Obstructive Sleep Apnea in Children: What are the Treatment Options?

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Abstract
Pediatric obstructive sleep apnea syndrome is a common disorder with important health consequences such as cognitive and behavioral problems, delay in somatic growth and cardiovascular complications. Polysomnography is used to diagnose and evaluate the severity of obstructive sleep apnea. The aim of this review is to discuss the definition, clinical findings, diagnosis and treatment of obstructive sleep apnea in children. But the emphasis of the review is on the treatment options for pediatric obstructive sleep apnea.

INTRODUCTION
Obstructive sleep apnea syndrome (OSAS) is a disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction (obstructive apnea) that disrupts normal ventilation during sleep and normal sleep patterns [1]. Pediatric OSAS is a common disorder with reported prevalence of 1-4% [2]. Snoring is the main manifestation of the disorder which is seen in 7.45% of children [2,3]. Other night time symptoms of OSAS include labored breathing during sleep, gasps/snorting noises/observed episodes of apnea, sleep enuresis (especially secondary enuresis) and sleeping in a seated position or with the neck hyperextended. Daytime symptoms are more subtle and include headaches on awakening, daytime sleepiness, attention-deficit/hyperactivity disorder and learning problems. On physical exam these children may have tonsillar hypertrophy, high-arched palate and adenoidal facies (Table 1) [1]. Obesity and micrognathia/retrognathia are risk factors for OSAS [4] (Table 2).

OSAS elevates the risk for neurocognitive deficits and reduces school academic performance, alters lipid homeostasis, and promotes the occurrence of cardiovascular morbidities such as systemic hypertension and endothelial dysfunction [5-10]. However, not all children with OSAS develop complications. Multiple factors such as the severity of OSAS, the magnitude of the inflammatory and oxidant stress responses, individual and genetic susceptibility factors, as well as environmental modifiers play a role in the associated morbidity [11,12]. To prevent associated morbidity, diagnosis and treatment of this condition is important in childhood. Although symptoms of OSAS are suggestive of diagnosis, using symptoms and physical exam alone for diagnosis cause over and under treatment in many children [13]. American Academy of Pediatrics (AAP) recommends that

| Table 1: Symptoms and signs of OSAS. |
| History | |
| Frequent snoring (≥ 3 nights/wk) | |
| Labored breathing during sleep | |
| Gasps/snorting noises/observed episodes of apnea | |
| Sleep enuresis (especially secondary enuresis) | |
| Sleeping in a seated position or with the neck hyperextended | |
| Cyanosis | |
| Headaches on awakening | |
| Daytime sleepiness | |
| Attention-deficit/hyperactivity disorder | |
| Learning problems | |

| Physical examination | |
| Underweight or overweight | |
| Tonsillar hypertrophy | |
| Adenoidal facies | |
| Micronodiathia/retrognathia | |
| High-arched palate | |
| Failure to thrive | |
| Hypertension | |
| Physical examination | |
| Underweight or overweight | |
| Tonsillar hypertrophy | |
| Adenoidal facies | |
| Micronodiathia/retrognathia | |
| High-arched palate | |
| Failure to thrive | |
| Hypertension | |

Table 2: Disorders or conditions predisposing to obstructive sleep apnea in childhood.

A. Adenotonsillar hypertrophy or allergic rhinitis
B. Obesity
C. Special craniofacial characteristics or profound craniofacial anomalies
   - Small mandible with/without mandibular malpositioning
   - Narrow nasomaxillary complex with/without high and narrow hard palate
   - Marked nasomaxillary (midface) deficiency (e.g., Apert syndrome, Crouzon syndrome, Pfeiffer syndrome, repaired cleft palate)
   - Marked mandibular hypoplasia (e.g., Pierre Robin sequence, severe juvenile rheumatoid arthritis, Treacher Collins syndrome, Nager syndrome, Stickler syndrome)
D. Abnormal neuromotor tone or control of breathing
   - Cerebral palsy
   - Duchenne muscular dystrophy
E. Combinations of the above disorders or conditions
   - Down syndrome
   - Achondroplasia
   - Prader-Willi syndrome
   - Mucopolysaccharidoses

