

Pediatric obstructive sleep apnea syndrome (OSAS) for the allergist: update on the assessment and management

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Objective: The purpose of this article is to provide an understanding of the epidemiology, pathophysiology, risk factors, potentially serious complications, diagnostic modalities, and treatment options available for pediatric obstructive sleep apnea syndrome (OSAS).

Data Sources: The Ovid, MEDLINE, and PubMed databases from 1950 to the present were searched for relevant articles regarding pediatric OSAS.

Study Selection: Articles describing the prevalence, mechanisms, risk factors, complications, and most recent updates on assessment and management of pediatric sleep-disordered breathing (SDB) were used for this review.

Results: The data suggest that SDB may be considered a disease continuum. It ranges in severity from mild obstruction of the upper airway, producing primary snoring, to increased upper airway resistance syndrome (UARS), to continuous episodes of complete upper airway obstruction or OSAS. The degree of sleep disruption, hypoxemia, hypercapnia, and upper airway airflow reduction are main factors in determining the severity of SDB. Mounting evidence implicates OSAS as a risk factor for decreased growth, impaired neurocognitive function, and cardiovascular morbidity. The first treatment of choice for OSAS in children remains tonsillectomy and adenoidectomy.

Conclusions: Sleep-disordered breathing is common in children and can cause minor as well as major disruption of sleep and health problems requiring intervention. Despite apparent symptoms and potentially severe consequences, SDB may be underdiagnosed and unrecognized. Therefore, a high index of suspicion and detailed clinical history and physical examination should be part of any clinical assessment of a child presenting with breathing difficulty during sleep.

Ann Allergy Asthma Immunol. 2011;107:104–109.

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by repeated episodes of upper airway occlusion that result in brief periods of breathing cessation or apnea and a marked reduction in airflow or hypopnea during sleep. The breathing pauses cause acute adverse effects, including oxyhemoglobin desaturation, brain arousals, and sleep fragmentation. Additional work in pediatric sleep disorders has shown that sleep-disordered breathing (SDB) is a continuum of severity from mild obstruction of the upper airway, producing primary snoring, to increased upper airway resistance syndrome (UARS), to continuous episodes of complete upper airway obstruction or OSAS.^{1–3} The degree of sleep disruption, hy-

poxemia, hypercapnia, and upper airway airflow reduction are main factors in determining the severity of SDB.

EPIDEMIOLOGY

Pediatric OSAS is a common underdiagnosed disorder. Up to 20% of normal children snore intermittently, and 7% to 10% are habitual or regular snorers.^{4,5} One percent to 3% of preschool children have OSAS,⁶ which correlates with the peak period of adenotonsillar hypertrophy, a major risk factor for this disorder. Sleep-disordered breathing is more common among boys, children who are overweight, and African Americans.⁷

PATHOPHYSIOLOGY

The cause of pediatric OSAS is not fully understood. It is thought to be attributable to a combination of structural, neuromotor, and other unknown factors. During inspiration, because of the action of the respiratory muscles expanding the lung volume, pressure generated within the airway is slightly lower than atmospheric pressure. While awake, the pharyngeal dilator muscles counteract this negative pressure and maintain airway patency by tonic contractions. Also, the

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Disclosures: The authors have nothing to disclose.

Received for publication January 31, 2011; Received in revised form March 1, 2011; Accepted for publication April 8, 2011.

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doi:10.1016/j.anai.2011.04.004

air usually will flow slowly and exert pressure on the pharyngeal walls. However, during sleep, as a result of decreased muscle tone, the pharyngeal dilator muscles relax and are unable to maintain airway patency.^{8,9} In the case of an upper airway narrowing, the air will flow faster and exert less pressure on the lateral walls, predisposing to collapse of the upper airway, the Venturi and Bernoulli effects.^{8,9} Upper airway collapsibility is more pronounced during rapid eye movement (REM) sleep, because of supraspinal inhibition of the pharyngeal dilator and intercostal respiratory muscles, leading to inability to contract and compensate for any increase in airway resistance present during this stage of sleep.

Therefore, when a child sleeps, an overall increase in upper airway resistance occurs, with a decrease in the compensatory mechanisms that can overcome this resistance. Any anatomic abnormality, whatever the cause, with consequent narrowing of the upper airways will augment the upper airway resistance, predisposing the child to obstruction.

