Consequences of Perennial Allergic Rhinitis in Children: Adenotonsillar Hypertrophy, Sleep Disordered Breathing and Behavioral Problems

Role of Allergic Rhinitis in Sleep Disordered Breathing and Behavioral Disorders in Children

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Case

• A 6 year old boy is referred to you by his pediatrician with the recent diagnosis of Attention Deficit Hyperactivity Disorder (ADHD). He has been placed on methylphenidate with some improvement in his school attentiveness and hyperactivity.

• The mother believes his problem is due to a food allergy, since he is more hyperactive after eating candy and sugary foods. She is not sure if dairy products make him worse, and has come specifically for food allergy testing. There was never a cutaneous reaction to any food, but mild eczema was noted as an infant.
Case

• Your history reveals that the patient snores and breathes with his mouth wide open every night. At times he stops breathing for a few seconds. He sometimes wets the bed. Interspersed with hyperactivity, he often falls asleep during school hours.

• Frequent ear infections and persistent middle ear fluid from 6 months to 2 years old has been replaced by recurrent tonsillitis, but not enough to see the ENT, according to the pediatrician. His nose is always blocked, at times with yellow or green discharge, which improves with antibiotics.
Case

- Physical Exam reveals “long face” with open mouth and allergic shiners. Nose is completely obstructed by swollen turbinates and thick mucoid discharge. Dental arch is somewhat narrow and high. Tonsils are markedly enlarged and almost “kissing”. Tympanic membranes are normal.

- Skin prick testing reveals 4+ reaction to dust mites, 2+ to molds and tree pollen, 1+ or negative to other aeroallergens and foods. Humeral immune evaluation is normal.
Case

• You recommend immediate ENT evaluation and sleep study. You also prescribe Mometasone Nasal Spray to be used for at least 2 months.

• After his exam, which reveals 50% obstruction by hypertrophic adenoids and a positive sleep study, the ENT physician schedules Tonsillectomy and Adenoidectomy.
Case

• However, prior to the surgery date one month later, the patient has markedly improved. He can breathe through his nose. Tonsils and adenoids are significantly smaller.

• He is no longer snoring or experiencing sleep apnea. The teacher reports that he is paying attention, and not hyperactive or falling asleep. A repeat sleep study is normal.

• Surgery is postponed and Mometasone nasal spray is continued.
Polysomnography

- The electrographic recording of simultaneous physiologic variables during sleep, currently considered the gold standard for objectively assessing sleep disorders.

- Physiologic parameters typically measured include gas exchange, respiratory effort, airflow, snoring, sleep stage, body position, limb movement, and heart rhythm.

- PSG may be performed in a sleep laboratory with continuous attendance.

Clinical Practice Guideline: Polysomnography for Sleep-Disordered Breathing Prior to Tonsillectomy in Children
Otolaryngology–Head and Neck Surgery 145(1S) S1–S15, 2011
Sleep-Disordered Breathing

- Characterized by an abnormal respiratory pattern during sleep and includes snoring, mouth breathing, and pauses in breathing.
- SDB encompasses a spectrum of disorders that increase in severity from snoring to obstructive sleep apnea.
- For example, obstructive sleep apnea (OSA) is diagnosed when SDB is accompanied by an abnormal PSG with obstructive events.

Practice Guideline: Polysomnography for Sleep-Disordered Breathing Prior to Tonsillectomy in Children
Otolaryngology–Head and Neck Surgery 145(1S) S1–S15, 2011
Prevalence of Atopy In Children Undergoing E.N.T. Surgery
Misra S., Silverman B.A., et. al.
Annual Meeting, American College of Allergy, Asthma & Immunology,

PREVALENCE OF ATOPY IN CHILDREN UNDERGOING ENT SURGERY. S. Misra, MD.