If a child or adolescent snores on a regular basis and has any of the complaints or findings of OSAS, clinicians should either obtain polysomnogram or refer the patient to a sleep specialist or otolaryngologist for a more extensive evaluation [1]. Selection of the appropriate therapeutic intervention is based on apnea hypopnea index (AHI), which corresponds to the number of obstructive and mixed apneas and hypopneas per hour of sleep. Polysomnographic criteria for scoring respiratory events for children were revised in 2013 in the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events [14]. According to these guidelines, obstructive apneas last for at least two respiratory efforts with a greater than 90% fall in nasal pressure signal amplitude for greater than or equal to 90% of the entire respiratory event compared with pre-event baseline amplitude. Hypopneas must last the duration of two baseline breaths with a fall in the amplitude of the nasal pressure or alternative signal that is greater than or equal to 30% of baseline airflow and is associated with an arousal, an awakening, or at least 3% desaturation. The obstructive sleep apnea syndrome is defined as an obstructive AHI score of 2 or more events per hour or an obstructive apnea index (OAI) score of 1 or more events per hour [15]. It is difficult to predict whether and when children with OSAS will develop complications. Not every child with severe OSA will manifest complications, while some subjects will have morbidity consequences with only mild OSA [16].

Although there is still continuing debate on the exact polysomnographic criteria that will effectively discriminate OSAS from habitual snoring, timely diagnosis and treatment of OSAS is very important. Children with moderate-to-severe OSA, or with mild OSA, but accompanied by morbidity, or by risk factors predicting persistence of the disorder should have priority for treatment [17].

Adenotonsillectomy

Hypertrophy of adenotonsillar tissue is a major contributor to the development of OSAS in otherwise healthy children. Anatomic impingement of the upper airway by enlarged upper airway lymphoid tissues will increase pharyngeal resistance, and may ultimately result in the episodic airway narrowing and collapse that characterizes OSAS [18]. AAP recommends that if a child is determined to have OSAS, has a clinical examination consistent with adenotonsillar hypertrophy, and does not have a contraindication to surgery, the clinician should recommend adenotonsillectomy (AT) as the first line of treatment [1].

In a recent randomized trial, as compared with a strategy of watchful waiting, surgical treatment for the obstructive sleep apnea syndrome in school-age children did not significantly improve attention or executive function as measured by neuropsychological testing but did reduce symptoms and improve secondary outcomes of behavior, quality of life, and polysomnographic findings, thus providing evidence of beneficial effects of early AT [19]. Although polysomnographic findings were normalized in the majority of children, response rate was 79%. Among children randomly assigned to early AT, the incidence of normalized polysomnographic findings was significantly higher among children who were not black, children who were not obese, and children who had a baseline AHI score at or below the median value. In a multicenter retrospective study evaluating the effectiveness of AT for OSAS in children, of the 578 children, only 157 (27.2%) had complete resolution of OSAS (i.e., post-AT AHI, 1/h total sleep time) [20]. In this study, age and body mass index z-score emerged as the two principal factors contributing to post-AT AHI, with modest contributions by the presence of asthma and magnitude of pre-AT AHI among no obese children.

Obese children are at an increased risk for OSAS; previous studies have shown that up to 27 percent of asymptomatic obese children have moderate to severe OSA, and 25 percent to 40 percent of obese patients with sleep symptoms have OSA [21]. Similar to the more recent studies, in a meta-analysis evaluating the effect of TA in obese children with OSAS, TA improved but did not resolve OSAS in majority of obese children. The weighted mean difference between pre- and postoperative AHI was a significant reduction of 18.3 events per hour. However, forty-nine percent of children had a postoperative AHI <5, 25 percent of children had a postoperative AHI <2, and 12 percent of children had a postoperative AHI <1 [21]. Furthermore, a recent randomized adenotonsillectomy study showed that AT for OSAS in children resulted in clinically significant greater than expected weight gain, even in children overweight at baseline [22]. The increase in adiposity in overweight children placed them at further risk for OSAS and the adverse consequences of obesity. Therefore AAP recommends to use clinical judgement to determine the benefits of adenotonsillectomy compared with other treatments in obese children with varying degrees of adenotonsillar hypertrophy.

