



Pediatric sleep disordered breathing: a narrative review

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Background and Objective: Pediatric sleep disordered breathing is a spectrum of ventilatory disorders associated with multisystem complications. This narrative review aimed to discuss the impact of obstructive sleep apnea (OSA) in pediatric patients, the presentation and phenotypic variations, sleep disordered breathing in special populations, screening for suspected sleep apnea, diagnosis and management of pediatric OSA.

Methods: We searched relevant English literatures published up to 2019 in PubMed.

Key Content and Findings: OSA is a multisystem disorder associated with various short term and long term complications. There are numerous challenges with screening and diagnosis which leaves high number of undiagnosed OSA. The approach to a child with suspected or confirmed OSA presenting for perioperative care is summarized.

Conclusions: This narrative review summarizes the impact of pediatric sleep disordered breathing, screening, diagnosis and management of patients with pediatric sleep disordered breathing, and thus indicates clinical management of pediatric sleep disorder.

Keywords: Sleep apnea syndromes; obstructive sleep apnea (OSA); respiration disorders; polysomnography (PSG); tonsillectomy

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Introduction

Sleep-disordered breathing (SDB) refers to a collection of ventilatory disorders characterized by recurrent partial or complete cessation of breathing resulting in multitude of night and day time symptoms (1). Sleep disordered breathing can be considered as a spectrum of breathing disorders ranging from benign snoring to obstructive sleep apnea (OSA) depending on the varying degree of airway obstruction. Primary snoring is the early stage where the patients present without any daytime symptoms or evidence of obstruction. Upper airway resistance syndrome (UARS) follows next when the symptoms begin to appear during the

day or night with increase in the upper airway resistance. When the upper airway resistance is significant enough to produce hypoxemia or hypercarbia without evidence of complete airway obstruction, it is called as obstructive hypopnea. OSA is the most severe form of SDB with evidence of intermittent or complete airway obstruction with or without symptoms of SDB (2,3) and snoring is on the other benign end of the spectrum.

Methods

In this narrative review, we are discussing the impact of OSA in pediatric patients, the presentation and phenotypic

variations, sleep disordered breathing in special populations, screening for suspected sleep apnea, diagnosis and management of pediatric OSA. Relevant English literatures published up to 2019 were searched in PubMed.

OSA

OSA in children is a disorder with significant comorbidity that causes poor sleep quality (4,5). There is evidence in the literature to support that treatment of OSA improves sleep quality (6). OSA in children is strongly associated with a range of complications including but not limited to the immediate perioperative period (7,8) and long-term behavioral problems like neurocognitive dysfunction, hyperactivity, inattentive behaviors (9-11). OSA is also associated with a variety of medical conditions like obesity, increased blood pressure, diabetes, changes in cardiovascular geometry (12,13) and increased mortality (14,15).

Prevalence

Prevalence of pediatric OSA varied between 1–5% depending on the population and age group studied and the prevalence of habitual snoring up to 27.5% depending on the study and definition used (16,17). The prevalence is significantly higher in obese children, patients with down syndrome, cerebral palsy, prematurity and craniofacial abnormalities. The prevalence is reported to be four to five-fold higher in obese children (18). Based on PSG in a large cohort of patients with down syndrome, the prevalence of OSA is reported to be 66% (19).

Short term and long-term complications

Short term complications: OSA independently increases the risk of perioperative respiratory adverse events including hypoxemia, prolonged oxygen supplementation, laryngospasm, pulmonary edema, need for noninvasive ventilatory support like positive airway pressure (BiPAP/CPAP), prolonged mechanical ventilation, reintubation, unanticipated inpatient and critical care unit admission among many others (8,20-22)

Long term complications: OSA is a multisystem disorder resulting in cardiovascular, neurological and metabolic complications in the long-term. Neuropsychological sequel of OSA include cognitive deficits, behavioral abnormalities, increased day time sleepiness, hyperactivity and/or attention deficit hyperactivity disorder (ADHD), depression and poor

quality of life (9,10,23-25). Cardiovascular complications include ventricular hypertrophy (right, left, biventricular), pulmonary hypertension, Cor-pulmonale, elevated blood pressure, autonomic instability (13,26-28). OSA also has been shown to affect growth, decrease in serum insulin-like growth factor (IGF) and associated with metabolic syndrome (29-31).

