Paediatric Respiratory Reviews 23 (2017) 68–71

Contents lists available at ScienceDirect

Paediatric Respiratory Reviews

Review

Obesity and common respiratory diseases in children

Melissa Xanthopoulos [1], Ignacio E. Tapia [2,*]

[1] Sleep Center, Division of Pulmonary Medicine, The Children's Hospital of Philadelphia, 3401 Civic Center Blvd, Philadelphia, PA 19104, USA
[2] Perelman School of Medicine at the University of Pennsylvania, Attending Physician, Sleep Center, Division of Pulmonary Medicine, The Children's Hospital of Philadelphia, 3401 Civic Center Blvd, Philadelphia, PA 19104, USA

EDUCATIONAL AIMS

The reader will be able to:

- Discuss the prevalence of obesity in childhood and populations disproportionately affected.
- Describe how obesity influences pulmonary mechanics and impacts paediatric respiratory symptoms and common disorders.
- Discuss respiratory disorders mostly commonly found in the presence of paediatric obesity.

ARTICLE INFO

Keywords:
Asthma
Lung function
Obstructive sleep apnoea syndrome
Obesity
Upper airway loading

SUMMARY

Obesity has become an important public health problem worldwide that disproportionally affects the underserved. Obesity has been associated with many diseases and unfortunately has not spared the respiratory system. Specifically, the prevalence of common respiratory problems, such as asthma and obstructive sleep apnoea, is higher in obese children. Further, the treatment outcomes of these frequent conditions is also worse in obese children compared to lean controls.

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Obesity is a major worldwide public health problem in children, adolescents, and adults. In 2013, 42 million preschool children (children under 5 years of age) were overweight or obese [1]. The prevalence of infant, childhood and adolescent obesity may be plateauing in some settings; however, there is a disproportionate absolute number of overweight and obese children living in low- and middle-income countries compared to in high-income countries [2]. Nonetheless, the risks of childhood obesity are greatest in lower socioeconomic groups in higher income countries. For example, over the past 30 years, the rate of obesity (defined as body mass index [BMI] $\geq 95^{th}$ percentile for age and gender) has doubled in children and tripled in adolescents in the United States [3]. The prevalence of obesity in children and adolescents aged 2-19 is 16.9%, whereas the prevalence of overweight or obesity in 2-19 year olds is 31.8% [3]. Importantly, non-Hispanic Black youth have significantly higher rates of overweight or obesity than their White counterparts (35.2% and 28.5%, respectively) [3]. In addition, an even more alarming trend is that the severity of obesity also continues to worsen [4,5]. In fact, 6.3% of children and adolescents in the United States are considered severely obese ($\geq$120% of the 95^{th} percentile or BMI ≥ 35 kg/m^2) and 2.3% are considered morbidly obese ($\geq$140% of the 95^{th} percentile or 40 kg/m^2) [4]. However, ethnic minorities are again disproportionately affected. The prevalence of extreme obesity (BMI-for-age $\geq$1.2 times 95th percentile or BMI $\geq$35 kg/m^2) in a large multiethinic cohort aged 2 through 19 in Southern California was 6.4%, with Hispanic Caucasian and African Americans presenting with higher prevalence (7.9% and 8.2%, respectively) [6]. Not surprisingly, minority and low socioeconomic groups disproportionately experience respiratory disorders, such as asthma and obstructive sleep apnea [7–10].

The respiratory system can be significantly adversely affected by obesity. Respiratory mechanics, respiratory muscle strength and endurance, airway resistance, lung volume and function, gas exchange, and control of breathing can all be negatively impacted by obesity [11], particularly as adiposity increases [12,13]. Table 1 shows the impact of obesity on pulmonary function and mechanics.

* Corresponding author. Tel.: +215 590 3749; fax: +215 590 3500.
E-mail address: tapia@email.chop.edu (I.E. Tapia).

http://dx.doi.org/10.1016/j.prrv.2016.10.002
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Table 1
Paediatric Obesity and Respiratory Disorders.

- Both paediatric obesity and paediatric respiratory disorders are increasing in prevalence worldwide.
- Children and adolescents from low income countries or low socioeconomic groups within high-income countries are at increased risk for obesity and respiratory disorders.
- Central adiposity, measured by waist to height ratio, is a better assessment than BMI of cardiometabolic and respiratory risk in paediatric patients.
- Obesity impacts all aspects of respiratory function, including mechanical, metabolic and ventilatory drive.

The amount of fat mass is only one aspect contributing to respiratory disorders and decreased pulmonary function. Fat distribution also plays a role. Central adiposity, or abdominal fat, has been related to impaired pulmonary mechanics, independent of BMI in adults [14], and has been shown to be associated with worsening lung function and respiratory symptoms in adults as well as children [15–17]. Central adiposity is characterized by increased adipose tissue in the anterior chest wall, anterior abdominal wall, and visceral organs [18]. Intra-abdominal fat is also considered more harmful to overall health than peripheral adiposity or subcutaneous fat [19]. In the paediatric population, central adiposity is assessed using waist to height ratio (WHtR). This is the waist circumference divided by height, both in centimeters. It has been recommended to use WHtR instead of BMI as it may be more predictive of cardiometabolic risk in children and adolescents, as well as increased early mortality [20,21].

