High Prevalence of Allergic Sensitization in Children With Habitual Snoring and Obstructive Sleep Apnea*

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Study objective: **To determine whether allergic sensitization occurs frequently in children with habitual snoring and whether allergy predicts the occurrence of obstructive sleep apnea syndrome (OSAS) in snoring children.**
Design: **Prospective study of 39 children with habitual snoring who were referred for polysomnography.**
Setting: **Pediatric pulmonary sleep disorders clinic in a tertiary referral center.**
Measurements: **Subjects underwent a complete history and physical examination. To assess for the presence of allergic sensitization, a multiantigen radioallergosorbent test (RAST) was performed on serum samples. Subjects then underwent nocturnal polysomnography to determine the presence and severity of OSAS.**
Results: **Fourteen subjects (36%) demonstrated sensitivity to allergens; this is higher than expected for the general pediatric population. The frequency of OSAS was increased in subjects with positive RAST results compared to those with negative RAST results (57% vs 40%; χ^2=9.11; p<0.01).**
Conclusion: **Allergy is frequently present in pediatric patients with habitual snoring. Furthermore, the presence of allergy is associated with an increased risk of OSAS in this population.**
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Key words: allergy; habitual snoring; obstructive sleep apnea syndrome; pediatrics

Abbreviations: $EtCO_2$=end-tidal carbon dioxide; OSAS=obstructive sleep apnea syndrome; SpO_2=arterial oxygen saturation measured by pulse oximetry; RAST=radioallergosorbent testing; REM=rapid eye movement; TST=total sleep time

Nocturnal snoring and obstructive sleep apnea syndrome (OSAS) are associated with adenotonsillar hypertrophy and chronic rhinitis in young children. Allergic diseases are common in children: allergic rhinitis, eczema, and asthma have a cumulative prevalence of 8.5 to 12.2% in school-aged children.[1-4] Allergic rhinitis or "hay fever" occurs in up to 7% of children.[1-3] Because rhinitis leads to nasal obstruction and increased upper airway resistance, sleep-related upper airway obstruction could result. The purpose of this study was to ascertain whether young children presenting with habitual snoring have a high prevalence of allergic sensitization and whether the presence of allergy predicts the presence or severity of OSAS.

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Materials and Methods

Patient Selection

Subjects, aged 1 to 7 years, who presented to the Johns Hopkins Pediatric Sleep Disorders Center for evaluation of habitual nocturnal snoring were recruited for study. Habitual snoring was defined as snoring that occurred most or all nights, according to parental observation.[5] The study was approved by the Joint Commission on Clinical Investigation of the Johns Hopkins Medical Institutions. Informed consent was obtained from parents, and assent was obtained from verbal children. A detailed history and physical examination were performed. Blood was obtained via venipuncture for multiantigen radioallergosorbent testing (RAST) analysis (Phadiatop Paediatric; Pharmacia Diagnostics; Uppsala, Sweden). This procedure has been found to have a high sensitivity and specificity for the diagnosis of atopic

disease in young children.[6] Children with positive RAST results were considered allergic; those with negative RAST results, nonallergic. Polysomnography was then performed to assess the presence and severity of obstructive sleep apnea.

RAST Analysis

The RAST analysis we used is specifically designed to detect atopic disease in children younger than 7 years of age. It uses a number of food and inhalant allergens, which are not specified; thus specific sensitizations cannot be determined. The inhalant allergens include representative (or cross-reacting) antigens from all geographic regions of the United States. Analysis was performed using standard RAST technique. Serum samples were incubated with paper disks to which common food and inhalant allergens were coupled. Disks were then washed and reacted with radiolabeled anti-IgE. After a second incubation and wash, disks were counted in a gamma counter to determine bound radioactivity. The mean counts per minute were compared to a reference sample and a positive control. A sample count higher than the reference sample is considered positive. The interassay coefficient of variation is reported by the manufacturer to be <10%.