Early diagnosis and treatment of pediatric OSA is important to minimize the risk of development of the above-mentioned complications. Treatment of OSA in children is primarily surgical mainly by tonsillectomy and adenoidectomy. Additional treatment is usually reserved for syndromic children and includes changes in facial architecture to improve risk of obstruction. Adenotonsillectomy has shown to improve the long-term outcomes in cardiovascular, cognitive, neuropsychological and quality of life measures in multiple studies (32-35).

Genotypes and phenotypes of OSA

The case for genetic basis of OSA has been made since more than four decades ago (36). There has been a number of clinical and epidemiological studies providing compelling evidence for familial clustering and probable genetic factors in the expression of OSA (37). In the Cleveland Clinic family study, the prevalence of OSA in the first-degree relatives of OSA patients ranged from 22% to 84%. It also showed that first degree relatives of OSA patients had a higher relative risk for OSA even after controlled for body mass index (BMI) (38,39). Several studies also have showed that OSA occur more commonly in African Americans which suggests the role of genetic components (38,40). Relatives of OSA patients have been shown to have similar craniofacial structures like narrow upper airways, retroposed maxilla, longer soft palate and high arched hard palate which may contribute to the familial tendency (41,42). Although multiple studies have shown strong familial tendency for sleep disordered breathing, conclusive evidence of a single genetic foci which can predict the occurrence of OSA is still elusive. Many gene association studies focusing on different genetic locations including apolipoprotein E4 (ApoE4), tumor necrosis factor (TNF) and angiotensin converting enzyme (ACE) so far have yielded mixed results (43-46). Fatal familial insomnia with mutation on the PRNP gene and Familial advanced sleep phase syndrome with mutation in the human PER2 gene have been identified as sleep disorders with definite genetic basis (39,47,48). Given that OSA has several risk factors and different phenotypic expressions, looking for a single genetic focus to identify the

OSA is not rational. Also, whether these genetic associations are causal or byproduct of OSA related complications is still remains to be determined.

Earlier studies of pediatric SDB suggested that the clinical signs and symptoms, presentation and pathophysiology of pediatric OSA was markedly different than the adult OSA. It is due to the fact that the pediatric OSA was caused by adeno-tonsillar hypertrophy rather than fatty infiltration of the soft tissues. However, with recent epidemic increase in the incidence of childhood obesity, more than 50% habitual snoring has been attributed to childhood obesity thus presenting with the similar pathophysiology of adult OSA (49). In many of these patients, OSA may still be persistent even after successful adenotonsillectomy which necessitates a different approach to treatment of OSA in obese children (50). Pediatric OSA phenotypes have been categorized into two subtypes: type 1 being primarily due to lymphadenoid hypertrophy without obesity and type 2 being primarily caused by obesity with minimal lymphadenoid hypertrophy mimicking the adult variant of OSA (49).

OSA and Inflammation

Elevated levels of inflammatory markers like CRP, IL-6, IFN- γ and TNF- α and decreased levels of anti-inflammatory cytokine IL-10 has been reported in non-obese pediatric patients with OSA and noted to return to baseline after treatment of OSA with adeno-tonsillectomy (51,52). Obesity itself is currently considered as a proinflammatory state (53,54) and the presence of OSA in addition to obesity exacerbates the chronic low-grade inflammatory state. Obese OSA children have higher levels of plasminogen activator inhibitor 1 and monocyte chemoattractant protein which activate the inflammatory pathways (55). Microarray analysis of RNA derived from peripheral leukocytes showed the presence of altered expression of gene clusters in pediatric OSA patients and majority of the altered gene clusters were involved in the activation of inflammatory pathways (56). The elevated levels of proinflammatory cytokines is not uniformly present in all the OSA patients suggests that environmental and genetic factors may play a role in the inflammatory process (57,58). OSA patients with high level of inflammatory markers found to have higher DNA methylation of inflammatory related genes when compared with OSA patients without high level of inflammatory markers (59). These epigenetic changes may explain some of the phenotypic variations and the

assessment of the DNA methylation of specific genes may help predict the pro-inflammatory risk of individual patients in the future.

