https://doi.org/10.5664/jcsm.10034

JCSM | Journal of Clinical Sleep Medicine

COMMENTARY

Pulmonary hypertension in children with severe OSA: Can CO_2 provide a clue?

Commentary on Maloney MA, Davidson Ward SL, Su JA, et al. Prevalence of pulmonary hypertension on echocardiogram in children with severe obstructive sleep apnea. *J Clin Sleep Med*. 2022;18(6):1629–1637. doi: 10.5664/jcsm.9944

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Obstructive sleep apnea (OSA) in children can be associated with a wide spectrum of metabolic and cardiovascular comorbidites.[1] The range of cardiovascular consequences that may arise from untreated OSA can include congestive heart failure, cor pulmonale, right ventricular hypertrophy, pulmonary edema, and pulmonary hypertension (PH). OSA is thought to be the primary catalyst of cardiac dysfunction in children without pre-existing cardiac disease, but the underlying pathophysiology of how this evolves is not yet fully understood. It is thought to stem from intermittent hypoxia due to abnormal gas exchange at the alveolar level, and a physiologic state of increased negative intrathoracic pressure that results from chronic upper airway obstruction. The downstream effects of increased negative intrathoracic pressure lead to progressive increase in pulmonary vascular resistance, inducing increased right-sided ventricular pressures.[2] The exact prevalence of PH in children with OSA is not known, but those with severe OSA are thought to be most at risk. The current guidelines from the American Heart Association and American Thoracic Society recommend echocardiography in pediatric patients with severe OSA (class I, level of evidence B).[3]

In this issue of the *Journal of Clinical Sleep Medicine*, the study by Maloney et al[4] explores the prevalence of PH in children with severe OSA. The authors also aimed to identify and examine the clinical determinants that may signal those at greatest risk for having PH in order to improve targeted screening for the disorder. The authors conducted a retrospective study of 318 children (ages 2–17 years) with severe OSA who had an echocardiogram performed within 1 year of their diagnostic polysomnogram. The cohort studied included children without comorbid conditions, but also those with known genetic syndromes, neuromuscular disease, and noncyanotic congenital heart defects. Children with history of cyanotic heart disease were excluded from the study. The authors compared patient characteristics of those with and without PH.

In this cohort, 26 of the 318 children were identified as having PH, yielding a prevalence of 8.2%. This represents a 2- to 4-fold higher prevalence compared with prior published studies of PH in children with OSA.[5,6] This study utilized a lower threshold for mean pulmonary artery pressure of 20 mmHg to define PH, compared to 25 mmHg utilized in the other studies, which may account for the higher prevalence noted in this study. The high percentage of children with comorbid medical conditions (65%) may also contribute to the increased prevalence. One of the authors' findings was that children with Down syndrome represented 46% of the group with PH. Of the 12 patients with Down syndrome, only 2 did not have a history of congenital heart disease. It certainly calls into question whether the history of Down syndrome, or other genetic conditions, predisposes one to both PH and OSA, and there may not be a significant independent contribution of the OSA to the pathophysiology of the PH. Specifically as it relates to Down syndrome, pulmonary vascular disease is a known clinical feature that predisposes to PH.[7]

One of the most intriguing findings from this study was that a significant proportion of the children diagnosed with PH were noted to also have sleep-related hypoventilation on polysomnogram. Surprisingly, higher obstructive apnea-hypopnea indices (OAHI), oxygen desaturation index (ODI), and more severe hypoxemia did not correlate with increased risk for PH. Instead, they found an independent correlation between the presence of sleep-related hypoventilation in children with severe OSA and PH. Twenty-five percent of the children with hypoventilation on polysomnogram were found to have PH. This is contrary to the widely held premise that hypoxemia is one of the primary drivers of PH in the setting of OSA. Based on this finding, the authors suggest prioritizing PH screening in children found to have hypoventilation on the polysomnogram. However, caution should be utilized when trying to extrapolate this finding to the general population. Of note, only 3 children (2.7%) without a comorbid condition were found to have PH, with only 1 child having hypoventilation. It was interesting to note that all 3 patients had a body mass index percentile > 99%.

Many questions regarding the risk of PH in children with OSA remain unanswered. It appeared from this article, as well as previous publications, that OSA severity does not have a strong correlation with the risk of PH. Hypoventilation may be a marker for PH in children with severe OSA, although these medical conditions may be associated sequelae from an underlying medical condition, such as Down syndrome. It is likely that the pathophysiology for PH in children with OSA is multifactorial, and different than in adults. The contribution of OSA to the pathophysiology of PH in

children is still not well known. This article, along with others, suggests that hypoxemia and severity of OSA may not serve as reliable indicators of PH in children. Prospective studies are required to determine the true prevalence of PH in children with OSA, which is likely low, especially in children without comorbid medical conditions.

CITATION

Kanney M, Hsu D. Pulmonary hypertension in children with severe OSA: can CO_2 provide a clue? *J Clin Sleep Med*. 2022; 18(6):1485–1486.

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SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication April 4, 2022
Accepted for publication April 4, 2022
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DISCLOSURE STATEMENT

Both authors have seen and approved the final manuscript. The authors report no conflicts of interest.