Pediatric Obstructive Sleep Apnea Syndrome

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KEYWORDS

• Children • Sleep-disordered breathing
• Obstructive sleep apnea syndrome • Sleep homeostasis

Obstructive sleep apnea (OSA) is a common and serious cause of metabolic, cardiovascular, and neurocognitive morbidity in children. The essential feature of OSA is increased upper airway resistance during sleep, resulting in intermittent partial or complete airway closure, associated with increased respiratory effort, sleep fragmentation, and/or gas exchange abnormalities. Consequently, children with OSA encounter a combination of oxidative stress, inflammation, autonomic activation, and/or disruption of sleep homeostasis. Causes of airway narrowing include soft tissue hypertrophy, craniofacial abnormalities, and/or neuromuscular deficits. There appears to be important individual genetic susceptibility and environmental factors that influence the expression of OSA sequelae.

The spectrum of *obstructive* sleep-disordered breathing ranges from persistent *primary snoring* to the frank, intermittent occlusion seen in *obstructive sleep apnea*. In most cases, partial obstructive events are also present, which share the pathophysiology and consequences of complete obstruction. Thus, the more inclusive term, *obstructive sleep apnea syndrome (OSAS)*, is be used in this article. Although primary snoring was traditionally defined as a benign condition, recent evidence suggests that snoring per se may be associated with adverse neurobehavioral outcomes.[1,2] In this review, the authors aim to encapsulate the salient features of pediatric OSAS, and focus on recent data regarding adverse consequences and treatment options.

EPIDEMIOLOGY

The epidemiology of pediatric OSAS has not been precisely established due to methodological limitations regarding diagnostic criteria and the paucity of population-based studies. OSAS occurs in children from neonates to adolescents, with little evidence of a systematic variability with age. Habitual snoring is nearly universally observed in pediatric OSAS, though the reliability of a negative clinical history of snoring is poor, particularly in older children. The prevalence of snoring and OSAS is predicated on the questionnaire phrasing and whether objective testing was performed. Considering representative questionnaire-based studies with a sample size of at least 1000, 4.2% "always snored"[3]; 10.9%"almost always" snored[4]; 11.7% snored "greater than or equal to 3 times per week"[5]; and 27% snored "sometimes."[6] The incidence of OSAS determined objectively in population-based studies was 2.2 to 3.8%.[7,8] The primary risk factors for pediatric

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OSAS and the putative mechanisms are listed in **Table 1**.

CLINICAL AND POLYSOMNOGRAPHIC FINDINGS IN PEDIATRIC OSAS

The principal symptoms and physical examination findings in children with OSAS are listed in **Boxes 1** and **2**. However, clinical history/questionnaires alone have poor sensitivity and specificity for the diagnosis of OSAS,[9] leading a consensus panel to recommend objective testing for snoring children.[10] Polysomnography represents the gold standard for establishing the presence and severity of sleep-disordered breathing in children, and can be performed in children of all ages. A comprehensive review of methodological considerations in pediatric polysomnography has recently been published.[11] There is minimal night-to-night variability in the respiratory variables during polysomnography.[12] Normative data from several large samples of nonsnoring, normal children after infancy (**Table 2**) indicate that (a) obstructive apneas and hypopneas very rarely occur; (b) inspiratory flow limitation and respiratory effort-related arousals are uncommon; and (c) oxygen saturation rarely drops below 90%, even during normal 10- to 15-second respiratory pauses following sighs or movements.[13–15]

Arousal from sleep is a protective reflex mechanism that restores airway patency, but is associated with sleep fragmentation. Although visible electroencephalographic arousals are present in only 51% of obstructive events in children, frequency domain analysis demonstrates additional evidence of sleep disruption.[16] Autonomic activation is present at the end of nearly all obstructive events, as measured by heart rate variability, blood pressure elevations, pulse transit time, and peripheral arterial tonometry. Children with OSAS have increases in slow wave sleep (23.5 vs 28.8%), decreases in rapid eye movement (REM) sleep (22.3 vs 17.3%), and decreases in spontaneous arousals.[17] Together, these observations provide evidence for a subtle disruption in sleep architecture, with increased sleep pressure and a homeostatic elevation in the arousal threshold.

