Congestion and Sleep Impairment in Allergic Rhinitis

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Summary

Allergic rhinitis is a disease with an increasing prevalence throughout the world that severely affects the quality of life of individuals suffering from it. Nasal congestion is the most common and bothersome symptom, and is often associated with sleep-disordered breathing, which is thought to be the reason for sleep impairment in individuals with rhinitis. The end result is a decrease in quality of life and productivity and an increase in daytime sleepiness. Treatment with intranasal corticosteroids has been shown to reduce nasal congestion. Data on sleep-related end points from clinical trials of intranasal corticosteroids indicate that this reduction is associated with improved sleep, reduced daytime fatigue, and improved quality of life. Other therapies, such as montelukast, also have a positive influence on congestion and sleep. This review examines nasal congestion and the associated sleep impairment of allergic rhinitis patients. It explores the adverse effects of disturbed sleep on quality of life and how these conditions can be reduced by therapies that decrease congestion. *(Asian Pac J Allergy Immunol 2011;29:297-306)*

Key words: *Sleep, Allergic Rhinitis, Quality of Life, Daytime Somnolence*

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Introduction

Allergic rhinitis (AR) is thought to affect up to 40% of the population, and its prevalence is increasing. Estimates suggest that it affects 20 to 40 million people in the United States, including up to 40% of children.[1,2]

Nasal congestion, rhinorrhea, sneezing, and pruritus of the eyes, nose, and throat, are troublesome symptoms in patients with perennial AR (PAR).[1] Typical sleep-related problems seen in AR include sleep-disordered breathing, sleep apnea, and snoring, all of which are associated with nasal obstruction.[3]

The importance of congestion is noted in children and adults. The recent publication of the Pediatric Allergies in America survey emphasized that congestion is the main symptom affecting children.[4] Furthermore, a survey conducted in more than 7000 adults showed that, sleep disturbance played a major negative role in rhinitis patients.[5]

Sleep impairment is a significant problem for patients with AR, and nasal congestion is of the main causes. In a recent survey of individuals with AR, 68% of respondents with PAR and 48% with seasonal AR (SAR) reported that their condition interfered with sleep.[6] The socioeconomic burden of rhinitis is significant. It is estimated that more than 6 billion dollars was spent on prescription medications for AR in 2000.[1,2,7] The socioeconomic costs of these disorders include the costs of treatment reduced productivity, and the use of inappropriate therapies. Patients' quality of life is significantly affected by AR, as has been shown using generic health-related quality-of-life questionnaires such as the Medical Outcomes Study Short Form Health Survey and disease-specific measures such as the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ).[8,9]

Treatments that improve the symptoms of AR, particularly those that reduce nasal congestion, have been shown to improve patients' sleep and quality of life. Unfortunately, the data to prove that nasal congestion results in sleep disturbance is limited. Thus, further research is warranted. This review explores the importance of congestion in patients suffering from rhinitis. It also addresses the adverse

effects of disturbed sleep on the quality of life of patients with rhinitis and how these effects can be reduced by therapies addressing the underlying problems affecting sleep.

With the prevalence of rhinitis being 15% to 40% depending on methods used and populations surveyed, more than 50% of these individuals have congestion as their main symptom. Even more concerning is the effect that congestion has on those who experience it. In a study by Stull et al.,[10] congestion had a much greater effect on patients than any other symptom of rhinitis assessed. Specifically, congestion, as compared with the other symptoms of rhinitis, accounted for 73% of the outcomes that included poor sleep, missed work, and activity impairment. According to the individuals in this cohort, 30% of impaired sleep was secondary to congestion. Congestion alone was calculated to have a direct cost of 3.4 billion and an indirect cost of 3.1 billion US dollars.

