IMPLICATIONS OF OBSTRUCTIVE SLEEP APNEA IN CHILDREN WITH OBESITY

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ABSTRACT:
Objective: Obstructive sleep apnea is a chronic and severe breathing-related disorder, caused by adeno-tonsillar hypertrophy and has major impact in children. Obesity is a signifiant risk factor in the pathogenesis of this disease through alteration of the anatomy and the collapsibility of airways which alters the respiratory control. The aim of this systematic review was to identify the oral implications in pediatric population with obstructive sleep apnea and to highlight the importance of healthy approaches and prevent the negative effects on general health in later childhood and adulthood. Materials and method: In this review was made a literature search of articles published in international indexed databases PubMed, Medline and Web of Science. We analized only original research articles in English using the following search terms: sleep apnea, obesity, pediatric, adenoid hypertrophy. Results: The articles were studied and analyzed to be according to the subject. The clinical presentation of a child with obstructive sleep apnea is quite representative and has elements which can be classified as symptoms and physical findings. Discussions: Obstructive sleep apnea syndrome in pediatric population is a complex condition associated with various risk factors and potential complications, which is influenced by genetic, environmental and lifestyle factors. Obesity represents one of the most important risk factor in obstructive sleep apnea syndrome in both adults and children. Pediatric patients with sleep apnea and obesity have numerous implications in neurobehavioral, cardiovascular and growth impairment. Studies showed that the underlying causes of this pathology is complex and the obesity is direct implicated as a principal risk factor. Conclusions: Obstructive sleep apnea in children and adolescents is a condition with a multi-factorial etiology. Obesity and obtructive sleep apnea syndrome represents actionable problems with increasing prevalence in our society. Whether approached individually or altogether, treatment of these problems can improve quality of life, ease associated psychological burden and have positive economic implications.

Keywords: obstructive sleep apnea, pediatric, obesity, adenoid hypertrophy, cardiometabolic risk

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a breathing disorder, frequently caused by adeno-tonsillar hypertrophy and is characterized by intermittent airway obstruction during sleep, leading to ventilatory perturbation and sleep fragmentation [1,2]. According to the guidelines, the prevalence of OSAS in the pediatric population is about 2% to 3% [1,3].

Obstructive sleep apnea syndrome in children has a negative impact on health and quality of life, because it is associated with cardiovascular morbidity, neuropsychological disorders and growth empairement, emphasizing the importance

of its early diagnosis and specific treatment [4-6]. For a better management is important to identify the risk factors of OSAS, which are tonsillar and adenoid hypertrophy, obesity, male gender, craniofacial deformity, neuro-muscular disorders, family passive smoking and low socioeconomic status [7,8].

Obesity is a multifactorial condition and one of the most frequent pathology encountered in practice worldwide. The prevalence of overweight and obesity is increasing, both in the pediatric population and in adults, with a high risk of comorbidities with multiple social and economic consequences [9]. The prevalence of obesity over time has almost tripled since 1975 according to the World Health Organization. In 2016, there were more than 650 million obese adults (13%) and for children and adolescents (5-19 years) the prevalence has increased substantially from 4% in 1975 to 18% in 2016. In the present time, there are 340 million overweight or obese children, of which respectively 124 million obese patients (6% of girls and 8% of boys) [10].

The third edition of the International Classification of Sleep Disorders defines OSAS as a polysomnography-determined obstructive respiratory disturbance with more than 5 events/h and associated with the typical symptoms like unrefreshing sleep, sleepiness in daytime, fatigue or insomnia, awakening with a gasping or choking sensation, loud snoring or over 15 obstructive events/h (even in the absence of symptoms) [11]. For the diagnosis of pediatric OSAS is essential a detailed clinical history, focusing on physical findings, nocturnal and diurnal symptoms and comorbidities and nocturnal oximetry and ambulatory polysomnography are mandatory [8]. Even though, obesity is an important risk factor in OSAS, there are not so many articles in which associates obstructive sleep apnea, childhood obesity, quality of sleep and cardiometabolic risks, important factors in prompt diagnosis and management of this pathology.

This review is aiming to identify the oral implications in pediatric population with obstructive sleep apnea and to highlight the importance of healthy approaches and prevent the negative effects on general health in later childhood and adulthood.

MATERIAL AND METHODS

In this review we identified and critically analised the most relevant published studies (original papers and reviews) in the scientific literature. The literature search of articles was made in electronic international indexed databases PubMed, Medline and Web of Science. The papers published up to November 2022 in each author's field of expertise were searched with the following keywords: obstructive sleep apnea, pediatric, obesity, adenoid hypertrophy. The resulting draft was discussed among authors to provide a theoretical point of view. The final version was then communicated and approved by all the co-authors.

RESULTS

A total of 604 articles were identified through databases. The articles were studied and analyzed to be according to the subject. Lastly, 30 articles were read entirely in final analysis. We analyzed two studies (one of them was excluded for its abstract), including a manual search in the reference lists of the selected articles. Ultimately, 20 articles with the specific subject were included in this review.

