doi: http://dx.doi.org/10.11606/issn.1679-9836.v99i2p164-169 Rev Med (São Paulo). 2020 March-April;99(2):164-9.

Obstructive sleep apnea and smoking: a literature review

Apneia obstrutiva do sono e tabagismo: uma revisão de literatura

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Alves JC, Silva JKLS, Furlan SF. Obstructive sleep apnea and smoking: a literature review / *Apneia obstrutiva do sono e tabagismo: uma revisão de literatura*. Rev Med (São Paulo). 2020 March-April;99(2):164-9.

ABSTRACT: Obstructive sleep apnea (OSA) is characterized by total or partial obstruction of the upper airways, which is highly prevalent and underdiagnosed in the general population and may have multiple deleterious consequences. Recent evicdences show a synergistic effect between smoking and OSA to the development of cardiovascular diseases and increased morbidity and mortality. However, the mechanisms by which smoking contributes to the development of OSA remain little discussed so far. The aim of the present study is to review the correlation of the effects of smoking in the development of OSA. This study was elaborated from a literature review in the databases Pubmed (104 articles), Scielo (42 articles) and Lilacs (9 articles) in the period between 1999 and 2017, totailing 155 articles. As inclusion criterion, only were used articles that correlated smoking with OSA, and articles which related OSA to other conditions were excluded, articles that used sleep questionnaires as a diagnosis method, which were not published in the stipulated period, and articles that were repeated in the used databases.

Keywords: Sleep apnea syndromes; Tobacco use disorder; Risk factors; Sleep apnea, obstructive; Snoring; Tobacco products.

RESUMO: A apneia obstrutiva do sono (AOS) é caracterizada por obstruções totais ou parciais das vias aéreas superiores, é altamente prevalente e subdiagnosticada na população geral e pode ocasionar múltiplas consequências deletérias. Evidências recentes mostram um efeito sinérgico entre o tabagismo e a AOS para o desenvolvimento de doenças cardiovasculares e aumento da morbimortalidade. No entanto, os mecanismos pelos quais o tabagismo contribui com o desenvolvimento da AOS, permanecem pouco discutidos até o momento. O objetivo do presente estudo é revisar a correlação dos efeitos do tabagismo no desenvolvimento da AOS. Este trabalho foi elaborado a partir de uma revisão da literatura nas bases de dados Pubmed (104 artigos), SciELO (42 artigos) e Lilacs (9 artigos) no período entre 1999 a 2017, totalizando 155 artigos. Como critério de inclusão, foram utilizados apenas artigos que correlacionavam o tabagismo com a AOS e foram excluídos artigos que relacionavam a AOS com outras condições clínicas, que utilizaram questionários de sono como método diagnóstico, que não foram publicados dentro do período estipulado que encontravam-se repetidos nas bases de dados utilizados.

Descritores: Síndromes da apneia do sono; Tabagismo; Fatores de risco; Apneia obstrutiva do sono; Ronco; Produtos do tabaco.

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INTRODUCTION

Obstructive sleep apnea (OSA) is a common clinical condition. It is estimated that at least 20-50% of the general population has some degree of apnea[1,2]. In a study carried out in the city of São Paulo by Tufik et al.[3], with a sample of 1042 individuals aged 20 to 80 years, the presence of OSA was found in almost one third of the adult population.

OSA is characterized by recurrent and intermittent episodes of upper airway collapse during sleep, which leads to total or partial cessation of airflow. These changes can, as a consequence, induce an exaggerated increase in negative intrathoracic pressure, increase in respiratory efforts, intermittent hypoxia and sleep fragmentation. This sequence of repeated events throughout the night, significantly compromises the quality of sleep[4].

This disease, which is often underdiagnosed and untreated in the general population, can have multiple consequences, which include not only snoring and sleep fragmentation, but also excessive daytime sleepiness, tiredness, cognitive dysfunction, symptoms of depression, low quality of life, traffic accidents risk, decreased productivity at work and increased risk of developing metabolic and cardiovascular diseases[5,6] such as heart failure, stroke and acute myocardial infarction. And when untreated, it is also associated with an increased mortality rate[7,8,9].

Obesity, advanced age, male gender, increased neck circumference and craniofacial abnormalities are well-established risk factors for the development of OSA[10]. Currently, smoking, which is a predisposing factor for pulmonary and cardiovascular diseases, is increasingly associated with OSA[11]. There is a synergism between smoking and OSA in which both increase the risk of developing cardiovascular disease. In addition, OSA may be independently responsible for nicotine addiction in smokers[1].

If OSA is common in the general population, it is even more common in smokers. Studies show that these individuals are three times more likely to develop OSA than non-smokers, with a prevalence of 35% vs 18% respectively, as shown in a study conducted in the United States[12]. Balkau et al.[13] found that men and women present similar risks for the development of OSA through smoking (1.5 times higher) when compared to non-smokers.