PATHOPHYSIOLOGY OF OSAS IN CHILDREN

Children with OSAS have increased upper airway resistance during sleep due to a combination of soft tissue hypertrophy, craniofacial dysmorphology, neuromuscular weakness, or obesity. However, most children with OSAS obtain long periods of stable breathing during sleep, indicating a role for other determinants of airway patency such as neuromuscular activation, ventilatory control, and arousal threshold.

Anatomy

Children with OSAS have narrower pharyngeal airways and increased nasal resistance compared with control children.[18,19] Adenotonsillar hypertrophy, maxillary constriction, and retro-/micrognathia are the most common anatomic abnormalities in OSAS. However, the correlation between apnea severity and adenotonsillar size is surprisingly variable.[20,21] Mouth breathing children habitually lower their mandible resulting in a high-arched palate, narrow maxilla, retrognathia,

Table 1
Epidemiologic risk factors for pediatric obstructive sleep apnea syndrome

Adenotonsillar hypertrophy	Increased airway resistance
Obesity	Fatty infiltration of airway, abnormal ventilatory control
Race (African American)	Craniofacial structure, socioeconomic
Gender (male)	Slight male predominance in prepubertal children, which increases markedly after puberty
Prematurity	Neurologic impairment, adverse craniofacial growth, abnormal ventilatory control
Craniofacial dysmorphology	Increased airway resistance
Neurologic disorders	Abnormal motor control of the upper airway
Nasal/pharyngeal inflammation	Allergy or infection increasing airway resistance
Socioeconomic/environmental	Neighborhood disadvantage, passive cigarette smoke, indoor allergens, sleep quality (noise, stress)
Family history of OSAS	Heritable craniofacial structure, neuromuscular compensation, arousal threshold, ventilatory control

Box 1
Symptoms of pediatric obstructive sleep apnea syndrome

Diurnal Symptoms
Sleep
- Excessive daytime sleepiness
- Napping
- Morning headaches
- Difficult arousing from sleep

Neurocognitive
- Aggressive behavior
- Poor school performance
- Depression
- Attention deficit
- Hyperactivity
- Moodiness

Upper Airway
- Mouth breathing
- Nasal congestion
- Frequent otitis media, sinusitis
- Nasal speech

Nocturnal Symptoms
Snoring
Witnessed apnea
Choking/snorting noises
Increased work of breathing
Paradoxic respirations
Enuresis
Restless sleep
Diaphoresis
Hyperextended neck
Frequent awakenings
Mouth breathing/dry mouth
Parasomnias

Box 2
Physical examination in pediatric obstructive sleep apnea syndrome

General
Obesity
Increased neck circumference
Failure to thrive
Sleepiness

Head
Nose
- Swollen nasal mucous membranes
- Deviated septum

Mouth
- Tonsillar hypertrophy
- High-arched palate
- Elongated soft palate
- Posterior buccal cross-bite
- Overbite
- Crowded oropharynx
- Macroglossia
- Glossoptosis

Face
- Midfacial hypoplasia
- Micrognathia/retrognathia
- Long face syndrome
  - Infraorbital darkening
  - Mouth breathing
  - Elongated midface
  - Nasal atrophy

Cardiovascular
Systemic hypertension
Loud P2

Extremities
Edema
Clubbing

and increased lower facial height. This constellation of findings has been termed the ''long face syndrome,'' and is associated with OSAS.[22,23] Thus not only does upper airway obstruction predispose to OSAS, but it also has an adverse effect on craniofacial development, posing an increased future risk of OSAS. Relief of upper airway obstruction during periods of rapid facial growth may at least partially normalize dentofacial abnormalities that predispose to OSAS.

