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Review Article

Smoking and Sleep Disorders

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ABSTRACT

Snoring and sleep apnea-hypopnea syndrome (SAHS) are two disorders of considerable relevance due to their high prevalence in the general population and their notable morbidity and mortality, particularly in association with their harmful effects on the cardiovascular system. As well as sex, age, weight, craniofacial malformations, alcohol consumption, and use of hypnotic drugs, it has been suggested that smoking may be a risk factor for developing sleep-disordered breathing. While there is solid evidence for the independent association between snoring and smoking in both children and adults, it is still unclear whether smoking constitutes an independent risk factor for developing SAHS, despite the many studies carried out to assess this link. This is probably because the association, if it exists, is very weak.

Tabaco y trastornos del sueño

Palabras clave:
Tabaco
Síndrome de apneas-hipopneas obstructivas del sueño
Ronquido

RESUMEN

El ronquido y el síndrome de apneas-hipopneas durante el sueño (SAHS) son dos enfermedades con una importante relevancia, debido a su elevada prevalencia en la población general y a su destacable morbimortalidad, asociada sobre todo a sus consecuencias nocivas sobre el sistema cardiovascular. Además del sexo, la edad, el peso, las malformaciones craneofaciales, el consumo de alcohol y los fármacos hipnóticos, se ha postulado que el tabaco puede constituir un factor de riesgo para desarrollar trastornos respiratorios durante el sueño. Si bien existe una evidencia sólida de la asociación independiente entre ronquido y tabaco tanto en niños como en adultos, en el caso del SAHS, a pesar de haber numerosos trabajos que evalúan dicha cuestión, todavía no está suficientemente claro si el tabaco constituye un factor de riesgo independiente para el desarrollo de SAHS, probablemente porque, si tal asociación existe, debe de ser muy débil.

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Introduction

Snoring and sleep apnea-hypopnea syndrome (SAHS) are the most common sleep-related respiratory disorders. Snoring is a very common disorder that affects between 16% and 33% of men and between 8% and 9% of women.[1-4] It has been associated with excessive daytime sleepiness even when SAHS is not present,[5-7] and with increased cardiovascular risk,[8] diabetes mellitus,[9] and pregnancy-induced hypertension.[10]

According to the national consensus document,[11] SAHS is defined as a clinical picture of excessive drowsiness and cognitive-behavioral, respiratory, cardiac, metabolic, or inflammatory disorders secondary to repeated episodes of upper airway obstruction during sleep. These episodes are measured using the respiratory disturbance index. Thus, a respiratory disturbance index of greater than 5 h^{-1} associated with symptoms linked to the disease and not attributable to other causes is considered diagnostic of SAHS. The respiratory disturbance index is defined as the total number of apneas, hypopneas, and respiratory efforts associated with sleep disruptions per hour of sleep. Population studies indicate that the prevalence of SAHS is approximately 2% in women and 4% in men, of middle age in the general population.[12,13] Due to its high prevalence, social and occupational repercussions, development of cardiovascular diseases[14-17] and cerebrovascular diseases,[18] its association with traffic accidents,[19] and its negative impact on both quality of life[20] and survival,[21] it is considered a first-order health care problem,[22-31]

The classic risk factors associated with respiratory sleep disorders (RSD) are male sex,[32,33] obesity,[32] age,[32,33] consumption of alcohol and muscle relaxants or hypnotic drugs,[32,33] and malformations of the upper airway, such as retromicrognathia or redundant edematous velum.[32,34] As well as these factors, it may be necessary to consider smoking, the risk factor *par excellence* for most respiratory disorders,[35-37] with important repercussions on health and quality of life,[38-41] and still not completely controlled by currently available interventions.[42-48] Smoking is highly prevalent in patients with SAHS and data in the literature indicate that it may act as a risk factor for developing the syndrome. This review analyzes the pathophysiologic bases, prevalence, and most relevant studies of the interaction between smoking and RSD in both adults and children.

Snoring and Smoking

Snoring can be defined as a complex acoustic phenomenon that appears during sleep due to the vibration of oropharyngeal structures and expresses the existence of resistance to the airflow in the upper airway.[49] Its complexity is due to the interaction of 1 or more levels of the oropharynx (nasal, oral, etc), which can lead to a labile airway that behaves in an unstable and heterogeneous manner.[50]

Snoring is a clinical symptom, the importance of which was, until a few years ago, reduced to a social phenomenon causing problems with partners and cohabitation problems. In the past 20 years, special attention has been paid to snoring, probably linked to the increased study of sleep disorders; this trend has favored the study of snoring and investigation of its causes, pathophysiology and repercussion on health. Currently, snoring is considered a symptom within the spectrum of disorders grouped in the category of RSD,[51] which range from simple snoring to established apnea. The presence of these symptoms, to a greater or lesser extent, leads to suspicion of an underlying disease, which may range from simple snoring (patients who snore but do not present daytime sleepiness) to snoring associated with excessive sleepiness without witnessed apnea, and an established diagnosis of SAHS. Below, we analyze the possible association between smoking and snoring and SAHS.

Snoring is a frequent phenomenon, although with considerable variability, according to the published studies. In general, its prevalence is 40% in men and 20% in women.[52] The prevalence studies carried out in Spain[12,53-55] are shown in Table 1. The principal limitation of these studies is that most of them are based on the use of clinical questionnaires, so that the measurement of smoking is a subjective perception.

