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Obstructive sleep apnea syndrome in the pediatric age: the role of the anesthesiologist

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Abstract. – OBJECTIVE: Childhood obstructive sleep disordered breathing (SDB) is a sleep-related upper airway obstruction that degrades sleep quality, ventilation and/or oxygenation; obstructive sleep apnea syndrome (OSAS) is one of the most common causes of SDB in children. The aim of this review is to evaluate the role of the anesthesiologist in pediatric OSAS.

MATERIALS AND METHODS: A literature review has been performed on the following topics: clinical aspects of pediatric OSAS, preoperative investigations including questionnaires, clinical parameters, laboratory polysomnography and home sleep apnea testing, anesthesiologic preoperative management, anesthesiologic perioperative management, anesthesiologic postoperative management including postoperative analgesia, postoperative nausea and vomiting (PONV), and post-tonsillectomy bleeding.

RESULTS: OSAS in children is a distinct disorder from the condition that occurs in adults; adenoidectomy and tonsillectomy are the first line of therapy in these patients. Even if these surgical procedures are frequently performed, they represent a great challenge for surgeons and anesthesiologists and are associated with a substantially increased risk of morbidity and mortality.

CONCLUSIONS: The role of the anesthesiologist is pediatric OSAS is crucial before, during and after surgery, as pediatric patients are at higher risk of preoperative, perioperative and postoperative adverse events including airway obstruction, PONV, and bleeding.

Key Words
OSAS, Children, Anesthesiologist, Anesthesia, Multidisciplinary approach.

List of Abbreviations

SDB: sleep disordered breathing; OSAS: obstructive sleep apnea syndrome; PSG: polysomnography; NSAIDs: non-steroidal anti-inflammatory drugs; AHI: Apnea Hypopnea Index; PONV: postoperative nausea and vomiting.

Introduction

Childhood obstructive sleep-disordered breathing (SDB) is a sleep-related upper airway obstruction that degrades sleep quality, ventilation and/or oxygenation. Obstructive sleep apnea syndrome (OSAS) is one of the most common causes of SDB in children. Prevalence of SDB and OSAS in children is respectively 12% and 3%[1].

Adenoidectomy and tonsillectomy are widely used surgical procedures in pediatric patients with SDB and in many cases represent the first line of therapy. After surgery, the resolution of OSAS occurs in nearly 82% of pediatric patients[2]. Furthermore, the effects of adenoidectomy and tonsillectomy include improvement of behavior, quality of life measures, neurocognitive functioning and academic performance.

Even if these surgical procedures are frequently performed, they represent a great challenge for surgeons and anesthesiologists and are associated with a substantially increased risk of morbidity and mortality[3]. In a study on malpractice claims after tonsillectomy Morris et al[4] found that children had more fatal respiratory failure events after tonsillectomy and adenoidectomy than adults (Table I).

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Table I. Severity ranking system based on polysomnography.

	Apnea-Hypopnea index	Oxygen saturation nadir
Normal	0-1	> 92
Mild OSA	2-4	
Moderate OSA	5-9	
Severe OSA	>10	< 80

OSAS = obstructive sleep apnea syndrome

In this review, we examine the most recent literature on pediatric OSAS and discuss the role of the anesthesiologist before, during and after adenoidectomy and tonsillectomy surgery.

Materials and Methods

A literature review has been performed on articles retrieved from PubMed and Scopus from the last 30 years on the following topics: clinical aspects of pediatric OSAS, preoperative investigations including questionnaires, clinical parameters and laboratory polysomnography and home sleep apnea testing, anesthesiologic preoperative management, anesthesiologic perioperative management, anesthesiologic postoperative management including postoperative analgesia, postoperative nausea and vomiting (PONV) and post-tonsillectomy bleeding.

Results

Clinical aspects of pediatric OSAS

OSAS is defined by the American Thoracic Society[5] as "a disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction (obstructive apnea) that disrupts normal ventilation during sleep and normal sleep patterns".

