Influence of smoking on sleep and obstructive sleep apnea syndrome

Influența fumatului asupra somnului și a sindromului de apnee obstructivă de somn

Oana-Claudia Deleanu[1,2], Diana Pocora[2], Ștefan Mihăicuță[3,4], Ruxandra Ulmeanu[2,5], Ana-Maria Zaharie[1,2], Florin Dumitru Mihălțan[1,2]

1. "Carol Davila" University of Medicine and Farmacy Bucharest,

2. "Marius Nasta" Institute of Pulmonology Bucharest

3. "Victor Babes" University of Medicine and Farmacy Timisoara

4. "Victor Babes" Hospital Timisoara

5. Faculty of Medicine and Pharmacy – Oradea University

Corresponding author :
Stefan Mihaicuta
E-mail: stefan.mihaicuta@umft.ro

Abstract

The various ill effects that tobacco smoking has on health have been largely studied, particularly on vascular, neoplastic, and respiratory diseases. Lately, the discussion about the negative impact of cigarette smoking moved towards sleep medicine. Tobacco consumption has been associated with sleep disordered architecture, both during regular intake and after withdrawal. Its effects on sleep disordered breathing (SDB) and especially obstructive sleep apnea syndrome (OSAS) still remain a matter of debate. It is unclear whether smoking represents a risk factor for OSAS or whether smoking cessation has any beneficial effects on OSAS and its therapy. There seems to be a synergistic effect between smoking and OSAS, both causing an increase in cardiovascular morbidity. Future studies are needed in order to establish the strength of this association. We aim to review the literature regarding the consequences of smoking on sleep architecture and SDB, adding emphasis on OSAS clinical implications and treatment.

Keywords: ***obstructive sleep apnea syndrome (OSAS), smoking, nicotine, sleep architecture, sleep disordered breathing, snoring, smoking cessation***

Rezumat

Diferitele efecte patogene ale fumatului asupra stării de sănătate au fost îndelung studiate, în special în ceea ce privește patologiile vasculare, neoplazice și respiratorii. În ultima vreme, interesul legat de impactul negativ al țigaretelor s-a mutat spre medicina somnului. Consumul de tutun a fost asociat cu modificarea arhitecturii somnului, atât pe parcursul consumului activ, cât și după renunțare. Efectele sale în cadrul tulburărilor respiratorii în timpul somnului (TRTS), și în special în sindromul de apnee în somn obstructiv (SASO) rămân încă în dezbatere. Este neclar dacă fumatul reprezintă un factor de risc pentru SASO sau dacă sevrajul fumatului are efecte benefice pe SASO sau tratamentul său. Pare a fi un efect sinergic între fumat și SASO, ambele crescând morbiditatea cardiovasculară. Studii viitoare sunt necesare pentru a dovedi puterea acestei asocieri. Ne propunem o trecere în revistă a datelor de literatură în ceea ce privește consecințele fumatului asupra arhitecturii somnului și TRTS, cu accent pe implicațiile clinice și tratamentul SASO.

Cuvinte-cheie: ***sindrom de apnee în somn obstructiv, fumat, nicotină, tulburări respiratorii în timpul somnului, sforăit, renunțare la fumat***

Smoking is a leading cause of mortality worldwide, killing one in 10 adults and causing 5 million deaths annually. It is estimated that if the current smoking trends continue, tobacco will be responsible for one in six deaths and account for more than 10 million deaths per annum by 2030[1,2]. The various ill effects that the use of tobacco has on health have been largely studied, particularly on vascular, neoplastic, and respiratory tract diseases. Smoking causes rhinitis[3], increased snoring, nasal obstruction and a volume increase in pharyngeal soft tissue[4] due to inflammation and increase of resistance in upper respiratory airway (UA) during sleep, causing sleep disordered breathing (SDB). Smoking withdrawal during the night can favor collapsibility of UA by reduction of muscular tone (otherwise stimulated by nicotine)[5,6].

In this moment, many questions regarding the relation between sleep and sleep pathology and smoking are still waiting to be answered.

1. Smoking and sleep

We cannot discuss about SDB without mentioning the effects smoking has on sleep, effects only recently discovered **(Table 1).**

1.1 Influence of nicotine on sleep and sleep related disorders

Sleep disturbance is commonly reported both by active and former smokers. Nicotine has a known potential for enhancing attention and maintaining a certain level of arousal. These effects are obtained by the central release of dopamine, norepinephrine, serotonin, acetylcholine, all of which have been implicated in the regulation of wakefulness, and by the stimulant effect nicotine has on cholinergic neurotransmission in the basal forebrain responsible for cortical arousal[7].

