Smoking, snoring and obstructive sleep apnea

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Abstract

Obstructive sleep apnea (OSA), with an apnea/hypopnea index (AHI) ≥5 events per hour , is recognized as an important cause of medical morbidity and mortality, being associated with a wide range of significant medical consequences, including arterial hypertension, cardiovascular diseases, metabolic diseases, neurological diseases and psychological effects. Tobacco smoking is considered a predisposing factor for pulmonary and cardiovasculary diseases and a risk factor for developing OSA. Since snoring is frequent in smokers and a common symptom, even a preclinical form of OSA, it is reasonable to speculate that smoking is an independent risk factor for snoring and may be associated with OSA. Current studies have observed there is a synergistic effect between smoking and OSA, both increasing the risk of cardiovascular disease through oxidative stress, endothelial dysfunction and abnormal inflammatory response. OSA, itself, could be responsible for nicotine addiction.

Keywords: *obstructive sleep apnea, tobacco smoking, risk factor, snoring*

Rezumat

Fumatul, sforăitul și sindromul de apnee obstructivă în somn

Sindromul de Apnee Obstructivă de Somn (SASO), la un indice de apnee/ hipopnee (IAH) ≥5 evenimente/ ora de somn, este recunoscut drept cauză importantă de morbiditate și mortalitate, fiind asociat cu o gamă largă de afecțiuni și consecințe patologice: hipertensiune arterială, boli cardiovasculare, boli metabolice, boli neurologice și efecte psihologice. Cum sforăitul este frecvent la fumători și un simptom comun, chiar formă preclinică de SASO, fumatul se consideră a fi un factor de risc independent al sforăitului și poate fi asociat cu SAS.

Cuvinte-cheie: *apneea obstructivă în somn, fumatul, factor de risc, sforăitul*

Introduction

Obstructive sleep apnea (OSA) is recognized as an important cause of medical morbidity and mortality, being underdiagnosed with an estimated frequency among adults of 9% in women and 24% in men, according to the Wisconsin cohort study, with an apnea/ hypopnea index (AHI) ≥5 events per hour[1]. The syndrome is associated with a wide range of co-occuring morbidities, that can be considered medical consequences of SASO, including: cardiovascular diseases (arterial hypertension resistant to treatment, arrythmia, myocardial infarction, sudden death)[2, 3], metabolic, neurological and psychic diseases and disorders.

In the past, the main risk factors evaluated for OSA were age, obesity, sex and craniofacial anomalies[5]. At present, smoking, as a predisposing factor in pulmonary and cardiovasculary diseases, is more and more frequently associated with OSA. Thus, smoking can act as a risk factor in developing OSA[6]; there is a synergism between smoking and OSA, both increasing the risk of cardiovascular disease[7], and not ultimately, OSA itself could be responsible for nicotine dependence in smokers[8, 9].

Epidemiological data

The study put forward by Bloom and his collaborators[10] at the beginning of 1988 proved that the risk of snoring is higher in smokers. Snoring can be considered a common symptom of OSA. In the absence of an OSA diagnosis, smoking may be considered an independent risk factor for snoring.

The main studies assessing the relationship between smoking and OSA carried out in the last two decades can be summarized as follows:

- In the research study conducted by Wetter et al., 811 active smoking individuals and former smokers were recruited, who were investigated polysomnographically at night and it was noticed that the active smokers "had more chances" to snore than non-smokers and they had a significantly higher risk of developing any form of OSA, especially a moderate or a severe one. Furthermore, a dose-response type of relation was found between smoking and OSA, which revealed that heavy smokers (≥40 cigarettes a day) have an increased susceptibility to developing OSA, irrespective of form, as compared to non-smokers[11].

The case-control study made by Kashyap et al aimed to determine the prevalence of smoking in 214 patients in relation to OSA (108 diagnosed with OSA and 106 control patients). The smoking prevalence in patients with OSA was of 35% versus 18% in control subjects without OSA. The conclusion of the study was that smoking is an independent risk factor for OSA, the risk of OSA being 2.5 times higher in smokers than in former smokers and non-smokers[6].

The research work of Moreno et al. used the Berlin questionnaire and showed, in its turn, that smoking is an independent risk factor for OSA in 10 truck drivers from 101 drivers included in the study[12].

The study carried out by Neruntarat et al investigated the medical and the non-medical staff in a hospital in a rural area in central Thailand and showed that OSA prevalence was 2 times higher in smokers than in non-smokers[13].

