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REVIEW

Obesity and obstructive sleep apnea in children

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Summary The prevalence and severity of obesity in children and adolescent is dramatically increasing worldwide with a corresponding increase in the prevalence of obesity-associated morbidities particularly those involving OSAS and metabolic and cardiovascular sequelae. Obstructive sleep apnea and obesity hypoventilation syndrome are important and serious consequences of obesity, and may in fact mediate components of the association between obesity and metabolic and cardiovascular morbidities, most likely via potentiation of inflammatory cascades. It is anticipated that the increased prevalence of obesity in children and adolescents in our society will be accompanied by a steady increase in the incidence of OSAS. In this review, we will examine our current understanding of sleep-disordered breathing and associated morbidities in obese children, and summarize the range of therapeutic modalities currently available for this high-risk population.

INTRODUCTION

The prevalence and severity of overweight in children and adolescent is dramatically increasing worldwide.[1,2] For example between 1980 and 2000, the prevalence of childhood overweight doubled among children 6–11 years of age and tripled among 12–17 year-old children in the United States.[3,4] Thus, in parallel to the increase in obesity secular trends among the adult population, excessive ponderal indices currently affect 15–17% of all children and adolescents and these figures are steadily rising.[5] The increase in both the prevalence of obesity and its severity has also translated into a corresponding increase in the prevalence of obesity-associated morbidities, such as type 2 diabetes mellitus and insulin resistance, dyslipidemia, systemic hypertension, atherosclerosis and ischemic heart disease, non alcoholic fatty liver/steatohepatitis, depression and decreased quality of life.[6–8] These short- and long-term morbid consequences of obesity, and more particularly the clustering of cardiovascular risk factors in the context of obesity, further stress the importance of increasing the public awareness to this problem, and prioritization of the overweight child and adolescent as a major public health concern and as an emergency. Indeed, we have increasingly become aware that many of the morbidities associated with obesity that have traditionally been viewed as problems of adults actually originate in childhood and adolescence.

Among the multiple morbidities associated with obesity, sleep-associated respiratory disturbances in general, and more specifically obstructive sleep apnea and obesity hypoventilation syndrome should be considered and evaluated.[9] As discussed further below, obstructive sleep apnea may represent an important mechanism underlying the association between obesity and metabolic and cardiovascular morbidities through potentiation of inflammatory cascades. During the past decade the childhood obstructive sleep apnea syndrome (OSAS) has become widely recognized as a common disorder with potentially serious clinical implications. Considerable insights have been gained into the associated morbidities and into the underlying

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mechanisms by which these complications arise from the basic disorder. It is expected that the increased prevalence of obesity in children and adolescents in our society and worldwide will be accompanied by a steady increase in the incidence of OSAS. Therefore, the classic presentation of children with OSAS as underweight children with adenotonsillar hypertrophy is being substantially replaced by more and more patients being overweight.[10] In this review, we will examine our current understanding of the sleep disordered breathing and associated morbidities in obese children.

OBSTRUCTIVE SLEEP APNEA SYNDROME

OSAS in children is characterized by recurrent events of partial or complete upper airway obstruction during sleep, resulting in disruption of normal gas exchange (intermittent hypoxia and hypercapnia) and sleep fragmentation.[11] The clinical spectrum of obstructive sleep-disordered breathing includes OSAS at one end, upper airway resistance syndrome UARS; traditionally associated with globally rather normal oxygenation patterns, but evidence for increased respiratory-related arousals, i.e., sleep fragmentation, and at the low end of this spectrum, a condition that has been termed either primary or habitual snoring. In other words, habitual snoring in the absence of apneas, gas exchange abnormalities and/or disruption of sleep architecture, which may occur in children and represent a relatively more benign manifestation of increased upper airway resistance during sleep. The usual nighttime symptoms and signs of OSAS in children include snoring, noisy breathing, snorting episodes, paradoxical chest and abdominal motion, retractions, witnessed apnea, difficulty breathing, cyanosis, sweating and restless sleep. Daytime symptoms can include mouth breathing, difficulty in waking up, moodiness, nasal obstruction, daytime sleepiness, hyperactivity, and cognitive problems. More severe cases of OSAS may be associated with pulmonary hypertension and cor pulmonale, systemic hypertension, failure to thrive, developmental delay, and in extreme cases sudden unexpected death. Despite recognition of OSAS in the late 1800's, this complex, yet relatively frequent disorder is only now being recognized as a major public health problem in the pediatric age range. Indeed, the prevalence of OSAS in children is currently estimated at up to 3% among 2-8 year-old children.[12,13] However, habitual snoring during sleep, the hallmark indicator of increased upper airway resistance is much more frequent in children and may affect up to 27% of children.[14–16]

Generally speaking, the pathophysiological mechanisms underlying the occurrence of obstructive sleep apnea are in many aspects quite different from those involved in adult OSAS. In the latter, OSAS is primarily, albeit not exclusively, associated with obesity, whereas the vast majority of cases of OSAS in children are due, at least to some extent, to enlarged tonsils and adenoids. Although the peak incidence of OSAS between 2 to 8 years of age was initially attributed to disproportionate growth of the upper airway lymphoid tissue during these years,[17] more recent work by Arens and colleagues suggests that the normative growth of lymphoid tissue in the upper airway is proportionate to the growth of other upper airway structures.[18–20] Thus, we should assume that a disproportionate proliferation of this tissue occurs in certain children, most likely as the result of multiple precipitating factors (e.g., respiratory viruses, allergens, passive cigarette smoking and other air pollutants, etc), and that the occurrence of this hyperplastic and/or hypertrophic growth will then predispose a subset of children to develop OSAS. The current understanding of childhood OSAS supports the existence of dynamic imbalance in upper airway function, whereby the combination of alterations in structural and anatomical characteristics, protective reflexes and neuromotor abnormalities of the upper airway are all implicated to a greater or lesser degree in any given child. As a corollary of such conceptual framework, several reports suggest that pediatric OSAS may be more common in those children with a family history of OSAS, children with allergy, children born prematurely, in African American children, and in children with chronic upper and lower respiratory tract diseases.[21–25] As discussed below, we should now incorporate the issue of obesity into the epidemiological considerations of OSAS in children.

OBESITY AS A RISK FACTOR FOR OSAS

The compelling evidence derived from the adult literature leaves no room for doubting that obesity is a risk factor for OSAS. What is currently known about obesity and risk for OSAS in children? Obese children are at increased risk for developing sleep-disordered breathing and the degree of OSAS is proportional to the degree of obesity.[21,26–31]

In the initial descriptions of OSAS in the modern era, Guilleminault and colleagues reported that 10% of 50 children who were diagnosed with OSAS were obese.[26] Mallory and colleagues showed the presence of polysomnographic abnormalities in 24% of 41 obese children.[29] Similarly, Silvestri and colleagues found evidence for partial airway obstruction in 66% and complete airway obstruction in 59% of the 32 obese children.[30] In a case-control study design, Redline and colleagues examined risk factors for sleep disordered breathing in children aged 2-18 years, and found that the risk among obese children was increased 4-5 fold.[21] In fact, for every increment in BMI by 1 kg/m^2 beyond the mean BMI for age and gender, the risk of OSAS increased by 12%. Similar trends demonstrating an increased risk of OSAS among obese and