OSAS in children is a distinct disorder from the condition that occurs in adults, such that the clinical manifestations, diagnostic criteria and, more important, treatment approaches need to be considered in an age-specific manner.

OSAS affects 1-3% of children[1]; the most prevalent age group is in pre-school age children between 3 and 5 years. The most common complaints are snoring and difficulty to breath during sleep; some children may also present difficult and noisy breathing during the day.

The etiology of pediatric OSAS is multifactorial and is specially associated to adenotonsillar hypertrophy. Actually, tonsillectomy with adenoidectomy (adenotonsillectomy) is the first treatment line in many pediatric OSAS patients[6].

Erickson et al[7] investigated epidemiological trends in tonsillectomy and adenotonsillectomy and reported that the indication to perform a tonsillectomy and adenotonsillectomy have substantially shifted in the last years: whereas in 1970 infections represented the main indication for tonsillectomy and adenotonsillectomy (88%), today the main indication is a pharyngeal obstruction (77%).

Preoperative investigations

The correct identification of OSAS patients is important for the anesthesiologist because it changes the perioperative and postoperative management as children with OSAS are at higher risk for perioperative airway obstruction[8].

Preoperative evaluation of a patient for potential identification of OSAS includes medical record review, patient and family interview and questionnaires, physical examination, laboratory polysomnography (PSG) and home sleep apnea testing. The diagnosis has historically been based on patient history and physical exam; however, it is important to underline that the hypertrophy of tonsils and adenoids is not correlated with the severity of OSAS. The in-laboratory PSG is the gold standard for the diagnosis of OSAS, but guidelines recommend this exam for definitive diagnosis only in specific cases. Actually, considering the cost of in-laboratory PSG and the inconvenience to the patient and caregiver, this is often not a reasonable option. When it is not possible to execute PSG, many children with symptoms of OSAS go unrecognized and thus may be at risk for perioperative respiratory adverse events.

Questionnaires are a simple practical tool to identify children with symptoms consistent with OSAS and SDB; the most common are the OSA-18[9], the Pediatric Sleep Questionnaire Sleep-Related Breathing Disorder[10] and the Snoring, Trouble Breathing, Un-Refreshed scales[11]. Schnoor et al[12] reported that the use of three core-questions (Does your child regularly snore at night? Does your child demonstrate labored breathing during sleep? Does your child have breathing pauses during sleep?) may facilitate the detection of pe-

diatric OSAS within the scope of the anesthesia survey. Unfortunately, given the subjectivity of questionnaires as a form of data collection, they failed to reach statistically significant results in detecting OSAS.

History and physical examination aimed to investigate typical symptoms such as snoring and apneas and excessive daytime sleepiness are crucial in the preoperative investigation; however, they have limitations in the ability to determine the severity of SDB. Actually, it is important to underline that presumptive diagnosis based on history and physical exam agrees with objective data obtained from PSG in about 30-50% of children[13] and neither tonsil size nor palate positions are reliable indicators of disease severity. Nolan et al[14] reviewed the biomedical literature for data comparing clinical and subjective tonsil size to objectively measured OSAS using PSG, and they found that the association between subjective pediatric tonsil size and objective OSAS severity is weak at best.

