42.2% of participants had at least one form of SDB [15]. Correa D. and Farney R. observed central sleep apnea (CSA) in a study of patients receiving methadone therapy [8]. With this type of sleep apnea, patients stop breathing or breathing is very low, and they cannot supply oxygen. It presents a more serious treatment challenge.

The major risk of methadone use is death from respiratory depression, especially when initiating therapy or changing doses [12]. Many studies have shown that methadone therapy leads to an increase in the incidence of sleep apnea symptoms, and the quality of sleep in these patients is very poor. This reflects on the quality of life of patients [13].

The data we obtained showed that addicts receiving methadone patients have trouble sleeping. The explanation of this in the literature is that unlike obstructive sleep apnea, in which the muscles of the throat are relaxed, in central sleep apnea (more common in opioids use), the brain does not send the correct signals to the muscles that control breathing.

We found that 79% of patients reported sleep problems. Different symptoms vary within various limits. Patients stop breathing for a certain period of time, have trou-

ble with sleep and wake up. These short, breath-taking awakenings are typical of central sleep apnea. Mood changes are also one of the symptoms of apnea, but they overlap with patients' mental state, and addiction treatment has many effects on them.

We observed other typical symptoms we observed in our patients have increased daytime sleepiness in 56.8% and morning fatigue in 44.4%. Many of these patients have insomnia (30.9%). A smaller percentage of those surveyed were found to have short sleep and snore.

What the partner of the respondents thinks is extremely important for conducting this survey. Some of the questions focused on what others were saying about the sleeper. In 83.9% of drug addicts, their partners did not notice the symptom of sleep apnea - cessation of breathing.

It is crucial that 27.2% percentage of patients nodded off or fell asleep while driving. This may be due to both fatigues from sleep apnea and opiates taken by the subjects. It is very difficult to distinguish the cause of this problem.

Other risk factors for sleep apnea are obesity and high blood pressure. In this study, we did not find it to affect drug addicts. A very small percentage of those surveyed had BMI ≥ 35 .

How to manage sleep apnea in methadone treated addicted?

Guilleminault C. (2010) showed the most accurate diagnosis of central sleep apnea is a combination of polysomnographic study and discussions with a multidisciplinary team. He has observed 2 abnormal breathing patterns in the diagnosed patients - reduced effort to inhale during an obstructive event and longer than expected respiration pauses [14].

Treating patients with sleep apnea as a result of opioids is extremely challenging. There are different study and opinions. According to Correa D. and Farney R. (2015), constant positive pressure apparatus is most commonly used for treatment, and different types of oxygen devices are used. Some patients may require a reduction in the opiate dose or the choice of another drug with less methadone toxicity (such as buprenorphine), as well as drug treatment with acetazolamide, theophylline and carbon dioxide [8].

Troitino A. et al. (2014) made a study in patients with sleep disorders, and his conclusion is that patients with central sleep apnea due to opiates are not significantly affected by CPAP (Continuous positive airway pressure therapy) treatment. Only 24% of addicted showed improvement compared with the control group with idiopathic central sleep apnea (38%) [16].

Guilleminault and the team also observe the same, but they report differences in obese patients and those with lower BMI. In their view, those with lower body weight have a different breathing pattern, which respond well to CPAP therapy [14].

Oxygen therapy corrects hypoxemia but does not affect patients' ataxic breathing. Patients may experience potentiation of hypoventilation or prolongation of central apnea/hypopnea. But oxygen therapy rarely causes respiratory depression, as opioids stabilize respiration if the

arousal threshold is low and the respiratory controller gain is high, associated with pain. Oxygen is added in addition to CPAP treatment for optimal treatment [8].

CONCLUSION:

We found in our study that there is a correlation between methadone therapy and the sleep of patients. De-

spite the high prevalence of sleep problems in drug addicts, this therapy is necessary and should be closely monitored by their psychiatrists. The key to improving the condition and reducing the risk of central sleep apnea is in monitoring patients, as well as a combination of different types of treatment.

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