Thirteen ped patients (pts) 18 mos - 10 yrs scheduled for ENT surgery (tonsillectomy, adenoidectomy and/or myringotomy) were randomly selected for allergy/immunology evaluation. 13/13 had obstructive airway symptoms, 2/13 had obstructive sleep apnea, 4/13 had recurrent tonsillitis, 10/13 had chronic serous otitis media, 10/13 had atopic symptoms of asthma, hay fever and/or eczema.

History of food allergy was found in 4/13 pts. Only 1/13 recognized sensitivity to inhalants. Family history was +ve in 10/13 for atopy. On physical exam 9/13 had swollen turbinates. Total IgE was high in 3/6 pts, selective IgA deficiency was found in 1/6, IgG level was high in 3/6 and IgG subsets were normal in 5/5. 3/10 were +ve to food by skin test. RAST was -ve in all. Skin test to inhalants was +ve in 6/9. Study suggests high prevalence of atopy in ped pts referred for ENT surgery. Allergy/immunology evaluation is recommended in most pts undergoing these procedures. Data from a larger population will be presented.
Is there any correlation between allergy and adenotonsillar tissue hypertrophy?


OBJECTIVES:

• Tonsil and adenoid are part of Waldeyers ring; the basic function of which is antibody formation, which later react against a great variety of antigens. The Adenotonsillectomy is the most common operation in small children but the exact reasons for adenotonsillar hypertrophy remain unknown. Some research has shown that allergy may be a risk factor for adenotonsillar hypertrophy.

METHODS:

• Through one year, two separated groups of children at the ENT and allergy ward of childrens hospital were enrolled in the study. The study group consisted of 117 children between 1 and 14 years old (with average of 6) who had adenotonsillar hypertrophy. The control group consisted of 100 children of similar age without adenotonsillar hypertrophy. Both groups were examined for the incidence of allergic disease, results of skin prick test, serum IgE levels and close contact to smoke.
Is there any correlation between allergy and adenotonsillar tissue hypertrophy?


RESULTS:
• In the study group 70.3% of children with adenotonsillar hypertrophy had positive skin prick test. But only 10% of children in control group had positive skin prick test.
• Increased serum total IgE level was confirmed in 48% of children with positive skin prick test in study group.

CONCLUSION:
• Allergy and sensitivity to different kinds of allergens are important risk factors for adenotonsillar hypertrophy in children.
• Allergy control may have role in reducing the rate of adenotonsillectomy in children suffering allergic reactions with adenotonsillar hypertrophy.
Allergic Rhinitis and Sleep Disturbance


Sleep disordered breathing and daytime quality of life in children with allergic rhinitis during treatment with intranasal budesonide

BACKGROUND:
• Nasal obstruction is recognized as an important cause of sleep disordered breathing. Congestion of the nasal mucosa and obstruction are common symptoms of allergic rhinitis. Daytime sleepiness is a common finding in symptomatic allergic rhinitis. Effective therapy of the nasal congestion of allergic rhinitis should alter sleep patterns in patients with symptomatic allergic rhinitis.

OBJECTIVE:
• To measure objective changes in polysomnograms (sleep studies) of children with allergic rhinitis before and after therapy with intranasal budesonide and to measure changes in the quality of life of these patients during treatment.

METHODS:
• Open clinical trial with objective measurements (polysomnography) and subjective data (Rhinitis Quality of Life Questionnaire [RQLQ]). Evaluations were performed before, during, and at completion of therapeutic intervention.
Sleep disordered breathing and daytime quality of life in children with allergic rhinitis during treatment with intranasal budesonide

RESULTS:
• The 14 studied children tolerated the procedures and treatment without problems. The mean number of sleep arousals per hour (all apneas and hypopneas) decreased from a baseline of 8.4 to 1.2 (P = .005) after treatment. The change was mainly in hypopneic episodes (7.5-0.9, P = .003). Objective responses on the RQLQ showed improvements consistent with improved sleep and lessened rhinitis symptoms.

CONCLUSIONS:
• Decreasing the nasal congestion associated with allergic rhinitis can improve sleep measured by objective sleep studies and lead to improvement in daytime quality of life.
Intranasal corticosteroids for nasal airway obstruction in children with moderate to severe adenoidal hypertrophy.

