20 Innovations in the Treatment of Pediatric Obstructive Sleep Apnea

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Abstract

Obstructive sleep apnea affects a large proportion of otherwise healthy children in the context of interactions between craniofacial elements, adenotonsillar hypertrophy and other anatomical factors, and neuromuscular reflexes of the upper airway. In light of the adverse consequences of sleep apnea, it is important not only to proceed with early diagnosis but also to implement adequate treatment that is guided by the pathophysiological determinants of the disease in each child. Here, we will describe the current standard of care approaches to the treatment of pediatric obstructive sleep apnea, and will also explore novel management strategies that should enable more personalized therapy in the near future.

Keywords

Adenotonsillar hypertrophy · Obesity · Tonsillectomy · Adenoidectomy · Orthodontics · Intra-oral appliances · Anti-inflammatory · Nasal corticosteroids · Leukotriene receptor modifiers · Myofunctional therapy · DISE · CPAP · Bilevel PAP · High flow nasal cannula · Mandibular advancement · Diet · Weigh management

20.1 Importance of Sleep

The American Academy of Sleep Medicine (AASM) and the National Sleep Foundation set forth recommendations for each age group on the total amount of sleep needed to promote optimal health in children (Paruthi et al., 2016; Hirshkowitz et al., 2015). These technical reports summarizing the extant literature and reflecting the consensus opinion of panels of experts indicated that sleeping less than the number of hours recommended could lead to behavior and academic problems, as well as various health issues, which prompted the endorsement of such recommendations by the American Academy of Pediatrics (AAP) (Hirshkowitz et al., 2015; Jenco, 2016). However, it is not only the duration of sleep that is important for health, but the quality and regularity as well. Indeed, reducing dis-

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ruption of sleep (i.e., sleep fragmentation) (Fatima et al., 2016; Ohayon et al., 2017; Phillips et al., 2020), as well as promoting regular bedtimes and sleep schedules (Spruyt et al., 2011), are critical to derive the best outcome from sleep at all ages, and particularly in growing children. Whereas sleep restriction, insomnia and delayed sleep-wake phase disorder are among the more common causes of short sleep duration in adolescents (Phillips et al., 2020), obstructive sleep apnea (OSA), with its concomitant microarousals is one of the most common causes of sleep fragmentation across the lifespan (Gipson et al., 2019; Zhang et al., 2017). Adult studies have shown that even mild OSA and even snoring with upper airway resistance syndrome can lead to poor sleep quality and can also be associated with comorbidities such as hypertension, obesity, diabetes and mood symptoms (Young et al., 2002; Pinto et al., 2016). Thus, maintaining a regular sleep schedule with the homeostatic need of sleep duration being preserved, and suffering from minimal disruption are all the more of paramount importance in children (Paruthi et al., 2016; Ohayon et al., 2017; Phillips et al., 2020; Gipson et al., 2019).

20.2 Diagnosis of OSA

The gold standard for the diagnosis of OSA remains as an in-laboratory diagnostic polysomnogram (PSG) (Gipson et al., 2019; Marcus et al., 2012; Dehlink & Tan, 2016). This is most effective when clinically correlated with a positive patient history and physical examination (Gipson et al., 2019; Marcus et al., 2012). Alternative approaches to the diagnosis of OSA in children are emerging. For a more detailed coverage of this topic, the reader is referred to a previous chapter by the authors in this book.

20.3 Overview of Treatment

Adenotonsillectomy (AT) remains the most common and first line management procedure for pediatric OSA (Marcus et al., 2012; Kaditis et al., 2016). However, there is currently no consensus algorithm for the management of pediatric OSA, or even a consensus regarding which cut-off values in the polysomnogram designate the need for certain interventions (Kaditis et al., 2012; Dehlink & Tan, 2016). An algorithm attempting to circumvent such issues was first proposed by Kaditis et al in 2011, and is presented in Fig. 20.1 below.