In relation to SDB, nicotine has a time-dependent effect across the sleep period. During the initial part of the sleep cycle, smokers may experience difficulty with

Table 1 Clinical effects of smoking behavior on sleep

Nicotine	Smoking as a complex habit	Smoking withdrawal	NRT	Bupropion	Increased gain during smoking cessation	Smoking-related diseases
1. Increased sleep latency 2. Decreased sleep efficiency 3. Decreased total sleep time 4. Decreased SWS 5. Increase number of arousals 6. Decreasing upper airway resistance = probably reducing the risk of OSAS	1. Insomnia 2. Sleep fragmentation 3. Nightmares 4. Difficulties waking up 5. Daytime sleepiness 6. Minor accidents 7. Depression 8. Probably increasing prevalence of restless leg syndrome 9. Increasing prevalence of bruxism 10. Increased prevalence of snoring	1. Sleep fragmentation (increased number of arousals) 2. Shift toward lighter stages of sleep 3. Sleepiness 4. Mood swings 5. Collapsibility of the upper airway = snoring and probable OSAS	1. Deterioration of sleep quality	1. Low-doses produce increased SWS and reduced stage 2 sleep 2. Higher-doses produce decreased SWS 3. Higher-doses increase REM density, activity and percentage.	1. Increased risk of OSAS	1. Hypoxemia 2. Hypercapnia 3. Hypoventilation 4. Central apnea (due to cardiovascular disease)

OSAS = obstructive sleep apnea syndrome; NRT = nicotine replacement therapy; REM = rapid eye movement; SWS = slow-wave sleep.

sleep onset due to the stimulating effects of nicotine[8] and a paradoxal decreased UA resistance as nicotine stimulates the UA muscle tone[9], effects that tend to reduce the occurrence of apneas. During the first few hours of sleep, nicotine may actually reduce SDB by decreasing UA resistance, although inducing difficulties in sleep onset.

In the later stages of the sleep cycle, as nicotine blood levels decline, UA resistance increases and a minor nicotine withdrawal appears which increases sleep instability. SDB among current smokers can be a reflection of the decline in nicotine blood levels throughout the night[10].

The effect nicotine delivered through a patch has on sleep was tested and it was proved that, besides its alerting effects causing later sleep onset, nicotine generates a dose-dependent reduction in sleep efficiency, slow-wave-sleep, REM sleep and total sleep time[11,12]. In rats, a sleep-suppressant effect has been reported after an acute administration of nicotine, reversed by repeated administration of nicotine, suggesting that compensatory mechanisms are triggered by chronic exposure[13].

1.2. Active and passive smoking, tobacco withdrawal and their relationship with sleep architecture and SDB

1.2.1. Active smoking and sleep architecture

Cigarette smoking has been associated with sleep disturbances, both during regular intake and after withdrawal: insomnia, sleep fragmentation **(Figure 1)**, nightmares, difficulties waking-up, daytime sleepiness, minor accidents and depression[5, 6, 14, 15]. These are partially explained by decreasing blood levels of nicotine during sleep which induces craving and are not linked to the wake-promoting effect of nicotine[7].

Most studies are based on patients' subjective reports of sleep disturbances, using questionnaires. Recent studies focused especially on objective measuring in order to provide solid, quality proof regarding the effects of smoking on objective sleep parameters **(Table 2)** and only two studies had the sufficient sample size and considered the potential effects of age and gender in assessing the independent relation between smoking and SDB: the Wisconsin Sleep Cohort[16] and Sleep Heart Health Study (SHHS)[17].

