Rhinitis and Sleep Apnea

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Introduction

Allergic rhinitis (AR), the most prevalent allergic disorder, and nonallergic rhinitis affect more than 25% of the population [1]. AR is characterized by local symptoms, such as nasal obstruction, itching, sneezing, rhinorrhea, and postnasal drip, as well as daytime sleepiness, fatigue, headaches, and malaise [1]. The latter systemic symptoms are especially related to poor performance and concentration at school and work, and to overall impairment of quality of life. It is generally accepted that complaints of sleepiness, fatigue, and malaise are secondary to the action of high levels of inflammatory mediators, such as tumor necrosis factor (TNF)-α, interferon (IFN)-γ, and other cytokines on the hypothalamus [2]. There is an increasing body of evidence, however, that the disabilities might be partially due to nasal congestion and sleep-disordered breathing [3–5].

Obstructive sleep apnea syndrome (OSAS) is characterized by: 1) complete or partial collapse of the upper airways during sleep, with consequent cessation of breathing, despite ongoing respiratory effort; and 2) coexistent daytime somnolence. OSAS is an important health problem, given its associated adverse consequences and its prevalence of at least 4%. Two kinds of clinical sequelae are associated with the disorder. Neuropsychiatric complications include sleepiness; depression; cognitive dysfunction; disruption of professional, family, and social life; and inattention that can result in road and industrial accidents. Cardiovascular complications include pulmonary and systemic hypertension due to chronic sleep-related hypoventilation, congestive heart failure, coronary heart disease, myocardial infarction, and stroke [6].

Obesity, increased neck circumference, aging, male sex, acromegaly, hypothyroidism, and relatively rare craniofacial abnormalities are strong risk factors for sleep-disordered breathing (SDB). Currently, the most important clinical risk factors are those of high prevalence that potentially can be modified [7]. Rhinitis meets these criteria, because it is a syndrome of high and increasing prevalence with relatively easily modified nasal congestion as a major contributing factor. Although earlier studies failed to demonstrate a linear correlation between nasal resistance and the severity of OSA [7–9], in 2000, Lofaso et al. [10] used stepwise multiple regression analysis to show that daytime nasal obstruction represented an independent risk factor for OSAS. Rhinitis had a weaker correlation than cephalometric landmarks, obesity, and male sex, but was stronger than age. Recently, several reviews discussing the role of nasal obstruction in the genesis of SDB have been published [11,12•,13].

Finally, OSAS might be a chronic inflammatory condition characterized by high levels of cytokines and inflammatory mediators that are similar to those of allergic rhinitis and asthma. Asthma might be more severe and difficult to control if OSA is present. Nasal continuous positive airway pressure (nCPAP) therapy can improve both the OSA and asthma [14,15]. The inflammatory mediators generated by OSA could possibly account for the cardiovascular and asthmatic complications [16•]. The cause of the OSA-related inflammation and its role in rhinitis are still open to debate.

Scope of Sleep-disordered Breathing

Sleep-disordered breathing is a large entity encompassing a variety of conditions of sleep-related regular respiratory
disturbances. One could represent it as a continuum [17•]: Intermittent snoring → Persistent or habitual snoring → Upper airway resistance syndrome → Mild OSAS → Severe OSAS → Obesity–hypoventilation syndrome.

The mildest form is snoring, ranging from intermittent to persistent, with lack of any detrimental effect on individual health. Snoring affects 35% of the middle-aged population, with a distribution of 44% men and 28% women. It becomes more common with age [18]. Snoring is produced by vibration of the soft palate and partially collapsed pharyngeal walls due to turbulent airflow. States causing nasal obstruction, such as nasal polyps, hypertrophied turbinate, and nasal septal deviation are often involved in this process. Recently, a population-based cohort study showed that nasal congestion at night is a strong independent risk factor for habitual snoring with an odds ratio of 4.9 [18].

At the other end of the spectrum is Pickwick or obesity-hypoventilation syndrome. This is the most severe form of SDB, and is characterized by persistent hypoxia and hypercapnia, high morbidity, and mortality.