Zhang L, Mendoza-Sassi RA, César JA, Chadha NK.

BACKGROUND:
• Adenoidal hypertrophy is generally considered a common condition of childhood. When obstructive sleep apnoea or cardio-respiratory syndrome occurs, adenoidectomy is generally indicated. In less severe cases, non-surgical interventions may be considered, however few medical alternatives are currently available. Intranasal steroids may be used to reduce nasal airway obstruction.

OBJECTIVES:
• To assess the effectiveness of intranasal corticosteroids for improving nasal airway obstruction in children with moderate to severe adenoidal hypertrophy.

SEARCH STRATEGY:
• Our search included the Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 2, 2007), MEDLINE (1951 to 2007) and EMBASE (1974 to 2007). All searches were initially performed in May 2007 and updated in April 2008.

SELECTION CRITERIA:
• Randomised controlled trials comparing intranasal corticosteroids with placebo or no intervention or other treatment in children aged 0-12 years with moderate to severe adenoidal hypertrophy.

DATA COLLECTION AND ANALYSIS:
• Data from the included trials were extracted and trial quality was assessed by two authors independently. Meta-analysis was not applicable and data were summarised in a narrative format.
Intranasal corticosteroids for nasal airway obstruction in children with moderate to severe adenoidal hypertrophy
Zhang L, Mendoza-Sassi RA, César JA, Chadha NK.

MAIN RESULTS:

• Five randomised trials, including a total of 349 patients, met the inclusion criteria of the review.
• All trials except one showed significant efficacy of intranasal corticosteroids in improving nasal obstruction symptoms and in reducing adenoid size.
• The first eight-week cross-over study showed that treatment with beclomethasone (336 micrograms/day) yielded a greater improvement in mean symptom scores than placebo (-18.5 vs. -8.5, P < 0.05) and a larger reduction in mean adenoid/choana ratio than placebo (right, -14% vs. +0.4%, p=0.002; left, -15% vs. -2.0%, p=0.0006) between week 0 and week 4.
• The second four-week cross-over study demonstrated that the nasal obstruction index decreased by at least 50% from baseline in 38% of patients treated with beclomethasone (400 micrograms/day) between week 0 and week 2, whereas none of the patients treated with placebo had such improvement (p<0.01).
Intranasal corticosteroids for nasal airway obstruction in children with moderate to severe adenoidal hypertrophy

Zhang L, Mendoza-Sassi RA, César JA, Chadha NK.

- The third randomized, parallel-group trial showed that 77.7% of patients treated with mometasone (100 micrograms/day) for 40 days demonstrated an improvement in nasal obstruction symptoms and a decrease in adenoid size, such that adenoidectomy could be avoided, whereas no significant improvement was observed in the placebo group.

- The fourth randomized, parallel-group trial showed that eight-weeks of treatment with flunisolide (500 micrograms/day) was associated with a larger reduction in adenoid size than isotonic saline solution (p<0.05).

- In contrast, one randomised, parallel-group trial did not find significant improvement in nasal obstruction symptoms and adenoid size after eight weeks of treatment with beclomethasone (200 micrograms/day).
Intranasal corticosteroids for nasal airway obstruction in children with moderate to severe adenoidal hypertrophy
Zhang L, Mendoza-Sassi RA, César JA, Chadha NK.

AUTHORS' CONCLUSIONS:

• Limited evidence suggests that intranasal corticosteroids may significantly improve nasal obstruction symptoms in children with moderate to severe adenoidal hypertrophy, and this improvement may be associated with a reduction of adenoid size. The long-term effect of intranasal corticosteroids in these patients remains to be defined.
Intranasal budesonide treatment for children with mild obstructive sleep apnea syndrome.
Kheirandish-Gozal L, Gozal D.

OBJECTIVES:
- Intranasal corticosteroids have been advanced as a nonsurgical therapeutic alternative for pediatric obstructive sleep apnea syndrome, particularly for patients with mild disease, and aims at reducing the size of hypertrophic adenotonsillar tissue.