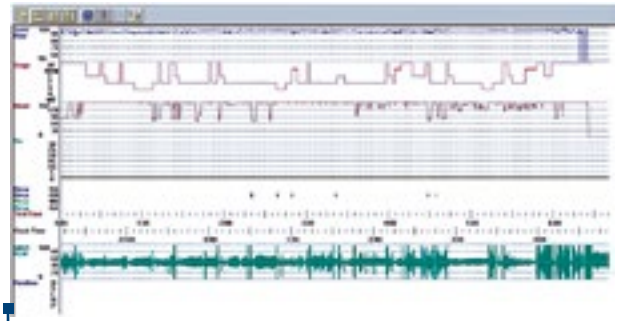

Figure 1: *Sleep architecture in heavy smokers*
Hypnogram of a 38 year old patient, heavy smoker (25 pack-years), highly dependent on nicotine (Fagerstrom score = 7), without any other comorbidities or sleep related disorders. Polysomnographic data: sleep efficiency 78%, arousal index 19,2/h, percent of sleep stages: stage 1- 15,2%, stage 2 – 68,8%, delta sleep – 10,7%, REM sleep - 5,3%. Diagnosis: sleep-onset and sleep-maintenance insomnia; REM=rapid eye movement.

Zhang demonstrated that sleep architecture disturbances among current smokers were not influenced by the amount of smoking quantified by pack-years and no differences were observed between former and never smokers. Contrary to other study results[11,12], smokers and non-smokers do not differ regarding rapid-eye

Table 2 Influence of smoking on sleep and sleep disordered breathing

REFERENCE	AIM OF STUDY	PARTICIPANTS	OBJECTIVE MEASUREMENTS	RESULTS
Wetter DW *et al.*, 1994[10]	Smoking as a risk factor for OSAS	811 subjects from Wisconsin cohort divided in groups: -never smokers -former smokers -current smokers	Sleep parameters analysis (PSG)	Current smokers are at greater risk of developing SDB compared to the other groups
Kashyap *et al.*, 2001[32]	Controlled study on prevalence of smoking among OSAS patients	214 patients divided in 2 groups: -108 patients with OSAS -106 controls (without OSAS)	No sleep study report	Smoking may be an independent risk factor for OSAS
Casasola *et al.*, 2002[54]	Evaluate the influence of cigarette smoking behavior on the sleep respiratory alterations	38 healthy volunteers, 2 groups: - current tobacco smokers (n = 18) - nonsmokers (n=20)	Sleep parameters analysis (nocturnal domiciliary polygraphic study)	Smoking: -isn't associated with ↑AHI -is associated with ↓nocturnal SaO_2 There is a significant correlation between PY index and night-time desaturation
Hoffstein *et al.*, 2002 [46]	Examine the relationship between smoking and OSAS	3509 subjects divided in groups by: -apnea severity -smoking status and severity	Sleep parameters analysis (PSG)	Smoking is not an independent risk factor for OSAS after adjustment for sex, weight and age
Zhang *et al.*, 2006[18]	Assess the impact of smoking on sleep architecture	6400 subjects from SHHS divided in groups: -never smokers -former smokers -current smokers	Sleep parameters analysis (PSG)	Smoking is independently associated with disturbance in sleep architecture
Conway *et al.*, 2008[33]	Evaluate the effects of smoking on sleep	1492 subjects divided in groups: -never smokers -former smokers -current smokers divided by smoking severity	Sleep parameters analysis (PSG)	Smoking is associated with arousal, desaturations during sleep, higher percent of stage 1, lower percent of SWS and higher Epworth score, but not with AHI.

AHI = apnea-hypopnea index; OSAS = obstructive sleep apnea syndrome; PSG = polysomnography; PY = pack-year; SDB = sleep disordered breathing; SHHS = Sleep Heart Health Study; SWS = slow-wave sleep.

movement (REM) sleep, perhaps because nicotine does not inhibit cholinergic regulation of REM sleep, but it's temporary withdrawal during the night can modify sleep continuity and shift the distribution of sleep architecture toward lighter stages of sleep[18].

Zhang extended the research using qualitative (spectral) analysis of electroencephalogram (EEG) which indicates that smoking induces a characteristic psychostimulant profile involving higher frequencies and peak alpha frequency at the expense of delta and theta power spectrum. These represent empirical evidence for the biological basis of smoking-related sleep onset insomnia and low quality of sleep[8].

It has been speculated that restless legs syndrome (RLS) and sleep bruxism are associated with smoking. If a causal relation between the amount of tobacco consumed and bruxism seems increasingly plausible[19-21], data regarding the effects smoking has on RLS are still contradictory. It has been reported that cigarette smoking aggravates RLS symptoms[22] or on the contrary, it alleviates them[23]. Either way, an increased prevalence of nocturnal smoking in patients with RLS has been observed[24]. Both RLS and bruxism are sleep related disorders, causing sleep fragmentation and poor quality sleep. More studies are needed to confirm the association.

