Management of Pediatric Obstructive Sleep Apnea

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Barry Steinberg, Rania A. Habib, and Yirae Ort

11.1 Introduction

Pediatric obstructive sleep apnea (OSA) remains controversial in the medical field. Not only does the definition of OSA change depending on the literature reviewed, but also the actual age group defined as the pediatric population varies. In 1996, the American Thoracic Society defined obstructive sleep apnea syndrome (OSAS) in children as a "disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction (obstructive apnea) that disrupt normal ventilation during sleep and normal sleep patterns" [1]. The upper airway includes the nose, nasal passages, paranasal sinuses, pharynx, oral cavity, and the portion of the larynx above the vocal folds. OSA must be distinguished from primary snoring. Primary snoring is defined by the American Sleep Disorders Association as "snoring without obstructive sleep apnea, frequent arousal from sleep, or gas exchange abnormalities" [2, 3]. Gas exchange abnormalities refer to hypoxia, hypoxemia, hypercapnia, or hypopnea.

The general census among the specialists that treat pediatric OSA is that it is an underdiagnosed condition that causes significant morbidity and reduction in the quality of life when left untreated.

B. Steinberg (✉)
Department of Oral and Maxillofacial Surgery, College of Medicine, University of Florida—Jacksonville, Jacksonville, FL, USA

Wolfsons Children's Hospital, Jacksonville, FL, USA
e-mail: barry.steinberg@jax.ufl.edu

R. A. Habib
Department of Oral and Maxillofacial Surgery, School of Dentistry, Louisiana State University, New Orleans, LA, USA
e-mail: rhabib@lsuhsc.edu

Y. Ort
Facial Cosmetic Surgery, Bellevue, WA, USA

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11.2 Epidemiology and Prevalence

The estimated overall prevalence of pediatric OSA is ~2–5% [4, 5]. Unfortunately, this percentage only includes patients who met the criteria for OSA based upon polysomnography. Snoring occurs in about 10% of pediatric patients [6]. Although snoring can be considered benign by itself, it can contribute to sleep-disordered breathing, especially when combined with obesity. Due to differences in practice, only about 10% of pediatric patients referred to the PCP for snoring are actually prescribed a sleep study. The prevalence of OSA is likely greatly underestimated because snoring is not present in all OSA patients, and such a small percentage of patients who snore actually receive a sleep study, the gold standard of the diagnosis of OSA [7, 8].

OSA is most common in preschool-aged children, aged 3–6. This is attributed to the size of the tonsils and adenoids relative to the posterior airway space and airway size [9]. The mean age of diagnosis is reported as 14 months ± 12 months. In this age group, OSA occurs equally in boys and girls and in highest prevalence among African Americans [4]. The frequency of OSA decreases after 9–10 years of age, with male predominance increasing after puberty [10].

The incidence of OSA increases in children diagnosed with craniofacial anomalies or syndromes. OSA in children with cleft lip and/or palate is 22–65%, 37–68% in syndromes with craniosynostosis, and 85% of children with Pierre Robin sequence [11–16].

11.3 Pathophysiology

The mechanisms by which the posterior airway obstruction occurs can be divided into two broad categories that include airway collapsibility and anatomic narrowing. Airway collapsibility can be caused by inflammation, hypotonia, tracheomalacia, and altered neuromotor reflexes. Pro-inflammatory cytokines that are increased in lymphoid tissue include TNF alpha, interleukin 6, and alpha 1. Inflammation may play a key role because it not only decreases the posterior airway space, but it also increases the risk of infection that causes collapse of the airway. Anatomic narrowing can occur anywhere in the respiratory tract and can be attributed to adeno-tonsillar hypertrophy, macroglossia, increased nasal resistance, craniofacial abnormalities, and lingual tonsil hypertrophy [17]. Lingual tonsil hypertrophy obliterates the vallecula and pushes the epiglottis posteriorly, which effectively narrows the airway. The craniofacial abnormalities that contribute to increasing the risk of OSA include retrognathia, micrognathia, midface hypoplasia, and abnormal anatomy of the cranial base. OSA is a complex condition, and it is important to remember that patients can possess multiple risk factors for developing OSA.