Minor risks of TA include pain and dehydration attributable to postoperative nausea/vomiting and poor oral intake;
while major risks are anesthetic complications, acute upper airway obstruction during induction or emergence from anesthesia, ostoperative respiratory compromise, hemorrhage, velopharyngeal incompetence, nasopharyngeal stenosis and occasionally death [1]. Commonly, the opioid codeine is given to young children post-AT. Codeine is a prodrug, the analgesic properties of which are dependent on its conversion to morphine. The metabolism of codeine to active morphine depends on the highly polymorphic CYP2D6 pathway. Identified polymorphisms in this gene have given rise to poor metabolizer, extensive and ultra-rapid metabolizer phenotypes resulting in varied amounts of morphine produced from a standard codeine dose. Children with a CYP2D6 ultrarapid metabolizer phenotype have increased risk of serious CNS depression and apnea [23]. Case reports suggest that analgesia with codeine or other opioids that use the CYP2D6 pathway after adenotonsillectomy may not be safe in young children with OSAS.

Some children are at increased risk for respiratory compromise after TA and these risk factors include: younger than 3 y of age, severe OSAS on polysomnography, cardiac complications of OSAS, failure to thrive, obesity, craniofacial anomalies, neuromuscular disorders and current respiratory infection. Children with these risk factors should be monitored closely as inpatients. Children with higher risk for residual OSAS need to be reassessed clinically and with polysomnogram if indicated.

Non-invasive ventilation

Non-invasive ventilation with CPAP (continuous positive airway pressure) is considered an effective treatment of OSAS in children. AAP recommends that clinicians should refer patients for CPAP management if symptoms/signs or objective evidence of OSAS persists after adenotonsillectomy or if adenotonsillectomy is not performed [1]. Positive airway pressure therapy was associated with significant improvements in attention deficits; sleepiness on the Epworth Sleepiness Scale; behavior; and caregiver- and child-reported quality of life in a prospective study [24]. A multicentre study evaluated PAP in 29 children who were randomly assigned either CPAP or bi-level positive airway pressure (BPAP) [25]. Patients demonstrated significant improvement in sleepiness, snoring, AHI, and oxyhemoglobin saturation while using PAP during the 6-month follow-up period. However, approximately one-third of patients dropped out, and for those who used PAP, objective adherence was 5.3±2.5 hours/night. Parents overestimated the hours of PAP use compared with the devices’ actual objective recordings of use. There was no significant difference in adherence between the CPAP and BPAP groups. A recent study examined to increase adherence to CPAP therapy by using a new technology [26]. This study has shown that both CPAP and Bi-Flex were efficacious in the treatment of children and adolescents with OSAS. Both modes resulted in major improvements in polysomnographic parameters. Subjective sleepiness, as measured by the Epworth Sleepiness Scale, improved with Bi-Flex and tended to improve with CPAP. However, adherence did not improve with Bi-Flex compared to CPAP. In patients using CPAP, objective assessment of CPAP adherence is important. If the patient is nonadherent, then attempts should be made to improve adherence or other treatment options should be considered. However, despite suboptimal adherence use, there was significant improvement in neurobehavioral function in children after 3 months of positive airway pressure therapy which suggests that caregivers should not be discouraged about CPAP use [24]. Also since children may need different masks and pressures as they grow they need to be monitored periodically for changing needs as well complications of masks.

Anti-inflammatory treatment

Nasal and oropharyngeal inflammation is present in children with OSAS and might contribute to the pathogenesis of breathing disturbances during sleep [27]. Local and systemic inflammatory markers and pro-inflammatory cytokines are increased in these children and promote lymphoid tissue proliferation [28]. Thus, systemic or topical anti-inflammatory agents were suggested to have a potential role in reversing adenotonsillar enlargement.

Nasal corticosteroids have been examined as an alternative to adenotonsillectomy in otherwise healthy children with OSAS. In a prospective, randomized, double-blind study, children with mild to moderate OSAS were treated with a 6-week course of nasal corticosteroids or placebo [29]. The researchers were able to demonstrate a moderate improvement in cases treated with nasal corticosteroids. This was associated with concomitant decreases of approximately 50% in the desaturation index and the movement arousal index. In contrast, the placebo group did not show any improvement [29]. Nasal corticosteroids work by exerting lympholytic action and effects on inflammation and upper airway edema. Several studies suggest that topical steroids may ameliorate mild OSAS [30,31]. However, the clinical effects are small and because the long-term effect of this treatment is unknown, the clinician should continue to observe the patient for symptoms of recurrence and adverse effects of corticosteroids.