Abnormalities in upper airway neuromotor control probably also contribute to the development of OSAS. This may explain why not all children with similar degrees of upper airway obstruction caused by adenotonsillar hypertrophy develop OSAS.

Once this upper airway obstruction occurs, impaired ventilation leads to oxyhemoglobin desaturation and hypercapnia with subsequent increased respiratory effort and arousal from sleep to reestablish airway patency. This cycle reoccurs several times during sleep, resulting in repetitive hypoxia and sleep fragmentation.

RISK FACTORS FOR OSAS IN CHILDREN

Several structural factors may lead to upper airway narrowing. The most common anatomic abnormality in children is adenotonsillar hypertrophy, with the most common site of obstruction the retropalatal region.^{10–12} Children with craniofacial anomalies that cause upper airway narrowing are also at increased risk of developing OSAS. Examples include retrognathia or micrognathia, midface hypoplasia, mandibular hypoplasia, and macroglossia.

Obesity represents a significant risk factor for OSAS, through increased fat pad deposition in the soft tissue of the neck. This accumulation increases the pharyngeal resistive load and narrowing and therefore airway collapse.

Chronic nasal obstruction is another predisposing factor for OSAS. The obstructed nose behaves like a Starling resistor model. This model can be described in terms of a hollow tube with partial obstruction at the inlet, corresponding to the nose, and a collapsible section downstream, corresponding to the oropharynx. According to this model, when air is drawn into the narrowed inlet, greater suction forces are generated downstream and may contribute to the forces that affect the collapsible segment. Therefore, when nasal obstruction develops, the downstream collapsibility of the oropharynx is increased (Fig 1).

Nasal obstruction induced by a variety of conditions, such as allergic and nonallergic rhinitis, frequently is associated

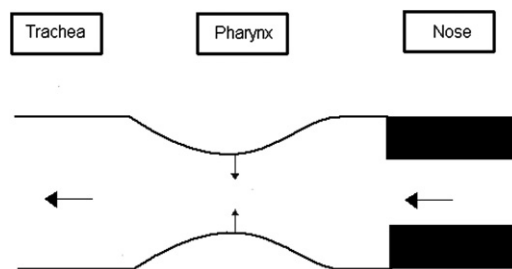


Figure 1. The Starling resistor model: when nasal obstruction develops, the down-stream collapsibility of the oropharynx is increased.

with SDB.¹³ Several studies show that sleep disruption in allergic rhinitis (AR) is directly related not only to SDB and an increase in microarousals during sleep but also to the release of several inflammatory mediators and cytokines involved in the allergic response. For example, inflammatory cytokines interferon gamma, tumor necrosis factor alpha, interleukin (IL) 1 β , IL-4, IL-6, and IL-10 are associated with disruption in sleep architecture with suppression of the REM stage of sleep, which is associated with restorative function.¹⁴ Therefore, its disruption results in reduced concentration and excessive daytime fatigue. As a result, patients with AR often have daytime somnolence, impaired mood, and diminished productivity. Treatment of rhinitis improves sleep quality and daytime sleepiness, possibly because of the reduction of inflammatory mediators and the mechanical reduction of congestion, leading to improvement in SDB.¹⁴

Children with decreased muscle tone because of congenital or acquired disorders, such as myotonic dystrophy, cerebral palsy, dysautonomia, and myopathies, may have pharyngeal muscular hypotonia with difficulty in maintaining adequate muscle tone to keep their airway open during sleep. Therefore, they are at risk of developing OSAS.¹⁵ Down syndrome has several risk factors for OSAS, such as midface hypoplasia, generalized hypotonia, macroglossia, increased oral secretions, and obesity.¹⁶

Sedatives and hypnotics, congenital disorders such as spina bifida, myelomeningocele, mucopolysaccharidosis, sickle cell anemia, strong family history of OSAS, and other conditions also are risk factors.

CLINICAL MANIFESTATIONS

The symptoms of OSAS in children can be divided into night and day. As in adults, loud, disruptive, continuous, and habitual snoring is the most common nighttime symptom, and OSAS is very unlikely without it.¹⁷ However, not all children who snore have OSAS. Between 6% and 12% snore at nighttime, and only between 10% and 30% of those have OSAS, based on polysomnography.¹⁷ In addition to snoring, parents may describe apneas, or breathing pauses, often followed by snorting or gasping, or they may notice that the child is struggling to breathe during sleep and has paradoxical chest wall movement, that is, out-of-phase rib cage and abdominal movement.