A study by the University of Wiscosin, comparing 811 active smokers and ex-smokers through the Polysomnography exam, showed that active smokers are twice as likely to snore and present a four times greater risk of developing OSA, especially moderate and severe[11]. Neruntarat et al.[14] investigated the staff of a hospital located in rural Thailand and the prevalence of OSA was twice as high in smokers as in non-smokers.

However, the mechanisms by which smoking contributes to the development of OSA remain poorly discussed so far. In this study, the mechanisms that can lead to the development of OSA will be reviewed and elucidated based on articles already published.

The aim of the present study is to review the correlation of the effects of smoking on the development of OSA.

MATERIAL AND METHODS

This study was elaborated from a literature review in the databases Pubmed, SciELO and Lilacs in the period between 1999 to 2017. The keywords used were selected from the Medical Subject Headings Section (MeSH): sleep apnea, smoking, risk factors, snoring. Exclusion criteria were: articles that were published before 1999 and articles that did not correlate OSA with smoking. Adding all the databases, 155 articles were found on the subject, 104 articles from Pubmed, 42 articles from SciELO and 9 Lilacs articles. After reading the titles of the articles, it was noted that some of them were repeated in different bases and others did not meet the criteria of this study. Then, 118 articles were selected for reading the abstract and of then, 73 that did not concern the purpose of this study or that just used sleep questionnaires as a diagnosis method were excluded.

Effects of smoking on sleep

Despite there are a lot of articles related to the subject, the effects of smoking on sleep are not well established and elucidated. Most of them are based on questionnaires and showed that smoking patients had greater difficulty falling asleep, staying asleep at night, difficulties to wake up and greater excessive daytime sleepiness[15,16]. These consequences can be attributed to the nicotine stimulants effects and the increased occurrence of snoring. Conway et al.[17], showed that patients did not smokers had a lower rate of awakenings during the night and smokers and ex-smokers presented increased N1 time, decreased slow waves and greater SpO2 time below 90% regarding to the non-smoking group.

Smoking as a risk factor for OSA

Epidemiological studies show that smoking, even in passive smokers, is associated with high prevalence of snoring and OSA[18,19]. Smoking cessation reduces the risk of developing OSA, however, inflammation and damage from smoking can alter mechanical and neural properties of the upper airways and increase the chances of collapsibility during sleep[10].

Smoking, active or passive, contributes to upper airway inflammation and has been associated with increased resistance of the nose and mouth, with apparent

worsening of mucociliary clearance[20,21]. Studies show that chronic cigarette use induces this chronic inflammation by several mechanisms: cell hyperplasia, edema of the upper airway, epithelial thickening, mucociliary dysfunction, changes in the viscoelastic properties of the mucus, in addition to affecting lung function, leading to an increased rate of respiratory infections[22,23].

Clinical manifestations of OSA as a consequence of smoking

Hypoxia

A type of dose-response was found between smoking and nocturnal hypoxia, in which the oxyhemoglobin desaturation during sleep was higher in smokers than in nonsmokers.

Trenchea et al.[11] demonstrated that patients who are smokers and diagnosed with OSA presented a significant lower SpO_2 while awake and during non-REM sleep regarding to non-smokers and the severity of nocturnal hypoxia in smokers was correlated with the number of packs of cigarettes per year.

Remodeling of the lower airway and the development of COPD (chronic obstructive pulmonary disease), chronic smoking consequences, cause disorders related to perfusion ventilation, worsening gas exchange, especially in REM sleep[24].

Hypercapnia

Smoking causes an increase in carboxyhemoglobin (COHb), leading to a shift to the left of the oxyhemoglobin curve. This increase in COHb values and the consequent deviation from the curve leads to a decrease in the SaO_2, which can induce difficulties in tissue oxygenation due to the increased demand for oxygen[11,20]. In addition, chronic exposure to cigarette smoking leads to decreased sensitivity of chemoreceptors to hypoxia, promoting long periods of apnea with important desaturation[11].

Snoring

Snoring is one of the main clinical manifestations of upper airway obstruction. It is estimated that in the adult population the prevalence of snoring is 16 to 33% in men and 8 to 19% in women, who get worse with aging[18,19]. In a study by Kauffman et al.[25], the prevalence in middle-aged men was higher than 60%. Studies show that snoring has a strong association with smoking, including passive smoking children[25].

Inflammation and increased airway resistance

Cigarettes have deleterious effects on the upper and lower airways and their chronic use can induce snoring, increasing the resistance of the upper airways[11]. In fact, the correlation between smoking and snoring, has been attributed to changes in mucociliary clearance and / or inflammation of the pharynx and soft palate. So, it is possible that this cigarette-induced inflammation in the upper airways could induce upper airway obstruction and other sleep disorders[20].