In the last decade, research[15,16] efforts have been made to identify laboratory biomarkers for pediatric OSAS. Gozal et al[17] assess that high-sensitivity C-reactive protein are higher in children with OSAS, and particularly in those who develop neurocognitive deficits as OSAS in children is associated with substantial neurobehavioral and cognitive dysfunction. However, more studies are needed to demonstrate the clinical utility in the use of serum biomarkers as screening tools for pediatric OSAS. Laboratory PSG and home sleep apnea testing are necessary before surgery. The American Academy of Sleep Medicine, the American Academy of Otolaryngology – Head and Neck Surgery, and the American Academy of Pediatrics published the guidelines[8] regarding the appropriate use of laboratory PSG for the diagnosis of OSAS in children. These guidelines recommend performing in-laboratory PSG in patients with complex medical conditions such as obesity, Down syndrome, craniofacial abnormalities, neuromuscular disorders, sickle cell disease, or mucopolysaccharidoses and in patients for whom the diagnosis is unclear or discordant with the history or physical exam. Overall, it is estimated that only 10% of children undergo a PSG prior to adenotonsillectomy for SDB[18]. Actually, PSG is expensive, time consuming, and labor intensive. For this reason, the researchers are studying home sleep apnea testing. Some individuals use overnight oximetry as a screening tool for OSAS, but compared with PSG, it has limited sensitivity and specificity[19]. Unattended monitoring with 4-7 channels (Type three studies) has sparse and conflicting data regarding utility in the pediatric population[20].

Preoperative management

Accessing the operating room is a cause of anxiety, especially for young patients and the presence of parents during induction of anesthesia may be helpful in reducing patient anxiety.

The anesthesiologists must consider the increased complications expected in OSAS patients and anxiolytics and sedatives must be carefully administrated in these patients (Table II). Premedication in children is performed with oral midazolam (0.5 mg/kg) or clonidine; both drugs have been shown to be effective and safe. Dexmedetomidine and ketamine have also been proposed although the safety of their use in pediatric patients with OSAS is still being studied.

Perioperative management

Perioperative respiratory adverse events may be more frequent in children with symptoms of SDB and OSAS. Although many of these events can be easily recognized and treated, some can be life-threatening and preventing measures must be taken in these patients.

Table II. Anesthesiology complication in OSAS children.

Preoperative	Perioperative	Postoperative
• Over sedation	• Difficult ventilation	• PONV
• Respiratory complications	• Difficult intubation	• Postoperative bleeding
• Anxiety	• Post obstructive pulmonary edema	• Over sedation
	• Inhalation	• Pain
	• Reintubation	• Respiratory complications

PONV: Postoperative nausea and vomiting.

Some adverse respiratory events may be explained by the intermittent hypoxia occurring in SDB. Breslin et al[21] demonstrated that chronic intermittent hypoxia increases the respiratory sensitivity of rats to morphine by upregulating expression of μ-opioid receptor and δ-opioid receptor in the medulla. For this reason, the use of perioperative opioid in children with OSAS should be carefully evaluated; the American Society of Anesthesiologists updated in 2014 the practice guidelines on perioperative management of patients with OSAS recommending reducing the dose of opioids used during surgery by half[22].

Other phases that deserve attention are the induction of anesthesia, ventilation, and intubation. Yang et al[23] recently evaluated the method and the effect of airway intervention before tracheal extubation after anesthesia after tonsillectomy under general anesthesia and adenoidectomy under nasal endoscope in children with SDB and reported that both methods are equally effective.

Several studies in the literature have shown that children with SDB are more likely to have a medium or high grade of Cormack-Lehane scale and they require more attention during intubation and ventilation. During the induction of anesthesia with volatile anesthetics, especially during spontaneous breathing, the relaxation of musculature can lead to the collapse of the upper airways causing a difficult mask ventilation. For this reason, it may be preferable to obtain a rapid induction with intravenous agents and perform a rapid airway intubation. Moreover, specific drugs must be avoided during induction; they include desflurane, as it can irritate airways, and suxamethonium that can cause significant side effects such as dysrhythmias, hyperkalaemia, sudden unexpected death, muscle pain, malignant hyperthermia, masseter spasm and prolonged neuromuscular blockade in face of cholinesterase deficiency.

Propofol is the most commonly used induction agent. During the maintenance phase, propofol decreases the incidence of PONV as compared to isoflurane; Sevoflurane is the most commonly used volatile agent for maintenance.

Postoperative practices

Postoperative practices include postoperative analgesia and postoperative care, as well as the management of postoperative complications such as nausea and vomiting and bleeding.

It is important to monitor postoperative therapy, because postoperative respiratory adverse events can be life-threatening.