SDB in special population

Children with syndromes are at high risk for post tonsillectomy complications. Overnight admissions are recommended in otherwise healthy children with down syndrome, craniofacial abnormalities, neuromuscular disorders, sickle cell disease, mucopolysaccharidoses, Prader-Willi syndrome, Achondroplasia, obesity and other conditions at a higher risk for OSA. There are numerous reviews on this topic particularly obesity and down syndrome are well studied. We provide more details regarding Pierre Robin syndrome and 22q11 syndromes.

Pierre Robin syndrome/sequence

Pierre Robin syndrome results from genetic anomalies at chromosomes 2, 11, or 17. It is frequently referred to as a sequence consisting of constellation of problems characterized by micrognathia, large posteriorly placed tongue (glossoptosis) which frequently results in airway obstruction. Uncorrected OSA leads to recurrent hypoxia, right heart failure, failure to thrive, feeding difficulties, and developmental impairment. PSG is indicated to assess the degree of airway obstruction and a multidisciplinary team is necessary to care for these children. Management includes positioning to side or prone to avoid airway obstruction, nasopharyngeal airway, or surgical interventions. Mandibular distraction is the most commonly performed procedure.

Prevalence of OSA in infants with Pierre Robin syndrome is as high as 85% (60). Children with Pierre Robin at risk for persistent OSA (1 out of 4 children) between the ages of 1 and 18 years particularly if they require respiratory support soon after birth (61). Infants treated with prone positioning alone are not as likely to develop persistent airway obstruction later in life (61). Significant reductions in apnea-hypopnea index (AHI) was seen in 9 out of the 45 evaluated children who underwent mandibular osteogenesis as evidenced by PSG (62). The severity of OSA did not decrease with increasing age as seen in non-Pierre Robin syndromic patients (62). A meta-analysis of 7 studies with 90 patients has shown the benefit of tongue-lip adhesion and tongue repositioning procedures in improving PSG parameters. Tongue-lip adhesion reduced the mean AHI by 50% and tongue repositioning

reduced it by 62.6% (63).

22q11 deletion syndrome and OSA

22q11 deletion is the most common microdeletion syndrome and results in variable phenotypes including DiGeorge syndrome. Children present with a range of symptoms and signs and cardiac involvement is very common. Structural anomalies and retrognathia results in an increased probability of obstructive breathing. The prevalence of OSA is as high as 58% in one retrospective review of children (64). The risk of OSA may be reduced with adenotonsillectomy (64). Children with 22q11 often required surgical treatment of velopharyngeal insufficiency which is characterized by poor palatal elevation and muscular hypotonia with an intact palate. With the repair of velopharyngeal insufficiency and surgical obstruction to the velopharynx, these children are predisposed to increased risk of OSA post-surgery (65). Monitoring of OSA is recommended and families should be counselled for post-operative CPAP or surgery (64,65).

SDB and secondhand (SHS) exposure

Secondhand smoke (SHS) exposure occurs in most parts of the world and most notably in Asian countries. Of the one billion children younger than 15 years studied from 21 countries, SHS exposure in home occurred in more than half of these children. Out of the countries studied, most exposures were reported from China, India, Bangladesh, Indonesia and the Philippines (66). Exposure to SHS has been associated with myriad of problems in children including exacerbation of asthma, respiratory infections, increased perioperative respiratory adverse events. A limited number of studies have shown that patients exposed to SHS have an increased risk of SDB. A systematic review on the association of SHS and SDB showed a significant association, albeit most studies were focused on snoring as the primary outcome (67). Few studies have explored the relation of SHS and OSA. A multicenter showed that both exposure to environmental tobacco smoke and African American race are associated with a 20% increase in AHI (68). Strategies to help reduce SHS exposure may be beneficial in reducing OSA severity.

Screening for SDB

Current literature suggests that the clinical symptoms

are unable to identify patients with clinically significant SDB (69). PSG is the gold standard for diagnosis of OSA. However, only 10% of the children with SDB undergo PSG testing for diagnosis preoperatively due to limited availability, cost and lack of adequate time to undergo the testing prior to surgery. Multiple questionnaires including the ASA checklist, OSA-18, Clinical Assessment Score (CAS-15) and pediatric sleep questionnaire (PSQ) among many other have been developed to screen pediatric patients at high risk for OSA. We performed a systematic review and found there were more than 15 different modes of diagnostic modalities for pediatric OSA screening of which most of them were questionnaires (70).