11.4 Risk Factors and Medical Conditions Associated with Pediatric OSA

11.4.1 Tonsillar and Adenoid Hypertrophy

The adenoids and tonsils reach peak growth relative to the size of the posterior nasopharynx and oropharynx during age 3–6 and can cause mechanical obstruction. Although adeno-tonsillar hypertrophy is thought to be the primary mechanism of upper airway obstruction in school-age children, studies have been unable to correlate the size of adeno-tonsillar hypertrophy to the degree of severity of OSA [18, 19].

11.4.2 Obesity

The prevalence of childhood obesity based on CDC data collected from 2011 to 2014 is 17%. The distribution includes 8.9% of 2–5-year-olds, 17.5% of 6–11-year-olds, and 20.5% of 12–19-year-olds [20]. The prevalence of OSA in obese pediatric patients approaches 50% [21]. This is attributed to increased neck circumference, intrathoracic pressure, leptin, and fatty submucosal infiltrates in the posterior airway space, as well as hypertrophy of the adenoids and lingual tonsils. Additionally, they also have decreased lung volumes and oxygen reserve [22]. In contrast to adults, however, the correlation between obesity and pediatric OSA is not very clear. Studies suggest there is an increased risk of OSA among obese adolescents aged 12 years and older; however, the risk of OSA was not significantly increased with increasing body mass among younger children [23].

11.4.3 Prematurity

Preterm babies are 3–5 times more likely to have OSA during childhood and two times as likely to develop OSA as an adult when compared to full-term babies. A recent retrospective study concluded that the negative impact of chronic lung disease of premature babies on gas exchange and lung volume combined with the abnormally decreased ventilatory drive all contribute to the development of OSA as they grow [24].

11.4.4 Craniofacial Deformities

Several congenital syndromes have various forms of disordered breathing or anatomic features that could contribute to OSA. These syndromes include but are not limited to Crouzon, Apert's syndrome, Pierre Robin sequence, Pfeiffer,

Treacher-Collins, Prader-Willi, Down syndrome (trisomy 21), Beckwith-Wiedemann syndrome, Klippel-Feil syndrome, Marfan's syndrome, and Fragile X [25, 26]. Among the craniofacial patients that undergo polysomnography, it was found that 22–65% of cleft lip ± palate, 40–60% of Apert/Crouzon/Pfeiffer craniosynostosis syndromes, and 85% of Pierre Robin sequence have OSA [11]. Craniofacial patients are complex because many have components of both central and obstructive sleep apnea [27]. Craniofacial dysmorphology in these patients often has key anatomic abnormalities that contribute to airway obstruction that include midface hypoplasia, choanal atresia, high and narrow palatal arch, macroglossia, glossoptosis, mandibular hypoplasia, microretrognathia, subglottic stenosis, laryngomalacia, tracheomalacia, and laryngeal atresia [28]. In addition, patients with craniofacial anomalies often have acute cranial base angles that correlate with increased risk of OSA [29].

OSA in children with craniofacial deformities is often multifactorial. A Down syndrome patient with trisomy 21 may have macroglossia, midface and mandibular hypoplasia, and hypotonia, which all contribute to posterior airway obstruction [30]. In Prader-Willi, the deleted chromosome 15 contributes to weak musculature due to hypotonia, poor feeding, and slow development. As these children age, they then develop constant hunger that leads to both obesity and insulin resistance. OSA in Prader-Willi patients could thus be attributed to hypotonia, obesity, and insulin resistance [31].

11.4.5 Neuromuscular Disorders

Children with neuromuscular disease suffer from pulmonary complications grouped into two main categories that include failure of the lung or failure of the respiratory pump [32]. Hypotonia of the muscles of the upper airway contributes to collapse of the posterior airway space during inspiration. Neuromuscular disease can produce narrowing of the posterior airway space on the level of the nasal and oropharyngeal area due to weakness of the pharyngeal and genioglossus muscles, respectively [33].

Other medical conditions associated with OSA in children include choanal stenosis, mucopolysaccharidosis, osteopetrosis, and sickle cell disease.