Obesity has been strongly associated with respiratory symptoms and diseases in youth, including exertional dyspnea, asthma, obstructive sleep apnea syndrome (OSAS), and obesity hypoventilation syndrome [22–24]. It has also been shown to impact breathing related to sedation and post-operative care [25].

OBESITY AND ASTHMA

Studies have shown that the prevalence of asthma is higher in obese children compared to lean controls. Further, large studies have shown that obese children are more symptomatic and more frequently seen in the emergency department. The reason for these is likely multifactorial. Lung function has been thought to play an important role on these associations based on previous studies in adults that have shown decreased functional residual capacity (FRC) and expiratory reserve volume (ERV) in obese participants with asthma [26]. However, lung volumes have not been consistently studied in obese children with asthma. Most studies have analyzed spirometry results in obese children with asthma and found that the forced expiratory volume at 1 second (FEV_1)/forced vital capacity (FVC) is the only lung function parameter reduced in overweight and obese asthmatic children compared to lean controls [27,28]. Interestingly, a study of obese children with and without asthma demonstrated that obese children with asthma had reduced post-exertional FEV_1/FVC only whereas non-obese asthmatics had a significant reduction of FVC, FEV_1, and forced expiratory flow between 25% and 75% of the vital capacity (FEF_{25-75}) [29]. Further research studying lung volumes in obese asthmatic children is needed.

Another important point to highlight regarding asthma and obesity in children is the response to inhaled corticosteroids. Data from the Childhood Asthma Management Program (CAMP) trial that followed asthmatic children over 4 years, reported that overweight and obese children had reduced response to inhaled budesonide [27]. Specifically, normal weight children treated with inhaled budesonide had a significant improvement in FEV_1, FEV_1/FVC and bronchodilator response throughout the duration of the trial. In contrast, overweight and obese children had a minor improvement in FEV_1 limited to the first half of the trial, and showed no improvement in any of the measures of lung function during the second half of the study. They also showed no FEV_1/FVC improvement throughout the trial. In addition, the risk of requiring an emergency department visit during the treatment with inhaled budesonide did not change in overweight and obese participants. However, this risk was reduced by 44% in normal weight children. These findings are important as they highlight the need for personalized medicine and further investigations in the growing population of obese asthmatics.

OBESITY AND OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS)

OSAS is a common paediatric disorder with prevalence estimates between 2-15% [30–32]. It is associated with intermittent hypoxemia, hypercapnia, and disrupted sleep. Often, children present with snoring, pauses in breathing, mouth breathing and daytime sleepiness or hyperactivity. The most common cause of OSAS in children 2-5 years of age is adenotonsillar hypertrophy. However, as the prevalence of obesity has dramatically increased over the past 30 years, it is now recognized as a significant contributor to OSAS, particularly in adolescence [32–34]. In a study of children and adolescents aged 2-18 years, obesity was the strongest predictor of OSAS, with an odds ratio of 4.59 [10]. In addition, the respiratory disturbance index has been found to increase in proportion to increasing body weight in children [35]. Further, another study of children and adolescents aged 3-14 years old reported that the prevalence of OSAS was 38.7% in children with BMI z-score less than 2 versus 60% in children with BMI z-score higher than 2. The OSAS odds ratio was 2.38 in children with BMI z-score higher than 2 [33]. The prevalence of OSAS in obese children and adolescents compared to the general population is clearly much higher.

The pathophysiology of the relationship between obesity and OSAS is likely multifactorial. It has been well recognized the importance of anatomy and neuromotor function in the pathophysiology of OSAS and the evidence suggests that obesity affects both anatomy and function. Specifically, obese children have been found to have fat deposits in the upper airway (UA) that can contribute to UA loading [36]. In addition, obese adolescents with OSAS have decreased response to hypercapnia during sleep, which is a marker of respiratory drive [37]. A recent study compared UA anatomy, measured by magnetic resonance imaging, and UA neuromotor function measured by activation of UA reflexes in obese adolescents with and without OSAS. This research showed that smaller nasopharyngeal airway volume (a marker of anatomy) and impaired UA neuromotor reflexes were synergistic risk factors for OSAS [38].

Short- and long-term effects of untreated OSAS in paediatric patients include physical and neurobehavioral consequences. Short-term consequences include increased cardiometabolic risk above that of having obesity alone, sleepiness, attention and executive dysfunction, mood concerns, and decreased quality of life [39–45]. There is little data regarding the long-term consequences of having paediatric obesity and OSAS. In adults, there is an association with increased morbidity and mortality, stroke, hypertension, and cognitive impairment and Alzheimer's disease [46–50].

First-line treatment for OSAS in paediatric patients is surgical removal of the tonsils and adenoids, if enlarged, even in obese patients. Removal of enlarged tissue decreases airway loading. However, paediatric patients with obesity are more likely to have residual OSAS following surgery than healthy-weighted peers. Most often, the residual OSAS is less severe following surgery. Weight loss should be strongly encouraged as it has been associated with lessening the severity of OSAS and even resolution [51–53]. However, it is unknown how much weight loss is needed to ameliorate OSAS. In addition, it takes time to lose weight in a

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