“Tossing and turning or having very restless sleep” is commonly described by parents. Children may sweat excessively during sleep, hyperextend their necks, and try to sleep sitting upright, using several pillows. Persistence of primary enuresis or the recurrence of bedwetting in a child previously dry at night also may be associated with OSAS.¹⁸

In adults, sleep fragmentation induced by repetitive apneas and hypopneas manifests as excessive daytime somnolence. In contrast, children with OSAS are more likely to manifest daytime sleepiness behaviorally through hyperactivity, irritability, aggression, and lack of concentration. They may have unrefreshed sleep, difficulty awakening, and headaches, despite adequate time in bed. The latter is thought to be caused by hypercapnia or hypoxia. Children with upper airway obstruction may mouth breathe and may have halitosis, nasal congestion, rhinorrhea, as well as a hyponasal voice, because of their lack of appropriate nasal airflow during speech.

COMPLICATIONS OF OSAS

Obstructive sleep apnea syndrome may lead to decreased growth,^{19–22} impaired neurocognitive function,^{17,23–30} and cardiovascular morbidity.^{31,32} Failure to thrive may be attributable to mechanisms not completely understood but likely related to an increase in nighttime energy expenditure secondary to the excessive work of breathing and disruption of the growth hormone pathway. A study by Freezer et al.²² showed that children with OSAS and failure to thrive had a significant increase in weight gain velocity and a catch-up growth period after tonsillectomy and adenoidectomy (T&A).²²

Children also have problems with inattention, hyperactivity, aggressiveness, daytime sleepiness, and depression, contributing to poor school performance.^{17,23–30} The neurocognitive morbidity usually arises from sleep fragmentation and abnormalities in gas exchange with resultant hypoxia and hypercapnia.

Obstructive sleep apnea syndrome–induced hypoxia can induce pulmonary vasoconstriction, subsequently leading to pulmonary hypertension and cor pulmonale.³¹ Systemic hypertension also may occur. Marcus et al.³² demonstrated diurnal elevation of the diastolic blood pressure in children with OSAS.³² In their study, the diastolic blood pressure index, the difference between the subject’s mean blood pressure during sleep and the blood pressure at the 95th percentile for age and height, significantly correlated with the apnea/hypopnea index.³²

DIAGNOSIS

Overnight polysomnogram (PSG; sleep study) is the “gold standard” for diagnosis and classification of SDB in children.³³

How Is PSG Performed?

Oronasal airflow is measured by a nasal cannula placed under the patient’s nose to monitor nasal breathing and snoring. Chest wall and abdominal wall movement during respiration

is usually measured by means of inductance plethysmography, by signals originating from 2 belts, 1 each around the abdomen and chest. A pulse oximeter determines oxygenation. A 2-lead electrocardiogram (ECG) is applied on the child’s chest to monitor heart rate and cardiac rhythm, and CO₂ is assessed by either a transcutaneous CO₂ monitor or an end-tidal CO₂ probe, helpful to assess hypoventilation. Electroencephalography, electro-oculography, and submental electromyography are used to monitor sleep architecture and arousals. The entire procedure is observed by a sleep technician who documents arousals, snoring, respiratory events, and abnormal sleeping positions and who attends to technical problems. Esophageal pH may be monitored if gastroesophageal reflux is clinically suspected.

Home audiotaping or videotaping: based on previous studies, sensitivity ranged from 71% to 94% and specificity from 29% to 80%. Positive predictive values (PPVs) ranged from 50% to 83%. The negative predictive value (NPV) ranged from 73% to 88%.¹⁰

Overnight oximetry has a PPV of 97% and an NPV of 47% when compared with PSG. It can be useful if a pattern of cyclic oxyhemoglobin desaturation is observed. False-positive results can occur in patients with other comorbidities such as asthma, making the test useful only in otherwise healthy children.¹⁰

Nap PSG during the day or observing the child for only the first 2 hours of night will underestimate the degree of OSAS because of the abbreviated sampling time and the decreased duration of REM sleep at these times. Studies show a PPV of 77% to 100% and an NPV of 17% to 49%.¹⁰

Unattended home PSG has been evaluated in only 1 study, with similar results compared with overnight sleep laboratory studies.¹⁰ The equipment used in this home PSG included respiratory inductive plethysmography (a method to determine ventilation without using oronasal sensors), oximeter pulse waveform, and videotaping, which are not used in the commercially available home sleep monitors. The utility of unattended home PSG in children using commercially available 4- to 6-channel recording equipment has not been studied. The quantitative correspondence between home and laboratory testing must be demonstrated before extrapolating home data to make clinical decisions for treatment and monitoring.