11.5 Clinical Presentation of Pediatric OSA

Nighttime symptoms include habitual snoring, witnessed apnea, frequent awakenings during sleep, night terrors, gasping for air, mouth breathing, neck hyperextension, secondary nocturnal enuresis, and frequent nocturnal awakenings. Daytime symptoms include lack of concentration, hyperactivity, inattention, restlessness, behavior problems, poor academic performance, daytime sleepiness, diaphoresis, nasal speech pattern, and mouth breathing. The consequences of obstructive sleep apnea in children manifest in various organ systems [34, 35].

11.5.1 Neurocognitive Sequelae

Several studies link pediatric OSA with a decrease in neurocognitive function that is often associated with decreased attention and/or concentration, hyperactivity, and aggressive behavior [36, 37]. The exact mechanisms by which OSA elicits neurocognitive deficits remain unclear. Research speculates that both sleep fragmentation and episodic hypoxia may lead to alterations within the neurochemical substrate of the prefrontal cortex with resultant executive dysfunction and neuronal cell loss [38, 39].

11.5.2 Cardiovascular Sequelae

Similar to adult patients, OSA can exert changes that affect the cardiovascular system in children. These adverse effects include systemic hypertension, changes in the left ventricular geometry, pulmonary hypertension, and endothelial dysfunction. Those changes are reflected in increased circulating levels of adhesion molecules and inflammatory responses within the microvasculature [40–43].

11.5.3 Weight Changes

While OSA in adults is strongly linked to obesity, weight changes in children with OSA can manifest either as obesity or as failure to thrive. Obesity can result from long-standing obstructive sleep apnea in association with insulin resistance and increased leptin levels resulting from lack of sleep. On the other hand, OSA can also cause increase work of breathing that causes the infant to burn calories in excess of those consumed and thus manifests as failure to thrive [44].

11.5.4 Insulin Resistance and Metabolic Syndrome

OSA, in the presence of obesity, increases the risk of developing metabolic syndrome in the pediatric population by increasing insulin resistance and lipid levels in the blood [45]. Leptin plays a role in regulating appetite, sleep, metabolic homeostasis, and respiratory control. Resistance to leptin is increased in pediatric patients, independent of the degree of obesity. Leptin acts as a respiratory stimulant in collaboration with central and peripheral chemoreceptors, so patients with leptin resistance have a weakened ventilatory response [46, 47].

11.5.5 Psychiatric Sequelae

Children with OSA experience decreased quality of life due to increased fatigue, irritability, impaired concentration, and depressed mood [48].

11.6 Diagnosis

Diagnosis of obstructive sleep apnea (OSA) in children versus adults is different in a few ways. A questionnaire-based screening in the pediatric population has low sensitivity and specificity—35% and 39%—respectively [49]. If a clinician has high suspicion that a child has OSA based on physical examination, further investigation and an appropriate referral to a specialist should be made. The presence of hyperplastic lymphoid tissues, large tongue, maxillary or mandibular hypoplasia, excessive overjet or crossbite, and obesity is suggestive of OSA in the presence of sleep disturbances and warrant further workup.

Overnight polysomnography is the gold standard for diagnosis; however, this procedure can often be difficult to perform in children due to poor cooperation with the attachment of monitoring devices and fear of sleeping in an unfamiliar environment. Polysomnography involves measuring several parameters including end-tidal CO_2, pulse oximetry, transcutaneous O_2 and CO_2 tensions (in infants and children <8 years), airflow at nose and mouth (pneumotachograph, thermistor), chest and abdominal wall motion (plethysmography), sleep state (EEG leads), electrooculogram, submental electromyogram (EMG study), electrocardiogram (ECG), and video monitoring with sound montage. Other alternative techniques such as nap polysomnography have been used in children, as it is shorter in duration and more convenient for the parent. However, this has a positive predictive value of 89% and a negative predictive value of 17%, which suggests that a child testing negative for OSA during a nap polysomnography should still undergo a more comprehensive evaluation and ideally an overnight polysomnography for definitive diagnosis if the patient's presentation strongly suggests OSA.