20.3.1 Weight Management for Obesity

Obesity and OSA are tightly interrelated. Obesity is a major risk factor for sleep-disordered breathing in children (Kanney et al., 2020; Redline et al., 1999). There is increasing frequency and severity of OSA when obesity is present, and obese children are much more likely to suffer from persistent OSA after customary treatment, which usually consists of surgical removal of adenoids and tonsils (Amaddeo et al., 2017; Barlow and Expert Committee, 2007). In a previous study, we showed that obese children with OSA ate more fast food, ate less fruits and vegetables, and were significantly less likely to engage frequently in organized sports (Alonso-Álvarez et al., 2015; Spruyt et al., 2010).

The American Academy of Pediatrics (AAP) outlines a four-stage approach to the diagnosis and management of childhood overweight and obesity (Barlow and Expert Committee, 2007). The first three stages comprise of lifestyle and behavior modifications, whereas medications and/ or bariatric surgery are considered during the fourth stage (Barlow and Expert Committee, 2007). Lifestyle changes employed in the treatment of obesity comprise caloric restriction (i.e., hypocaloric diet and other nutritional modifications aimed at minimizing for example the glycemic index) and increasing caloric expenditure (i.e., exercise or non-exercise thermogenesis) (Cuda et al., 2016). Roche et al explored the effect of this first-line intervention for obesity, and showed that a combination of aerobic exercise and a balanced diet led to weight loss, but did not affect the AHI (Roche et al., 2018). They

