**R E V I E W**

**Updates on management of pediatric obstructive sleep apnea**

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**ABSTRACT**

Obstructive sleep apnea (OSA) affects about 1%–5% of the pediatric population. The consequences of untreated OSA in children include neurocognitive deficits, behavioral problems, poor school performance as well as systemic and pulmonary hypertension. The treatment options for pediatric OSA are numerous with a variety of surgical and non-surgical interventions. As our understanding of the complexities of OSA grows, the options for management have continued to expand as well. The objectives of this review are to describe the commonly prescribed treatments for pediatric OSA including adenotonsillectomy as well as use of positive airway pressure. We also highlight other surgical and non-surgical interventions available. In addition, we provide updates on current research focusing on newer diagnostic and experimental treatment modalities.

**KEYWORDS**
Obstructive sleep apnea, Sleep disordered breathing, Polysomnography, Adenotonsillectomy, Pediatric

**Introduction**

Obstructive sleep apnea (OSA) is defined as complete or partial collapse of the upper airway leading to oxygen desaturations and arousals from sleep. It is a medical condition that spans infancy to adulthood and is estimated to affect 1%–5% of the pediatric population. Contributing factors to the pathophysiology of pediatric OSA include: obesity, adenotonsillar hypertrophy, impaired neuromotor tone, and a high loop gain (exaggerated ventilatory response to respiratory perturbations). Children at increased risk of OSA include those with genetic disorders such as Down syndrome, craniofacial abnormalities and neuromuscular disorders. Children with OSA often present with caregiver complaints of snoring or difficulty breathing during sleep as well as daytime symptoms of hyperactivity and excessive daytime sleepiness. The consequences of OSA in children include neurocognitive problems, behavioral problems, poor school performance, and cardiovascular risks. As a result, untreated OSA can lead to significant health care burden. The diagnosis of OSA is made by overnight polysomnography (PSG) performed in a sleep laboratory. The severity of OSA is based on classification of obstructive apnea and hypopnea index (AHI), derived from the PSG. Most centers classify pediatric OSA as mild if the AHI is between 1 to 5 events per hour, moderate > 5 to ≤ 10 events per hour and severe if the AHI is greater than 10 events per hour. Adenotonsillectomy has been the treatment of choice in children with OSA with success rates as high as 80%. However, residual OSA can occur postoperatively in children, particularly those with underlying comorbidities (e.g. Down syndrome, obesity). In addition, some children in other high-risk populations such as neuromuscular diseases or infants with craniofacial abnormalities (e.g. Pierre Robin sequence) may not be candidates for adenotonsillectomy. Alternative treatment options for pediatric OSA include both surgical and non-surgical interventions.
those who underwent a period of watchful waiting. Participants who had surgery compared to 46% of treatment of pediatric OSA with adenotonsillectomy was a landmark randomized control trial looking at the upper airway thereby making collapse less likely to occur. The Childhood Adenotonsillectomy Trial (CHAT) that showed a resolution of apnea in 79% of the trial participants who had surgery compared to 46% of those who underwent a period of watchful waiting. While their primary outcomes measures of attention and executive function were not significantly different compared to controls, secondary outcomes including sleepiness scores, parent reported behavior, quality of life and polysomnographic measurements improved in the treatment group. A subsequent Cochrane review of the literature on the effects of adenotonsillectomy versus non-surgical management concluded that there is moderate quality evidence that adenotonsillectomy provides benefits in terms of quality of life, OSA symptoms, and behavior but there is no difference in neurocognitive performance or attention when compared to watchful waiting.

While adenotonsillectomy is an effective treatment for pediatric OSA, it is not without risk. The most common post-operative complication is respiratory compromise manifesting as persistent overnight desaturations that may require supplemental oxygen. This occurs in about 9.4% of cases with resolution during the recovery period. Primary hemorrhage (occurring within 24 hours of surgery) and secondary hemorrhage (occurring after 24 hours of surgery) occurs at a rate of 2.4% and 2.6% respectively. Other complications include post-operative pain and dehydration due to inadequate fluid intake. Risk of death is between 1 in 16 000–35 000 cases. Identifiable risk factors for post-operative complications include: children younger than 3 years, severe OSA, cardiac complications, failure to thrive, obesity, craniofacial anomalies, neuromuscular disorders, and concurrent respiratory infections. When discussing surgical management of pediatric OSA, parents should be counseled on the success rate, benefits, and risks of the procedure.