Use of opioids following tonsillectomy with or without adenoidectomy in OSAS children may not be safe. The central nervous system depressing effects of codeine or hydrocodone and their respectively potent morphine or hydromorphone metabolites can further compromise respiratory drive[24]. Approximately 8-10% of children are slow or non-metabolizers of codeine, and no amount of codeine will provide adequate analgesia. More concerning, 0.5-2% of children are rapid metabolizers, converting codeine to morphine and producing a much higher blood level of the drug than normally expected[25]. Therefore, it is important to stress out that some patients can be rapid metabolizers of codeine, which is rapidly transformed into morphine, and that children with OSAS have a greater sensitivity to morphine for desaturation. For these reasons in April 2017, the Food and Drug Administration[24] placed a restriction on the use of codeine and tramadol medication in children, elevating the previous "warning" that was added in 2013.

Nonsteroidal anti-inflammatory drugs (NSAIDs) can be considered as an alternative to opioids for postoperative analgesic therapy. Even if NSAIDs inhibit platelet aggregation and prolong bleeding time, the Cochrane Database has determined in 2013 that in the pediatric population there is no increased risk of bleeding in the postoperative period[25].

In addition to the administration of NSAIDs in the postoperative period, palate injection of ketamine has proved useful in reducing pain. Lesser palatine and glossopharyngeal nerve blocks combined with general anesthesia improves the operative conditions and provides excellent postoperative analgesia[26].

Postoperative care

Statham et al[27] analyzed a sample of 2315 patients younger than 6 years undergoing adenotonsillectomy; of these, 149 (6.4%) developed a postoperative respiratory complication. The authors noticed that postoperative complications were more frequent in children younger than 3 years compared to children aged 3 to 5 years. Higher incidence of postoperative complications is also present in children with neuromuscular disorders, craniofacial morphology alterations, Down's syndrome or pulmonary

disease[27,28]. Down's syndrome patients have predisposing factors to OSAS including large tongue, narrow nasopharynx, hypoplastic mandibula, muscular hypotonia, obesity, tracheal abnormalities, and lymphoid hyperplasia[29]. For their anatomical features of head and neck anatomy, these patients often require an adenotonsillectomy[29-31].

The majority of children undergoing adenoidectomy and tonsillectomy are discharged the day of the surgery. The 2011 Academy of Otolaryngology - Head and Neck Surgery guidelines suggested inpatient postoperative care for children with severe OSAS (AHI ≥10/h), SpO_2 nadir <80%, and/or age <3. In 2012, the American Academy of Pediatrics also published guidelines[8] recommending postoperative admission for children with OSAS aged <3 years, obese, or with SpO_2 nadir <80%, or peak PCO_2 ≥60 mm Hg. While the American Society of Anesthesiologists did not issue specific guidelines for postoperative admission for children with OSAS, it recommended monitoring these patients until they can maintain their oxygen saturation on room air at rest, and preferably while sleeping[22].

Children with severe OSAS and those with comorbidities may also require postoperative intensive care unit admission.

Postoperative nausea and vomiting

A major problem in pediatric patients undergoing tonsillectomy and adenotonsillectomy is the high incidence of PONV. Antiemetic drugs can reduce PONV; however, their use is not always safe. The combination of paracetamol, NSAIDs, and fentanyl provide excellent analgesia with minimal PONV after elective tonsillectomy and adenotonsillectomy[32].

Dexamethasone is widely used to prevent PONV in pediatric tonsillectomy. In one study from Czarnetzki et al[33] the use of high doses of dexamethasone was associated to bleeding after tonsillectomy; however, high doses were not required to produce an anti-emetic effect. According to recent studies, dexamethasone could also have an analgesic effect although further research is needed.