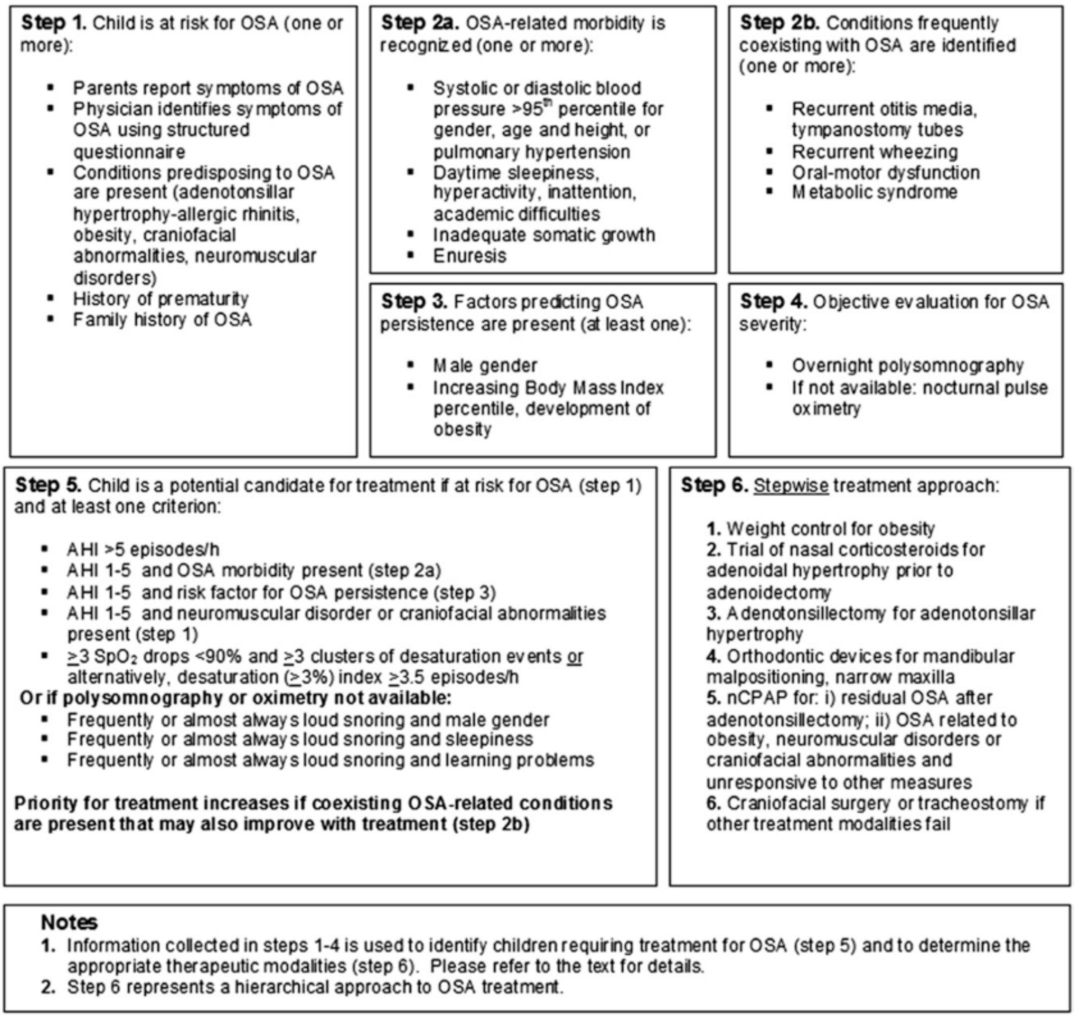

Fig. 20.1 Algorithm for the diagnosis and treatment of pediatric OSA, as proposed by Kaditis et al. (2012)

concluded that their subjects had severe obesity and despite the significant weight loss, remained in the same Body Mass Index (BMI) category, and that greater weight loss was required to see an improvement in AHI (Roche et al., 2018). Conversely, in another study they showed that a comprehensive obesity management program yielded improvements in metabolic dysfunction independently of the changes in AHI (Roche et al., 2020). Verhulst and colleagues found that weight loss was successful in treating OSA in 31 obese teenagers. In addition, a positive association between the severity of OSA at the start of the treatment and the amount of weight loss achieved was detected (Verhulst et al., 2009). Metformin, phentermine, liraglutide, topiramate and orlistat are the medications currently used in pediatrics for weight loss (Cuda et al., 2016; Page & Freemark, 2020; Pharmareviews.in, 2021). Only orlistat is FDA-approved for this indication (Cuda et al., 2016). They have all been studied for weight loss for various pediatric age groups, but to the best of our knowledge none of these medications has specifically been examined as far as its effect on AHI after weight loss. Jaramillo et al conducted a retrospective chart review of patients who underwent laparoscopic sleeve gastrectomy and found that most had resolution of their comorbidities after weight loss from surgery, and this includes 16 of 18 patients not needing their CPAP anymore (Jaramillo et al., 2017). Thus, when OSA is present in the context of obesity, it is important to emphasize that all efforts should be made to improve dietary habits and daily physical activity to not only reduce the likelihood of residual OSA, but also to improve the cardiometabolic dysfunction that is frequently present in these children (Koren et al., 2016a, b).

20.3.2 Anti-Inflammatory Therapy

Systemic and local (topical) anti-inflammatory therapy is now commonly used in the management of pediatric OSA and includes intranasal steroids and montelukast.

It is recognized that in OSA, there is evidence of accelerated proliferation of inflammatory cells in the airways, such as eosinophils, lymphocytes and mast cells (Brockmann & Bertran Salinas, 2021). Corticosteroids will inhibit chemical messengers like cytokines, chemokines, and adhesion molecules ultimately reducing the recruitment of inflammatory cells to tissues such as the adenoids or tonsils (Brockmann & Bertran Salinas, 2021). Corticosteroids will also operate via inhibition of proliferation, hence potentially reducing the hyperplasia and hypertrophy of these tissues that play such a fundamental role in enhancing the risk of OSA (Brockmann & Bertran Salinas, 2021).

Interestingly, only a few randomized controlled studies have been carried out to date. Generally speaking, the extant literature clearly supports the efficacy of the anti-inflammatory approaches in the treatment of OSA in children (Gozal et al., 2021). The initial study by Brouillette et al studied the effects of intranasal fluticasone on the AHI in a triple-blind randomized trial, and found that the AHI in the study group decreased from around 10.7 events per hour to 5.8 events per hour after 6 weeks of use (Brouillette et al., 2001). Since then, most studies have particularly explored the impact of this treatment in mild cases, based on the ethical equipoise that delaying surgical treatment in more severe OSA cases may not be appropriate (Brockmann & Bertran Salinas, 2021). In a recent study, Kajiyama and colleagues confirmed the validity of such approach, and showed that although adenotonsillectomy could be presented in a substantial proportion of mild and moderate OSA cases by medical treatment, severely affected children were significantly less likely to benefit from such approach (Kajiyama et al., 2021). Notwithstanding, there appears to be some advantage in efficacy when combination treatment with intranasal corticosteroids and montelukast is implemented rather than intranasal steroids alone (Liming et al., 2019; Kuhle et al., 2020). Overall, the empirical experience of our group over several years seems to indicate a substantial benefit from anti-inflammatory approaches in mild to moderate OSA, with up to >80% of children not requiring surgical intervention (Kheirandish-Gozal et al., 2014). We should also indicate that the younger ages (<6–7 years) seem to be more responsive to treatment than older children, likely because in older children the lymphadenoid tissues in the upper airway are more likely to be more rigid and less malleable due to increased fibroelastic structural content.