There are no standard imaging studies used in the diagnosis of OSA. Lateral cephalometric radiograph can demonstrate several indicators for higher likelihood of obstructive sleep apnea, such as posterior airway space, elongated soft palate, acute cranial base angles, and mandibular plane to hyoid distance. However, definitive correlation between these measurements alone and OSA has not been firmly established [50]. CT provides 3D images of the upper airway, allowing detailed views of the cross-sectional area, volume, and shape. Although some studies suggest CT scan for evaluating patients with OSA, it is not often used in pediatric population due to concerns with unnecessary radiation. It is worthy to note that lying in a supine position while awake does not duplicate the soft-tissue architecture produced in the altered neuromuscular activity found during sleep. Fiberoptic nasopharyngoscopy can be used as an adjunct to confirm the diagnosis and to identify the anatomic location and structural and/or functional abnormality that may contribute to obstructive sleep apnea. It requires patient cooperation; therefore, it serves greater diagnostic value in older children.

Polysomnographic criteria for defining OSA in children shares similarity to the criteria used with adults, but there are some significant differences. In adults, an apneic event is defined by the duration of the lack of breath which is 10 seconds. In children, an apnea event is classified by one or more missed breaths and is considered apnea even with the event lasts less than 10 seconds. Breath cycle, rather than time, is used in the children because the baseline pediatric respiratory rate is

faster than that in adults until they reach late adolescence. Hypopnea is defined as ≥50% reduction in airflow measured by nasal air pressure transducer, accompanied by an arousal or ≥3% decrease in oxygen desaturation. This slightly varies from the criteria for adults, which is defined by ≥30% reduction in nasal airflow, accompanied by ≥4% oxygen desaturation [51].

Another factor that differs is the measurement of hypoventilation. For adults, sleep hypoventilation is defined as arterial $PCO_2 > 55$ mmHG for ≥ 10 minutes or an increase in arterial $PCO_2 \geq 10$ mmHg above the awake supine value. For pediatric patients, hypoventilation is defined as arterial $PCO_2 > 50$ mmHg for >25% of total sleep time or an arterial $PCO_2 > 53$ mmHg during any period of total sleep time [52].

The criteria for defining OSA in the pediatric population has a much lower threshold than adults. An apnea-hypopnea index (AHI) >1.5 is considered abnormal in children where in adults an abnormal AHI is >5. Although there are several different indices as well as varying opinions among the experts, most sleep centers define the severity of OSA in children using the following parameters: AHI < 1 normal, AHI 1.5 ≤ 5 mild OSA, AHI 5 ≤ 10 moderate OSA, AHI > 10 severe OSA [53].

11.7 Management

The most common first-line treatment for children with OSA is adenotonsillectomy. Meta-analysis literature shows the success rate of tonsillectomy and adenoidectomy to be approximately 79–85% in the pediatric population [54, 55]. However, long-term outcome studies in patients after adenotonsillectomy are lacking, and it is often difficult to identify whether recurrence or persistence of OSA occurs due to other factors such as obesity or existing lingual tonsil hypertrophy [56].

A less commonly used surgical treatment for pediatric OSA is uvulopalatopharyngoplasty (UPPP). This is because children, with or without sleep apnea, do not demonstrate as much redundant palatopharyngeal tissue as adults. However, UPPP is found to have some benefit in children with abnormal upper airway neuromuscular tone. This is seen in children with cerebral palsy, Down syndrome, or high Mallampati score due to redundant lateral pharyngeal tissue [57].

A reasonable option in non-surgical candidates is continuous positive airway pressure (CPAP). Depending on the facial structure and size of the child, CPAP can be administered via facial mask as in adults or via nasal masks. Due to logistical issues, nasal CPAP is generally the preferred method in most pediatric patients [58]. Successful treatment requires parental support in addition to patient compliance and frequent clinician assessment. Children with poor parental support and those with behavior problems that cannot tolerate the CPAP may thus not benefit from CPAP as a treatment modality.