In summary, abbreviated or screening techniques, such as videotaping, nocturnal pulse oximetry, and daytime nap PSG, are helpful when positive. However, because of their poor predictive value, an overnight PSG should be performed if the results are negative and there is a high index of suspicion for OSAS. Home sleep PSG is not yet validated for children.

Diagnostic criteria for SDB

Diagnostic criteria for OSAS in pediatric and adult patients are provided in the American Academy of Sleep Medicine International Classification of Sleep Disorders 2.³³ Up to 5 apneas per hour are normal for adults; however, in children, having more than 1 apnea per hour is considered abnormal.³³

All of the following criteria should be met for diagnosing pediatric OSAS³³:

1. Caregiver reports snoring, labored or obstructed breathing, or both.
2. Caregiver observes at least 1 of the following: paradoxical breathing, movement arousals, diaphoresis, neck hyperextension, excessive daytime sleepiness, hyperactivity or aggressive behavior, impaired growth, morning headaches, or enuresis.
3. PSG shows ≥ 1 respiratory event/hour.
4. PSG demonstrates at least 1 of the following: respiratory-related arousals, oxygen desaturation, hypercapnia, or negative esophageal pressure swings.
5. Conditions are not better explained by another sleep disorder, medical or neurological condition, medication use, or substance abuse.

The American Academy of Sleep Medicine Updated Scoring Manual³⁴ defines UARS as snoring more than 50% of the total sleep time and more than 10 related arousal events per hour.

A careful and thorough clinical history and physical examination should be performed before determining whether a sleep study is warranted. Isolated snoring, without other risk factors and clinical signs or symptoms of SDB, is seldom sufficient to order a sleep study. Polysomnography is performed to confirm the diagnosis of OSAS when it is suggested by the clinical history, to differentiate between OSAS and primary snoring, to assess the severity of the OSAS, to evaluate symptoms such as excessive daytime sleepiness or failure to thrive, and to evaluate the success of an intervention, such as T&A, especially when posttreatment residual symptoms or risk factors for OSAS exist. Other situations exist in which obtaining a sleep study may be beneficial (Table 1).

Whether preoperative PSG should be performed routinely before T&A in otherwise healthy children with clinically suspected SDB and demonstrable adenotonsillar enlargement is a subject of debate. Until further data are available, at a minimum, preoperative sleep studies should be performed in children who are younger than 3 years old and in those with severe symptoms or significant associated disease.

TREATMENT

Surgery, not medical management as in adults, is the primary treatment for children with OSAS, because adenotonsillar hypertrophy is usually the most important cause of airway obstruction. T&A is curative in 80% of cases.^{35–37} Whether the size of the tonsils and adenoids predicts the number of respiratory events during sleep is unknown.³⁸ Therefore, the size of tonsils and adenoids alone should not be the determining factor as to whether to operate, because OSAS results from relative narrowing of the upper airway rather than their absolute size.

Tonsillectomy and adenoidectomy is the first choice of treatment even for those patients who have additional risk factors such as Down syndrome. All patients should undergo

Table 1. Conditions in which obtaining a sleep study may be beneficial^{10,35–39}

1. To confirm the diagnosis of OSAS when clinically suspected
2. To differentiate between OSAS and primary snoring
3. To assess the severity of the OSAS
4. To evaluate symptoms such as excessive daytime sleepiness, growth delay, or failure to thrive
5. To evaluate the success of an intervention, such as T&A, especially when posttreatment residual symptoms or risk factors for OSAS exist
6. Postoperative assessment after T&A or other oronasopharyngeal surgery for children with severe preoperative OSAS
7. Titration of patient with OSAS treated with continuous positive-airway pressure [CPAP] or bilevel positive airway pressure [BiPAP]
8. PSG with esophageal pH monitoring to assess the relationship of gastroesophageal reflux with respiratory events such as nocturnal asthma, cough, apnea, or hypoxemia
9. Unexplained congestive heart failure, cor pulmonale, or pulmonary hypertension
10. Refractory enuresis after age 6
11. Atypical attentional or behavioral disorders, especially if accompanied by or alternating with hypersomnolence

clinical evaluation 6 to 8 weeks after surgery, and high-risk patients or children with severe OSAS may need reevaluation by doing a postoperative polysomnogram to examine for residual disease.