The American Society of Anesthesiologists (ASA) Task Force on Perioperative Management of Patients with OSA has recommended a checklist (ASA checklist) as a routine screening tool for OSA in surgical patients (71) which contains 14 questions for pediatric patients. The ASA checklist in adult patients over 18 years of age undergoing surgery is shown to be fairly sensitive and predict higher risk for postoperative complications (72,73). PSQ consists of 22 questionnaires (Yes/No/Unknown) and a score of ≥ 8 is positive for OSA. It has been validated in research setting but may not be reliable to assess the OSA risk at individual patient level (74). However, it may be a better tool in assessing the neurobehavioral morbidity and its response to adenotonsillectomy as a follow up tool (75). Tait *et al.* developed a short version of PSQ, STBUR that did not correlate with PSG indices but shown to be predictive of pediatric respiratory adverse events (PRAE) (76). Similarly, PSQ was unable to predict the OSA in severely obese adolescent patients (77). A short 6 questionnaire version adapted from PSQ was shown to correlate with PSG in predicting postoperative oxygen requirement (78). Raman *et al.* developed another short 6 questionnaire version adapted from PSQ with good predictive utility for moderate to severe OSA (79). External validation of these short questionnaires is currently limited. In the childhood adenotonsillectomy trial (CHAT) with more than 450 pediatric patients, both ASA checklist and PSQ failed to demonstrate good reliability in predicting the presence or severity of OSA (80,81). OSA-18 questionnaire and child health questionnaire have been reported to better assess the impact of OSA on the child's overall quality of life and multiple studies have utilized either questionnaire to show sustainable improvement in the quality of life after adenotonsillectomy (82,83). CAS-15 is another questionnaire which has been reported to

Table 1 Indications for polysomnography

American Academy of Otolaryngology—Head and Neck Surgery (91)
<2 years of age
Obesity
Down syndrome
Craniofacial abnormalities
Neuromuscular disorders (neuropathies, cerebral palsy, congenital myopathies, muscular dystrophies, myotonias, myasthenia gravis)
Sickle cell disease
Mucopolysaccharidoses
Moderate to severe congenital heart disease
Uncertainty in the need for tonsillectomy
Discordance between physical examination and reported SDB severity
Other children with increased surgical and anesthesia risks
American Academy of Pediatrics (16)
Children undergoing tonsillectomy for SDB
If not available—referral to ENT surgery or sleep medicine
American Academy of Sleep Medicine (92)
In all patients with SDB undergoing tonsillectomy

PSG, polysomnography; SDB, sleep disordered breathing; ENT, ear, nose and throat.

have correctly diagnose 72% patients referred for PSG in an office-based setting (84). With any questionnaires, the answers to the questions can be very subjective, inherently biased by under- and over-reporting of the symptoms and we are yet to find a screening questionnaire that is able to predict the diagnosis or the severity of OSA reliably and consistently (81).

Portable devices with either single channel monitoring such as nocturnal pulse-oximetry readings, nasal airflow or multichannel monitoring devices combining various data have been used in addition to the questionnaires to predict the risk of OSA as a cheaper alternative to the in-laboratory PSG testing. This is described further in the ambulatory sleep apnea testing part of this article.

Anthropometric measures such as neck circumference has been well documented as OSA predictors in adults. With increasing incidence of childhood obesity, these measures may become more relevant in pediatric patients as

well. In one study, neck circumference-height (NHR) ratio was shown to predict SDB in pediatric patients (85). Sagittal abdominal diameter has been shown to correlate with AHI and oxygen nadir of PSG in severely obese adolescent patients (77). In one study, adding anthropometric measures such as neck circumference and BMI did not significantly improve the predictive validity of the pediatric OSA screening questionnaire (79).

Serum biomarkers such as C-reactive protein (CRP) and IGF-1, genetic susceptibility of apolipoprotein E (ApoE) allele and epigenetic modifications of increased DNA methylation of inflammatory genes all have been studied to associate OSA with inflammation and resulting neurocognitive dysfunction and to predict the risk OSA (52,59,86,87). These markers are currently in the very early stages of research and further studies are needed before they can be incorporated into clinical practice (88).