Airway Mechanics

The upper airway is a highly compliant tube in which small changes in pressure produces large changes in airway cross-sectional area. The luminal pressure at which airway collapse occurs is termed the *critical closing pressure* (Pcrit). The Pcrit is an index of both the viscoelastic and neuromuscular properties of the pharynx. Children

Table 2
Polysomnographic data in normal children

Sleep	
EEG arousal index (per h TST)	9 ± 3
Sleep efficiency (%)	89 ± 7
Stage 1 (% TST)	5 ± 3
Stage 2 (% TST)	42 ± 8
Slow wave sleep (% TST)	26 ± 8
REM sleep (% TST)	20 ± 5
REM cycles	4 ± 1
Periodic leg movement index (per h TST)	1 ± 1
Respiratory	
Obstructive apnea index (per h TST)	0.0 ± 0.1
Obstructive apnea/hypopnea index (per h TST)	0.1 ± 0.1
Central apnea index (per h TST)	0.5 ± 0.5
$P_{ET}CO_2 \geq 50$ mm Hg (% TST)	2.8 ± 11.3
Peak $P_{ET}CO_2$ (mm Hg)	46 ± 3
S_pO_2 >95% (% TST)	99.6 ± 1
S_pO_2 90%–95% (% TST)	0.4 ± 1
S_pO_2 <90% (% TST)	0.05 ± 0.2
Desaturation index (≥4%, per h TST)	0.4 ± 0.8
S_pO_2 Nadir (%)	93 ± 4

Data are presented as mean ± SD.
Abbreviations: EEG, electroencephalograph; REM, rapid eye movement; TST, total sleep time.
Data from Refs.[14,17,125–128]

with OSAS have a higher Pcrit than control subjects[24] and children with habitual snoring.[25] Pcrit correlates with the severity of OSAS, and decreases following adenotonsillectomy.[25] Of note, the Pcrit in OSAS patients after adenotonsillectomy does not decrease to level of control subjects[24] or even primary snorers,[25] suggesting that subtle abnormalities of anatomy or neuromuscular control remain after treatment.

Neuromuscular Compensation, Arousal, and Ventilatory Control

Upper airway muscles that are phasically activated during inspiration, such as the genioglossus, increase both the luminal size and stiffness of the airway. During wakefulness, children with OSAS have increased genioglossus activity compared with control children.[26] At sleep onset, pharyngeal dilator activity is reduced, ventilatory variability increases, and an apneic threshold slightly below eupneic levels is observed in non-REM sleep. Airway collapse is offset by increased pharyngeal dilator activity in response to hypercapnia and negative luminal pressure. Respiratory control mechanisms modulate ventilation and, therefore, pharyngeal dilator activation, in non-REM sleep. Arousal from sleep immediately opens the airway and normalizes gas exchange abnormalities. However, arousal may also be considered an adverse epiphenomenon that potentiates obstructive cycling by augmenting ventilatory overshoot, interfering with sleep homeostasis.[27] Paroxysmal reductions in pharyngeal dilator activity related to central REM processes likely account for the disproportionate severity of OSAS observed during REM sleep.

Obesity

The prevalence of childhood obesity has tripled in the last 25 years, and is presently estimated to be 17% to 18%. Obese children are more likely to snore than lean children.[28] The incidence of OSAS in obese children is high at 36%,[29] and may exceed 60% if habitual snoring is present.[30] The risk of having moderate OSAS increases 12% for each 1 kg/m^2 of body mass index (BMI; calculated as the child's weight in kilograms divided by height in meters squared) above the mean.[31] Nevertheless, the relationship between BMI and OSAS severity is often poor, suggesting

that *fat distribution* is of considerable importance.[32] Obesity can contribute to the severity of OSAS by influencing the dimension and collapsibility of the upper airway, as well as altering ventilatory control. Both OSAS and obesity are considered chronic, low-grade systemic inflammatory states and may act synergistically to produce cardiovascular, metabolic, and neurocognitive morbidities (**Box 3**). Obesity and OSAS are also associated with an impaired quality of life and sleepiness.[33–35]

Most obese children with OSAS will also have adenotonsillar hypertrophy.[30] However, when obese and lean children with OSAS are matched for disease severity, the obese children have less adenotonsillar hypertrophy, but significantly higher Mallampati scores (indicating more crowding of the oropharynx).[32] This finding also supports the concept that a central distribution of adiposity poses the greatest risk for OSAS. Obese children with OSAS have more obstructive events in the supine position, whereas nonobese children with OSAS are more severe in the prone or side positions.[36] This result suggests that there are important physiologic differences between obese and nonobese airways.