1.2.2. Second-hand smoke, sleep architecture and SDB

Some recent studies suggested that passive smoking also influences sleep. Yolton *et al.* reported delays in sleep onset, more-frequent SDB (increasing risk with the magnitude of exposure), parasomnias and daytime sleepiness among children with asthma exposed to second-hand smoke[25]. The pathological mechanism is most likely related to the fact that smoke exposure acts as an UA irritant, increasing symptoms of SDB.

1.2.3. Tobacco withdrawal and pharmacological treatments for smoking cessation - effects on sleep architecture and SDB

People who quit smoking often complain of disturbed sleep. There is some objective proof that sleep fragmen-

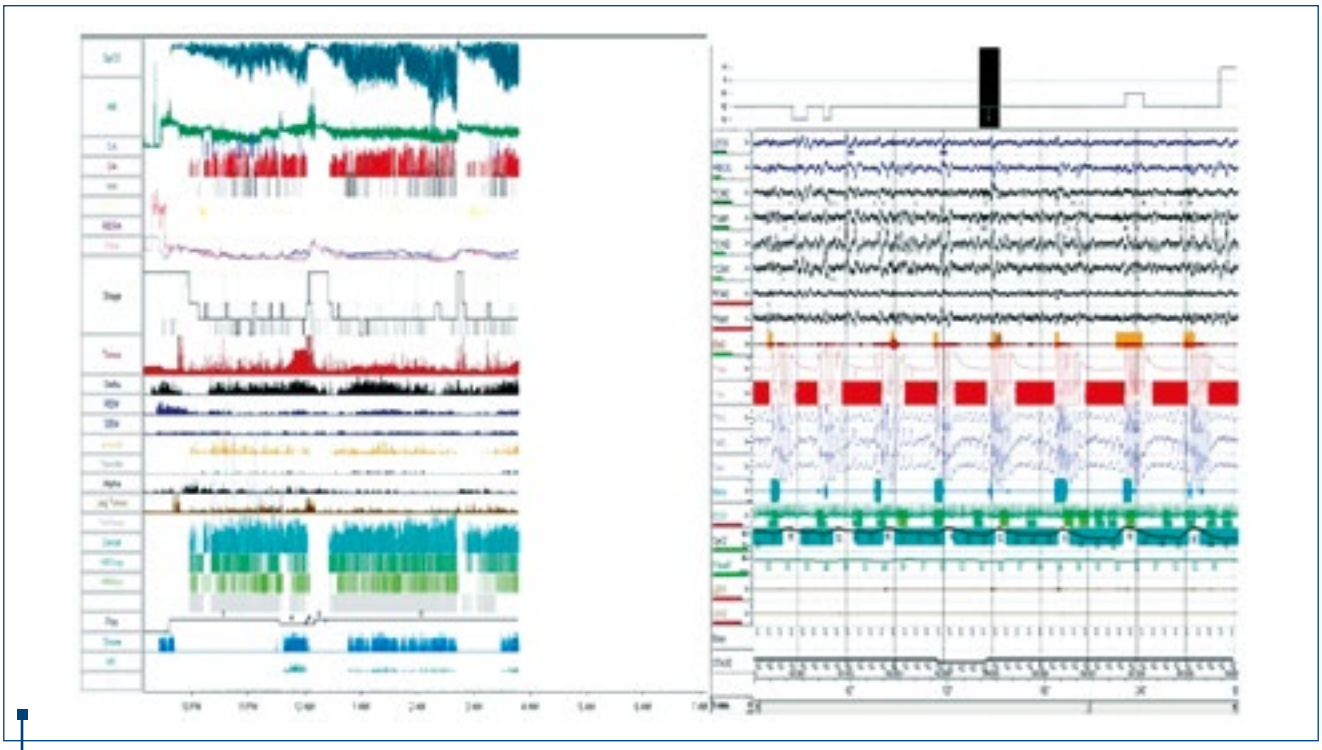

Figure 2: *Sleep study in a patient suffering from severe OSAS*
Left image: *entire night registration viewing mode- oxygen saturation (SpO2) varying significantly during sleep periods, with numerous respiratory events (OA=obstructive apnea, CA=central apnea, MA=mixed apnea, HYPO=hypopnea), and a profoundly altered sleep architecture (high percentage of stage 2 sleep, without REM sleep, high arousal index);*
Right image: *a polysomnographic images (5 minutes epoch) which reveals numerous obstructive apneas seen as the absence of registration waves on flow sensor (*Flow) and thermistor (Flow) with the persistence of thoracic and abdominal movements registered by two sensor belts as waves (THO, ABD), followed by arousals (visible on electroencephalogram C3M2, C4M1, O1M2, O2M1, F3M2, F4M1 and marked in orange on the electromyogram - EMG) and oxygen desaturations (registered on the SpO2 channel). REM=rapid eye movement.*

tation commonly occurs during the acute withdrawal period. Frequent arousals related to smoking cessation have daytime consequences that include sleepiness, mood swings and negative cardiovascular effects due to the repetitive bursts of sympathetic nervous system activation[26].