Children with mild OSA may benefit from a reduction of upper airway inflammation using topical intranasal application of corticosteroids [59]. Similarly, montelukast receptor blocker was found to be effective in reducing symptoms in children with mild OSA [60]. Since appropriate duration of these treatments and their

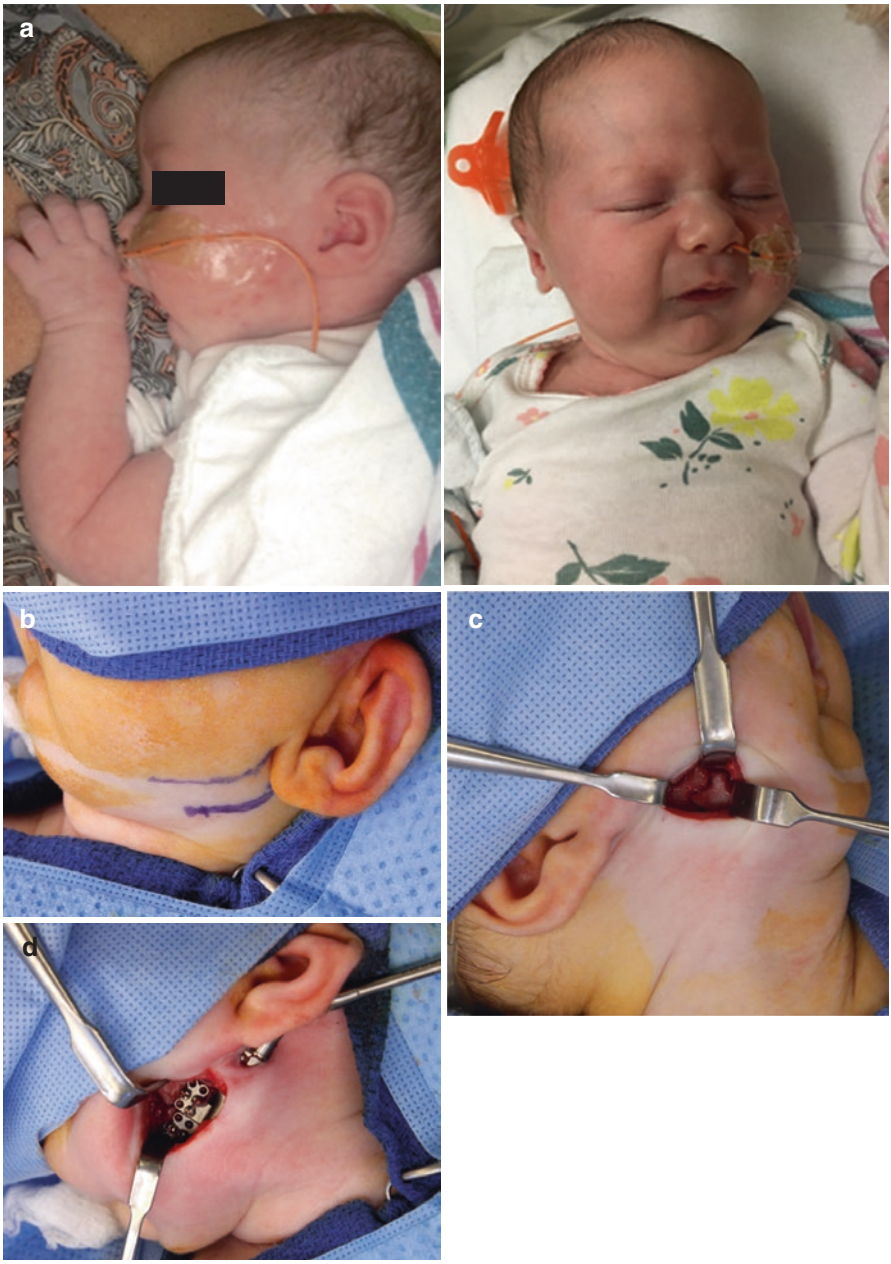

Fig. 11.1 (**a**) Preoperative photos of an infant with OSA and feeding problems due to micrognathia and Pierre Robin Sequence. Note that the mandible is hypoplastic and retrognathic. (**b**) Intraoperative marking outlining the inferior border of the mandible and incision site. (**c**) Mandibular osteotomy. (**d**) Mandibular distractor placement. (**e**) Post-operative photographs demonstrating advancement of the mandible into a prognathic position. (**f**) Intraoperative photograph demonstrating good bony consolidation following removal of mandibular distractor