In the Pediatric Allergies in America survey, congestion was found to be the main symptom affecting children, with 52% of respondents reporting that they experienced congestion most days of the week. Seventy-five percent of the respondents stated that congestion was the most bothersome symptom. When providers were asked a similar question, 92% believed that congestion was the worst symptom.[4] Patients with AR were more likely to go to work and participate suboptimally. Similarly, those in this cohort were less likely to be happy, energetic, peaceful, and full of life. Parents rated their children with rhinitis as being less healthy, less productive, having limited ability to work, and more likely to have difficulty performing tasks. Parents also thought that their child's rhinitis affected the child's ability to perform in school, activities, and sports. Lastly, 40% stated that allergies affected their sleep, 32% had difficulty getting to sleep, 26% awakened at night due to sleep problems, and 29% had a lack of good sleep.[4]

When adults were asked about their sleep, those with AR were more likely to have poor sleep compared to patients with nonallergic rhinitis and those without rhinitis symptoms. Only 3.2% of patients with AR symptoms in the previous month had 100% quality sleep during this time. This compared with 19.2% who had no symptoms of rhinitis.[5]

Evidence of Sleep Impairment

As noted, rhinitis is associated with sleep problems, daytime somnolence, and fatigue. The symptoms of AR—in particular nasal congestion—adversely affect sleep, and the degree of sleep impairment is used in the Allergic Rhinitis and its Impact on Asthma guidelines to classify AR severity.[4] Sleep disturbances associated with AR include sleep-disordered breathing (ranging from snoring to obstructive sleep apnea [OSA] and/or hypopnea) and microarousals,[11–13] Individuals with frequent night-time symptoms of rhinitis have been shown to be more likely to have chronic excessive daytime sleepiness or chronic nonrestorative sleep than those who rarely have such symptoms.[15] Studies using actigraphy have demonstrated objective evidence that adults with PAR have more sleep disturbance than healthy control participants.[16]

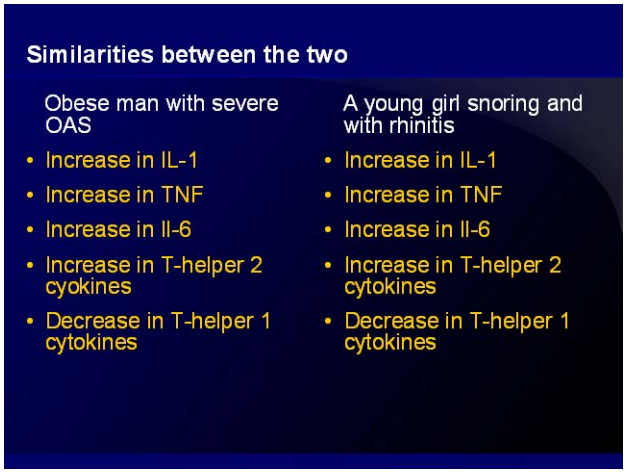
Studies in children have demonstrated that AR and allergic sensitization are associated with snoring.[17] A recent publication by Bixler et al.[18] demonstrated that rhinitis was an independent variable for disordered sleep in children. In a study in patients with asthma, the presence of concomitant AR was independently related to difficulties in inducing sleep and to daytime sleepiness.[19]

Mechanisms of Sleep Impairment

Identifying the mechanisms involved in sleep impairment in AR is important in determining how to reduce the impact of the disease on patients. For example, the daytime fatigue experienced by patients with AR could be attributed to sleep impairment resulting from nasal congestion or other rhinitis symptoms[20,21] or to the effects of inflammatory cytokines on sleep or producing fatigue directly.[22] Current evidence suggests that symptoms (particularly nasal congestion) and underlying pathophysiologic changes of the disease contribute to reduced sleep quality and daytime somnolence.[20]

Nasal congestion occurs when capacitance vessels dilate in the cavernous tissues of the nasal turbinates.[23] Nasal congestion reduces the internal nasal diameter, increases airway resistance to nasal airflow, and results in nasal obstruction.[23] In addition to subjective clinical assessments of the severity of nasal congestion, the degree of congestion (nasal patency) can be evaluated objectively by measures of nasal airflow (eg, peak nasal inspiratory flow), assessment of airway resistance/conductance (rhinomanometry), and acoustic rhinometry, which