Diagnosis of SDB

Diagnosis of SDB in pediatric patients can be challenging due to wide variety of presenting symptoms including snoring, behavioral and cognitive defects, nocturnal enuresis, headaches, poor school performance and cardiovascular symptoms. A high degree of suspicion and thorough history and physical examination focused on craniofacial anatomy and adeno-tonsillar examination is necessary prior to referring the patients with high degree of suspicion for OSA to a formal sleep study. However, demographics, clinical history, physical examination findings including tonsil size, and caregiver reports from questionnaires does not seem to predict the severity of OSA (80,89,90). So overnight in-laboratory PSG is still considered to be the gold standard diagnostic test for SDB.

Polysomnography (PSG)

The indications for PSG are outlined in *Table 1*. PSG measures a number of parameters including electroencephalography; electrooculography; electromyography; electrocardiography; and nasal airflow, respiratory effort, and oxygen saturation. The PSG report usually contains the AHI which is the total number of episodes of apnea and hypopnea per hour of sleep, oxygen saturation nadir, peak and average end tidal carbon-dioxide level and respiratory disturbances index (RDI). Apnea is defined as a decrease in flow of 90% or more for two breaths or more. Hypopnea is defined as a decrease in flow 50%

or more coupled with a 4% decrease in oxygen saturation, decrease in the heart rate or electroencephalographic evidence of arousal. The severity of OSA is calculated by the AHI. ASA Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea defines OSA severity of pediatric patients based on AHI as mild (AHI 1–5), moderate (AHI 6–10) and severe (AHI >10) (71). The criteria for measuring the severity of OSA varies widely based on the laboratory and the ASA task force advises that the laboratory's assessment of severity should take precedence over the actual number of AHI in the report (93).

Ambulatory sleep apnea testing

As mentioned earlier, it is not realistic to get an overnight PSG in every child who is suspected to have SDB due to multiple factors including but not limited to scarcity of resources, socio-economic factors, cost, prolonged wait time etc. Alternatives to the full attended nocturnal PSG have been explored including single channel devices such as nocturnal oximetry, nasal airflow, nasal pressure variations, electrocardiogram for heart rate variability and multichannel devices which include three or more of the parameters.

Nocturnal pulse-oximetry trend graph alone as a single channel monitoring device has yielded mixed results. In one study it was shown to have 97% positive predictive value in children above the age of 12 months with suspected OSA and offer a possible cheaper alternative to PSG testing in patients with adeno-tonsillar hypertrophy (94,95). Patients with significant desaturations on overnight pulse-oximetry can be prioritized for adenotonsillectomy without waiting for PSG testing where PSG testing is limited availability. It is shown to correlate with increased risk of PRAE which might help plan the perioperative care in these patients (96,97). However, other studies contradict the predictive value of pulse-oximetry alone for the diagnosis of OSA (98).

Adding additional data like nasal airflow and respiratory rate to the pulse-oximetry can increase the sensitivity of the diagnosis. Many commercially available multichannel recording devices include The ApneaLink Plus (ResMed Corporation, Poway, CA, USA), eXim Apnea Polygraph (Bitmed, SIBEL Group), Embletta® Gold™III (Embla, Broomfield, CO, USA) among others. The ApneaLink Plus is a portable multichannel screening device that records nasal airflow by nasal pressure transducer, respiratory effort, pulse rate, and hemoglobin saturation by pulse oximetry. In a small study of 25 severely obese pediatric patients, the

ApneaLink autoscore correlated well with the Obstructive Apnea-Hypopnea Index (OAHI) score (99). This has been validated to reliably identify SDB in children older than 10 years (100). The multichannel recording devices have a better success rate of acquiring data and correlating with PSG when the initial setup was performed by a technician or a nurse when compared to caregiver setup (101-103). In pediatric patients, age might also be a factor in determining the success of the ambulatory PSG with good correlation with attended PSG has been found in children with age 6 or older versus higher discordance in younger children (104). According to the American Academy of Sleep Medicine (AASM) guidelines, portable monitors may be used as an alternative to in-laboratory PSG in patients with high pre-test probability of having moderate to severe sleep apnea. However, they are not appropriate for screening asymptomatic patients, patients with comorbid conditions or central sleep apnea (105,106).