Adenotonsillectomy in obese children with OSAS results in a marked reduction in apnea/hypopnea index (AHI; expressed as the number of apneas and hypopneas per hour of sleep), but 76% have residual OSAS.[37,38] One series reported that 56% of obese children with OSAS required continuous positive airway pressure (CPAP) following adenotonsillectomy.[39] Weight loss in obese children of 18.7 kg over 20 weeks resulted in a reduction in the AHI from 14.1 to 1.6 per hour.[40] However, another study reported that 38% of obese children had an AHI of more than 2/h after a 24-kg weight loss over 5 months.[41] Bariatric surgery in adolescents resulting in an average 58 kg weight loss over 5 months resulted in a reduction in the AHI from a median of 9.1 to 0.7 per hour, with only 1 child with residual OSAS.[42] Postoperative respiratory complications are higher in obese children with suspected OSAS.

Box 3
Sequelae of pediatric obstructive sleep apnea

- Metabolic
  - Elevated C-reactive protein
  - Insulin resistance
  - Hypercholesterolemia
  - Elevated transaminases
  - Decreased insulinlike growth factor
  - Decreased/altered growth hormone secretion
- Neurocognitive
  - Decreased quality of life
  - Aggressive behavior
  - Poor school performance
  - Depression
  - Attention deficit
  - Hyperactivity
  - Moodiness
- Cardiovascular
  - Autonomic dysfunction
  - Systemic hypertension
  - Absent blood pressure "dipping" during sleep
  - Left ventricular dysfunction
  - Pulmonary hypertension
  - Abnormal heart rate variability
  - Elevated vascular endothelial growth factor

SEQUELAE OF PEDIATRIC OBSTRUCTIVE SLEEP APNEA

Metabolic Sequelae

Failure to thrive was reported in 27 to 62% of cases in early case series of pediatric OSAS.[43,44] The probable origin is a reduction of insulinlike growth factor (IGF) and growth hormone secretion. IGF binding protein 3 (IGFBP-3), which is correlated to growth hormone secretion, is decreased in children with OSAS. Also, both IGF-1 and IGFBP-3 were observed to increase following adenotonsillectomy, and catch-up growth, including height and weight, occurs.[45,46] In fact, increases in BMI *z*-scores occur in both lean and obese children following OSAS treatment.[46,47] More recently, the increased awareness of the adverse consequences of OSAS has made the presentation of failure to thrive rare, and indeed, obesity is present in nearly half of cases.[48] Leptin is an adipocyte-secreted peptide secreted that regulates metabolism, hunger, and inflammation, and stimulates ventilation. Leptin levels are increased in children with OSAS,[49] and decrease after treatment with CPAP.[50]

Obesity in children is associated with insulin resistance, dyslipidemia, and hypertension, termed the "metabolic syndrome," which is associated with adverse cardiovascular outcomes into adulthood.[51] Other factors that may influence the

expression of the metabolic syndrome include genetics, diet, physical activity, and possibly, OSAS. The role of OSAS in the development of the metabolic syndrome in children is complex and is limited by cross-sectional data. In *obese* children, OSAS has been independently associated with insulin resistance,[52–54] dyslipidemia,[52,54] and blood pressure dysregulation.[52,55] By contrast, OSAS does not appear to increase the risk of insulin resistance in *lean* children[56] or *morbidly obese* children. The combination of obesity and OSAS likely magnify the proinflammatory comorbidities observed in both conditions.

Cardiovascular Sequelae

Children with OSAS have cardiovascular abnormalities ranging from autonomic dysfunction to structural heart disease (see **Box 3**), and may be predisposed toward more serious morbidity and mortality as adults. The pathophysiology is multifactorial including altered sympathovagal balance, oxidative stress, production of inflammatory cytokines, vascular remodeling, and endothelial cell dysfunction. In children with OSAS, urinary levels of catecholamines are elevated,[57] and sympathetic drive is increased based on heart rate variability, peripheral arterial tonometry, pulse transit time, and beat-to-beat blood pressure. Of importance is that these abnormalities are present in OSAS patients during both wakefulness[58] and sleep,[59] suggesting generalized autonomic dysfunction. Complicating the role of OSAS in the genesis of cardiovascular morbidity is the profound effect of obesity, genetic susceptibility factors, and the environment.