Table 1. This table lists the cytokines that have been associated with obstructive sleep apnea and allergic rhinitis.



assesses the volume and area of the nasal cavity by analyzing reflected sound waves.[24]

Nasal congestion is often worse at night time and early morning hours. Although congestion tends to increase when an individual lays down, mechanisms in healthy patients compensate to reduce congestion, which does not happen in rhinitis sufferers.[25] The normal overnight decline in serum cortisol is one of these mechanisms and is likely to contribute to night-time worsening. Similarly, in patients with asthma, lower cortisol levels are associated with greater airway obstruction.[26] A large study in patients with AR confirmed that nasal congestion worsened overnight and peaked at about 6 AM, showing a clear, large-amplitude, circadian variation similar to asthma.[27] This seems to be one explanation for why patients with nasal congestion often complain that they have difficulty sleeping at night and feel fatigued during the day.

Studies of treatments for nasal congestion associated with AR have suggested that congestion is largely responsible for the disturbed sleep and daytime fatigue that occurs with this condition.[12] Early studies using objective assessments of sleep indicated that nasal congestion in patients with AR is associated with an increase in the number of microarousals[13] and apneic episodes of apnea.[11] When developing the Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire (NRQLQ), Juniper et al.[29] found that a stuffy nose and sinus congestion were among the most troublesome symptoms to patients with allergic rhinoconjunctivitis who experienced sleep disturbance.

Additional support for the direct effect of congestion on sleep includes a population-based study (n =4927) investigating the role of acute and chronic nasal congestion in the development of sleep-disordered breathing. Those with frequent nocturnal symptoms of rhinitis were more likely to report habitual snoring, chronic nonrestorative sleep, and excessive daytime fatigue compared to those who never had symptoms. Individuals with nasal congestion caused by AR were 1.8 times more likely to have moderate to severe sleep-disordered breathing than those with AR without nasal congestion.[30] The role of congestion as a risk factor for habitual snoring was confirmed in a population-based cohort study (n =4916).[31] The switch to oral breathing that occurs as a result of nasal congestion may be the key factor behind this association, compromising the airway and leading to sleep-disordered breathing.[3]

Other symptoms, such as sneezing, rhinorrhea, and nasal pruritus, may contribute to reduced sleep quality and sleep disturbance in individuals with AR. One study concluded that rhinorrhea was troublesome to patients with AR and interfered with sleep. Ocular itching has also been demonstrated as a cause of sleep disturbance.[29] Two studies confirmed the association between ocular itch from AR and subjective sleep difficulty.[32,33]

The inflammatory mediators, such as histamine and cytokines released during allergic reactions, may directly affect the central nervous system, which contributes to disturbed sleep and fatigue or sleepiness during the day.[34–36] Histamine is involved in the regulation of the sleep–wake cycle and arousal.[34] Higher levels of the cytokines interleukin (IL)-1β, IL-4, and IL-10 in allergic patients compared with healthy individuals have been shown to correlate with increased latency to rapid eye movement (REM) sleep, decreased time in REM sleep, and decreased latency to sleep onset.[36] Because the restorative function of REM sleep is important, its disruption may contribute to daytime fatigue, difficulty concentrating, and poorer performance in individuals with AR.[36] Inflammatory cells and mediators show circadian variation, with levels peaking during the early-morning hours.[37] These changes of cytokines could explain the higher level of AR symptoms upon waking and why overnight sleep is particularly affected.

Table 2. Demonstrates the associated symptoms that are noted with elevation of specific cytokines that can worsen sleep or cause daytime somnolence or fatigue.