Polysomnography

Polysomnography was performed during natural, nocturnal sleep. Physiologic signals were recorded continuously on a recorder (Grass model 78-D; Grass Instruments Inc; Quincy, Mass). Sleep stages were measured using two leads (C_3A_2/C_3O_1) of EEG, right and left electro-oculograms, and submental electromyogram. Thoracoabdominal movement was measured using mercury-filled strain gauges. Nasal-oral airflow was monitored using a three-bead thermistor positioned over the nostrils and the mouth. Arterial oxygen saturation (SpO_2) was monitored by pulse oximetry (Nellcor N-1000; Nellcor Inc; Hayward, Calif), and the pulse oximeter waveform was recorded to detect motion artifact. ECG was simultaneously recorded. End-tidal carbon dioxide ($EtCO_2$) was measured continuously via a nasal cannula (Nellcor N-1000).

Polysomnography Scoring

Polysomnograms were scored by a polysomnographic technician who had no knowledge of clinical or laboratory evidence of allergy. Obstructive apnea was defined as cessation of nasal-oral airflow, with continued respiratory efforts, lasting for at least two respiratory cycles and associated with a fall in SpO_2 of ≥4%. Obstructive hypoventilation was defined as a decrease in nasal/oral airflow associated with nadir SpO_2 ≤92% and/or peak $EtCO_2$ ≥50 mm Hg. OSAS was diagnosed when at least one of the following was present: obstructive apnea occurring at least once per hour; obstructive hypoventilation leading to peak $EtCO_2$ >53 mm Hg; and obstructive hypoventilation leading to desaturation (decrease in SpO_2 of at least 4%) >1.4 times per hour.[7,8] Primary snoring[5] was diagnosed when snoring was present but was not accompanied by any of these criteria.

Statistical Analysis

Presence and severity of obstructive sleep apnea were compared between children with and without positive RASTs using the χ^2 test and Student's *t* test. Results are given as mean±SD.

RESULTS

Presence of Allergic Sensitization

Among 156 eligible subjects, 132 were asked to participate. Eighty-five subjects declined and 47 consented; in eight of these subjects, blood could not be obtained. Among the 39 subjects studied (24 male; mean age, 4.7±1.8 years), 14 (36%) had a positive RAST, indicating sensitivity to one or more inhalant or food allergens. Characteristics of allergic vs nonallergic patients are summarized in Table 1. Seven children were obese (weight to height ratio greater than the 95th percentile, National Center for Health Statistics percentiles), five in the allergic group and two in the nonallergic group. Among subjects with a positive RAST (allergic subjects), 58% had other features suggestive of allergic disease: a history of eczema or wheezing, a history of allergies or asthma in a first-degree family member, or physical examination findings of allergic shiners, eczema, or wheezing. Among subjects with a negative RAST (nonallergic subjects), 47% had one or more of these features (χ^2=0.13; NS).

Polysomnographic Findings

Respiratory and Sleep Variables in Allergic vs Nonallergic Subjects: Gas exchange was similar between allergic and nonallergic subjects (Table 2). Total sleep time (TST) was decreased in allergic subjects compared to nonallergic subjects; there was a trend toward decreased sleep efficiency in allergic subjects (p=0.06) (Table 2). Rapid eye movement (REM) sleep comprised 21% of TST in allergic subjects and 20% of TST in nonallergic subjects; this was not significantly different when compared as either percentage of sleep time or as total REM time.

Frequency of Obstructive Sleep Apnea Syndrome: Overall, 18 subjects (46%) were found to have OSAS. Eight of 14 (57%) allergic subjects had OSAS, compared to 10 of 25 nonallergic subjects (40%) (χ^2=9.11; p<0.01). When data were reanalyzed

Table 1—*Characteristics of Allergic vs Nonallergic Subjects*

	Allergic	Nonallergic
n	14	25
Gender, F/M	6/8	9/16
Age, yr, mean±SD	4.4±1.7	4.8±1.9
Weight/height percentile		
<5	0	0
5-50	4 (29%)	13 (52%)
50-95	5 (36%)	10 (40%)
>95	5 (36%)	2 (8%)

Table 2—*Sleep and Blood Gas Parameters in Allergic (+RAST) vs Nonallergic (−RAST) Subjects*

	Allergic	Nonallergic
n	14	25
TST, min	330±55	363±40*
Sleep efficiency, %	81±13	88±10
REM, %TST	21±6	20±5
OEI†	4.0±5.3	2.2±3.8
Nadir SpO_2, %	90±6	90±10
Peak $EtCO_2$, mm Hg	49±4	49±7

*$p<0.05$.
†OEI=obstructive event index (No. of obstructive apneas plus episodes of obstructive hypoventilation per hour).

using a stricter diagnostic standard of five episodes of obstructive apnea or obstructive hypoventilation per hour, four of 14 allergic subjects had OSAS, compared to four of 25 nonallergic subjects ($\chi^2=6.62$; $p<0.01$). Only three children with OSAS were obese; two of these subjects were allergic.