Drug induced sleep endoscopy (DISE)

Majority of the children with OSA will improve with adeno-tonsillectomy. However, about 10–20% of patients with persistent OSA after adenotonsillectomy will need additional studies (107). DISE is the endoscopic evaluation of the airway under a drug induced state of sleep without any airway support to mimic the airway collapse under natural sleep to localize the level of obstruction to plan for further surgical interventions (108,109). Various anesthetic agents including propofol, ketamine, dexmedetomidine, remifentanyl, benzodiazepines and combination of these agents have been used with varying degrees of success for DISE (110,111). In our personal experience, Ketamine bolus 1 mg/kg with dexmedetomidine bolus 2 mcg/kg over 10 min followed by 2 mcg/kg infusion provides the optimal condition and best successful completion rate for the DISE study (109).

Ciné magnetic resonance imaging (MRI) sleep study

Ciné MRI sleep study is another airway evaluation tool for persistent sleep apnea post tonsillectomy to locate the level and magnitude of airway collapsibility and obstruction (112,113). Anesthetic concerns remain the same as the DISE study to mimic natural sleep and maintain natural airway without airway adjuncts. Reviewing the PSG report to determine the nadir SpO₂ will help guide the anesthesiologist when to intervene with airway support.

Table 2 Perioperative management of tonsillectomy (91)

Guidelines for perioperative management of tonsillectomy

Ibuprofen 5–10 mg/kg q 6–8 hours

Acetaminophen <1 month—7.5 mg/kg; 1 mo–2 years—10 mg/kg, and >2 years—15 mg/kg q4–6 hours for a maximum of 75 mg/kg or 4,000 mg over 24 hours

Education on pain assessment and management

Single intraoperative dose of intravenous dexamethasone

NO routine antibiotics (indicated during endocarditis prophylaxis for cardiac conditions, concomitant peritonsillar abscess)

NO codeine or codeine containing analgesics

In patient monitoring

<3 years old

Severe OSA—AHI \geq 10 events/hour, oxygen saturation nadir <80% or both (higher AHI or other PSG parameters may be considered)

Low threshold for admission

Complicated medical histories including cardiac complications of OSA

Down syndrome

Neuromuscular disorders

Failure to thrive

Craniofacial anomalies

Current/recent respiratory infection

Obese children (BMI $>95^{\text{th}}$ percentile) without PSG quantification of OSA severity

Behavioral disturbances that could potentially contribute to poor oral intake or difficulty in pain management

Admission to ICU

Severe OSA with an AHI >30 events/hour

Syndromic children with known difficult airway

Any child with severe comorbidity that would require ICU admission

OSA, obstructive sleep apnea; AHI, apnea-hypopnea index; BMI, body mass index; PSG, polysomnography; ICU, intensive care unit.

Dexmedetomidine is shown to provide ideal conditions for the Cine MRI sleep studies (114).

Treatment of SDB

Surgical options

Adenotonsillectomy

Pharyngeal obstruction is caused by faster growth of pharyngeal lymphoid tissue as compared to facial bones between the ages of 2 and 6 contributing to OSA. Hence, adenotonsillectomy is the first line treatment for pediatric OSA and relieves symptoms in 80% of cases (115).

The most recent clinical practice guidelines in children

having tonsillectomy for OSA and infectious causes was released in 2019 by American Academy of Otolaryngology-Head and Neck Surgery (91). This is an update of the previous guidelines released in 2011 (116). There are guidelines published on OSA by the American Academy of Pediatrics and the AASM that may differ from this guideline (16,92).

We are providing a summary of the updated guidelines published in 2019 (*Table 2*). The 2019 guidelines provide recommendations on the perioperative management of children aged 1 to 18 years undergoing tonsillectomy. The guidelines exclude children with neuromuscular disease, diabetes mellitus, chronic cardiopulmonary disease, congenital head and neck anomalies, coagulopathies or

immune deficiency pathologies. The guidelines recommend detailed history of associated comorbidities in children with SDB. PSG is recommended for the following children with SDB: <2 years of age, obesity, down syndrome, craniofacial abnormalities, neuromuscular disorders, sickle cell disease, mucopolysaccharidoses, uncertainty in the need for tonsillectomy, and discordance between physical examination and reported SDB severity. The important take away points for anesthesia management includes administration of a single dose of intraoperative dexamethasone, and ibuprofen or acetaminophen or both for analgesia.