In an open-labelled study, the leukotriene receptor antagonist montelukast was found to be clinically effective in reducing disease severity in children with mild OSA [32]. In a recent double blind, placebo-controlled trial, montelukast effectively reduced polysomnographic findings, symptoms, and the size of the adenoidal tissue in children with non-severe OSA [33].

Adenoidal regrowth might occur in children after surgical intervention and is associated with recurrent symptoms. Kheirandish et al reported an open trial exploring the effect of a combined anti-inflammatory approach in children with persistent OSA after a surgical treatment [34]. Twenty-two children with residual mild OSA postsurgery were offered a combined therapy consisting of intranasal budesonide and oral montelukast for a period of 12 weeks. Compared with the 14 children receiving no therapy, there was considerable improvement in the polysomnographic respiratory measures and in the radiographic measures of airway size, thus suggesting a new approach to residual OSA after adenotonsillectomy.

Weight loss

Clinicians recommend weight loss in addition to other therapy if a child/adolescent with OSAS is overweight or obese [1]. In a nonrandomised investigation, weight loss by 35% in children with OSA and a mean body mass index z-score of
2.4–2.8 was related to a significant decrease in the severity of intermittent upper airway obstruction during sleep [35]. Kalra et al showed a significant improvement in OSAS after bariatric surgery, in association with a mean weight loss of 58 kg [36]. Along with many other health-related benefits, achieving weight loss and increasing exercise seem to be beneficial for OSAS and should be recommended along with other interventions for OSAS in obese children and adolescents. However, in children with OSA and obesity who do not respond to weight loss nCPAP may be effective in ameliorating apnoeas and hypopneas.

**Orthodontic treatment**

Children with OSAS may have a narrow and long face, with large tonsils, narrow upper airway, maxillary constriction and/or some degree of mandibular retrusion. Oral appliances may help improve upper airway patency during sleep by enlarging the upper airway and/or by decreasing upper airway collapsibility, thereby enhancing upper airway muscle tone. There are 3 types of available oral appliances for patients with OSAS: 1) Mandibular advancing device: advance or downwardly rotate the mandible and thus draw the tongue forward through its attachments to the genial tubercles. 2) Tongue retaining devices: hold the tongue in an anterior position during sleep. 3) Palatal lift devices: reduce the vibration of soft palate, and thus snoring. Several pediatric studies showed improvement in OSAS by using oral appliances [37]. 32 patients with symptoms of obstructive sleep apnea, malocclusion, and a baseline apnea index >1 event/h were studied and 19 subjects were assigned to a 6-mo trial of an oral appliance. Treated subjects had lower apnea (p<0.001) and hypopnea index (p<0.001), in untreated subjects these values were unchanged. Rapid mandibular expansion is an orthodontic procedure designed to increase the transverse diameter of the hard palate by reopening the midpalatal sutures. It does this by means of a fixed appliance with an expansion screw anchored on selected teeth. After 3 to 4 months of expansion, a normal mineralized suture is built up again. It is typically used in children with maxillary constriction and dental malocclusion.

In a study of 14 children (age 9.7 years) who completed the 12-month rapid maxillary expansion treatment, AHI decreased and the clinical symptoms had resolved by the end of the treatment period [38]. Twenty-four months after the end of the treatment period [38], Twenty-four months after the end of the treatment period [38].

**Orthodontic treatment should be encouraged in pediatric OSAS, and an early approach may permanently modify nasal breathing and respiration, thereby preventing obstruction of the upper airway. Additional surgical procedures and tracheostomy are treatment options which are reserved for complex cases such as patients with craniofacial anomalies.**

In conclusion, OSAS is a common disorder in children with important consequences. Although AT improves OSAS in most cases, a combination of different treatment modalities is necessary for the successful alleviation of upper airway dysfunction during sleep.

**REFERENCES**