Hoflstein's study underlined a higher prevalence of active smokers and heavy smokers (a greater number of pack-years) among the subjects with AHI >50/h. Taking into account that heavy smokers smoked equal or more than 30 pack-years (PA), he noticed that they had a higher AHI than non-smokers, without a statistically significant relationship between smoking and the AHI value[14].

The research work of Casasola et al. highlighted a dose-response relation between smoking and nocturnal hypoxia, showing that the desaturation period of the oxyhemoglobin during sleep was significantly higher in smokers than in non-smokers. Severe nocturnal hypoxia of smokers was significantly correlated with the number of pack years[15].

According to the study conducted by Conway et al., active smokers have more chances of spending over 5% of the total sleeping time at a saturation of the oxyhemoglobin (SaO_2) lower than 90%, with smoking playing an important part in sleep fragmentation[16].

Pathophysiological mechanisms

So far, several pathophysiological mechanisms of the possible relationship between smoking and OSA have been evoked:

I. Smoking - a risk factor in OSA

Smoking can contribute to the inflammation of the upper respiratory airways (URA). Active or passive smoking has been associated with increased airflow resistance at the nose and mouth, with an apparent change of the mucociliary clearance[17]. Smoking induces chronic inflammation of the URA by several mechanisms: cellular hyperplasia, edema, thickening of epithelium and ciliary disfunction[18, 19]. This was recently demonstrated in a transversal study of Virkkula et al., which involved 2523 subjects and demonstrated a cause-effect relationship between smoking and chronic inflammation of URA by reducing the dimensions of the nasal cavity and therefore by decreasing the airflow[20]. Moreover, in this study smokers have higher chances to develop severe snoring early in life, with an important nasal obstruction and lower volumes of nasal air, irrespective of the sleeping position[20].

The negative effects of smoking also affect the pulmonary function, with an increased rate of respiratory infections, of obstructive respiratory diseases like the chronic obstructive bronchopulmonary diseases (COPD and bronchial asthma)[21, 22]. In chronic bronchitis, the increased sputum production may contribute to the increased resistance of the upper airways, leading to snoring and OSA[23].

Thus, through these mechanisms, smoking continually affects breathing during sleep and increases smokers' vulnerability to OSA.

At the beginning of 1963 it was demonstrated that nicotine increases ventilation by affecting the neuronal structures in the neighbourhood of the ventrolateral surface of the spine[24]. In the 1980s, studies on animals proved that nicotine reduces the resistance of the upper airways[25, 26] by stimulating the muscles of the upper respiratory airways, including the genioglossus, more than the diaphragm[25].

Starting from these data, recent research has demonstrated that simply prescribing nicotine chewing gum before sleeping has decreased the number of obstructive ans mixed sleep apneas, but has not influenced, as expected, central type apnea. Taking into consideration that the levels of nicotinemia gradually decrease during the night, the number of sleep apneas may rise as a consequence of the "rebound effect". There is an individual sensitivity, explaining why the nighttime effects of nicotine do not necessarily affect all smokers.

The precise effects of nicotine on OSA may include smoking induced inflammation, the obesity effect on the muscles of the upper respiratory airways, the rebound effect of nicotine.

Hypoxia is specific for OSA. Casasola et al.[15] and Conway et al.[16] have demonstrated that smokers are more susceptible to develop long term hypoxia, which might consecutively worsen OSA. Bonsignore et al.[28] have shown that smokers with OSA have a significantly lower arterial blood oxygen pressure (PaO_2) during wake state, and a reduced saturation (SaO_2) while sleeping during non-REM sleep.

Remodelling of the lower respiratory airways and the chronic decrease of the pulmonary function induced by smoking can be other pathophysiological mechanisms of OSA emergence[29]. Taking into account sleep effects upon ventilation, remodelling of the respiratory airways induced by chronic tobacco smoking might worsen the ventilation-perfusion gas exchances, thus contributing to the smaller, but significant changes of SaO_2, especially during REM sleep[30].

Smoking produces a major increase in carboxihemoglobin (HbCO), causing deviation to the left of the dissociation curve of oxyhemoglobin. Such a change may induce difficulties in tissue oxygenation due to the increased need for oxygen[15]. Furthermore, the chronic exposure to smoking leads to the decrease of the sensitivity to hypoxia and, thus facilitates longer periods of apnea, with important desaturations.