Pharmacological treatments play an important role in smoking cessation and there is some evidence which suggest that smoking-cessation treatment causes disrupted sleep, mostly in women[26]. A randomized clinical trial administering nicotine transdermal patch to non-smoking snorers showed that snoring was reduced, the number of apneas was not influenced and sleep quality deteriorated[12].

Although the effects of bupropion on sleep architecture have not been studied in healthy human subjects, it's effects on depressed individuals demonstrated that low-dose administration increased slow-wave sleep at the expense of stage 2 and higher-doses produced the opposite effect[27,28] and increased REM density, activity and percentage. Further studies are needed on influence of smoking-cessation treatment on sleep.

The effect of weight gain has to be mentioned, as it is a consequence of smoking cessation. Medium weight gain after smoking cessation is about 2 kg, but 10% of those who discontinue smoking experience a greater than 13 kg increase in weight [29]. Significant weight gain after smoking cessation can contribute to development of OSAS in susceptible individuals.

2. Smoking and sleep-disordered breathing

2.1. Relation of smoking with UARS and snoring

A relatively new topic of discussion is the upper airway resistance syndrome (UARS), which was defined after finding multiple arousals during sleep preceded by increased breathing effort without apnoea or hypopnoea, more clearly revealed by continuous recording of esophageal pressure[30].

The decreasing in UA resistance after nicotine administration has been demonstrated by Gothe[31] and Kashyap[32]. They imply a possible association between smoking and UARS. Moreover, not even the smoking habit is associated with apnea-hypopnea index (AHI) ≥5, but its influence on arousal index, Epworth score and oxyhemoglobin desaturation during sleep can suggest a key role in UARS[33].

If the role smoking habits play in UARS still needs to be clarified, the association between smoking and snoring has been extensively studied. Snoring is a frequent phenomenon (with up to 40% prevalence in men and 20% in women) occurring during sleep due to the vibration of oropharyngeal structures and is the expres-

sion of airflow resistance in the UA[34]. It is not only a condition that creates great discomfort to the patient and sleep disruption, but a higher risk of cardiovascular disease was also demonstrated[35,36].

Smoking proved to be an independent risk factor for snoring. The magnitude of this association differs significantly between studies, probably because of methodological factors and the different populations studied (mainly men)[37-39].

On 15,555 studied men and women, randomly selected from the general population, and Franklin concluded that current smoking, ex-smoking and passive smoking are major risk factors for habitual snoring; there was a direct relationship between snoring frequency and the amount of tobacco smoked or the exposure to passive smoking[40].

The association between snoring and smoking might be explained by several mechanisms: smoking increases the inflammatory response of the UA (histological changes in the sinus mucosa)[4,41] and provokes edema of the larynx due to potent mucosal irritants and ciliotoxins. Also smoking increases resistance in the nostrils[3] due to increased mucus secretion, and favors collapsibility of the URA by progressive reduction in blood levels of nicotine at night and reduced muscle tone[10].

Increased snoring in smokers, however, does not necessarily indicate an increase in the prevalence of OSAS in smokers.

2.2. Obstructive sleep apnea syndrome

The main respiratory events occurring in OSAS during sleep are apnea and hypopnea, meaning the absence, respectively the reduction of respiratory flow lasting longer than 10 seconds **(Figure 2).** Many factors have been identified to contribute to these events: modified airway anatomy, tissue characteristics, neuromuscular function and sleep–wake instability[42].

OSA became a first-order health care problem due to its high prevalence (25% in middle-aged men, 9% in women[43]), social and occupational repercussions, risk for development of cardiovascular and cerebrovascular diseases, its association with traffic accidents and its negative impact on both quality of life and survival[44,45].