Montelukast is a leukotriene receptor antagonist and acts via cysteinyl leukotriene receptor-1 in tonsils and adenoids (Brockmann & Bertran Salinas, 2021). Several studies have shown that use of montelukast can be used in the short-term treatment of mild to moderate OSA (Brockmann & Bertran Salinas, 2021; Liming et al., 2019; Kuhle et al., 2020; Ji et al., 2021; Kheirandish-Gozal et al., 2016; Bao et al., 2021). Kheirandish-Gozal et al showed in a double-blind randomized trial that use of montelukast for 16 weeks improved AHI from 9.2 events per hour to 4.2 events per hour (Kheirandish-Gozal et al., 2016). In vitro studies have confirmed decreased proliferation in tonsillar and adenoidal tissue after exposure to montelukast (Dayyat et al., 2009). Of note similar results were reported by Goldbart and colleagues in a preceding RCT (Goldbart et al., 2012). Several issues remain unaddressed however and will need to be delineated to allow for a more uniform implementation of these approaches. These issues will need to include whether specific ages are more likely to respond favorably, what anatomical attributes need to be considered (e.g., extent of tonsillar or adenoidal hypertrophy, Mallampati score, degree of retrognathia, etc…), the duration and dosage of treatment, when to use this approach either as single vs. combined therapy, etc…

20.3.3 Orthodontic Management

Certain craniofacial features have been frequently linked to pediatric OSA. Syndromic children usually present with craniofacial malformations, which could include midface hypoplasia, mandibular hypoplasia, macroglossia, or a narrowed oropharynx (Fernandes Fagundes et al., 2021). These children should be screened regularly by both their primary care physicians, and oral health providers (Fernandes Fagundes et al., 2021). Validated questionnaires can be used for screening, albeit being fraught with limited reliability, and clinical imaging and/ or referrals to specialists such as ENT are periodically needed (Fernandes Fagundes et al., 2021). Orthodontic treatment is currently deemed beneficial in the management of OSA in children in the presence of certain craniofacial features or malformations associated with OSA problems (Fernandes Fagundes et al., 2021). However, more expansive training of orthodontic specialists in sleep medicine and development of more standardized interventions along with the appropriate underlying clinical trial evidence may propel orthodontic options to the high priority standing of treatment choices. Presented below are two orthodontic procedures currently employed in the management of some children suffering from OSA.

20.3.3.1 Rapid Maxillary Expansion

Rapid Maxillary Expansion (RME) is used for correction of dental crowding in pre-pubertal children with the presence of maxillary skeletal constriction (Fernandes Fagundes et al., 2021; Júnior et al., 2018). Overall, the purpose of the procedure is to increase the volumetric space within the oral cavity while facilitating improved positioning of the tongue, the latter generally being displaced backwards and reducing further the pharyngeal introitus (Júnior et al., 2018; McNamara Jr et al., 2015). Hence, it may be an adjunct treatment in children who have residual OSA (Fernandes Fagundes et al., 2021). RME is also performed in selected pediatric cases when nasal obstruction symptoms are predominant (Júnior et al., 2018). It then leads to reduced nasal airway resistance and improved respiratory pattern (Júnior et al., 2018; McNamara Jr et al., 2015; White et al., 1989; Kiliç & Oktay, 2008). In recent years the selection of rapid vs. intermediate vs. slow maxillary expansion using the customary expanders has prompted renewed interest in the advantages and disadvantages of each approach (Luiz Ulema Ribeiro et al., 2020; Adobes Martin et al., 2020; Hoxha et al., 2018). Villa et al showed that after 12 months of RME, a 20% reduction in AHI was anticipated, and that RME appears to be a safe and efficacious intervention in selected cases with more complex forms of OSA in which adenotonsillectomy alone is insufficient to normalize the breathing patterns during sleep (Villa et al., 2015).