A possible explanation for these changes involves the abnormal functioning of the peripheral chemoreceptors without excluding the defficient functioning of central chemoreceptors due to the adverse effects of smoking on the brain development in the fetal period.

Smokers have a higher prevalence of developing sleep disturbances[11]. This has been confirmed in studies which have shown that smokers have a greater latency of the falling asleep period, inefficient sleep and a lighter transition from one sleep stage to another[32, 33]. Furthermore, Conway et al. have noticed that active smokers with ≥ 15 PA report a worsening of sleep quality, with frequent prolonged awakenings while fully abstaining from nicotine[16, 34, 35].

The reduced levels of nocturnal nicotine is associated to the decrease of neurotransmitters release at the central nervous system, inducing unstable sleep. Through the stimulating effects of the decrease of nocturnal nicotine concentration, smoking can interact with OSA symptoms, causing great sleep fragmentation, with worsening of sleep quality and significant daytime sleepiness.

II. The effect of smoking on OSA clinical manifestations

II.1. Smoking and the OSA cardiovascular damage

OSA and chronic smoking are independent cardovascular risk factors[3, 36, 37]. The major mechanisms involved in inducing cardiovascular diseases (CVD) in OSA patients include oxidative stress, the abnormal inflammatory response and the endothelial disfunction[38, 39]. In a long term, smoking also induces CVD through the same pathophysiological mechanisms[40, 41].

The preliminary study made by Lavie et al. investigated the oxidative stress and the circulating inflammatory markers in OSA patients and revealed, in smokers with OSA, significantly increased levels of circulating triglycerides and inflammatory markers, including reactive C protein, ceruloplasmin, haptoglobin, as well as lower levels of high density lipoproteins (HDL) and cholesterol as compared to non-smokers with OSA, thus indicating a synergic effect between smoking and OSA in increasing the cardiovascular risk[7]. In smokers with severe OSA, they have established the highest level of ceruloplasmin and the lowest level of HDL, which suggests

that these patients have a greater cardiovascular risk than smokers with slightly moderate OSA forms and non-smokers with OSA[7].

Furthermore, a study carried out by Bonsignore et al. has indicated that smoking patients with OSA have a lower baroreceptor sensitivity only while being awake and a greater cardiovascular variability during wakefulness and while sleeping[28].

II.2. Smoking and the endocrine effect of OSA

While evaluating OSA and the impact of smoking on the total serum testosterone level, Kirbas et al. have noticed serum levels of total testosterone lower in patients with OSA with a negative correlation with AHI[42, 43, 44]. At present, a statistical correlation between serum testosterone and the number of PA smoked[45, 46] has not been demonstrated, although earlier studies supported this idea[43, 44].

II.3. Sleep apnea: a predisposing factor in nicotine dependence?

A provoking and rather intriguing hypothesis was formulated at the beginning of the 1990s by Wetter et al. and Schrand, who stated that smoking can represent a form of self-therapy in patients with OSA who reveal hypersleepiness symptoms, depression, and cognitive disfunctions, persons susceptible of being incompetent in their work and ostracized by their co-workers at the work place[9, 11].

Since it has been demonstrated that under the influence of nicotine, these patients put up with these symptoms, patients with severe OSA can be encouraged to solve their social problems of this kind by smoking, to preserve their vigilance.

At the same time, there is a valid reciprocal assumption (the reverse is also true), that is, in untreated OSA patients with severe depressive symptoms and cognitive disfunctions, CPAP therapy requires that smoking withdrawal should be an absolutely necessary precondition.

As far as the mechanism of nicotine addiction is concerned, the immediate continuation of the life preservation activities is encouraged. In the long term, hypoxia increases the dopamine release in the body and the nicotine, in its turn, will also increase the levels of dopamine in the brain. It is known that nicotine increases ventilation and decreases the upper respiratory airways resistance.

Conclusions

The influence of tobacco smoking on the respiratory system is unquestionable.

The stimulating effects of decreased nocturnal level of nicotine represent latent mechanisms through which smoking can be considered a pathogenic mechanism of OSA.

The co-occurrence of smoking and OSA is, at least partially, supported by the reduced risk of OSA, noticed in former smokers, after an adequate period of smoking withdrawal.

OSA may be responsible for the nicotine addiction. Thus, on one hand, giving up smoking is advisable when doctors consider therapy for OSA, while, on the other hand, smoking is recommended to untreated OSA patients with severe symptoms, such as daytime sleepiness, depression, and cognitive dysfunction. ■

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