2.2.1. Smoking prevalence in patients with OSAS

Smoking prevalence in patients suffering from OSAS is not very well documented. Kashyap *et al.* found that smoking has a higher prevalence among patients with OSAS of 35%, compared to 18% in controls (without OSAS). He hypothesized that cigarette smoke may be an independent risk factor for OSAS as current smokers had a 2.5 times greater probability of having OSAS than former smokers and nonsmokers combined (OR=2.5, CI:1.3-4.7, p=0.0049), and a 2.8 times greater probability of having OSAS than former smokers alone (OR=2.8, CI:1.4-5.4, p=0.0028) after elimination of confounding factors. Ex-smokers were not more likely to have OSAS compared to never smokers (OR=1.2, CI: 0.55-2.7, p=0.64), suggesting that active smoking is the risk factor, not lifetime exposure[32].

Hoffstein demonstrated that, although smoking status and amount of pack-years smoked was not associated with an increased AHI, there was a greater number of current smokers and higher average of pack-years among patients with AHI ≥50 than among those with AHI <10[46].

2.2.2. The importance of smoking and OSA association

a) Cardiovascular disease

Many cohort studies have suggested that OSAS is a risk factor for mortality associated with cardiovascular disease[16,47]. The effects smoking has on the cardiovascular system and the mortality it generates have been exhaustively documented[48,49]. However, these studies had a relatively small number of participants, included mostly advanced forms of OSA, are not randomized and registered a limited number of deaths, except Wisconsin Sleep Study Cohort and SHHA that brought strong evidence about independent association of OSAS with all-cause and cardiovascular disease–related mortality[17].

In relation to OSAS, it is important to mention the synergistic effect these two diseases seem to have. They increase the risk of arterial hypertension, promote atherosclerosis and increase cardiovascular morbidity. The pathophysiological mechanism by which they cause these effects is mainly related to the oxidative stress and inflammation, due to synergistic effect on some biochemical cardiovascular risk markers. Smokers with severe OSAS have a greater cardiovascular risk than smokers with mild-moderate OSAS and never-smokers[50].

The results of Marin indicate that patients with severe OSA smoking at least 20 cigarettes per day have greater cardiovascular risk compared to smokers with mild forms of disease or non-smoking OSAS patients[44,50].

b) The overlap syndrome

The association between OSAS and chronic obstructive pulmonary disease (COPD) is known as overlap syndrome (OS) and should be well investigated in smoking patients, firstly because the common risk factor (represented by smoking) and secondly because of the altercated pathological mechanism that disrupt both sleeping, but also oxygenation during the night, with a great impact on health, comorbidities and mortality[51]. About 0.5-1% of population suffers from OS[52]. The poor quality of sleep reported by patients has led to sleep analysis using objective and subjective measurements, which reveal that patients with OS suffer greater and longer sleep-related desaturation than COPD patients having the same degree of bronchial obstruction, having a higher risk for COPD exacerbations and a higher mortality risk[53]. They also have a greater risk of hypercapnic respiratory failure, pulmonary hypertension and other cardiovascular disease[52,54,55], leading to a greater cardiovascular mortality.

Overlap syndrome is a complex, individual disease, which deserves a separate debate.

2.2.3. Smoking as a risk factor for OSAS

There are some well conducted studies trying to demonstrate the role of smoking as a risk factor for OSAS. Smoking causes chronic nasopharyngeal inflammation and increasing UA resistance[3,4,41] leading to collapse

during sleep. In addition, smoking might cause a diminished arousal response to apnea, favoring an increased frequency and duration of apneic episodes, a theory which has been clearly proven only in neonates[56].

Recent studies **(Table 2)** used polysomnography (PSG) for an objective measurement. Wetter conducted the first epidemiologic study on patients who underwent PSG, in order to analyze the relationship between smoking and OSAS, and found that smokers had a greater tendency to present snoring and moderate-to-severe SDB than nonsmokers. A dose-response association was discovered, especially in heavy smokers (>40 pack-years), who proved to have 40 times the risk of never-smokers in developing SDB[10].

Kashyap reported that the prevalence of current smokers among patients with AHI>10 was higher compared to normal controls[32]. Up to date, Hoffstein published the largest population study which contradicted previous data: a higher percentage of active smokers were detected only among severe patients (AHI>50/h). Even though smokers had 1.5 times the risk of non-smokers in having OSAS, after adjustment for age, sex and BMI, the difference disappeared. The cause of disagreement with previous results may be the greater severity of OSAS in the selected population[46].