Non-invasive ventilation

While adenotonsillectomy is the mainstay of treatment for pediatric OSA, OSA may persist in high risk populations. Non-invasive positive airway pressure (PAP) is an effective treatment for children with residual OSA or in those whom adenotonsillectomy is not an option. This therapy involves use of a machine that generates positive air pressure which is connected to an interface such as a nasal mask. PAP delivery to the upper airway alleviates obstruction during sleep. Commonly used modes of PAP in children include continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BPAP). More recently, a mode of CPAP called auto-adjusting CPAP (AutoPAP) is becoming more frequently prescribed, particularly in older children. AutoPAP devices have active monitoring of the patient’s breathing through proprietary software which provides feedback to the machine in order to adjust the pressure settings to provide just enough pressure to overcome apneas. Side effects of CPAP therapy include nasal congestion, recurrent epistaxis, and mouth dryness. Newer masks designs and materials make pressure ulcers and skin breakdown less common, but younger children may develop midface hypoplasia from the pressure, especially if PAP is worn for prolonged periods. While CPAP has been shown to be effective in treatment of OSA, adherence to therapy remains a major barrier to its use. Objective monitoring of adherence is important as parents often overestimate CPAP use. Adherence can be obtained from the PAP device via a secure digital (SD) card or uploaded onto an online server via modem. Studies investigating barriers to PAP adherence showed that strong family support, maternal education, and strong caregiver self-efficacy were associated with improved PAP use in children with OSA. Strategies improving CPAP adherence include behavioral therapy and multidisciplinary support, however there are few studies with limited numbers of participants and further work is needed to develop a systematic approach. CPAP and other non-invasive ventilation modes remain a safe option that should always be considered in patients deemed unsafe for surgery or who have residual apnea after adenotonsillectomy, but ensuring adherence may require involvement of a multidisciplinary team as well as strong family support.

Other non-surgical treatment modalities

In situations where pediatric OSA is refractory to surgery, or the patient is not safe for surgery due to comorbid medical conditions, non-surgical therapies and medications are available. These options are becoming more widely acceptable and safe, particularly in children with mild to moderate OSA.

Anti-inflammatory medications

Anti-inflammatory agents commonly used in the treatment of OSA include steroids and leukotriene receptor antagonist. These medications target upper airway inflammation present in children with OSA to decrease tonsil and adenoid size. Analysis of tonsillar tissue from...
children with OSA have shown increased expression of leukotriene C4 synthase as well as leukotriene receptors 1 and 2 compared to healthy controls. In vitro studies have also shown increased tonsillar tissue proliferation with exposure to leukotriene D4 (LTD4) and a reduction with leukotriene receptor antagonists, e.g., montelukast. Several clinical studies have demonstrated the efficacy of leukotriene receptor antagonists in children with OSA. In a double blinded randomized placebo-controlled study of 57 children with mild OSA, the average AHI reduction was from 9.2 events/h to 4.2 events/h in the treatment group (n = 27) versus no change in the placebo group (n = 28).

Similar to montelukast, intranasal steroids have also been shown to be effective in treatment of pediatric OSA. Their anti-inflammatory effects reduce tonsil and adenoid size. In a randomized double blind placebo trial of 6 weeks of intranasal budesonide versus placebo in children with mild OSA, the authors showed an average AHI reduction from 3.7 events/h to 1.3 events/h in the treatment group (n = 48) and no reduction in AHI within the placebo group (n = 32).

Several studies have also reported a combination of leukotriene receptor antagonist and intranasal steroids to be effective in treatment of OSA. The benefit of this combination versus monotherapy is however unknown, as there are no randomized controlled trials comparing them. In children with mild OSA, not medically safe for surgery, and those who failed adenotonsillectomy, nasal steroids and leukotriene receptor antagonists are potential treatment options, but monitoring for resolution of symptoms is needed.

High flow nasal cannula

High flow nasal cannula has shown promise as an alternative treatment to CPAP in some studies. This therapy is a constant stream of humidified air delivered via a soft plastic nasal cannula into the upper airway. Small studies to date have shown statistically significant improvements in AHI with use of high flow nasal cannula. Though the exact mechanism is unclear, theories to its effectiveness include stenting of the airway, reduction of congestion by heat and humidity, and stimulation of the upper airway tone. Larger studies are needed to further evaluate the mechanism and effectiveness of high flow nasal cannula, however, one can consider this therapy in younger OSA patients as well as those intolerant of CPAP.