Multiple Pro-Inflammatory Factors in Allergic Rhinitis Affect Sleep and Symptoms

Mediator	Effect on Sleep
Histamine	Balance between wakefulness and sleep, arousal; ↑ nasal obstruction, rhinorrhea, & pruritus
CysLT	↑ Slow-wave sleep, ↑ Sleep-disordered breathing; ↑ Nasal obstruction, rhinorrhea
IL-1	↑ Latency to REM and ↓ REM duration
IL-4	
IL-10	
Bradykinin	↑ Sleep apnea; ↑ Nasal obstruction & rhinorrhea
Substance P	↑ Latency to REM, arousal; ↑ Nasal obstruction

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Similar cytokine milieus also have been found in AR and OSA, as shown in Table 1. As can be seen, cytokine changes associated with sleep apnea may promote a T-helper type 2 cell phenotype, further causing allergic-type inflammation and leading to an increase in nasal congestion. Multiple cytokines can affect sleep and are noted in Table 2. In addition, elevation of some of the cytokines seen in both disorders, such as tumor necrosis factor, IL-6, and IL-1, can cause fatigue and other nonspecific constitutional symptoms during the day.[38]

The potential of autonomic dysfunction playing a role in sleep is also being explored. The extent that excessive cholinergic activity and a decrease in adrenergic tone have on congestion and associated sleep disturbance is unknown. What we do know is that automonic disturbance is associated with mild OSA. The abnormalities noted by Woodson et al.[39] may precede OSA and possibly be part of the pathologic mechanism. The importance of this mechanism on AR and associated congestion and sleep disturbance needs to be further explored.

In summary, multiple mechanisms affect sleep quality in rhinitis. Nasal obstruction has been studied the most and is very important to sleep quality. However, as pointed out previously, other symptoms of rhinitis can influence sleep quality and inflammatory mediators and neurogenic stimulation may play a role.

Sleep Impairment and Quality of Life

Individuals with AR suffer impaired cognitive function and reduced work productivity and performance.[40–42] AR can affect children's learning ability and performance at school and cause somnolence and inability to concentrate.[43] These effects may be a direct result of allergic symptoms but are likely to be exacerbated by sleep impairment.[44] Sleep-disordered breathing and sleep disturbance are known to be directly associated with decreased quality of life in the general population,[45] as evidenced by experimentally induced sleep fragmentation in healthy individuals being associated with impaired mental flexibility and attention, increased daytime sleepiness, and impaired mood.[46,47] Adolescents with AR have difficulty getting a good night's sleep and experience problems doing schoolwork,[48] and children with rhinitis and snoring have poorer school performance than healthy individuals.[49] Daytime fatigue, difficulty concentrating, and impaired psychomotor performance are commonly reported by individuals with AR and may

Table 3. This table includes most of the therapies indicated for rhinitis and their adverse effects and benefits for sleep.

	Congestion	Rhinorrhea	Affect on Sleep	Eye Symptoms
Intranasal steroids	+++	+++	++++	++
Oral antihistamines	+	++	+	++
Intranasal antihistamines	+	++	+	+
Oral decongestants	++	-	-	-
Intranasal decongestants	++++	-	=	-
Intranasal cromones	+	+	-	-
Anticholinergics	-	++	+	-
Antileukotrienes	++	+	++	++

reduce their ability to perform the physical and social tasks of daily living.[9,41,50] An Internet-based survey of 1322 people with self-reported rhinitis found that PAR and SAR interfered with sleep (68% and 51% of respondents, respectively) and their ability to carry out their daily routine (58% and 48%, respectively).[6]

One of the largest surveys to examine the impact of rhinitis was carried out by Meltzer et al.[5] using a self-reporting questionnaire. They surveyed 3831 people with rhinitis and 3193 without rhinitis. Sleep quality was assessed using quality-of-life instruments specific for rhinitis.[51] Those with rhinitis missed more work/school, had poorer quality of life, and had decreased productivity.