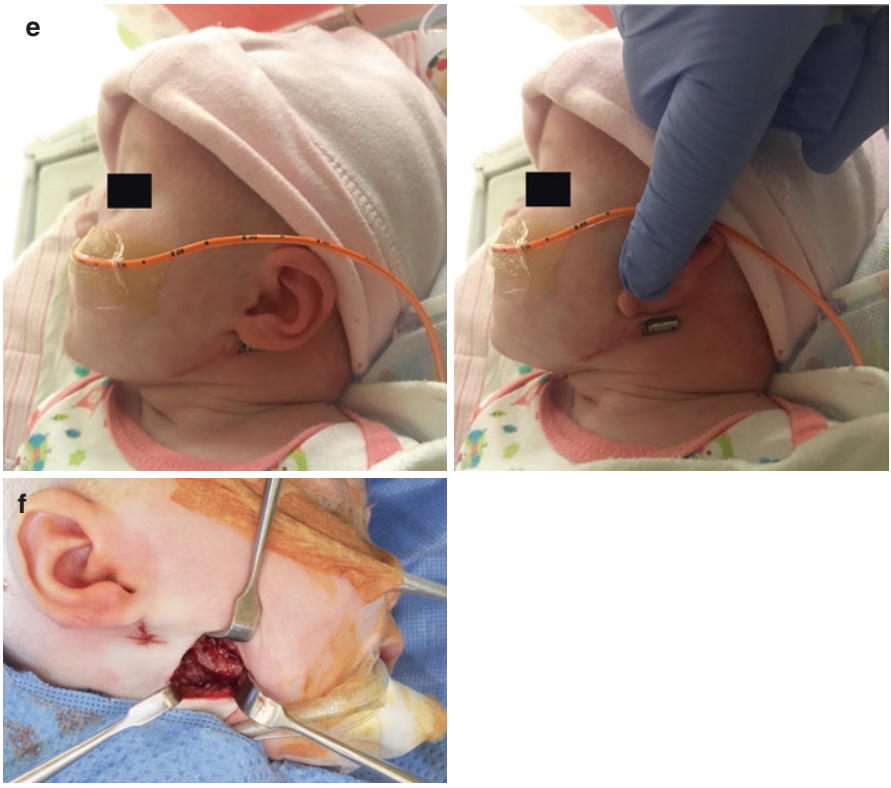

Fig. 11.1 (continued)

long-term effects have not been established, these are considered adjuncts to therapy and are not recommended as first line treatment for OSA.

Severe OSA due to certain craniomaxillofacial skeletal abnormalities may benefit from distraction osteogenesis (DO). The goal of DO is to diminish the need for tracheostomy or to help in early decannulation in patients who already have a surgical airway. Meta-analysis studies in the literature suggest the success rate of mandibular DO for treatment of pediatric OSA is approximately 90–96% [61]. Indications for mandibular DO in the pediatric population include severe hypoplasia, failure of nonsurgical airway such as CPAP, or failure of previous surgical intervention. Distraction osteogenesis is rarely the first-line treatment modality. Many patients with non-syndromic micrognathia will undergo catch-up growth, outgrowing their airway issues and obviating the need for surgery [62]. Complications of mandibular DO include vector control, which may lead to poor occlusal or functional relationship potentiating the need for secondary jaw surgery later in life. Other complications include TMJ trauma or ankylosis, facial asymmetry, inadequate consolidation, and relapse [63]. Figure 11.1a–f depicts the treatment sequence for an infant diagnosed with Pierre Robin sequence who had feeding difficulty and

OSA secondary to microretrognathia. After successful mandibular distraction, the patient resumed oral feeds and had resolution of OSA symptoms.

The most definitive treatment to establish a protected airway remains the tracheostomy. It is associated with numerous complications that include but are not limited to scars, granulation tissue, accidental decannulation, tracheal stenosis, tube occlusion and fistula. In a retrospective study reviewing the complications in pediatric tracheostomies, Carr et al. found that 77% had complications of which 43% were considered serious [64]. Trachestomy should thus be reserved for the most severe cases of OSA that cannot be successfully treated with any other methods.

11.8 Summary

Pediatric OSA has many similarities to that described in the adult population. However, it tends to be more complex with more potential causes when compared to the older population. Differences in anatomy and neurologic development are factors add to these age related variations. The treatment paradigm also is somewhat different with remaining growth entering into the equation.

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