Severity of OSAS: Overall, the severity of OSAS was similar between allergic and nonallergic subjects (Table 3). $EtCO_2$ levels were higher in nonallergic subjects. TST and sleep efficiency were not different between allergic and nonallergic subjects with OSAS.

Discussion

We have demonstrated a high prevalence of allergy in a group of children with habitual snoring. Although a control group of nonsnoring children was not studied, the 36% incidence of allergic sensitization found in this cohort is approximately three times that reported in prevalence studies of allergy in children.[2-4] The prevalence of allergy in this population is not known, making it possible that these findings simply represent a high degree of allergic sensitization in children in Baltimore. Even if this is true, this finding may have important implications for diagnosis and treatment.

Table 3—*Sleep and Breathing in Subjects With OSAS, Allergic (+RAST) vs Nonallergic (−RAST) Subjects*

	Allergic	Nonallergic
n	8	10
TST, min	317±72	340±51
Sleep efficiency, %	78±17	81±13
OEI*	7.18±5.6	5.3±3.5
Nadir SpO_2, %	86±5	82±13
Peak $EtCO_2$, mm Hg	49±2	55±7†

*See table 2 for expansion.
†$p<0.05$.

Pathophysiologically, upper airway allergy causes edema and mucus secretion in the nasal mucosa. This increases nasal resistance, and hence, may predispose children to the development of partial or complete upper airway obstruction during sleep. Environmental measures or pharmacologic agents that decrease mucosal edema and mucus may decrease airway obstruction. For example, a recent study[9] demonstrated improvement in adenoidal obstruction with the use of nasal beclomethasone, a frequently prescribed therapy for allergic rhinitis. Finally, these data support a finding previously reported by our group: history and physical examination alone are inadequate in diagnosing OSAS in children presenting with habitual snoring.[10]

The multiantigen RAST used in this study was chosen as a simple, reproducible means to screen for allergic sensitization. This test has been verified to have a high sensitivity (92%) and specificity (88%) for diagnosis of atopic disease in young children.[6] A personal or family history suggestive of allergy occurred very frequently in this population, making it unlikely that the observed findings are due to a large number of false-positive test results. The relatively small number of subjects consenting to the study raises the question of whether self-selection contributed to the high prevalence of allergy in this population, and it is possible that these findings are relevant only to a subset of children with OSAS who have a high frequency of allergic features.

It is possible that the presence of allergy increases the likelihood that a child with habitual snoring will have OSAS. These data do not show a difference in respiration during sleep in allergic vs nonallergic patients overall, perhaps because of the relatively high frequency of OSAS in this referred snoring population. However, the overall frequency of OSAS was increased in allergic subjects. Allergy may increase the risk of obstructive sleep apnea by its effects on upper airway resistance. Whether allergic children have a higher frequency of snoring or obstructive sleep apnea than the general population cannot be answered by these data, but deserves study based on these findings.

A number of risk factors for the development of OSAS in children have been described. These include adenotonsillar hypertrophy, craniofacial abnormalities, and neuromuscular disorders.[11-13] These findings suggest that allergy is common in young children with primary snoring and OSAS. Because there is overlap between symptoms of upper airway allergy and of OSAS, including chronic rhinitis and mouth breathing, clinicians should be aware of the potential presence of allergy in subjects with OSAS and vice versa. We suggest that patients with OSAS who have features of allergic disease be assessed for

allergy, and that environmental and pharmacologic therapy be considered when allergy is documented. The RAST test used in this study is a useful screening test, but its utility may be limited because of the lack of specific sensitization information. Further studies regarding the effect of treating allergy in children with OSAS would be helpful in clarifying who should be screened and how allergic subjects with OSAS should be treated.

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