A number of risk factors have been linked to snoring, including age, sex, alcohol consumption, the use of certain drugs (hypnotic drugs, muscle relaxants), and obesity. Prevalence increases with age[56,57] (from 20 years of age in men and 40 years of age in women) and tends to decrease from the 7th decade on. It has also been shown that smoking is more frequent in men.[49] Obesity (body mass index [BMI]>25 kg/m^2) is the factor that has traditionally been most associated with snoring, the frequency of which increases in correlation with a higher BMI.[12,58] Alcohol consumption has also been linked to snoring, particularly when consumed late in the day. This effect is caused by increased relaxation of the oropharyngeal musculature, which makes it more collapsible and, therefore, leads to snoring.

Many anatomic disorders of the nose may accompany snoring, such as a deviated nasal septum, congestion and/or nasal polyps, enlarged uvula or soft palate, micrognathism, macroglossia, overdeveloped pharyngeal arches, tonsillar hypertrophy, and laryngeal polyps.[59-61] Snoring is also more frequent in the supine position, due to the posterior movement of the tongue, which, in the presence of other factors, can favor obstruction of the airway.

Several hypothesis may explain the potential association between snoring and smoking. First, smoking increases the inflammatory response of the upper airway.[56,62] Histologic changes have been reported in the sinus mucosa, such as hyperkeratosis or leukoplakia on the nasal mucosa of smokers.[63] Furthermore, smoking increases resistance in the nostrils, especially in young adults with asthma or rhinitis.[64] As well as cancer and other premalignant lesions linked to smoking, the larynx may also present Reinke edema—-a disease that is directly linked to tobacco smoke and that causes chronic irritation of the vocal cords and edema. Another reported pathogenic mechanism is the relationship between the onset of snoring with progressive reduction in blood concentrations of nicotine at night and reduced muscle tone due to this process[65] which favors collapsibility of the upper airway and, potentially, snoring.

Several studies have aimed to determine whether smoking is also a risk factor for snoring. In 1988, Bloom et al[56] published a study in which they evaluated the potential risk factors associated with snoring in 2187 white subjects from the Tucson Epidemiologic Study of Obstructive Airways Disease. Data were collected by means of self-completed questionnaires, which included questions on the presence and frequency of snoring and on consumption of alcohol and other drugs. Depending on smoking habits, participants were classified as nonsmokers, ex-smokers and active smokers and a complete smoking history of the latter 2 groups was included. A higher prevalence of snoring was observed in men than in women in subjects under 54 years of age, with a tendency to equalize in subjects over 64 years of age. Prevalence of smoking was also higher in obese subjects, even after adjusting for age and sex. The effect of obesity was greater in the younger group of women, with a 3-fold higher prevalence of snoring in obese women. The prevalence of smoking was higher in smokers than in nonsmokers, whereas ex-smokers presented a tendency to increased, though not significant, prevalence of smoking. Furthermore, after adjusting for obesity, the effect of smoking was shown to be greater in nonobese subjects. A correlation was also found between snoring and smoking intensity, with a prevalence of 43.9% in smokers of more than 30 cigarettes per day compared to 24.3% in smokers of 30 cigarettes per day or fewer (Figure 1). Interestingly, the prevalence of smoking appears to equal that of nonsmokers in the 4 years after smoking cessation.

Another similar study published the following year by Kauffmann et al[66] included 457 male Parisian police officers aged between 22

Table 1
Studies of Snoring Prevalence in Spain

Authors	Publication Year	Location	Results
Marín et al[53]	1997	Zaragoza	Severe (habitual) snorers >18 years of age Men: 63.6% Women: 36.3%
Zamarrón et al[55]	1999	Santiago de Compostela	Age: 20 to 70 years Snorers: 40.4% Snoring as a probably risk factor of AMI
Vela Bueno et al[54]	1999	Madrid	Age: >18 years 11.9% daily snoring
Duran et al[12]	2001	Vitoria	35% (ages: 30–70 years) Men: 46% Women: 25%

Abbreviation: AMI, acute myocardial infarction.

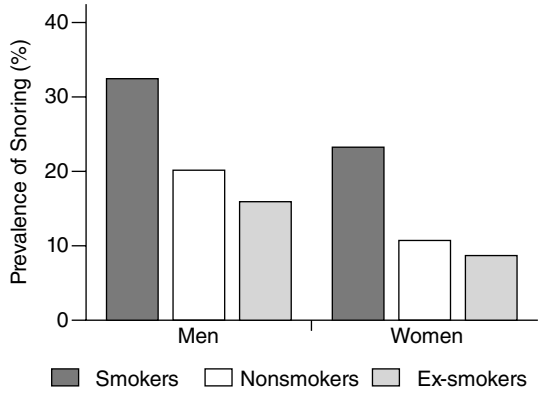

Figure 1. Effect of smoking on the prevalence of snoring. EX indicates ex-smokers; S, Smokers; NS, Never Smoked. (Adapted from Bloom et al[56])

and 54 years, who completed a questionnaire on respiratory symptoms, including snoring. Smoking was established in grams per day and participants were classified as nonsmokers, ex-smokers (at least 1 month without smoking), moderate smokers (<20 g/day), and heavy smokers (>20 g/day). Parents' smoking habits, alcohol consumption, and BMI were also recorded. Sixty percent of the subjects snored regularly and this was significantly linked to symptoms of rhinitis, ager, BMI, and smoking; there was also a correlation with the amount smoked daily. When logistic regression was performed, differences were detected between ex-smokers and nonsmokers (odds ration [OR], 1.67), between moderate smokers and heavy smokers (OR, 2.10), and between very heavy smokers and nonsmokers (OR, 2.89). The results support the data obtained by the group in the study by Bloom.[56] Nevertheless, these studies are limited by the fact that they are based on health questionnaires, with the inherent bias that this system may contain; furthermore, sleep studies were not performed and this makes objective comparison with other studies difficult.