Blood pressure (BP) dysregulation has been reported in children with OSAS compared with controls during wakefulness[55,60] and sleep,[55] though frank hypertension is rare.[55,61] Children with severe OSAS (AHI >5 events/h) have an increased morning BP surge, elevated mean 24-hour BP, and lack the normal ''dipping'' of BP at sleep onset (**Fig. 1**).[55,62] The sensitivity of the baroreflex system is reduced in children with OSAS, impairing their ability to maintain cardiovascular homeostasis.[63] Of note, BP dysregulation and lower baroreflex gain is observed even in children with mild OSAS (AHI 1–5 events/h), supporting the need to intervene at early stages in the disease.[55] Paradoxically, some children with OSAS develop orthostatic hypotension and therefore are reported to have low systemic blood pressure and orthostatic hypotension.[61]

Children with OSAS have been reported to have echocardiographic evidence for left ventricular hypertrophy,[64] right ventricular hypertrophy,[64]

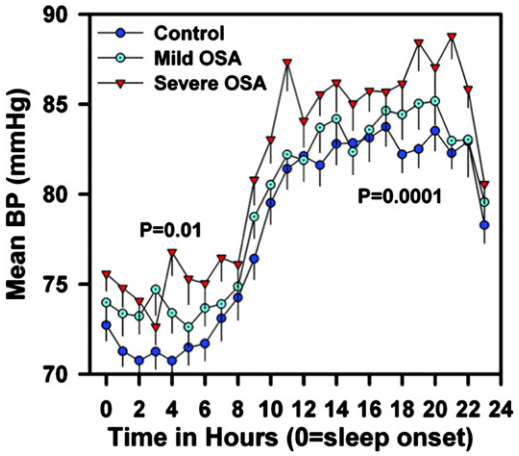

Fig. 1. Group mean 24-hour ambulatory BP recording for children with mild OSA (AHI 1–5/h), severe OSA (>5/h), and a control population. Sleep onset is at time 0. Children with severe OSA have significantly greater mean BP during wakefulness and sleep. (*From* Amin R, Somers VK, McConnell K, et al. Activity-adjusted 24-hour ambulatory blood pressure and cardiac remodeling in children with sleep-disordered breathing. Hypertension 2008;51:84–91; with permission.)

and decreased left ventricular function,[65] without clinical symptoms. The increase in systolic BP, morning BP surge, and BP variability has been associated with increasing left ventricular wall thickness.[55,63] Thus, the subtle changes in BP homeostasis observed in children with OSAS may be an intermediate phenotype, leading to significant cardiovascular morbidity over time. Improvement of left ventricular function has been observed following treatment of OSAS.[65] Right and left ventricular hypertrophy has been associated with an increased risk of postoperative complications in children with OSAS, and is suspected to be a risk factor for adverse cardiovascular outcomes in adulthood.

The recurrent episodes of hypoxemia and arousal associated with OSAS are associated with oxidative stress and systemic inflammation, independent of obesity. Children with OSAS have elevated serum levels of tumor necrosis factor α (TNF-α), C-reactive protein (CRP),[66] interferon-γ (INF-γ),[67] interleukin (IL)-6,[68] and IL-8.[67] Pathology studies of tonsillar tissue from children with OSAS demonstrate increased expression of TNF-α and IL-6, compared with children with recurrent tonsillitis.[69] In addition, levels of IL-8,[70] IL-6,[66,68] and CRP[54,71] decline following treatment of OSAS. Of note, children with a family history of premature cardiovascular disease were more likely to have residual endothelial cell dysfunction following treatment.[72]