Children with OSAS are at 25% increased risk for postoperative respiratory compromise after T&A compared with 1% of children undergoing adenotonsillectomy for other indications.³⁹ Those at highest risk include children with severe OSAS, associated medical conditions, or children younger than 3 years of age.⁴⁰ Patients with complications of OSAS, a manifestation of disease severity, are also at highest risk. High-risk patients are not candidates for outpatient surgery, and, after surgery, they should be observed overnight in a pediatric intensive care unit or hospital facility.

Uvulopalatopharyngoplasty has been performed in special subgroups in which neuromotor tone is an important contributor, for example, with cerebral palsy and Down syndrome. Other craniofacial surgeries may be considered on an individual basis, but it is not usually indicated for normal children whose facial bones are still growing. Tracheostomy, which is the definitive treatment for upper airway obstruction, should be reserved for severe refractory or life-threatening situations.

The use of continuous positive-airway pressure (CPAP) is another treatment option for pediatric OSAS. It works by delivering CPAP that pneumatically splints the upper airway, maintaining its patency and ensuring less collapsibility and thus normalization of breathing and oxygenation.⁴¹ It is used for children in whom a surgical intervention is not possible or desired or in whom surgery does not result in complete resolution of symptoms. It may be helpful for patients with neuromuscular diseases and children with anatomic abnor-

malities of the upper airway.^{41–45} If obesity appears to play a role, weight reduction should be encouraged. Continuous positive-airway pressure also may be beneficial for this subgroup.

Continuous positive-airway pressure is noninvasive and has a relatively minimal side effect profile. Compliance with CPAP, although greater than in adults, is still an issue in children,⁴⁵ in whom compliance ranges from 50% to 100%.^{46,47} Once CPAP therapy is started, children must be frequently monitored, at least yearly, for mask refitting and CPAP re-titration. Body shapes in adolescence are changing rapidly. Therefore, CPAP therapy may be preferable to non-reversible approaches such as surgery. Also, in this age group, OSAS oral dental appliances can affect oral airway shape during this phase of rapid facial growth, limiting their usefulness in this population.

Avoidance of environmental tobacco smoke and other indoor pollutants, indoor allergens, and sleeping in the supine position are adjunctive measures that may be helpful to treat childhood OSAS but have not yet been prospectively evaluated. Therefore, implementation of these adjunctive therapies should not delay specific treatment of OSAS.

The Role of Intranasal Glucocorticosteroids (INCS) and Leukotriene Modifier Therapy in Pediatric OSAS Treatment

Intranasal glucocorticosteroids (INCSs) have a modest helpful effect in pediatric OSAS. Alexopoulos et al demonstrated that 4 weeks of intranasal budesonide improves both polysomnography findings and symptoms in children with mild sleep-disordered breathing. The clinical effect is maintained for several months after treatment is stopped.⁴⁸ Similar beneficial effects of improving SDB and daytime quality of life was shown in children with allergic rhinitis treated with intranasal budesonide.⁴⁹ In a triple-blind, parallel design, placebo-controlled study of 25 children with OSAS and adenotonsillar hypertrophy, intranasal fluticasone improved SDB, oxyhemoglobin saturation, and arousal frequency compared with placebo.⁵⁰ Oral montelukast treatment induced significant reductions in adenoid size and respiratory-related sleep disturbances in children with mild SDB.⁵¹ Combined anti-inflammatory therapy that consists of montelukast and intranasal budesonide effectively improved or normalized respiratory and sleep disturbances in children with residual SDB after T&A.⁵² Whether withdrawal is associated with recurrence is unknown; therefore, follow-up is essential.

CONCLUSION

Sleep-disordered breathing is common in children and can cause minor as well as major disruption of sleep and health problems requiring intervention. Clinicians must be alert to the full range of clinical manifestations of SDB in children. Despite apparent symptoms and potentially severe consequences, SDB may be underdiagnosed and unrecognized. Therefore, a high index of suspicion, detailed clinical history, and physical examination should be part of any clinical

assessment of a child presenting with breathing difficulty during sleep.

ACKNOWLEDGMENTS

The authors would like to thank Dr Roger Fox, Dr Robert Pesek, Dr David Fitzhugh, Dr Jim Parkerson, Dr Ahmed Butt, and Dr Salman Aljubran for their suggestions in editing this manuscript.

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