Synergistic effect of smoking and OSA on the cardiovascular system

The effects of smoking and OSA on the development of cardiovascular diseases and in the rate mortality increasing are well established and documented. It is important to mention the synergistic effects of these two conditions: both promote increased blood pressure, increase the risk of developing atherosclerosis and increase cardiovascular morbidity[28]. The pathophysiological mechanisms that cause this effect are mainly related to increased oxidative stress and inflammation that act directly on cardiovascular risk biomarkers[29]. Studies show that smokers with severe OSA are more likely to developing cardiovascular disease than smokers with mild or moderate OSA and non-OSA smokers[7,29].

OSA as a predisposing factor in nicotine dependence

Sleep disorders can play a stimulating role in the non-cessation or initiation of smoking. The symptoms caused by sleep disorders - depression, fatigue, anxiety, cognitive impairment - resemble those of nicotine withdrawal and these symptoms could, therefore, increase desire and necessity to smoke. In fact, nicotine withdrawal patients commonly report problems with sleep, however, many of these symptoms are only exacerbated by the absence of nicotine, reflecting the disorders already previously developed due to smoking[16]. Patients with untreated sleep disorders have greater difficulties in smoking cessation, increasing the chances of failure[28].

The effects of nicotine in the upper airway are already well established, which can lead to an increase in upper airway tonus during sleep, suggesting a protective effect against OSA. Interestingly, nicotine has been used in treatment of OSA although with still inconclusive results[20].

As nicotine levels decline during sleep, upper airway resistance increases, generating greater sleep instability and a dose-dependent reduction in sleep efficiency, REM sleep and total sleep time[29].

Regardless of the possible beneficial relationship between nicotine and OSA, smoking can get worse the consequences of OSA, mainly, on the individual's oxygenation at night, increasing stress oxidative, blood pressure, the risk of developing cancer, cardiovascular diseases and decreasing life expectancy[20].

Importance of smoking cessation in patients with OSA

OSA is associated with an increased risk of

developing cardiovascular disease, greater hospitalization rates, increased mortality rates and high costs on health services[16,30]. Thus, the identification of a modifiable risk factor for OSA, such as smoking, becomes an important step towards reducing and preventing the consequences caused by it[16].

Smokers with OSA have sleep fragmentation and sleep deprivation, as consequences increase the consumption of nicotine to counteract these effects of sleep deprivation[31]. The treatment of OSA and its consequences are important measures that contribute to the successful cessation of smoking[32,33].

Currently, smoking cessation efforts have not had the desired effect, mainly in more dependent patients compared to less dependent ones[34,35]. This can be explained by some studies that relate this difficulty with stimulation of pleasure centers that encourage the continuity of addiction, since the cycle of intermittent hypoxia that occurs in OSA leads to an increased release of catecholamines at levels of dopamine (DA)[36,37]. The next question is how adaptation to addiction occurs. Long-term hypoxia can be characterized as responsible for the increase in the number of nicotine-binding sites in smokers, and this increase in nicotine will cause an increase in DA levels in the brain, thus increasing the cycles respiratory and oxygenation, consequently there is an increase in the stimulation of the pleasure centers that lead to compulsive activity and addiction[33,38].

Short-term smoking cessation has some deleterious effects, such as: increased daytime sleepiness and worsening of sleep disorders with increased apnea and hypopnea rate[39,40,41]. The process of nicotine abstinence, as well as the respiratory and pulmonary effects caused by smoking can be exacerbated soon after its cessation, however, they will have an important decline after a certain time[19].

In this way, many studies have already demonstrated that smoking cessation is an important intervention for reduce OSA[16,26,34,35].

Behavioral intervention therapies (smoking cessation, weight loss and physical activity) can provide the individual with an efficient reduction in the severity of OSA[16]. According to studies by the Commission Research on Sleep Disorders Research, identify early modifiable behavior, such as smoking, becomes an important step to avoid and reduce the impact of the associated clinical consequences OSA, only using health promotion and prevention resources[42].

Smoking cessation before 30 years would prevent more than 90% of lung cancer deaths and individuals who quit smoking showed a pattern of survival similar to that of individuals who never smoked[21]. A study carried out in the United Kingdom showed that, in individuals who stopped smoking, the risk of lung cancer has dropped sharply over time cessation[43,44]. According to Prabhat Jha et al.[45], men who quit smoking at 50, 40 or 30 years of age had accumulated risks of lung at 75 years of 2%, 3% and 6%, respectively, in contrast to the 16% risk for individuals who continued to smoking.

CONCLUSION

Chronic smoking lead to increased upper airway resistance, hypoxia, hypercapnia and snoring due to inflammatory factors and changes in mucociliary clearance, besides being responsible for changes sleep phases, which can be attributed to the stimulating effect of nicotine.

The association of smoking and OSA can increase blood pressure, increase the load atherosclerosis and increased cardiovascular morbidity.

Short-term smoking cessation has some harmful short-term effects on the quality of smoking. sleep, however, is necessary due to its harmful effects related to cardiovascular morbidity and mortality.

Authors' participation: *Alves JC*: review of articles and text development. *Silva JKLS*: review of articles and text development. *Furlan SF*: text development and final corrections.

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Received: October 27, 2017
Accepted: November 11, 2019