Moreover, this correlation has not been shown in other population studies, such as that carried out on 294 Australian men aged between 40 and 60 years. All of the included subjects underwent a simplified domiciliary sleep study, in which 4 variables were recorded: snoring, heart rate, oxygen saturation, and body position. Snoring was measured by means of a microphone located on the throat for subsequent visual analysis. The overall prevalence of active smoking was 18%. Of the men studies, 81% snored for more than 10% of the night and 22% snored for more than half the night. Smokers snored for a greater percentage of the night than nonsmokers (40.9% compared to 31.3%) and the risk of snoring for more than half of the night was approximately 2 times greater among smokers than among nonsmokers (OR, 2.32). However, this risk was not linked to the number of cigarettes smoked.[58]

Larsson et al[67] carried out a study, using a validated questionnaire, to establish the prevalence of self-reported snoring, apnea and daytime sleepiness in patients with chronic bronchitis, recurrent bronchospasm, rhinitis, and diagnosed asthma in the general population of Sweden. The study included 5682 subjects from the general population (aged between 20 and 69 years). The questionnaire included questions on symptoms and respiratory disease, smoking and profession. Snoring was reported by 10.7% of the population, apnea by 6.8%, and daytime sleepiness by 28.3%. Age, male sex, chronic bronchitis, diagnosed asthma, rhinitis, and smoking were significantly linked to snoring and to snoring associated with daytime sleepiness. The OR was 1.55 for snoring in active smokers and 1.52 for snoring associated with daytime sleepiness. This relationship was maintained after adjusting for obstructive airway diseases. Apnea was also greater in smokers.

Stradling and Crosby[59] carried out a study of prevalence in 1001 men randomly selected from the general population, aged between 35 and 65 years. Each participant was administered a questionnaire on the possible factors associated with snoring and SAHS, including questions relating to alcohol consumption and smoking, nasal congestion and lesions, prior nasal surgery, history of adenotonsillectomy, use of sedatives, hypnotic drugs and other drugs. The study recorded anthropometric data, lung-function data (forced expiratory volume in the first second, forced vital capacity, and rest pulse oximetry), information on snoring (corroborated by the subject's partner where possible), and occupational data. Nighttime pulse oximetry was performed on all participants. The study also included a polysomnography study in the hospital in subjects with more than 5 desaturation episodes (of at least 4%) per hour of study. Analysis of the discontinuous variables showed a significant association between snoring and smoking. The prevalence of frequent snorers was 15% in the 632 nonsmokers compared to 30% in the 105 smokers of more than 15 cigarettes per day. Multiple linear regression showed that smoking was significantly associated with nasal congestion, neck circumference, and smoking.[59]

In 2004, Franklin et al[68] published a novel study in which they attempted to establish the impact of active and passive smoking and obesity on snoring. The study included a total of 15 555 men and women randomly selected from the general population, aged between 25 and 54 years, from several northern European countries, who answered a postal questionnaire. The questionnaire included a 5-point scale, based on the Basic Nordic Sleep Questionnaire, on snoring in the previous months. The participants were classified as nonsmokers, ex-smokers, and active smokers, and their degree of smoking was also quantified in grams of tobacco per day (1 g per cigarette and 5 g per cigar). Passive smokers were considered to be nonsmokers exposed on a daily basis to tobacco smoke in the home.

Chronic bronchitis was defined by indicative symptoms without a known diagnosis of asthma, and obesity was established as a BMI of greater than 30 kg/m^2. Habitual snoring was reported by 18.3% of subjects. Snoring was more prevalent in smokers (24%) and ex-smokers (20.3%) than in non-smokers (13.7%). It was also more frequent in passive smokers (19.8% compared to 13.3% in those not exposed to tobacco smoke in the home). A clear dose-response relationship was observed between smoking and the prevalence of snoring, which was higher in those who smoked more than 20 g of tobacco per day (Figure 2). Active and passive smoking were maintained as independent factors for snoring after adjusting for male sex, BMI, country, and age. Habitual snoring was most prevalent in the 4.1% of patients with clinical criteria for chronic bronchitis compared to those without these criteria (34.9% compared to 17.6%). Active smoking and chronic bronchitis were found to be independent and additive risk factors with for smoking. The risk attributable to snoring was 17.1% in active smokers and 2.2% in passive smokers. However, while the data are clear, they are subject to certain limitations, such as the lack of information on alcohol consumption and objective measurement (eg, lung function), and the possible existence of a bias in information relating to the social environment of the different countries, which might explain differences in prevalence of snoring and smoking in the different centers.[68]

Another, more recent, study examined another risk factor not considered in earlier studies: exposure to smoke from using biomass as a fuel. This study included patients from an epidemiologic study to establish the characteristics of respiratory symptoms during sleep and of other diseases, in order to determine the risk factors and their relationship to the observed snoring and apneas. A total of 12 270 people took part in the study; these were the parents and grandparents of the pupils of 20 randomly selected primary schools in rural and urban areas of Turkey. The data were collected using questionnaires on sleep-disordered breathing and state of anxiety. Snoring and apnea were more frequent in participants from rural areas, particularly in women exposed to biomass smoke. These differences were maintained after adjusting for sex, age, BMI, income, and level of education. The rate of smokers was similar in both rural and urban areas.[69] Nevertheless, the greater psychological stress of specific individuals may have led them to overestimate this dimension when self-assessing respiratory symptoms during sleep.