METHODS:
- Of 71 possible candidates, 62 children with polysomnographically diagnosed mild obstructive sleep apnea syndrome were recruited onto a double-blind, randomized, crossover trial of intranasal budesonide (32 microg per nostril at bedtime) or placebo for 6 weeks followed by an additional 6-week treatment in the alternative treatment arm after allowing for a 2-week washout period. Polysomnographic assessment and radiographs for assessment of adenoid size were performed after completion of each phase.
Intranasal budesonide treatment for children with mild obstructive sleep apnea syndrome.


RESULTS:
• There were significant improvements in both polysomnographic measures (sleep latency, slow-wave sleep, and rapid-eye-movement sleep), in the magnitude of respiratory disturbance (apnea/hypopnea index, nadir pulse oxygen saturation), and in adenoid size among the 48 children who completed the treatment phase compared with 32 children who received placebo in their initial arm, with normalization of sleep measures in 54.1% of the treated children. Furthermore, discontinuation of treatment for 8 weeks for 25 children revealed a sustained duration of the initial treatment effect.

CONCLUSIONS:
• A 6-week treatment with intranasal budesonide effectively reduced the severity of mild obstructive sleep apnea syndrome and the magnitude of the underlying adenoidal hypertrophy, and this effect persisted for at least 8 weeks after cessation of therapy. These findings justify the use of topical steroids as the initial therapeutic option in otherwise healthy children with mild obstructive sleep apnea.
OBJECTIVES:
• Examine statistical effects of sleep-disordered breathing (SDB) symptom trajectories from 6 months to 7 years on subsequent behavior.

METHODS:
• Parents in the Avon Longitudinal Study of Parents and Children reported on children's snoring, mouth breathing, and witnessed apnea at ≥2 surveys at 6, 18, 30, 42, 57, and 69 months, and completed the Strengths and Difficulties Questionnaire at 4 (n = 9140) and 7 (n = 8098) years. Cluster analysis produced 5 "Early" (6-42 months) and "Later" (6-69 months) symptom trajectories ("clusters"). Adverse behavioral outcomes were defined by top 10th percentiles on Strengths and Difficulties Questionnaire total and subscales, at 4 and 7 years, in multivariable logistic regression models.
RESULTS:

• The SDB clusters predicted ≈20% to 100% increased odds of problematic behavior, controlling for 15 potential confounders. Early trajectories predicted problematic behavior at 7 years equally well as at 4 years. In Later trajectories, the "Worst Case" cluster, with peak symptoms at 30 months that abated thereafter, nonetheless at 7 years predicted hyperactivity (1.85 [1.30-2.63]), and conduct (1.60 [1.18-2.16]) and peer difficulties (1.37 [1.04-1.80]), whereas a "Later Symptom" cluster predicted emotional difficulties (1.65 [1.21-2.07]) and hyperactivity (1.88 [1.42-2.49]). The 2 clusters with peak symptoms before 18 months that resolve thereafter still predicted 40% to 50% increased odds of behavior problems at 7 years.

CONCLUSIONS:

• In this large, population-based, longitudinal study, early-life SDB symptoms had strong, persistent statistical effects on subsequent behavior in childhood. Findings suggest that SDB symptoms may require attention as early as the first year of life.
A Clinical Overview of Sleep and Attention-Deficit/Hyperactivity Disorder in Children and Adolescents

• Compelling evidence of a wide range of neurobehavioral and neurocognitive deficits in children with both clinical symptoms of and polysomnographically-confirmed SDB, including inattention, impaired memory, and executive functions, mood disturbance, externalizing and internalizing behavior problems, and academic difficulties (Chervin & Archbold, 2001; Chervin, Dillon, Bassetti, Ganoczy, & Pituch, 1997; Huang et al., 2007; Beebe, 2006).