The results were sustained in the same year by Casasola, who demonstrated on healthy volunteers subjected to nocturnal domiciliary polygraphy that cigarette smoking doesn't seem to be associated with increased apneic activity during sleep, but is related to a lower nocturnal oxygen saturation which was significantly correlated with pack-years index[57].

On the other hand, Kim proved that compared to non-smokers, moderate-to-severe OSAS was more common, with higher apnea index, hypopnea index and desaturation index, and related that to a thickness of the lamina propria of the uvula, increasing with OSAS severity[58].

The question of whether and how smoking habits and sleep are related is only partially answered[6,15,18,46]. Only a few studies analyzed former-smokers[10,18,32,46] or the degree of exposure (pack-years index)[32,46]. Conway highlighted the association of the amount of pack-years smoked with sleep fragmentation and night-time oxyhemoglobin desaturation, which was stronger in current smokers compared to former smokers[33]. When comparing sleep architecture in all status groups, the author reached the same results as Zhang[18]: active smokers had a higher percent of stage 1 sleep and a lower percent of slow-wave sleep compared to non-smokers. The author also found a relation between smoking habits and sleep fragmentation by proving that current and former smokers registered higher arousal index compared with never-smokers and that the arousal index was also dependent of the amount of nicotine exposure (higher arousal index among subjects with pack-years ≥15 compared to subjects with pack-years <15). Higher exposure to smoking (pack-years ≥15) was also related to higher Epworth score, suggesting once more that smoking severity plays a role in sleep disturbances. On the other hand, they found no differences in mean AHI among current, former and non-smokers[33].

These findings are objective proof of previous reports of nocturnal awakenings, difficulty in maintaining sleep and in waking-up, poor quality sleep inducing lower daytime performances, but contradict the theory of an association between smoking and AHI[5,6].

2.2.4 Smoking as self-treatment in OSAS patients

OSAS is an important cause of altered sleep quality and quantity, impaired attention or cognition, irritability and daytime sleepiness[42]. Smoking withdrawal only adds to these effects by creating cravings, depression, increased frequency and duration of lapses in attention, delayed response to stimuli, sleep fragmentation and shift toward lighter stages of sleep[59,60].

Hamidovic and de Wit conducted a questionnaire-based study, on healthy smokers before and after two days of smoking abstinence leading to increased subjective feelings of fatigue. The study revealed that sleep deprivation increases smoking in order to counter its effects[61].

Moreover, tobacco withdrawal during 12 hours of overnight smoking cessation can alter cognitive abilities, deficits which can be reversed by administration of nicotine[60].

It is only natural to assume that the combined effects on diurnal symptoms of OSAS and smoking abstinence could increase the need these patients have to smoke in order to counteract the fatigue or difficulty concentrating.

Actually the concept of administering nicotine in order to treat OSAS symptoms is no novelty. Gothe reported on 8 subjects that nicotine gum administrated prior to sleep reduces UA resistance followed by a decrease in the total number and duration of obstructive and mixed apneas in the first hours of sleep[31]. A randomized placebo-controlled trial willing to evaluate the acute effect of the use of transdermal nicotine patches trial in 20 non-smoker patients with mild OSA didn't observe AHI or snoring improvement after nicotine administration, but a significant negative effect on sleep architecture[12].

At the time being, the use of nicotine is not considered a therapeutic option for improving the respiratory obstructions that characterize OSAS.

2.2.5 The importance of smoking cessation in OSAS

As we discussed before, smokers deprived of sleep, including those with OSAS, can increase the consumption of nicotine to counteract the effects of sleep deprivation[61]. Treating OSAS and its consequences might be a necessary step on the road to a successful tobacco cessation[62]. In this case, understanding the OSAS-tobacco relationship is mandatory for the development of a tobacco prevention program. In routine clinical practice, OSAS patients should be treated with continuous positive airway pressure (CPAP). A healthier lifestyle, including smoking cessation, should be strongly recommended also. Non-compliance to CPAP therapy is an important issue and smoking seems to be playing a

significant role, especially in old people[63], maybe because of the odor that smoking induces to the CPAP mask.

Yegneswaran and Shapiro made a bold statement after their analysis of data from the Busselton Health Study[47]: non-compliance to CPAP treatment for those with severe OSAS is even more dangerous than smoking heavily[64]. Their results were contested by Marshall[65] who claim that the majority of scientific evidence does not support Yegneswaran and Shapiro's conclusion, but fortunately raising suspicion was enough to pave the way for new questions regarding the growing importance of smoking cessation in OSAS patients.