On analyzing the available scientific evidence, the results of the studies examined appear to be uniform, showing that, as well as the classic factors associated with snoring, such as age, BMI, male sex, and alcohol consumption, smoking constitutes an independent risk factor for smoking, though the magnitude of this association differs significantly between studies; this is probably due to methodological factors and to the fact that the populations studied are different.

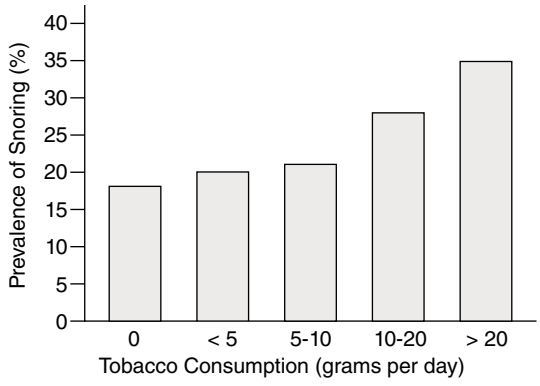

Figure 2. Prevalence of snoring and daily tobacco consumption. (Adapted from Franklin et al[68].)

Smoking and Sleep Apnea–Hypopnea Syndrome

As mentioned above, the association between snoring and smoking appears to be accepted. Furthermore, snoring is one of the symptoms that most commonly lead to consultations in patients with SAHS. Although the prevalence of SAHS among snorers has not been established, it reaches 50% of severe snorers in some series.[70,71] For this reason, it has been thought that smoking may be a factor associated with SAHS, together with obesity, age, and sex.

Before analyzing the available evidence, we should consider whether pathophysiologic bases exist that might explain a positive or negative association between smoking and SAHS. As has been stated, smoking causes chronic inflammation of the nasopharyngeal mucosa,[56,62-64] which leads to a reduction in its caliber and facilitates its collapse during sleep. Furthermore, smoking may be associated with a reduced arousal response to apnea, which would favor a greater frequency and duration of these apneas; however, to date, this has only been clearly shown in neonates.[72] Despite the certainty that smoking is associated with alterations in normal sleep architecture,[73,74] a provocative hypothesis has been formulated that asks whether patients with SAHS smoke as a form of self-treatment, as smoking would help them to remain more awake and to reduce their appetite and weight.[75] Moreover, neither tobacco nor nicotine have been shown to have harmful effects on the mechanics or muscular control of the upper airway[76] and, as will be discussed below, attempts have been made to test it as an alternative treatment in SAHS.[77,78]

The aforementioned studies by Bloom et al[56] and Kauffmann et al[66] are epidemiologic studies carried out on the general population, and the data were collected by means of questionnaires, without sleep studies to provide objective data on the events occurring during the night. Wetter et al[65] carried out the first epidemiologic study to approach the question of whether smoking is a risk factor for developing sleep-disordered breathing. The study included 811 people from the United States. All participants underwent an in-hospital polysomnography study and, according to the results, 5 categories of sleep-disordered breathing were established: a) no abnormalities (no snoring and an apnea hypopnea index [AHI] of less than 5 h^{-1}); b) snoring (snoring and AHI<5 h^{-1}); c) mild disorder (AHI between 5 and 15 h^{-1}); d) moderate-to-severe disorder (AHI>15 h^{-1}); and e) any type of disorder (AHI>5 h^{-1}). The study found that smokers snored more than nonsmokers (OR, 1.31; 95% confidence interval [CI], 0.92–1.86), even after adjusting for age, sex, BMI, and caffeine and alcohol consumption (OR, 1.26; 95% CI, 0.86–1.85), and had a greater tendency to present moderate-to-severe sleep-disordered breathing. This tendency was also observed when comparing ex-smokers with nonsmokers, although this association disappeared after adjusting for other factors. A dose-response association was also established between smoking and sleep-disordered breathing; this association was stronger in smokers of more than 40 pack-years (OR, 40.47; 95% CI, 2.37-50). Smokers of fewer than 20 cigarettes per day presented an increased risk of any type of sleep-related disorder (OR, 4.11; 95% CI, 1.41-11.99). Limitations of the study include the fact that objective measurements of smoking were not performed; this information was analyzed according to the responses to the questionnaires self-administered by the patients.