Post-tonsillectomy bleeding

Post-tonsillectomy bleeding is an emergency and can lead to rapid deterioration of hemodynamics[34,35]. The incidence of bleeding following tonsillectomy is 0.5-2% depending on the surgical technique and may have serious complications including death[34,35]. The bleeding is most likely to occur within the first 24 hours after surgery and 6-10 days after tonsillectomy. The main factors to be considered in post-tonsillectomy bleeding are potential hypovolemic shock, pulmonary aspiration, and potential difficult intubation due to bleeding obscuring the view and oedema from the previous surgery[3,36].

Most clinicians perform preoperative investigations such as clotting profile, full blood count, grouping and cross-matching of blood, to reduce the incidence of bleeding during and after tonsillectomy. However, although these exams may be useful in patients who have a history suggestive of a major bleeding disorder, routine preoperative coagulation studies are not recommended in all patients[37,38].

Discussion

Children with OSAS are at higher risk for perioperative airway obstruction; therefore, the correct identification of OSAS patients is important for the anesthesiologist because it changes the perioperative and post-operative management. Preoperative evaluation of a patient for potential identification of OSAS includes medical record review, patient and family interview and questionnaires, physical examination, laboratory PSG and home sleep apnea testing. The in-laboratory PSG is the gold standard for the diagnosis of OSAS, but guidelines recommend this exam for definitive diagnosis only in specific cases; however, when it is not possible to execute PSG, many children with OSAS are unrecognized and may be at risk for perioperative respiratory adverse events.

Preoperative management is mainly aimed at reducing anxiety and agitation and is often performed using oral midazolam.

Perioperative respiratory adverse events are more frequent in children with OSAS and some of these events can be life-threatening. The use of perioperative opioid in children with OSAS should be carefully evaluated as chronic intermittent hypoxia, typical in patients with SDB, upregulates the expression of opioid receptors and therefore increases the effects of these drugs. Other phases that deserve attention are the induction of anesthesia, ventilation and intubation, as the relaxation of musculature can lead to the collapse of the upper airways causing a difficult mask ventilation.

It is important to monitor postoperative therapy especially in children with OSAS, because postoperative respiratory adverse events can be life-threatening. The use of opioids in OSAS children is not safe as they can have a stronger depressing effect on the central nervous system. NSAIDs are instead recommended to control postoperative paid.

A major problem in pediatric patients undergoing tonsillectomy and adenotonsillectomy is the high incidence of PONV; dexamethasone is currently used to prevent this complication and may have a significant role especially in children with SDB and OSAS.

Post-tonsillectomy bleeding is an emergency and could lead to rapid death[34,35,36]. Unfortunately, preoperative coagulation studies in all pediatric patients undergoing tonsillectomy have not shown to be cost-effective and their role seems to be limited to patients who have a history suggestive of a major bleeding disorder.

Further studies to understand preoperatively potential indicators of higher risk of post-tonsillectomy complications are necessary. Several studies have identified age, comorbidities, opioid doses, severe OSAS and obesity as risk factors for postoperative complications after tonsillectomy. In a recent paper from Jaryszak et al[39], the authors attempted to use preoperative PSG to identify risk factors for postoperative respiratory complications in pediatric patients undergoing tonsillectomy. Data revealed that patients who suffered a postoperative respiratory complication had the following risk factors: BMI greater than 95%, >30 AHI, 22.6 hypopnea index and a nadir oxygen saturation of 74%[39]. Further research is necessary to identify patients preoperatively at risk of developing postoperative complications. PSG in the preoperative period may be a useful tool to help identify these patients.

Conclusions

OSAS in children is a distinct disorder from the condition that occurs in adults, and adenoidectomy and tonsillectomy are the first line of therapy in many of these patients. The anesthesiologist must be able to recognize preoperatively children affected by OSAS and to manage possible complications. Therefore, the role of the anesthesiologist is children with OSAS is crucial before, during and after surgery, as pediatric patients are at higher risk of preoperative, perioperative and postoperative adverse events including airway obstruction, PONV, and bleeding.

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Conflict of Interests

The authors declare that they have no conflict of interest.

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