The updated guidelines recommend against routine antibiotic use and administering codeine or codeine containing medications in children less than 12 years of age (*Table 2*). Our practice is not to use codeine or codeine containing medications and they should not be prescribed to any child undergoing tonsillectomy due to varied metabolism of codeine by CYP2D6 (14,117,118). FDA received reports of 24 deaths related to use of codeine of which 21 was in children <12 years of age. In 2013, FDA issued a black box warning concerning the use of codeine in tonsillectomy. Although most opioids undergo metabolism with CYP2D6, oxycodone is minimally metabolized and at this moment appears to be a relatively safe to be used as an analgesic (91).

Education on assessing and managing pain should be provided to families. Emphasis should be provided to both pharmacologic and non-pharmacologic modes of treatment for post-operative pain. Intraoperative single dose dexamethasone is an important component of multimodal treatment. Although there are concerns for postoperative bleeding, this has not been shown in most studies. The beneficial effects of dexamethasone are its anti-inflammatory effect, reduces swelling and pain. The commonly indicated dose is 0.5 mg/kg (dose range =0.15 to 1.0 mg/kg) with a maximum dose based on local hospital protocols with a range of 8 to 25 mg (119).

Tonsillectomy for OSA carries a high risk for perioperative respiratory adverse events. Although most children are operated are outpatients, in patient overnight monitoring is indicated in children <3 years old or those who have severe OSA measured by an AHI \geq 10 events/hour or oxygen saturation nadir <80% or both. It is also prudent to admit any obese child for overnight monitoring if quantification of SDB severity with PSG has not been obtained prior to surgery. These criteria are based on expert consensus due to lack of data on the threshold for severe OSA for PSG predictive of complications or appropriate age (91).

A follow up for postoperative complications should be performed. Admission to intensive care unit is indicated if the AHI is >30 or there is underlying comorbidity with difficult airway or based on local hospital policies.

The updated 2019 tonsillectomy guidelines emphasize the administration of acetaminophen or ibuprofen or both based on efficacy from systematic review and randomized controlled trials. The goal is to potentially avoid the use of opioids. Although there are theoretical concerns of bleeding with the use of ibuprofen it has been found to be safe after tonsillectomy. The use of ketorolac is controversial and most physicians elect not to use it with tonsillectomy. Acetaminophen is recommended in an age dependent dosage with a maximum of 75 mg/kg or 4,000 mg in 24 hours whichever is lower. Although effect site concentrations can be achieved with either oral, rectal or intravenous routes, it is the authors preference to use routine intravenous acetaminophen for tonsillectomies (120). This is because with postoperative use children often have difficulty swallowing and the preemptive analgesic effect is absent. Intraoperative use could also reduce the use of opioids. Rectal administration is not favored due to requirement of high loading dose which significantly limits subsequent doses. Preoperative oral acetaminophen use is not followed due to risk of inadvertent medication error with intraoperative intravenous formulation (121). The 2019 guidelines emphasize the use of education materials and brochures to promote the routine use of acetaminophen and ibuprofen and avoid the routine use of opioids.

The CHAT study which was the first randomized controlled trial to compare watchful waiting to tonsillectomy reported that the overall success rate for OSA (AHI <2 events/hour) in children having tonsillectomy was 79%. The risk factors for persistent OSA were age greater than 7 years, obesity, asthma, certain ethnicities, and increased baseline OSA (AHI >4.7 events/hour) (107,122). The CHAT study also found improvements in standard measures of quality of life, sleep and behavior (122).

In children who underwent adenotonsillectomy, resolution of OSA was less likely in children with obesity and higher AHI at baseline. Children with severe OSA and significant comorbidities or syndromes were excluded from this study. The resolution rate was 39 percent in patients with severe obesity or severe OSA, compared with 74 percent in uncomplicated patients (123).