In 2001, Kashyap et al[79] published a study of patients and controls to determine the prevalence of smokers among patients with SAHS and to determine whether smoking is an independent risk factor. They included 214 participants (106 in the control group [AHI<5 h^{-1}] and 108 patients [AHI>10 h^{-1}]), all of whom underwent a nighttime in-hospital polysomnography study. Smoking was associated with a greater risk of SAHS, even after adjusting for BMI, sex, age, and alcohol consumption. Furthermore, significant differences were observed when comparing smokers with nonsmokers and ex-smokers: the risk of SAHS was 2.7 times greater in smokers than in

nonsmokers and ex-smokers as a group (OR, 2.7; 95% CI, 1.2-5.7), even after adjusting for the other variables.

Hoffstein[80] published the largest population study to date, with the aim of determining whether smoking is a risk factor for developing SAHS; the results contradicted previous data. The study population consisted of patients referred to a specialist with suspected sleep-disordered breathing. The study included 3509 patients, who provided a detailed history of smoking and underwent an in-hospital nighttime polysomnography study. The prevalence of smoking was similar in patients without apnea and patients with SAHS. A higher proportion of active smokers (27%) was only detected in more severe patients (AHI>50 h^{-1}); moreover, the total accumulated dose of tobacco was higher in these patients. In the statistical analysis, patients were stratified according to severity of AHI and, subsequently, according to their smoking history, and a univariate and multivariate regression were performed to establish the correlation between pack-years and AHI. The risk of snoring for smokers was twice that for nonsmokers; however, after adjusting for age, sex, and BMI, the possible additional risk of smoking was not significant. Also, when patients were divided into snorers and nonsnorers, no association was found between smoking and snoring after adjusting for age, sex, and BMI; this finding differed from the results of the studies by Bloom et al,[56] Kauffmann et al,[66] and Kashyap et al.[79] Using the same cutoff in the definition of SAHS (AHI>5 h^{-1}) as that used in the Wisconsin Sleep Cohort,[65] the study reproduced the results of the study by Hoffstein[80] since, although the risk of SAHS was 1.5 times greater in smokers, this difference disappeared after adjusting for age, sex, and BMI. The probable explanation of the disagreement with the results of previous studies is that the populations samples were different; in this study, the population included patients who were smokers with strongly suspected sleep-disordered breathing, predominantly men, with severe apnea, and this may have attenuated the possible independent effects of smoking on this disease, unlike in the studies carried out in the general population (Table 2).

One of the most recent studies on snoring and SAHS was carried out on 3136 Brazilian adults, using domiciliary questionnaires.[81] The independent variables considered were age, sex, skin color, marital status, socioeconomic level, smoking, alcohol consumption, regular physical activity, and BMI. The questionnaire also included questions on the sleep period (mean hours of sleep, latency period). Prevalence of snoring was 50.5% and that of obstructive apnea was 9.9%. After adjusting for different variables, habitual snoring was more frequent in men, older subjects, active smokers (OR, 1.15; 95% CI, 1.07-1.25), regular drinkers, and obese subjects. Moreover, the presence of reported apnea was associated with male sex, age, active smoking (OR, 1.60; 95% CI, 1.25-2.05), and obesity. As in other studies, the use of questionnaires with dichotomous variables or value scales and the fact that sleep studies were not conducted favored bias in the information, particularly in subjective variables such as snoring and experienced apnea. Also, the definitions of habitual snoring and experienced apnea may differ and this would help to explain the different results.[80,81]

Several studies have been published that provide interesting data, although their sample sizes are smaller. Blazejova et al[82] compared BMI, prevalence of obesity, arterial hypertension, and smoking in 356 patients with SAHS (287 men and 69 women aged between 25 and 64 years) and in 2353 people representing 1% of the Czech general population. They observed differences in the group of men aged between 35 and 64 years in prevalence of systemic arterial hypertension and differences in the 45-64 years age group in prevalence of smoking; this indicates that the prevalence of smoking in patients with SAHS is greater than that in a sample of the general population. Casasola et al[83] carried out a study to evaluate the effect of smoking on sleep-disordered breathing in the general population. They studied 38 healthy volunteers (21 men and 17 women aged between 30 and 54 years), who underwent home sleep monitoring. AHI, and apnea and oxygen desaturation indexes were determined and the nocturnal hypoxia index was calculated. Carboxyhemoglobin concentrations in blood were measured in all participants before and after the sleep period. No significant differences were found in the AHI and apnea and oxygen desaturation indexes between smokers and nonsmokers. Furthermore, smokers presented a higher nocturnal hypoxia index than nonsmokers and significant correlations were found in smokers between this index, smoking levels measured in pack-years, and carboxyhemoglobin concentrations. Oxygen saturation was significantly lower in smokers than in nonsmokers. Another important fact is that the AHI and desaturation showed a significant relationship to habitual snoring. Although it was not possible to establish an association between smoking and sleep apnea, it was shown that smoking is associated with reduced nocturnal oxygen saturation.

At present, while the pathophysiologic bases that might justify a potential association between smoking and SAHS, no study has definitively shown this association. The contradictory results are probably due to the differences in the populations studied and the methods used. Nevertheless, these discrepancies show that, if smoking is associated with SAHS, it is a weak association, so that smoking would be of less importance in the pathophysiology of nighttime apnea.