20.3.3.2 Mandibular Advancement

Mandibular advancement devices (MAD) involve changing the mandible to a more forward position in relation to the maxilla. This increases the sagittal dimension of the oropharyngeal area and reduces collapsibility of the airway there (Fernandes Fagundes et al., 2021). This treatment modality is already regularly employed in the treatment of mild-to-moderate OSA in adults, especially those with a history of non-compliance or non-tolerance of Positive Airway Pressure (PAP) Therapy (Ramar et al., 2015). A systematic review and meta-analysis by Noller et al found a dramatic improvement in AHI (89% decrease) in patients with mandibular insufficiency when treated with either mandibular advancement or mandibular distraction (Noller et al., 2018). Another systematic review and meta-analysis, this time by Schwartz et al, found that CPAP is still more efficient in reducing AHI, but has less compliance (Schwartz et al., 2018). There was no difference in quality of life with MAD (Schwartz et al., 2018).

20.3.4 Surgical Treatment of Pediatric OSA

As mentioned above, adenotonsillectomy (T&A) is considered the first-line treatment for pediatric OSA by the AAP, AASM and the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) (Marcus et al., 2012; Aurora et al., 2011; Mitchell et al., 2019). The gold standard technique involves removal of the tonsils along with the capsule (i.e., tonsillectomy) (Sarber & Ishman, 2021). Another approach, tonsillotomy, refers to the removal of the tonsillar tissues, while leaving the tonsillar capsule in place (Sarber & Ishman, 2021). This has been shown to be associated with less bleeding and pain (Konstantinopoulou et al., 2015; Borgström et al., 2019) but is associated with a higher rate of tonsillar re-proliferation and recurrence of OSA in a substantial proportion of the children (Sarber & Ishman, 2021). T&A is associated with improved AHI, behavior and quality of life (Sarber & Ishman, 2021; Marcus et al., 2013; El-Kersh et al., 2017; Fehrm et al., 2020; Song et al., 2016). Obesity, age > 7 years, black race, OSA severity before surgery, and presence of genetic and metabolic syndromes (especially those associated with craniofacial and neuromuscular disorders) negatively affect the outcomes of T&A and are inherently fraught with a high risk of residual OSA that may require additional interventions (Konstantinopoulou et al., 2015; Sarber & Ishman, 2021; Connolly et al., 2020; Della Vecchia et al., 2020).

20.3.4.1 Drug Induced Sleep Endoscopy (DISE)

DISE is a technique to evaluate the upper airways while the patient is deeply sedated. The sedation state using specific drugs is considered as a viable simulation of natural sleep. DISE is presently used to aid in surgical decision-making for children with persistent OSA, and sometimes used in decision making for those children at risk for persistent OSA (Sarber & Ishman, 2021; Baldassari et al., 2021). Dynamic evaluation of the upper airway during sedation allows for identification of additional sites of obstruction that could be potentially addressed surgically (Sarber & Ishman, 2021; Baldassari et al., 2021). DISE is required for patients being considered for a hypoglossal nerve stimulator to evaluate the degree and pattern of velopharyngeal collapse (Sarber & Ishman, 2021). Of note, nerve stimulation devices are not currently approved by the FDA for use in children, but have gained popularity among adults who are refractory to CPAP.

20.3.4.2 Nasal and Nasopharyngeal Surgery

Nasal surgery has been shown to improve AHI, and reduce CPAP pressures (Hoxha et al., 2018). Septoplasty has historically been avoided in children due to concerns about its effects on nasal growth (Cingi et al., 2016). More recently, limited septoplasty has been shown to be safe especially for children older than 6 years of age (Cingi et al., 2016). Turbinoplasty is a commonly performed procedure to improve nasal breathing in children with turbinate hypertrophy (usually associated with chronic allergic rhinitis) and signs of nasal airway obstruction (Sarber & Ishman, 2021; Wright et al., 2020).