Neuropsychological Sequelae

Children with symptoms of OSAS have been reported to have a wide range of neuropsychological dysfunction, including cognition,[73] hyperactivity,[74] sleepiness,[33] memory,[75] executive function,[76] attention,[77] school performance,[78,79] and behavior.[77] Parents and teachers both report disruptive behavior including aggression, conduct, and emotional control.[80] Even mild OSAS or primary snoring (increased respiratory effort without discrete obstructive events) is associated with adverse neurodevelopmental outcomes.[2,75,76,81] Children with attention-deficit hyperactivity disorder (ADHD) have a high incidence of OSAS both subjectively and objectively.[82] In contrast, the incidence of ADHD by DSM-IV-R (*Diagnostic and Statistical Manual of Mental Disorders* Fourth Edition—Text Revised) criteria was 28% in a population of children undergoing adenotonsillectomy for predominantly obstructive indications.[83] Treatment of OSAS with adenotonsillectomy has been shown to improve hyperactive behavior,[83] inattention,[84] sleepiness,[84] behavior,[85] school performance,[78] and cognition.[86,87] However, a history of frequent or loud snoring between 2 and 6 years of age was associated with lower academic performance at 13 to 14 years old, suggesting that OSAS-induced deficits incurred during periods of brain development may not be fully reversible.[88]

Excessive daytime sleepiness (EDS) is rarely reported by children with OSAS themselves. Parental reports vary with the type of questionnaire used, from 7% ("moderate/severe EDS") using a single question,[9] to 49% ("problematic subjective sleepiness") using the more comprehensive 4-item Pediatric Sleep Questionnaire-Sleepiness Subscale (PSQ-SS).[89] There was a good correlation between the subjective PSQ-SS questionnaire and the objective Multiple Sleep Latency Test (MSLT).[89] Objective sleepiness in children with OSAS evaluated with an MSLT varies between approximately 13% and 40%.[33,89] Of importance is that parents will not report EDS in over 50% of cases in which the mean MSLT sleep is less than 12 minutes, indicating pathologic sleepiness. Objective sleepiness is positively associated with AHI, oxygen desaturation, respiratory arousal index (number of arousals per hour of sleep), and BMI.[33] Obese children with OSAS are more likely to have objective sleepiness than lean children with OSAS, at all levels of OSAS severity.[33]

DIAGNOSTIC AND TREATMENT PARADIGM

The optimal methodology and criteria for the diagnosis of OSAS in children has not been established. Previous efforts to define OSAS severity with threshold levels of the AHI (mild 1–5/h, moderate 5–10/h, severe >10/h), gas exchange abnormalities, or sleep fragmentation have proven unsatisfactory, because they fail to account for the individual trait susceptibility to the neurocognitive, cardiovascular, and metabolic sequelae of OSAS. Thus the threshold amount of OSAS associated with adverse consequences varies widely among children. Therefore, current efforts to diagnose and classify OSAS are using the *personalized medicine* paradigm, in which the genomic and molecular profile of an individual is combined with clinical and polysomnographic phenotyping. Toward this end, a hybrid approach to the diagnosis and treatment of OSAS in children has been proposed, combining polysomnographic indices, symptoms, and biomarkers,[90] but this has not been rigorously studied.

Despite advances in the recognition of abnormal respiratory patterns during sleep, there is no clear consensus on the severity of childhood OSAS that warrants treatment. The choice of therapy is predicated on the etiology, severity, natural history, and therapeutic options available for the increased upper airway resistance. Most clinicians consider adenotonsillectomy as the first line of treatment in the setting of adenotonsillar hypertrophy. However, with a compatible clinical history and physical examination of allergies, the threshold level of OSAS necessary for treatment with intranasal steroids and leukotriene antagonists is low. By contrast, it is recognized that the initiation of *CPAP* is fraught with difficulties in tolerance and may itself be disruptive of sleep. Thus, initiating CPAP therapy requires more polysomnographic evidence of obstruction (usually AHI >5 events/h), more profound gas exchange abnormalities (SpO_2 <90%), increased sleep fragmentation (arousal index >15/h), or neurobehavioral symptoms. Finally, children with severe OSAS polysomnographically, and severe manifestations including failure to thrive, pulmonary hypertension, and marked aberrations in daytime functioning, would mandate consideration of all available therapies, including medically supervised weight loss and, if life-threatening, tracheotomy.