In the middle of the continuum is OSAS. Some additional terms are needed to outline this disorder. Apnea is defined as cessation of airflow for at least 10 seconds. It could be central, obstructive, or mixed. Central sleep apnea, which is rare and beyond the scope of this review, is due to absence of brainstem-derived respiratory efforts. Obstructive sleep apnea is much more common and results from complete obstruction of the upper airways, despite persistent ventilatory effort. Hypopnea results from incomplete upper airway obstruction, and is defined by at least a 30% reduction of airflow. The apnea–hypopnea index (AHI) is the average number of apnea and hypopnea events per hour of sleep. AHI less than 5 is considered normal. OSAS is characterized by an AHI of 5 or higher, and is associated with a 4% decrease in oxygen saturation. OSA is divided into three severity levels: mild with AHI of 5 to 15; moderate with AHI of 15 to 30; and severe with AHI higher than 30. Apnea and hypopnea always cause arousal. These repetitive arousals underlie sleep fragmentation, resulting in daytime sleepiness. OSA, together with daytime sleepiness, constitutes OSAS [19].

Subgroups of patients have excessive daytime sleepiness because of repetitive nocturnal arousals, without apnea, hypopnea, or oxygen desaturation. In these cases, the airflow channel of the nocturnal polysomnogram shows less severe inspiratory flow limitation. Inspiratory esophageal pressures show repetitive, increased upper airway resistance. The respiratory efforts aimed at overcoming this increased upper airway resistance result in transient arousals. The term respiratory effort-related arousal (RERA) is applied to this event.

Guilleminault et al. [20] noted that the repetitive RERAs were pathognomonic for the condition and introduced the term “upper airways resistance syndrome” (UARS). Because nasal resistance is responsible for at least 40% of total airway resistance, its increase could result in UARS. UARS is the mildest form of SDB and shows better sleep fragmentation responses with treatment of nasal congestion than other OSA patients [12••, 21]. Like OSA, UARS is characterized by excessive daytime sleepiness and fitful sleep. However, snoring is not present in all patients. Although UARS was often placed between snoring and OSAS, it could be a distinct disorder [22]. Unlike OSA, UARS patients are predominantly nonobese, younger women with histories of fainting, cold extremities, low blood pressure, and postural hypotension [22]. These patients frequently complain of sleep-onset insomnia, fatigue, headaches, depression, irritable bowel syndrome (IBS), bruxism (teeth grinding), gastroesophageal reflux disease, and rhinitis [23]. The arousal threshold for increased inspiratory effort is elevated in OSA, but is lower than normal in UARS. As a result, UARS patients wake up very easily in response to even mild increases in respiratory effort. Guilleminault and Chowdhuri [22] hypothesize that different functional arousal pathways are dysfunctional in the two syndromes. Blunted mechanoreceptor responses predominate in OSA patients, whereas UARS patients have intact or even increased sensitivity of mechanoreceptor systems.

Electroencephalograms (EEGs) show that delta sleep and the percentage of sleep spent in alpha rhythms are relatively increased in UARS patients. Delta sleep is decreased in OSA patients. UARS patients have evidence of “alpha–delta sleep.” This is the appearance of waking alpha rhythms that intrude into the slow-wave delta rhythm that characterizes deep sleep. This EEG finding is not a feature of OSA. Curiously, “alpha–delta sleep” is widespread in disorders characterized by chronic fatigue. These include chronic fatigue syndrome, fibromyalgia, migraine/tension headache syndrome, IBS, and temporomandibular joint syndrome (TMJ). Gold et al. [23] demonstrated a correlation between UARS and increasing prevalence of alpha–delta rhythm, IBS, headache, and sleep-onset insomnia. Patients with OSA had low correlations with these conditions. Rhinitis was present in approximately 30% of UARS patients in this study.

Levander [24], in a recent review on the pathophysiology of dysfunctional disorders, discussed the concept of “sensory sensitization dysfunctional disorder” that could be applied to the functional somatic syndromes mentioned earlier and to dry eyes and mouth syndrome (SICCA syndrome), gastralgia, interstitial cystitis, chronic prostatitis, vestibulitis syndrome, and nonallergic rhinitis. Nonallergic rhinitis shows a significant overlap with chronic fatigue syndrome: 76% of chronic fatigue syndrome patients have significant rhinosinusitis complaints [25]. It is tempting to speculate that UARS is part of the spectrum of sensory sensitization dysfunction disorders. Coexisting nonallergic rhinitis could be an additional aggravating factor for UARS, resulting in increased inspiratory effort due to nasal obstruction.