Oxygen therapy

The partial or complete obstruction of the upper airway in OSA leads to airflow limitation and subsequent oxygen desaturation. The use of supplemental oxygen in management of OSA has been used to treat desaturations and is also thought to alter the respiratory response (loop gain) to hypoxemia. Oxygen therapy has been of particular interest in infants as CPAP is not FDA approved for patients weighing less than 13 kg. In one retrospective review of 23 infants, 0.25–1.0 L/min of supplemental oxygen was administered during the second half of a split-night sleep study and there were significant improvements to overall oxygen saturation, oxygen nadir, and AHI. Two studies of supplemental oxygen in older children have also shown improvements in oxygen saturation and nadir but mixed results on reduction in AHI with one study showing no changes in number of events and another showing a reduction in AHI. On average, carbon dioxide levels remained unchanged on supplemental oxygen, however several individual patients in one study did develop hypercapnia. Oxygen therapy may be considered as a temporizing measure in young neonates with mild OSA where growth is expected to improve their symptoms. However, it is advisable to monitor patients for hypercapnia when initiating oxygen therapy.

Oral appliances

Mandibular advancement devices (MAD) are an effective treatment of mild to moderate OSA in adults. These oral appliances are devices fitted to the dentition of a patient and passively moves the jaw anteriorly. This motion puts anterior tension on the muscular dilators of the pharynx thereby dilating the posterior pharynx. There is little literature on the use of oral appliance therapy for the treatment of OSA in children. A recent systematic review of the literature revealed a total of seven articles looking at oral appliance therapy in pediatric OSA for which two were randomized control trials that were included in a meta-analysis. The results of this meta-analysis suggest benefit from use of a MAD for treatment of pediatric OSA with an average AHI decrease of 1.75 events/h (P < 0.00001). Oral appliance therapy does appear to show benefit as a treatment modality in the pediatric population. However, there are still concerns about the consequences of chronic long term use of these devices in young children and whether the devices can alter facial and dental development. Further studies will be needed to determine efficacy of this therapy along with any long term consequences.

Weight loss

Obesity is an epidemic within the pediatric population with an estimated 18.5% of patients falling into the obese weight range. Obesity is a known risk factor for OSA and obese children also have higher rates of residual OSA after adenotonsillectomy. Weight loss can be achieved through dietary modifications, intensive weight loss program and more recently, bariatric surgery. An intensive weight loss program conducted on obese teenagers in a residential facility showed significant reduction in their OSA from an average AHI of 3.8 events/h to 1.9 events/h. In another study of obese adolescents that underwent bariatric surgery, AHI declined postoperatively from a baseline mean of 14.6 events/h to 4.5 events/h at 3 weeks and 5.0 events/h at 5 weeks. However, pediatric bariatric
surgery is only reserved for adolescents under extreme health circumstances. The American Society for Metabolic and Bariatric Surgery has advised that surgery should only be considered in adolescents who have completed physical maturity (95% of adult stature by radiograph) and who have a BMI >35 with comorbidities including Type II Diabetes, pseudotumor cerebri, or moderate to severe OSA (AHI >15). While sustained weight loss can be achieved in children, the process is time consuming and often requires motivated families with adequate support system for the child. As such, weight loss is not frequently used independently as a treatment of OSA and, other conventional treatments (e.g. CPAP) should be utilized as well.

Positional therapy

OSA has been shown to be worse in supine position in adults. The mechanism is likely related to the collapse of the tongue into the oropharynx further worsening obstructive events. Devices used to maintain sleep in a lateral position include homemade products such as tennis balls sewn to the back of a shirt or a backpack worn during sleep as well as medically designed back pillows/padding, all with the end goal of making supine sleep uncomfortable. There are also now devices that can be worn on the neck that vibrate when a patient rolls off their side as a method for behavioral modification. Studies in children have shown mixed results regarding whether OSA severity is worse in the supine versus lateral position. While studies in adults have demonstrated improvement in OSA with positional therapy, there have been no studies evaluating its effectiveness in children and the long term practicality and safety of positional therapy in children has not been established.

Watchful waiting

The pediatric population encompasses a period of constant growth and development where factors contributing to OSA such as obesity, neuromuscular tone, and allergies can improve with time. In the Childhood Adenotonsillectomy Trial (CHAT), patients were randomized into watchful waiting and early adenotonsillectomy. Seventy-nine percent of children who received adenotonsillectomy had resolution of their OSA but interestingly, 46% of patients who were in the watchful waiting group also had their AHI normalize without any intervention. Factors associated with non-resolution of OSA after watchful waiting include; obesity, African American ethnicity, and AHI greater than the median for the study which was 4.7 events/h. Watchful waiting is therefore a considerable option when counselling patients with mild OSA who have no significant comorbidities.

Other surgical/procedural treatments of OSA

Other surgical and/or procedural treatment options for pediatric OSA are available in specific patient populations and are highlighted in this section.