Pharmacologic Therapy

Leukotrienes and their receptors are increased in adenotonsillar tissue[91] and exhaled condensate[92] of children with OSAS. Topical intranasal steroids have been shown to decrease adenoidal hypertrophy and improve symptom scores of obstructed breathing.[93] Aqueous beclomethasone decreased the adenoid/choanae ratio from 91%

at baseline, to 77% at 1 month, and 62% after 6 months.[93] Several studies have documented reduction in the AHI following a course of nasal steroids: (1) 5 weeks of intranasal fluticasone decreased the AHI from 11 to 6/h[94]; (2) 6 weeks of intranasal budesonide decreased the AHI from 3.7 to 1.3/h[95]; (3) 4 weeks of intranasal budesonide reduced the AHI from 5.2 to 3.2/h.[96] The improvement in OSAS severity after discontinuing intranasal steroid therapy appears to be stable after at least 2 months polysomnographically,[95] and after at least 9 months symptomatically.[96] Children whose symptoms improve with nasal steroids are less likely to have an adenotonsillectomy within 2 years, compared with nonresponders (54% vs 83%).[97] The combination of budesonide and montelukast in children with mild residual OSAS following adenotonsillectomy resulted in a reduction in the AHI from 3.9 to 0.3 per hour after 3 months of therapy.[98] The long-term success of anti-inflammatory therapy has not been established.

Positive Pressure/Oxygen Therapy

CPAP delivered noninvasively through nasal or oronasal interface is a highly efficacious therapy for pediatric OSAS, though long-term compliance is often problematic.[99–101] CPAP is typically reserved for moderate to severe OSAS not amenable to surgical or pharmacologic treatment. A properly fitted mask and adequate age-appropriate behavioral training is crucial to the success of CPAP therapy.[102,103] The minimum daily duration of CPAP therapy required to mitigate the adverse effects of OSAS is unknown. In a prospective study of children with severe OSAS, CPAP compliance monitored electronically after approximately 1 month of therapy revealed that CPAP usage of longer than 4 hours, longer than 5 hours, and longer than 6 hours per night was observed in only 54%, 48%, and 31% of patients, respectively.[104] The reported side effects of CPAP in children include skin erythema, eye irritation, congestion, rhinorrhea, and maxillary growth impairment.[105] CPAP was reported to be equally as efficacious as bilevel ventilation for the treatment of OSAS in children.[105]

Oxygen therapy has a limited role in the treatment of children with OSAS. Two studies have evaluated the effect of supplemental oxygen in children with OSAS, with disappointing results. Improvements in oxygen saturation are evident, but there is no significant decrease in OSAS severity.[106,107] In addition, 2 children with OSAS developed a marked increase in P_{CO_2} on supplemental oxygen (>75 torr).[106] Thus, oxygen therapy will not alleviate the sleep fragmentation or hypoventilation associated with OSAS.

Surgical Therapy

Successful treatment of children with OSAS is predicated on identifying the origin of the increased upper airway resistance. In most children with documented OSAS and adenotonsillar hypertrophy, an adenotonsillectomy is the recommended first-line therapy. Following adenotonsillectomy, children with OSAS have reported improvements in quality of life,[108] behavior,[85] attention,[83] growth,[109] cognitive scores,[86,87] and school performance.[78] However, residual OSAS may be present polysomnographically in more than 40% of cases postoperatively.[37,38] Moreover, there is no consensus on whether the adenoids, tonsils, or both need to be removed. A retrospective study in children undergoing adenoidectomy for obstructive symptoms reported that 27% subsequently had a tonsillectomy.[110] Selected patients may benefit from treatments of additional sites of obstruction, such as turbinectomy, deviated septum repair, maxillary expansion, mandibular distraction, maxillary distraction, tongue reduction/advancement, or lingual tonsillar removal.[111]

Parental reports of OSAS symptomatology post adenotonsillectomy are usually favorable, though objective testing often reveals considerable residual obstruction. Complete normalization of OSAS (AHI<1) following adenotonsillectomy was observed in only 25% of patients, with 46% having persistent mild OSAS (1<AHI<5), and 29% having at least moderate OSAS (AHI>5).[37] Children with residual OSAS following adenotonsillectomy are most likely to have obesity, severe OSA, enlarged turbinates, deviated septum, neurologic disorders, or craniofacial malformations.[37,38] Together, these studies indicate that adenotonsillar hypertrophy is only one of several important determinants of OSAS in children. A recent meta-analysis of the cure rate of adenotonsillectomy for OSAS (defined as an AHI <1) was only 60%, though there was a marked improvement in OSAS in the majority of children.[112]