• Several recent reports have documented a significant increase in parent-reported SDB symptoms specifically in children being evaluated for or diagnosed with ADHD, and have suggested that as many as 25% of ADHD diagnoses may be linked to symptoms of sleep-disordered breathing such as habitual snoring (Chervin & Archbold, 2001; Chervin et al., 1997).

• Habitual snoring is also reported to be three times more common in children with ADHD (33%) than in other child psychiatric (11%) or general pediatric populations (9%) (O’Brien et al., 2003a).
Not all studies have found an association between polysomnographically (PSG)-confirmed SDB and ADHD (Sangal, Owens, & Sangal, 2005).

Severity of neurobehavioral and neurocognitive deficits does not appear to be “dose-dependent”, suggesting that disease severity alone does not account for the extent of impairment.

Studies which have looked at changes in behavior and neuropsychological functioning in children following treatment (usually adenotonsillectomy) for SDB have also largely documented significant improvement in daytime sleepiness, neuropsychological measures of impairment, behavior, and academic performance post-treatment (Wei, Mayo, Smith, Reese, & Weatherly, 2007; Gozal, 1998; Ali, Pitson, & Stradling, 1996);

In one study, 50% of children initially meeting DSM-IV criteria for ADHD no longer did so one year after adenotonsillectomy (Chervin et al., 2006).
Allergic rhinitis in children with attention-deficit/hyperactivity disorder

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Allergic rhinitis in children with attention-deficit/hyperactivity disorder

Background:

• Both allergic rhinitis and attention-deficit/hyperactivity disorder (ADHD) are common pediatric conditions associated with learning difficulties and sleep disturbances.
• There are conflicting research data regarding the association between ADHD and atopic disorders.

Objective:

• To determine the prevalence of allergic rhinitis in patients with physician-diagnosed ADHD.

Methods:

• Patients 5 to 18 years of age who presented with a Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition diagnosis of ADHD to an outpatient pediatric psychiatry clinic were screened for allergic rhinitis with focused history, physical examination, and skin prick testing to common aeroallergens.
Allergic rhinitis in children with attention-deficit/hyperactivity disorder

Results:

• Thirty patients were interviewed, with 23 of these undergoing physical examination and skin prick testing.
• Eighty percent reported allergic rhinitis symptoms, whereas 61% had at least 1 positive prick skin test result.
• Forty-three percent showed typical physical signs of allergic rhinitis, 100% had a positive atopic family history, and 53% had other associated atopic disorders.
Conclusions:

• Most children with ADHD displayed symptoms and skin prick test results consistent with allergic rhinitis.
• Nasal obstruction and other symptoms of allergic rhinitis could explain some of the cognitive patterns observed in ADHD.
• This might result from sleep disturbance known to occur with allergic rhinitis.
• Therefore, evaluation and treatment of allergic rhinitis could benefit patients with ADHD.
Allergic Rhinitis and Inner-City Children—Is There a Relationship to Sleep-Disordered Breathing?

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Allergic Rhinitis and Inner-City Children—Is There a Relationship to Sleep-Disordered Breathing?

Background:
• Allergic rhinitis (AR) causes increased upper airway resistance and may lead to undiagnosed sleep-disordered breathing (SDB).
• This problem may be further complicated in the pediatric inner-city population where indoor allergens such as rat, cockroach, and mouse may contribute to morbidity.

Objective:
• To determine the pattern of aeroallergen sensitization in inner-city pediatric patients with SDB.
• To determine if intranasal corticosteroid treatment improves SDB, using a validated Pediatric Sleep Questionnaire (PSQ).
Allergic Rhinitis and Inner-City Children—Is There a Relationship to Sleep-Disordered Breathing?

Methods:

• Patients (ages 2–18) were evaluated for AR and completed the PSQ prior to treatment.
• Skin prick testing (SPT) to aeroallergens, including inner-city culprits (rat, cockroach, and mouse), was performed.
• Patients with a history of AR, a positive SPT evaluation, and at least one positive response on the PSQ were treated with intranasal mometasone furoate monohydrate, environmental control, (±) antihistamines.
• After 6 weeks of treatment, PSQ responses were reassessed.
Allergic Rhinitis and Inner-City Children—Is There a Relationship to Sleep-Disordered Breathing?