The clinical presentation of a child with OSAS is quite representative and has elements which can be classified as symptoms and physical findings. The symptoms are classically divided into diurnal and nocturnal [12-14] (Tabel 1).

Tabel 1. Symptoms of Obstructive Sleep Apnea Syndrome

Diurnal	Nocturnal
Daytime sleepiness, headache, nasal speech, inattention, hyperactivity, mood instability, depression, irritability and even aggressiveness	Snoring, witnessed apnea, oral breathing, paradoxical thoracic movements, sleepwalking, nightmares and nocturnal enuresis

In general examination, the patients present obesity, long face syndrome, craniofacial alterations and elevated systemic blood pressure. On the local physical examination, more frequently is observed adeno-tonsillar hypertrophy, inflammation of the nasal mucosa, hypertrophy of the inferior turbinates, ogival palate, deviation of the nasal septum, or macroglossia. [15,16].

The long-term complications are more present in the adult population, but they may also occur in the pediatric population with OSAS. In fact, several studies have shown an increased risk of cardiovascular and pulmonary complications, such as pulmonary hypertension or right heart failure [8]. In addition, children affected by severe OSAS may develop an early metabolic syndrome, characterized by: obesity, insulin resistance, systemic hypertension, and dyslipidemia.

DISCUSSIONS

Obstructive sleep apnea syndrome in pediatric population is a complex condition associated with various risk factors and potential complications, which is influenced by genetic, environmental and lifestyle factors. Obesity represents one of the most important risk factor in obstructive sleep apnea syndrome in both adults and children [8]. Obesity is a complex disorder which affects patients with OSAS through two mechanisms: the presence of fat in the pharyngeal soft tissue which reduces the caliber of the lumen and increases the collapse of the structures, respectively the presence of fat in the thoracic and abdominal walls reduces importantly the respiratory function [17].

According to NCD Risk Factor Collaboration, since 1975 to 2016, the mean body mass index (BMI) in children and adolescents increased worldwide, up to 18.6 kg/m^2 (18.4–18.7) for girls and 18.5 kg/m^2 (18.3–18.7) for boys in 2016. Furthermore, childhood obesity is also a persistent phenomenon and about 50% of obese children are also likely to be obese adults [18]. It is considered that each addion in BMI over the 50th percentile is associated with a risk for OSAS of approximately 10% [19].

Obesity is associated with a progressive dysfunction of the adipocytes that form adipose tissue because of a positive energy balance. This tissue not only stores energy, but also acts as a dynamic endocrine organ, essential for hormone and cytokine (adipokine) secretion [20]. If it is a dysfunction of adipocytes, will lead to the stimulation of adipokines, particularly TNF-α and interleukins 6 and 1. These defects lead to inflammatory responses, localy and generaly, in addition to abnormal secretion of peptides such as leptin,

adiponectin, etc., found not only in the adipocyte, but also in the gut and brain. The dysfunction of the adipocytes leads to leptin resistance and ghrelin dysfunction, which are crucial to food intake, insulin resistance, and the dysregulation of glucose and lipid control [21]. Overweight and obese children and adults, with or without OSAS, will develop these dysfunctions in the organism. The consequences of these modifications in organism affect the respiratory, cardiovascular, metabolic and cerebral systems.

A few studies found that chronic inflammation and oxidative stress in severe paediatric obesity are apparently affecting the sleep, through disorders such as OSAS or disrupted sleep [22,23]. The examination of two important inflammatory cytokines such as IL-6 and TNF-α it confirms that OSAS in both adults and children promotes a persistently low intensity inflammatory state. However, the inflammatory processes in OSAS presents a substantial heterogeneity, indicating substantial modulation by genetic factors as well as by environmental and lifestyle influences [23].

In a study performed by Gaines et al. it was presented that C-reactive protein (CRP) and leptin levels are elevated in obstructive sleep apnea. They also found that an increase in waist circumference in boys from childhood to adolescence can be associated with increased CRP and the increase of CRP since childhood predicts sleep apnea in adolescence [24].

Adenoid and/or tonsil hypertrophy is another important risk factor and the most common cause of upper airway reduction of lumen in children [8]. Adenoid hypertrophy determine the obstruction of the posterior nostrils and the nasopharynx and tonsillar hypertrophy determine important pharyngeal stenosis which can obstruct airflow, consequently contributing to the development of OSAS. The adenoids and tonsils are lymphoid tissues, that are more developed at the age between 3 to 6 years and there are different adenoid and tonsil sizes that can have a different impact on patients, explaining why in some cases the hypertrophy determine just snoring as symptom [25]. The clinical grading of tonsillar size can be evaluated by the Friedman Grading Scale (Table 2).