Craniofacial surgery/procedures

Craniofacial morphology is also an important contributing factor to the size and shape of the upper airway. Retrognathia and mandibular hypoplasia are craniofacial abnormalities that are associated with many syndromes including craniosynostosis, Pierre-Robin Sequence, and Treacher-Collins Syndrome. A narrow maxilla or retrognathic mandible can compress the nasopharynx and oropharynx as well as displace the tongue base posteriorly leading to increased risk of OSA.

Mandibular distraction osteogenesis and mandibular advancement are surgeries that involve intentional fracturing of the mandible and advancing the jaw into a new position. Mandibular advancement surgery moves the jaw into a new position immediately. Distraction osteogenesis is reserved for more severe cases where the jaw is gradually advanced using plates and screws in order to safely advance the mandible to a greater distance. A meta-analysis conducted on mandibular advancement surgery outcomes in children showed a mean AHI decrease from 41.1 events/h to 6.0 events/h. Complete resolution was achieved in only 25.5% of patients despite an 89% reduction in AHI, highlighting the fact that patients with mandibular insufficiency tend to have particularly severe OSA. Mandibular advancement surgeries should be considered in children with craniofacial abnormalities who have mandibular insufficiency and severe OSA.

Rapid maxillary expansion (RME) is a procedure used to expand the hard palate in patients with maxillary constriction. It involves placement of an appliance anchored to a patient’s dentition that spans the hard palate. An expansion screw is turned daily by the parent to apply force against the patient’s dentition, causing expansion of the hard palate at the palatal suture, widening the maxilla without fracturing it. In a cohort of 31 children with OSA and no evidence of adenotonsillar hypertrophy but with bite malocclusion due to maxillary constriction, RME improved AHI to less than 1 event/h in all patients. These results were maintained at 12 year follow up without OSA recurrence. A systematic review of RME use in treatment of OSA concluded that in 17 different studies totaling 314 patients, RME resulted in a 70% reduction of AHI from an average of 8.9 events/h to 3.3 events/h. Referral to an orthodontist for RME should be considered in patients with small tonsils or who have residual OSA after adenotonsillectomy and evidence of maxillary constriction and malocclusion.

Lingual tonsillectomy/ tongue base reduction

The tongue plays a major role in the pathophysiology of OSA. Macroglossia and glossoptosis lead to a posteriorly positioned tongue that is more likely to collapse into the airway during sleep. This is seen in conditions like Down syndrome, Pierre-Robin sequence, and Beckwith-Wiedemann syndrome resulting in OSA. Enlargement of the lingual tonsils can occur similarly to
enlargement of the adenoids or palatine tonsils. Tongue base reduction surgery involves the surgical removal of the lingual tonsils with or without a portion of the posterior tongue musculature in order to reduce the amount of posterior tongue collapse.\textsuperscript{65} A systematic review of the literature showed that among 114 patients from 9 different studies, there was an average 48.5\% reduction in AHI.\textsuperscript{66} The majority of patients had underlying syndromes; however non-syndromic children had greater reductions in AHI (59\% vs 40\%).\textsuperscript{66} The extent of tongue base reduction is limited by risks to the critical nerves and blood vessels to the tongue as well as maintain proper function with swallowing and speech and therefore this treatment option may be challenging.

**Supraglottoplasty**

Laryngomalacia is a congenital condition characterized by excessively redundant or floppy upper airway tissue that leads to obstruction. It typically presents as stridor in newborns and infants and is a recognized cause of OSA in this age group.\textsuperscript{67,68} Typically, congenital laryngomalacia improves as the patient grows and surgery is reserved only for patients who exhibit failure to thrive or significant respiratory distress.\textsuperscript{67,68} Supraglottoplasty is a surgical treatment that reduces the redundant upper airway tissue and preventing collapse.\textsuperscript{67,68} Studies have shown improvement in AHI in patients with laryngomalacia and OSA after supraglottoplasty.\textsuperscript{69,70} It may be difficult to determine whether or not a patient has laryngomalacia, particularly if it only occurs in sleep. Laryngomalacia may therefore be an under recognized etiology for OSA and one can consider additional diagnostic testing such as drug induced sleep endoscopy (DISE) or other dynamic imaging modalities like Cine MRI for further evaluation. A systematic review of laryngomalacia and OSA showed that 77\% of patients who were identified as having sleep related laryngomalacia were diagnosed by drug induced sleep endoscopy.\textsuperscript{71}

**Tracheostomy**

Tracheostomy involves the surgical placement of a tube from the midline neck through an incision into the trachea. Tracheostomy completely bypasses the upper airway collapse and is a definitive treatment for the management of OSA.\textsuperscript{71} In children, the use of tracheostomy has been reserved for the most severe and refractory patients, mostly in children with craniofacial abnormalities or neuromuscular dysfunction, nonresponsive to other treatment modalities.\textsuperscript{73} Tracheostomy, although therapeutic, is associated with long-term complications including frequent infections, accidental decannulation and death. In addition, there is associated lower quality of life. There is also an increased burden of care on the family for tracheostomy care.\textsuperscript{73} For these reasons, tracheostomy remains an infrequently used treatment modality in management of pediatric OSA and providers should weigh the severity of disease burden and the complications of tracheostomy when making the decision to pursue this therapy.