On the other way, as in any situation a clear position against smoking habit should be embraced, an overview of smoking cessation effect on OSAS symptoms must be taken into account. The effect of interrupting smoking may be interpreted on short term (acute withdrawal period) or long term (becoming an ex-smoker instead of current smoker). As the aggravation of OSAS symptoms is temporary in the first case (being related to nicotine withdrawal, and not to an increase of AHI)[26], an effect of long term smoking cessation on OSA should be well described.

The risk of OSAS is the same in never smokers and former smokers (contrary to the active smokers), supporting the role of smoking cessation for preventing development of OSAS[32].

Regarding the sleep quality, long-term smoking cessation is beneficial: comparing former smokers with current smokers, the latter have worse sleep quality (less total sleep time, longer sleep onset latency, increased difficulty falling asleep, maintaining sleep, and waking up earlier)[66].

Studies evaluating the role of smoking cessation on OSAS severity, and also on specific obstructive mechanisms are lacking for the moment. Even if studies have demonstrated that current smokers have a higher risk of severe OSAS (as compared to non-smokers)[67], a prospective study assessing the objective polygraphic or polysomnographic studies before and after smoking cessation is not available.

Smoking cessation impact also other comorbidities (as COPD, chronic bronchitis, bronchial asthma, but also heart failure or ischemic heart disease), offering a better control of these diseases and diminishing the appearance of their nocturnal symptoms. For the OSAS patient, this may be equal to the improvement of OSAS related symptoms (as excessive daytime somnolence, insomnia, nocturnal dyspnea)[68].

2.2.6. Future directions

The relation between OSA and smoking is not well described yet. Even if major acquisitions have been made in this direction, there are still many things to be discovered. Objective measurement (of both smoking history and OSAS severity) should be used in pertinent, longitudinal studies. The effect of smoking cessation on OSA severity, as well as on objective assessment of each of the intricate comorbidities should be a priority, as it offers a huge argument in the fight against smoking. Adjusting for COPD and all other associated (and confounding) conditions will allow an independent assessment of the risk of smoking and OSAS[68].

A precise time from the smoking withdrawal to the annihilation of smoking-related risk of OSAS is not known yet and should be investigated.

Also, the reverse must be taken into account, and evaluating the impact of CPAP use for OSAS treatment on the cessation success rates is a necessity.

Studying the effect of electronic cigarettes on OSAS characteristics is mandatory, especially in the context of the huge marketing pressure related to them.

Discussion

Although demonstrated mostly by studies without objective measurements of sleep parameters, smoking influences sleep architecture and sleep deprivation seems to stimulate tobacco consumption.

At the moment, although the pathophysiological bases justifying the association of smoking and snoring are definite (via nicotine, nicotine withdrawal, smoking as a habit), the potential association between smoking and OSAS has not been definitively clarified. If such a relation exists, it has a weak significance. While reports of the effects smoking habits have on AHI are still contradictory, recent studies using objective sleep measurements showed that difficulties in falling asleep, maintaining sleep and daytime sleepiness in smokers are supported by a high arousal index and oxyhemoglobin desaturations during sleep. These mechanisms induce oxidative stress and disturbances in the normal redox state of cells, affecting mainly the cardiovascular system. Evidence of a synergistic effect of smoking and OSAS especially on cardiovascular morbidity and mortality would be of great interest, both clinically and epidemiologically. With such proof, smoking cessation may become a critical component in treating OSAS and its consequences.

The way smoking withdrawal and smoking cessation therapy (nicotine replacement therapy, bupropion) affect sleep, independently or synergically, is a matter of open debate. Prospective, randomized studies are needed in order to establish the beneficial effect smoking cessation has on OSAS. Future studies to investigate the recovery time for sleep respiratory parameters after smoking cessation and the effect of smoking on CPAP therapy are required.

Conclusions

Clinicians need to asses smoking status when considering treatment for OSAS. Even if there are no studies to prove the association of smoking and AHI and the best approach for treating smoking in patients with associated OSAS has not been established yet, due to the high prevalence of smoking among individuals with OSAS, patients should be well-informed to avoid smoking in order to prevent greater impairment of sleep parameters and potentially additive effects on the cardiovascular system. ■

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