Studies of subjective and objective measurements of sleep impairment and its impact on patients' quality of life have emphasized the significance of this problem for those with AR. Many instruments have been used to assess effect on sleep; however, most are not specific for rhinitis. Disease-specific quality-of-life measures (eg, the RQLQ) include a domain that measures the effects of disease and/or treatment on sleep.[29] These questionnaires focus on the problems for which patients seek help and thus are more sensitive to changes in patients' quality of life than generic health status questionnaires The NRQLQ assesses the functional impairments most problematic for patients with nocturnal symptoms,[29] including sleep problems, symptoms during night-time and awakening problems during waking hours.

General questionnaires that assess daytime sleepiness and sleep quality include the Epworth Sleepiness Scale,[52] the Pittsburgh Sleep Quality Index,[53] the Calgary Sleep Apnea Quality of Life Index,[54] and the University of Pennsylvania Functional Outcomes of Sleep Questionnaire.[55] Poor sensitivity and specificity may limit their use in assessing the mild to moderate sleep disturbance often noted in patients with rhinitis.

Only a few studies have objectively assessed sleep (using polysomnography) in AR.[11,13,15,17,21-22,31,56,57] In one study, 25 patients with SAR and 25 healthy volunteers underwent 2 consecutive nights of polysomnography before and during pollen season.[22] There were statistically significant differences between the two groups in sleep parameters, including increases in the apnea index (number of apneas per hour), hypopnea index (number of hypopneas per hour), apnea–hypopnea index, snoring time, amount of REM sleep, and sleep latency. The changes were considered by the authors not to be clinically

relevant, as values remained within normal limits (below 5 episodes of apnea hypopnea per hour), but nonetheless did worsen during times with rhinitis symptoms. Of note the authors did not assess for microarousals, which can fragment sleep. The study found a statistically significant increase in daytime sleepiness (assessed subjectively using the Epworth Sleepiness Scale) in patients with SAR compared with healthy individuals, reinforcing the known poor correlation between subjective and objective measures of sleep disturbance.

Effects of Therapy

Therapies that reduce nasal congestion may improve sleep impairment and daytime sleepiness and thereby improve quality of life. In addition, therapies that reduce inflammation may have a positive influence on quality of life by reducing inflammatory mediators, such as tumor necrosis factor, which can cause constitutional symptoms. Table 3 includes most of the available therapies for use in rhinitis.

Sedating antihistamines are contraindicated in those experiencing daytime sedation, fatigue, and functional impairment and thus should be avoided. Non-sedating oral antihistamines are widely used to treat AR and relieve nasal symptoms such as rhinorrhea, sneezing, and pruritus, but have less effect on nasal congestion Some studies, however, have shown an improvement in sleep and quality of life following therapy with an oral or topical antihistamine.[58,59] Although non-sedating antihistamines are tolerated well and often improve sleep and quality of life, data have suggested that the increased sedation secondary to first-generation antihistamines and topical intranasal administration of sedating antihistamines may exacerbate daytime somnolence.[58,59]

Oral decongestants reduce nasal congestion but may have adverse effects on sleep because of their stimulatory effects and their association with systemic side effects, such as tachycardia and urinary retention. Topical decongestants seem to improve sleep in patients with nasal obstruction,[60] but because of the risk of rhinitis medicamentosa ("rebound" congestion), they should not be used for long periods.

The anticholinergic agent ipratropium bromide is not considered effective in relieving nasal congestion; however, limited data suggest that sleep and quality of life may be improved following treatment.[61]

Leukotriene receptor antagonists[62] or a combination of an antihistamine and a leukotriene receptor antagonist[63] have shown some efficacy in improving sleep and quality of life in patients with AR or sleep-disordered breathing. The cause of the improved sleep and daytime somnolence may be a reduction in congestion, a reduction in inflammatory mediators, or a combination of the two. Even in young children with large adenoids, especially those with high levels of inflammatory mediators, montelukast has been shown to be an effective intervention.[64]