Adenotonsillectomy for OSAS is associated with postoperative bleeding (3% of cases), pain, and respiratory decompensation (20% of cases), including pulmonary edema, upper airway obstruction and, rarely, death.[113–115] Adenoidectomy alone has a lower risk of postoperative bleeding (<0.5%). The first postoperative night may be associated with significant OSAS, resulting in profound desaturation.[116] However, the majority of children with mild OSAS will improve

on the first postoperative night.[117] Patients at high risk for postoperative complications include children younger than 3 years, or those with prematurity, craniofacial abnormalities, obesity, neuromuscular weakness, cerebral palsy, cor pulmonale, or severe OSAS.[118,119] Careful postoperative monitoring of high-risk patients in a pediatric intensive care unit is recommended. Children experiencing respiratory distress postoperatively have been reported to benefit from positive airway pressure.[118]

Dental Therapy

Craniofacial growth in children is determined by both genetic and environmental factors. Chronic mouth breathing results in aberrant facial development, including maxillary constriction. Rapid maxillary expansion, using an orthodontic appliance to deliver a lateral force to the upper posterior molars, opens the midpalatal suture transversely and therefore widens the nasal cavity. Over a period of about 3 weeks, the intermolar distance increases approximately 3.9 mm, and the nasal pyriform opening increases 1.3 mm.[120] After 4 months of therapy, rapid maxillary expansion decreases nasal resistance[120] and improves OSAS in children with maxillary constriction.[120–122] Children with OSAS due to both maxillary constriction and adenotonsillar hypertrophy generally require both rapid maxillary expansion and adenotonsillectomy to resolve the OSAS.

Children with OSAS and dysgnathia (87% deep/retrusive bite, 13% cross-bite) were randomized into a 6-month trial of a custom mandibular advancement device versus an untreated control group.[123] Twenty-six percent of the children in the treatment group discontinued therapy for unknown reasons. As a group, follow-up polysomnography revealed a decrease in the AHI from 7.1 to 2.6 events per hour, but 20% of the patients had a residual AHI above 5 events/h.[123] Another pediatric study similarly demonstrated that mandibular advancement devices reduced the AHI from 8 to 4 events per hour.[124] Nevertheless, there are insufficient long-term efficacy data using mandibular advancement devices to treat OSAS in children with dysgnathia.

SUMMARY

OSAS is a common and serious cause of metabolic, cardiovascular, and neurocognitive morbidity in children. The essential feature of OSAS is increased upper airway resistance during sleep, resulting in intermittent partial or complete airway closure, increased respiratory effort, sleep fragmentation, or gas exchange abnormalities. Consequently, children with OSAS encounter a combination of oxidative stress, inflammation, autonomic activation, and disruption of sleep homeostasis. Causes of airway narrowing include soft tissue hypertrophy, craniofacial abnormalities, or neuromuscular deficits. Most children with OSAS obtain long periods of stable breathing during sleep, indicating a role for other determinants of airway patency such as neuromuscular activation, ventilatory control, and arousal threshold. There appear to be important individual genetic susceptibility and environmental factors that influence the expression of OSAS sequelae. In some children even mild OSAS can result in adverse neurocognitive and cardiovascular sequelae. The choice of therapy is predicated on the etiology, severity, natural history, and therapeutic options available for the increased upper airway resistance. Most clinicians consider adenotonsillectomy the first-line treatment in the setting of adenotonsillar hypertrophy. However, anti-inflammatory therapy with intranasal steroids and leukotriene antagonists is helpful in many cases. CPAP is generally reserved for children without surgically correctable obstruction, or significant residual OSAS following other treatments. Preliminary data suggest that the consequences of pediatric OSAS are at least partially reversible with appropriate therapy. However, there is concern that exposure to OSAS during critical developmental intervals may result in lasting neurocognitive deficits.

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