Table 2. Clinical grading of tonsillar size

Grade	Description
0	The tonsils are not seen
I	Tonsils present in tonsillar fossa
II	Tonsils visible beyond anterior pillars
III	Tonsils extended 3/4 of way to midline
IV	Tonsils completely obstructing airway (kissing tonsils)

Adapted after Gulotta G et al., *Risk Factors for Obstructive Sleep Apnea Syndrome in Children: State of the Art*

Many studies confirms that adenoid and tonsilar hypertrophy are not significantly associated with OSAS severity [25,26].

Individuals of all ages need sleep as it is an opportunity for the body to restore its normal processes, conserve energy, improve mental development and promote physical growth, especially the development of children [27]. Sleep quality and duration has been associated with obesogenic behaviors and obesity

prevalence in both adulthood and childhood [28].

The National Sleep Foundation 2015 recommendations acknowledged the individual variability in appropriate sleep durations and defined inadequate sleep as < 12 hr in infants 4–11 months, < 11 hr in toddlers 1–2 years of age, < 10 hr in preschoolers 3–5 years of age, and < 8 hr in school-aged children and teenagers 6–17 years of age [29].

The interruption of sleep, which appears with abnormal breathing, can determine metabolic changes in part through the process of epigenetics, triggered by environmental events. Obesity associated with fatty infiltration of the upper airway will always determine the sleep disordered breathing pathology, initial from simple flow limitation to obstructive sleep apnea syndrome [30].

According to Narang I et al., obesity facilitate the development of OSAS, with a high prevalence of this pathology among obese children. Also, there is a higher proportion of children with OSAS who are obese, which means that both OSAS and obesity can coexist and potentiate the adverse impacts of one another [31]. The prevalence of OSAS is increasing globally due to the growing occurrence of obesity in society. A prospective cross-sectional, multicenter study, the NANOS study, assessed the corelation of obesity and adenotonsillar hypertrophy to pediatric OSAS and found that 46.6% of obese children had obstructive sleep apnea [32].

Adenotonsillectomy is considered by many authors as the first-line therapy in children with moderate or severe OSAS and even the gold standard of surgical treatment [1,33]. Brietzke et al. demonstrated that the surgical treatment can determine the resolution of polysomnographic findings in 83% of pediatric patients with OSAS without other comorbidities [33]. Several studies have demonstrated the efficacy, but also suggested follow up on long-term, especially in children with comorbidities, in order to avoid residual OSAS [34,35].

In spite of the fact that adenotonsillectomy represents the first line therapy for children, several studies have reported that obesity increases the risk of persistent OSAS after surgery [36-38].

Polysomnography represents the cardiorespiratory monitoring during sleep performed at the patient's home. The examination has high sensitivity and specificity on adult patients, but its effectiveness in children is strongly related to their age [8].

Polysomnography prior to adenotonsillectomy is indicated for children with conditions that can increase the risk of perioperative respiratory complications, which includes obesity, Down syndrome, craniofacial abnormalities, neuromuscular disorders, sickle cell disease or mucopolysaccharidosis [39]. The main purpose of the polysomnography in children with high-risk is to improve the accuracy of diagnostic, define the severity of OSAS and to optimize perioperative planning.

Several studies have suggested recommendations that all children after several months postoperative adenotonsillectomy should have a clinical reevaluation to determine whether they present snoring and that the symptoms of OSAS had been resolved, especially in those children with higher risk of persistent disease, like severe obesity or craniofacial syndromes. Furthermore, a postoperative polysomnography should be taken in consideration even in the absence of snoring or other symptoms, so that we can

determine whether additional treatment is necessary for residual OSAS [40].

In the management of obesity-related OSAS in children and adolescents the most important is weight-loss, especially in patients that have previously performed adeno-tonsillectomy surgery without clinical results. Andersen I.G. et al. conducted a prospective study on a lot of 62 children and adolescents overweight and with obesity and they observed a favorable evolution in 38% of them after 6 months of obesity treatment and in 44% after one year of weight-loss [41]. The treatment of severe obesity requires also a multidisciplinary approach with lifestyle changes, nutrition and medications. Psychosocial issues and the quality of life are important components in evaluating the patients diagnosed with obesity [42]. An interventional study by Roche et al. demonstrated that a 9-month lifestyle modification programme with weight loss and enhanced cardiorespiratory fitness exercises improves sleep duration and changes sleep architecture [43].

CONCLUSIONS

Obstructive sleep apnea in children and adolescents is a condition with a multi-factorial etiology. Obesity is a public health problem and an important risk factor that influences the evolution of obstructive sleep apnea in pediatric population. Obesity and obtructive sleep apnea syndrome represents actionable problems with increasing prevalence in our society. The effective prevention of obesity in children may reduce the occurrence of pediatric OSAS.

Whether approached individually or altogether, treatment of these problems can improve quality of life, ease associated psychological burden and have positive economic implications.

ACKNOWLEDGEMENTS

Not applicable.

CONFLICT OF INTEREST AND FUNDING

All authors read and approved the final manuscript.

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