Pediatric Sleep Questionnaire
Please answer the following questions about your child: YES NO
•1. While sleeping does your child snore more than half the time?
•2. While sleeping does your child always snore?
•3. While sleeping does your child snore loudly?
•4. While sleeping does your child have heavy or loud breathing?
•5. While sleeping does your child have trouble breathing or struggle to breathe?
•6. Have you ever seen your child stop breathing during the night?
•7. Does your child tend to breathe through the mouth during the day?
•8. Does your child have a dry mouth on waking up in the morning?
•9. Does your child occasionally wet the bed?
•10. Does your child wake up feeling unrefreshed in the morning?
•11. Has a teacher or other supervisor commented that your child appears sleepy during the day?
•12. Is it hard to wake your child up in the morning?
•13. Is your child overweight?
•14. Does your child seem to not listen when spoken to directly?
•15. Does your child have difficulty organizing task and activities?
•16. Is your child easily distracted by extraneous stimuli?
•17. Does your child fidget with hands or feet or squirm in seat?
•18. Does your child seem like he or she is “on the go” or often acts as if “driven by a motor”?
•19. Does your child interrupt or intrudes on others (e.g., butts into conversations or games)?

Questions 1–9 related to breathing/snoring; questions 10–13 related to sleepiness; questions 14–19 related to behavior.
Allergic Rhinitis and Inner-City Children—Is There a Relationship to Sleep-Disordered Breathing?

Results:

• Of the 23 patients recruited in this study, 100% had SDB as per screening PSQ responses;
• 100% had 1 positive SPT, 78% of which were SPT-positive to cockroach, mouse, or rat.
• For PSQ questions (1–13), prior to treatment, patients’ average PSQ score = 6.00 ± 2.65 (SD) questions; following treatment, 2.35 ± 1.90 (SD), with an improvement of 3.65 (p < 0.0001).
• For PSQ questions (1–9) (breathing/snoring), pretreatment = 4.48 ± 2.19 (SD); posttreatment = 1.52 ± 1.5 (SD), with an improvement of 2.96 (p < 0.0001)
• For PSQ questions (10–13) (sleepiness), pretreatment = 1.52 ± 0.83 (SD); posttreatment = 0.83 ± 0.94 (SD), with an improvement of 0.70 (p = 0.0016).
• For PSQ questions (14–19) (behavioral issues), pretreatment = 3 ± 1.95 (SD); posttreatment = 2.3 ± 2.14 (SD), with an improvement of 0.70 (p = 0.0842). This was not significant, but patients with behavioral disorders were not preselected.
Conclusion:

• Children suffering from AR have increased nasal obstruction leading to sleep-disordered events.

• This study demonstrated that adequate treatment, that is, intranasal steroids, may significantly improve SDB.

• In inner-city children, elimination of indoor allergens such as cockroach, mouse, or rat may further improve SDB.
Conclusions

• Allergic Rhinitis (AR) in children, with or without secondary Adenotonsillar Hypertrophy (ATH) is associated with Sleep-Disordered Breathing (SDB).
• Treatment with intranasal corticosteroids (INC) improves AR, Adenoid Hypertrophy, and SDB.
• ADHD is also associated with SDB and improves with adenotonsillectomy when both are present.
• AR and ADHD are highly associated, probably due to nasal obstruction in AR or secondary ATH, both causing SDB, which in turn results in daytime behavioral changes, i.e. inattentiveness and hyperactivity.
• Therefore INC treatment of children with both AR and ADHD or similar behavioral issues should improve behavior.
Larger prospective studies are needed to:

• Evaluate change in polysomnography, sleep and behavioral scales for patients with concomitant AR and ADHD, ADD, or other behavioral disorders, who are treated with INC.

• Further examine how ATH and its treatment with INC affects the relationships between AR, sleep, and behavior.