20.3.4.3 Oropharyngeal Surgery

Uvulopalatopharyngoplasty (UPPP) involves removal of excessive tissue of the lower soft palate and uvula (Sarber & Ishman, 2021). Because of complications such as velopharyngeal insufficiency, voice changes, globus, and airway stenosis, the traditional technique has undergone many modifications over the years (Sarber & Ishman, 2021). UPPP has been shown to improve OSA in children who are neurologically impaired (Kosko & Derkay, 1995; Kerschner et al., 2002), and in those with severe obesity (Com et al., 2015).

20.3.4.4 Tongue Surgery

Tongue base reduction (i.e., base-of-tongue surgery, BOT) can be achieved through lingual tonsillectomy (Sarber & Ishman, 2021). Other surgeries in this category include tongue suspension and true reduction (Camacho et al., 2017). All three were evaluated by Camacho and colleagues in a systematic review and meta-analysis. BOT was shown to reduce AHI in both syndromic and non-syndromic children. However, the majority of reports involve very small series or even isolated case reports.

20.3.4.5 Tracheotomy

Tracheotomy allows for complete bypass of the obstructed upper airway structures for the treatment of OSA. It is considered as a salvage treatment option for children with severe OSA after other options have failed (Sarber & Ishman, 2021). Although used in the past, every effort should be made to avoid this intervention.

20.3.5 Positive Airway Pressure (PAP) Therapy

PAP preserves airway patency during sleep by stenting the collapsible segments of the airway. Thus, PAP reduces the inspiratory work of breathing in the setting of increased airway resistance. Though PAP therapy is the first-line treatment for adult OSA (Patil et al., 2019), it is often reserved for cases of persistent OSA (i.e., refractory or residual OSA) after T&A, or in those children with otherwise little or no evidence of adenotonsillar hypertrophy (Dehlink & Tan, 2016; Gozal et al., 2020). Usually, continuous pressures are delivered throughout the complete respiratory cycle (i.e., inspiratory and expiratory phases; CPAP). However, when a very high positive end-expiratory pressure is required, or if the patient has a neuromuscular condition or obesity hypoventilation syndrome, bi-level PAP (BIPAP) may be implemented, whereby the expiratory pressure administered is inferior to the inspiratory pressure and permits more comfortable respiratory efforts while maintaining airway patency throughout the respiratory cycle. Though PAP therapy is very effective, adherence is usually a major problem (Gozal et al., 2020; Hawkins et al., 2016; Bhattacharjee et al., 2020). Behavioral interventions such as desensitization (Gozal et al., 2020) or family member modeling (Puri et al., 2016) have been developed and shown to increase compliance or adherence to treatment.

20.3.6 Myofunctional Approaches

Orofacial myofunctional therapy helps to re-establish correct habits and functioning of the orofacial muscles to avoid residual OSA after surgical and orthodontic treatment (Villa & Evangelisti, 2021). The treatment must be as early as possible for protecting airway health and sleep quality (Villa & Evangelisti, 2021).

Children with OSA traditionally present with alterations in posture and mobility of the orofacial musculature, and oropharyngeal muscle hypotonia is also implicated in the pathogenesis of OSA (Villa & Evangelisti, 2021). Exercises may improve function and reduce such impairments (Gozal et al., 2020). These exercises aim to correct functions such as swallowing, breathing, speech, and chewing. Exercises can be categorized into: (1) nasal breathing rehabilitation; (2) labial seal and lip tone exercises; and (3) tongue posture exercises (Fehrm et al., 2020).

Overall, myofunctional exercises lead to decreased mouth-breathing, re-establish nasal breathing and improve orofacial muscle performance (Villa & Evangelisti, 2021). However, their efficacy has not been critically evaluated even if preliminary results are encouraging in children (Camacho et al., 2015). In addition, adherence to these exercises has been problematic.

In summary, a large array of different approaches has emerged over the last several decades aimed at resolving OSA in the pediatric age group. It is likely that as multi-disciplinary approaches become the standard, rather than the exception, we will witness rapid evolution of integrative personalized therapies that are tailored to the specific patient, finally replacing the one treatment fits all approach which has dominated to the present day.

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