Smoking and Sleep Disorders in Children

Childhood SAHS differs from adult SAHS both in its etiology and in its clinical manifestations, diagnosis, and treatment. It is a form of sleep-disordered breathing characterized by partial, prolonged obstruction of the upper airway and/or and intermittent complete obstruction that interrupts ventilation during sleep and normal sleep patterns. The guiding symptom in boys is snoring and conventional polysomnography is the gold-standard test for diagnosing the condition. The American Thoracic Society considers a diagnosis of SAHS in children to be an AHI of 3 h^{-1} or greater, provided the patient presents associated indicative clinical signs and symptoms. The most common cause of SAHS in children is hypertrophy of the tonsillar and adenoid lymphoid tissue; resolution is usually complete following adenotonsillectomy. Other surgical procedures may be used (uvulo-palato-pharyngoplasty, maxillofacial surgery, etc), depending on the presence of other causes. If adenotonsillectomy fails, the second line of treatment is continuous positive airway pressure.[84]

Primary or simple snoring is snoring not accompanied by disorders recorded by polysomnography. Its harmless nature is currently the subject of debate as it has been associated with neurocognitive disorders and low achievement at school.[85-87]

The diseases caused by passive smoking in children may be the result of exposure to tobacco smoke before and/or after birth. The prevalence of smoking in pregnant mothers is high. In a Spanish study,[88] 43.4% of pregnant women were smokers before pregnancy and, of these women, 42.2% ceased smoking. At the end of pregnancy, 25.2% of women in the study continued to smoke.

In the US, the prevalence of exposure to tobacco smoke in children varies between 35% and 80%, depending on the method of measurement used and the population studied.[89] In a recent Spanish study,[90] approximately 56% of children and adolescents, aged between 6 and 18 years, were exposed to tobacco smoke from one of the parents.

Some components of tobacco smoke, including nicotine, cross the placental barrier.[90] The placentas of pregnant women exposed to tobacco smoke present pathologic abnormalities (ischemic necrosis, retroplacental infarction, increased intervillous space, etc) that, together with increased concentrations of carboxyhemoglobin in the blood of the pregnant woman, lead to a higher number of complications during pregnancy and more intense fetal hypoxia.[91]

Table 2
Main Studies on the Link Between Smoking, Snoring, and Sleep Apnea–Hypopnea Syndrome

Authors	Population	No. of Patients	Sleep Study	Smoking History	Results
Bloom et al[56] (1988)	General population	1359	No	Non-smokers, ex-smokers, and active smokers Pack-years	1. 38% (compared to 20%) of snorers among smokers of >30 pack years 2. 15-fold risk of snoring among male smokers and obese men
Kauffmann et al[66] (1989)	General population	457	No	Non-smokers, ex-smokers, and active smokers Grams of tobacco/day	1. 70% (compared to 50%) of snorers among smokers of >20 g/day 2. 3-fold risk of snoring among heavy smokers
Wetter et al[65]	General	811	Yes	Non-smokers, ex-smokers, Cigarettes/day	3-fold risk of AHI > 5 in active smokers and active smokers(1994) population
Kashyap et al[79] (2001)	SAHS consultation	214	Yes	Non-smokers, ex-smokers, and active smokers	35% (compared to 18%) of smokers with SAHS 2.5-fold risk of SAHS in smokers (adjusted)
Hoffstein[80] (2002)	SAHS consultation	3267	Yes	Non-smokers, ex-smokers, and active smokers Pack years	No greater risk among smokers after adjusting for sex, weight, and age
Franklin et al[68] (2004)	General population	15 555	No	Non-smokers, ex-smokers, and active and passive smokers Grams of tobacco/day	1. Snoring more prevalent in smokers (24%) and ex-smokers (20.3%) than in non-smokers (13.7%) 2. Snoring more prevalent in passive smokers (19.8%) than in people not exposed to smoke (13.3%) 3. Higher prevalence of snoring in smokers of >20 g tobacco/day (P<.0001) 4. Active and passive smoking as independent risk factors for snoring

Abbreviation: AHI, apnea-hypopnea index.

By means of complex interactions between the neurochemical and vascular systems, exposure to nicotine during pregnancy affects the development of the regions of the brain stem associated with regulating waking and with cardiorespiratory homeostasis. Several studies have shown that children exposed to tobacco smoke during or after pregnancy have a higher waking threshold; ie, they have an abnormal capacity for both spontaneous arousals and evoked arousals in response to auditory stimuli or when subjected to hypoxia and/or hypercapnia.[72,92,93] The effect of exposure to nicotine has also been observed on the modulation of arousal in rat models, which revealed difficulty in autoresuscitation after brief periods of induced hypoxia.[94] All this appears to be of considerable relevance, as arousals are thought to be a defence mechanism that protect against potential respiratory lesions during sleep. Arousal in SAHS is associated with increased muscle tome in the upper airway and this makes it possible to re-establish the permeability to the passage of air and to reinstate breathing.[95]

Several studies have been published in recent years, linking exposure to tobacco smoke during or after pregnancy to sleep-disordered breathing in childhood (Table 3). A study that included 509 subjects (267 boys and 242 girls; 115 neonates in the first week of life and 394 approximately 11 weeks old), whose mothers were stratified into nonsmokers (did not smoke during pregnancy), mild smokers (between 1 and 9 cigarettes per day), and smokers (? 10 cigarettes per day), linked smoking during pregnancy to increased frequency and duration of obstructive apnea in children. Furthermore, the link between maternal smoking and the number of apneas in the children was dosis-dependent. The relative risk of obstructive apnea in the children of mothers who smoked during pregnancy was 2.76 (95% CI, 1.63-4.69). Smoking during pregnancy, together with low birth weight and profuse sweating during sleep, were identified as independent risk factors for obstructive sleep apnea.[96]

Franco et al[92] studied 68 children (26 neonates and 42 children aged between 4 and 21 weeks) and found that those exposed to tobacco smoke during pregnancy presented a higher frequency of obstructive apnea (median, 3.1 h^{-1}) than those not exposed (median, 1 h^{-1}), although the mean duration of obstructive apnea, unlike in the study by Kahn et al,[96] was similar in both groups.