Intranasal corticosteroids are considered first-line therapy when nasal congestion is a major symptom. They relieve nasal symptoms, including nasal congestion, and decrease inflammatory mediators secreted from activated lymphocytes, epithelial cells, mast cells, and other inflammatory cells.[65] All intranasal corticosteroids presently available are effective and reduce nasal congestion. The improvement in nasal congestion is subjective and objective, with the objective evidence assessed by an increase in peak nasal inspiratory flow in AR patients treated with intranasal corticosteroids.[66]

Alleviation of nasal congestion using intranasal corticosteroids may have beneficial effects on sleep, daytime sleepiness, and quality of life in patients with inflammatory nasal conditions. Three small studies in adults and children with PAR found that intranasal budesonide reduces nasal congestion, subjective daytime somnolence, and fatigue and thus improving sleep quality and patients' quality of life.[56,67,68] Another intranasal corticosteroid, flunisolide, improved subjectively assessed nasal congestion and sleep problems in patients with PAR compared with placebo, although daytime fatigue and sleepiness did not show significant improvement[21]. Berlin et al.[69] found that flunisolide was superior to azelastine nasal spray in improving nasal congestion, sleep, and daytime sleepiness in patients with PAR. In another study that included patients with PAR, intranasal fluticasone significantly improved subjective assessments of sleep compared with placebo and decreased daytime sleepiness and fatigue by more than 10%.[57]

Mansfield and Posey[70] replicated these findings and demonstrated an improvement in daytime sleepiness and improved cognitive function. The study was placebo-controlled and double-blinded, adding significance to the results. Although the study was conducted in adults, similar data exist for children.

Fluticasone propionate nasal spray improved nasal symptoms, quality of life, and verbal memory in children with SAR.[71] Furthermore, intranasal fluticasone improved AR associated with OSA syndrome; treatment resulted in a significantly lower frequency of apnea/hypopnea and subjective improvements in nasal congestion and daytime alertness, although snoring noise and sleep quality were unchanged compared with placebo.[72]

Data indicate that all intranasal corticosteroids improve quality of life in patients with AR. Milgrom et al.[61] showed that beclomethasone dipropionate controlled nasal congestion and improved quality of life in children with PAR or nonallergic rhinitis, reducing the negative effects of rhinorrhea on mood, concentration on school/work, and sleep. Two recent studies in AR patients found that intranasal triamcinolone acetonide relieved nasal congestion and improved health-related quality of life (including sleep) as assessed using the RQLQ,[73] the NRQLQ, and the Pittsburgh Sleep Quality Index.[74-76]

Further research is warranted on the effect that immunotherapy has on improving sleep quality and daytime somnolence. Data associated with the benefit of immunotherapy on these symptoms and outcomes are extremely limited. Such trials should use sleep-related measures as primary end points and include subjective and objective assessment of sleep parameters. Another important study that needs to be conducted is one that assesses subjective and objective instruments used to monitor sleep disturbance in patients with rhinitis so that the effectiveness of these instruments can be determined and we can determine the best instruments to use to assess sleep quality in patients with rhinitis.

Conclusion

Sleep impairment associated with rhinitis has a significant impact on patients' quality of life. Nasal congestion, one of the most common and bothersome symptoms of rhinitis, is thought to be a major cause of sleep impairment and sleep-disordered breathing. Recent research has suggested that the poor sleep associated with nasal congestion is an important therapeutic target. However, evidence indicates that other rhinitis symptoms, inflammatory mediators released because of rhinitis, can also disturb sleep and lead to an increase in daytime somnolence and limitations.

Treatment with intranasal corticosteroids has been shown to significantly reduce nasal congestion in AR patients, and in those with congestion, they should be considered the drug of choice. Montelukast may be a second-line therapy in those intolerant to intranasal corticosteroids. In turn, sedating antihistamines should be avoided, as they may amplify the sedation and decrease productivity in those already compromised.

Disclosure

Dr. Craig has conducted research for GlaxoSmithKline, Schering, Novartis, Genentech, and Merck & Co. and served as a speaker for Teva Pharmaceuticals, Genentech, Schering, Novartis, and Merck & Co. No other potential conflicts of interest relevant to this article were reported.

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