**Newer diagnostic and treatment modalities in pediatric OSA**

The mainstay of diagnosis of pediatric OSA is by PSG which is a multichannel recording of sleep typically occurring in an accredited sleep laboratory. Severity of OSA is classified as mild, moderate or severe, based on the obstructive apnea-hypopnea index (AHI).\textsuperscript{12} Although the diagnosis of OSA is based on identification of flow limitations, respiratory effort, and oxygen desaturation during polysomnography, these measurements indirectly describe the upper airway collapse. Visualization of the upper airway during collapse does not occur during routine polysomnography. Drug induced sleep endoscopy (DISE) and Cine magnetic resonance imaging (Cine MRI) are two methods employed to help visualize and identify the level and nature of the upper airway collapse in patients with OSA.

DISE is a procedure where patients are given sedative medications while a flexible endoscope is placed through the nose to visualize the upper airway. As the patient becomes increasingly sedated but breathing spontaneously, the upper airway will collapse, and this is thought to be a correlate to the collapse that occurs in sleep. This technique is becoming increasingly employed especially in children with residual OSA after adenotonsillectomy. It was first described by Croft and Pringle in 1991, and their initial cohort of patients included 15 pediatric patients.\textsuperscript{74} A more recent systematic review described 375 patients over 11 different studies where DISE was used to identify a site of upper airway collapse in patients with residual OSA after adenotonsillectomy.\textsuperscript{75} Despite identifying a site of collapse in 100\% of these patients, treatments and outcomes after DISE directed therapy were limited and focused mostly on lingual tonsillectomy and supraglottoplasty.\textsuperscript{75,76} There is also still ongoing debate about whether use of sedation truly mimics sleep and therefore, whether the physiologic information obtained is truly meaningful.\textsuperscript{77,78}

Cine MRI takes sequences of MRI images to dynamically visualize the upper airway.\textsuperscript{79,82} It is superior to DISE in that it allows for visualization of the upper airway in its entirety. However, there is no literature on whether Cine MRI has helped guide treatments or whether it improves surgical outcomes. The process for obtaining MRI images is also difficult and time consuming requiring patients to lay still in a machine for a prolonged period. Children require sedation for this procedure, which brings up the controversy regarding whether sedation truly mimics sleep.

Regardless of the controversies in the diagnostic modalities described above, treatment of OSA may be difficult in medically complex patients or those who fail initial adenotonsillectomy. DISE and Cine MRI are increasingly playing a role in identifying the site of collapse in OSA.
and can guide alternative surgical treatment.

**Neurostimulation**

Hypoglossal nerve stimulation (HGNS) is a novel surgical treatment of OSA. It was introduced in 2014 and is currently FDA approved for the treatment of OSA in adults. An implantable device is surgically placed with a pressure sensor placed in the intercostal muscles of the chest and a stimulating electrode placed around the hypoglossal nerve. The device senses breathing during sleep and sends electrical stimulus to the hypoglossal nerve causing the tongue to protrude during inspiration.

HGNS has been implanted in a case series of 20 children with Down syndrome. There was an average 85% reduction in AHI among these patients and an average use of 9.21 hours a night. This treatment is however not currently FDA approved in children. Neurostimulation may be potentially beneficial in treating OSA in the complex pediatric patient intolerant of CPAP.

**Conclusion**

While the mainstay of treatment of most children with OSA is adenotonsillectomy, children with medical comorbidities are at risk for residual OSA despite this procedure. Numerous surgical and non-surgical options for treatment of persistent disease have shown efficacy although data comparing these interventions is limited. As such, these interventions should be tailored to each child’s needs, underlying comorbidities as well as availability and expertise of the practitioner. Future prospective trials are needed to determine if newer advanced diagnostic imaging techniques can improve OSA resolution rates in children undergoing surgery. Ultimately, it is important to have a thorough discussion with the patient, caretaker, and healthcare team regarding benefits and risks of all the different treatment options to achieve an agreeable and effective treatment plan.

**CONFLICT OF INTEREST**

The authors declare no conflicts of interest.

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