As well as the effect of maternal smoking during pregnancy on sleep-disordered breathing in children, other authors have studied the effect of exposure to tobacco smoke from the parents on these disorders. In a study of 1615 children aged between 6 and 13 years, Corbo et al[97] found that passive smoking was associated with snoring. The prevalence of habitual smoking increased significantly with the number of cigarettes smoked by the parents (5.5% in children of nonsmokers and 8.8% in children of smokers of 20 or more cigarettes per day).

Another study of 5728 children aged between 5 and 7 years, the main aim of which was to link sleep-disordered breathing with attention deficit hyperactivity disorder, found an increased risk of snoring, in a subsample of 3374 children, in the children of parents who smoked: father, OR=1.83 (95% CI, 1.43-2.35); mother, OR=2.86 (95% CI, 2.14-3.82); both parents, OR=4.35 (95% CI, 3.17-5.96). A subgroup of children with symptoms of attention deficit hyperactivity disorder underwent a polysomnography study, although the effect of exposure to tobacco smoke from the parents was not studied in association with the presence or absence of SAHS.[98] Ersu et al[99] studied 2147 schoolchildren in Istanbul to determine the prevalence of snoring and to evaluate the symptoms of sleep-disordered breathing in children. The overall presence of habitual snoring in children aged between 5 and 13 years was 7%. A greater proportion of the parents of children who habitually snored were smokers (mothers, 46.2%; fathers, 65.5%) than the parents of children who did not snore (27.5% and 53.8%, respectively). The harmful effect of smoking on snoring in children was greater if the mother smoked, as the risk of the children snoring was more than double that when the father smoked (OR, 2.3 and 1.6, respectively). The authors attribute this finding to the fact that Turkish children traditionally spend more time with their mothers. The final conclusion of this study was that exposure to tobacco smoke in the home increased the probability of habitual snoring in childhood, particularly if the mother smoked.

Kaditis et al[100] studied 3680 Greek children and adolescents (aged between 1 and 18 years) and found an association between habitual snoring and exposure to tobacco smoke in the home (prevalence of 69% for passive smoking among habitual snorers and 31% among nonsnorers). As in the study by Ersu et al,[99] the children of parents who smoked had a higher risk of snoring than those of parents who did not smoke; this risk was maintained even after adjusting for male sex, chronic nasal obstruction, infections of the lower tracheobronchial tree, parents or siblings who snored,

asthma, or adenoidectomy in the mother (adjusted OR, 1.4). In this Greek study, a polysomnography study was performed on 70 children randomly chosen from among the 307 snorers who had not undergone adenoidectomy or tonsillectomy. The estimated frequency of SAHS in this subgroup of children was 4.3%, although, unfortunately, the potential effect of exposure to tobacco smoke from the parents was not studied in this group of children diagnosed with SAHS. In a similar vein, Paavonen et al[101] of the Helsinki group carried out a retrospective cross-sectional study to determine whether very low birth weight (<1500 g) was associated with the risk of sleep-disordered breathing, defined as chronic snoring, in young adults (aged between 18 and 27 years). Chronic snoring was found to be more prevalent in the children of mothers who had smoked during pregnancy than in children of mothers who were nonsmokers (26.3% compared to 11.3%). The results lead to 2 interesting conclusions: premature children with very low birth weight have an increased risk of snoring in adulthood, but besides low birth weight, the most important independent risk factor for snoring is a history of maternal smoking during pregnancy (adjusted OR, 3.04).

A recent study with a large sample size (in a population of 6811 British children aged between 1 and 4 years) to determine the prevalence, severity, and risk factors of snoring found a prevalence of habitual snoring in children of 7.9%. After adjusting for the other environmental study factors, age, sex, ethnic group, and socioeconomic factors, passive smoking in the home was found to be an independent risk factor for habitual snoring in children; this risk increased if both parents were active smokers (OR, 1.46 if only 1 parent smoked and 2.09 if both parents smoked). The fact that the association between passive smoking and snoring in children showed a dose-response relationship and the fact that this association was stronger in younger children who spent more time in the home, and that a third of cases of habitual snoring could be attributed to exposure to smoke (passive smoking and vehicular traffic) reveals the possible existence of a causal link between both entities.[102]

Most studies published on sleep-disordered breathing mention habitual smoking. Studies on SAHS are less plentiful, probably because diagnosis of SAHS requires performing polysomnography studies. In the case of snoring, questionnaires completed by the parents tend to be the method used for measurement.

Of the other forms of sleep-disordered breathing, due to its severity and high social and family impact, we will briefly mention sudden infant death syndrome. This syndrome is defined as the sudden death of an infant under 1 year of age, which cannot be explained after a thorough investigation of the case, with complete autopsy, examination of the place of the death and a review of the clinical history.[103] Maternal smoking is a risk factor for this syndrome[104] and the risk increases with the number of cigarettes smoked per day.