The surgical technique can be either intracapsular or extracapsular with each has its advantages. Intracapsular tonsillectomy was associated with shorter duration of

postoperative pain and faster return to normal life compared with traditional extracapsular tonsillectomy (124-126). Meta-analyses have shown that symptom recurrence was more common among children undergoing intracapsular tonsillectomy compared to extracapsular tonsillectomy as revealed in these meta-analyses (125,126). A practice pattern survey of US Otolaryngologists showed that 73% performed complete extracapsular tonsillectomy for a surgical indication of SDB (127). Follow up evaluations of post-surgical patients for resolution of symptoms is important as those with persistent symptoms require a repeat PSG. In children with risk factors for persistent disease, a PSG is recommended even in the absence of symptoms suggestive of SDB (16).

Uvulopalatopharyngoplasty

Uvulopalatopharyngoplasty is a surgical procedure performed to open airway spaces by reducing soft tissues contributing to airway obstruction. It has been used in cerebral palsy, down syndrome and other disorders where abnormal airway tone contributes to OSA. The surgical procedure strengthens the hypotonic pharyngeal musculature (128,129). Increasingly variants of this surgical procedure are performed where in only part of the soft tissue debulking is done. Expansion of lateral pharyngoplasty can benefit children with pharyngeal wall collapse. Supraglottoplasty is typically considered in infants with laryngomalacia and OSA (130,131).

Tongue debulking

Tongue debulking is occasionally used in patients with significant macroglossia related to syndromes such as Beckwith-Wiedemann syndrome and trisomy 21. They are generally avoided because of the highly vascular nature of the tongue but offer a solution in persistent OSA after adenotonsillectomy in patients who have an identified obstruction at the level of the base of the tongue (132). Newer techniques such as partial midline glossectomy and tongue suspension are evolving as surgical options (133).

Facial bone distraction

Maxillary expansion is an option in patients who are pre pubertal and have a narrow palate and persistent OSA with minimal adenotonsillar tissue. It may be used in combination with adenotonsillectomy in patients who have both conditions (134,135). Mandibular distraction is performed in children with Pierre Robin syndrome and other micrognathic conditions to relieve airway obstruction.

The distraction devices are being placed internally eliminating the need for external pins (136).

Hypoglossal nerve stimulation

Hypoglossal nerve stimulation is a treatment modality that has been used to alleviate airway obstruction due to tongue malposition by applying low-voltage electric pulses to the hypoglossal nerve in synchronization with diaphragmatic excursion, activating the muscles that move the tongue forward (137,138).

Tracheotomy

Tracheotomy may be a first line therapy in the rare instance of contraindications for other surgeries along with presence of failure to thrive. Tracheotomy could be a last resort in multimodality treatment failed significant OSA (139).

Non-surgical treatment options

There are various non-surgical treatment options available to treat or reduce the severity of OSA.

Weight loss

Weight Loss can lead to a marginal (5–10%) improvement in AHI in children with SDB. Weight loss could also happen as a surgical outcome, since improved quality after surgery could lead to weight loss. Weight loss is frequently recommended as a part of SDB treatment particularly when there is underlying obesity even when surgery is an option (140,141).

Positive airway pressure

CPAP and BiPAP while useful as surgery sparing noninvasive treatment modalities in SDB have their limitations in being less useful in younger children due to compliance. They are invaluable in management of residual sleep apnea after surgery in the immediate postoperative period. Standard precautions are followed for indications and contraindications like at risk of aspiration (142).

Pharmacotherapy

The use of pharmacotherapy in the treatment of pediatric OSA is summarized in a review (143). Medications that have been evaluated are intranasal steroids and leukotriene receptor antagonists (e.g., Montelukast). In milder cases montelukast along with inhaled steroids might be useful in reducing tissue inflammation and treatment of postoperative residual OSA (144,145).

Conclusions

Pediatric SDB is a spectrum and OSA is the most severe variant with a prevalence of up to 4% or higher in children. There are numerous challenges with screening and diagnosis which leaves high number of undiagnosed OSA. The approach to a child with suspected or confirmed OSA presenting for perioperative care is summarized. The recently published guidelines on tonsillectomy by American Academy of Otolaryngology is endorsed by various other societies. The guidelines provide a comprehensive view of perioperative management of a child with sleep disordered breathing presenting to an anesthesiologist and otolaryngologist for perioperative management.

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Footnote

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