In conclusion, exposure to tobacco smoke during and after pregnancy appears to be an avoidable factor for developing sleep-disordered breathing in childhood and is better established in the cases of snoring than in SAHS.

Effect of Smoking and SAHS on Cardiovascular Risk

SAHS is a risk factor doe developing arteriosclerosis and cardiovascular morbidity.[17,105,106] The pathogenic mechanisms that favor this association include oxidative stress,[107,108] activation of inflammatory cells and mediators,[109] and increased adherence between leukocytes and inflammatory cells,[109] Smoking is also considered a cardiovascular risk factor associated with a greater prevalence of arteriosclerosis and has similar pathogenic pathways to that of SAHS. Smokers with SAHS have been shown to have higher levels of triglycerides and inflammatory markers (C-reactive protein, ceruloplasmin, and haptoglobin) and lower levels of high-density cholesterol than nonsmokers of the same age, weight, and with the same AHI. The highest concentrations of inflammatory molecules have been detected in patients with more severe SAHS who smoked, showing that there is a synergetic effect between smoking and SAHS in some of the biochemical markers of cardiovascular risk.[110] Although the data are preliminary, everything appears to indicate that patients with severe SAHS who smoke at least 1 packet per day have a higher cardiovascular risk than smokers with mild SAHS or patients with SAHS who do not smoke.[17,110]

Treating Smoking Dependence in Patients With SAHS

Administration of nicotine, either intravenously or topically applied to the anterior region of the medulla, increases the activity of the upper airway muscles, such as the genioglossus and the posterior cricoarytenoid. It has also been shown to cause reduced resistance of the upper airway in animal models.[78,111,112] The results of these lines of research led to the spread of the idea of using nicotine

Table 3
Studies Linking Exposure to Tobacco Smoke During or After Pregnancy to Sleep-Disordered Breathing in Children

Authors	No. of Patients	Age	PSG	Exposure to Tobacco Smoke	Results
Corbo et al[97], 1989	1615	6–13 years	No	After pregnancy	Increased prevalence of habitual snoring in children of parents who smoke compared to nonsmokers (8.8% compared to 5.5%)
Kahn et al[96], 1994	509	1–11 weeks	Yes	During pregnancy	Independent relative risk of obstructive apnea of 2.76
Franco et al[92], 1999	68	1–21 weeks	Yes	During pregnancy	Increased frequency of obstructive apnea in exposed children
O'Brien et al[98], 2003	5728	5–7 years	Yes (although the effect of smoking was not studied)	After pregnancy	Increased risk of snoring in children of smokers
Ersu et al[99], 2004	2147	5–13 years	No	After pregnancy	Exposure to tobacco smoke in the home increased the probability of habitual snoring in childhood, particularly if the mother smoked.
Kaditis et al[100], 2004	3.680	1–18 years	Yes (although the effect of smoking was not studied)	After pregnancy	Association between habitual snoring and exposure to tobacco smoke (adjusted OR, 1.4)
Pavoneen et al[101], 2007	327	18–27 years	No	During pregnancy	Chronic snoring more prevalent in adult offspring of mothers who smoked during pregnancy compared to children of nonsmokers (26.3% compared to 11.3%). Independent risk factor
Kuehni et al[102], 2008	6811	1–4 years	No	During pregnancy	Association between habitual smoking and 1 or 2 parents who smoke (OR, 1.46 and 2.09, respectively). Independent risk factor

Abbreviations: OR, odds ratio; PSG, respiratory polysomnography.

as a substance that could constitute a treatment modality in SAHS. Gothe et al[78] studied the effect of nicotine (administered in the form of chewing gum) in 5 patients with severe SAHS. They found a reduction in the total number of apnea episodes and of the length of sleep time with apnea, particularly a reduction in the number of episodes of obstructive and mixed apnea. Nevertheless, this is a preliminary non-controlled study with very few patients and the results cannot therefore be generalized. A subsequent study with a more appropriate design was therefore carried out to evaluate the acute effect of the use of transdermal nicotine patches in a randomized placebo-controlled trial in 20 patients with mild SAHS who were nonsmokers. Nicotine was not found to produce improvements in the AHI or in the snoring of the patients but it did have a significant negative effect on their sleep architecture, as it increased latency and a reduction in sleep efficiency, total sleep time, and percentage of REM sleep was detected.[77] The use of nicotine is not currently considered as an option for improving the respiratory obstructions that characterize SAHS.

To our knowledge, there are no studies that have examined the best approach for treating smoking in patients with associated SAHS. Some evidence exists that smoking cessation is accompanied by sleep fragmentation in the initial cessation period as part of the tobacco abstinence syndrome[113] and that certain drugs used to treat smoking, such as bupropion and nicotine, may lead to sleep disorders such as insomnia.[113] However, the role of each of these drugs has not been clearly defined.

In routine clinical practice, the greatest emphasis is on treating patients with mechanical therapeutic modalities, which have clearly shown their efficacy and effectiveness; however, on many occasions, insufficient effort is dedicated to recommending and helping patients to adopt healthier lifestyles, including smoking cessation, due to the high prevalence of smoking in the population with SAHS and to its probable harmful and potentially additive effects on the cardiovascular system.

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