The Role of Co-Morbidities

Sofia Konstantinopoulou, MD,[a] Georgios A. Sideris, MD,[b] and Lourdes M. DelRosso, MD[a]

Medical conditions can impact sleep and breathing in children. Gastroesophageal reflux disease, allergic rhinitis and asthma are common in children and often coexist with obstructive sleep apnea. Appropriate identification and management of these conditions can improve nocturnal and diurnal symptoms of sleep disordered breathing. We discuss the relationship between these medical conditions and obstructive sleep apnea in children

Curr Probl Pediatr Adolesc Health Care 2016;46:7-10

Introduction

Medical conditions can impact sleep in children. In this article we will discuss gastroesophageal reflux disease, allergic rhinitis, and asthma in relationship to pediatric obstructive sleep apnea syndrome (OSAS).

Gastroesophageal Reflux

Gastroesophageal reflux (GER) is common in children of all ages. Overall, 70% of infants are affected by GER, with prevalence decreasing to 50% at 4 months of age, 10% at 1 year and 4% in older children.[1,2] GER refers to the retrograde movement of food contents from the stomach into the esophagus secondary to transient relaxation of the lower esophageal sphincter, considered a normal physiologic process in children and adults. Gastroesophageal reflux disease (GERD) occurs when GER is accompanied by symptoms. In infants symptoms include vomiting, regurgitation, irritability, poor weight gain, and respiratory symptoms. In toddlers symptoms include vomiting, decreased appetite, coughing, wheezing, and laryngitis. In older children and adolescents, the symptoms can be similar as in adults and include heartburn, abdominal pain and regurgitation.[1]

During wakefulness, GER usually occurs after meals and is rapidly cleared by swallowing. During sleep, GER episodes usually occur during arousals secondary to relaxation of the lower esophageal sphincter. Children with sleep disorders that increase sleep fragmentation such as OSAS are therefore at higher risk of GERD. Sleep also decreases esophageal peristalsis, saliva production, and swallowing contributing to prolonged GER episodes.[3]

OSAS and GER are physiologically interrelated. GER episodes in infants result in laryngeal closure to prevent aspiration resulting in apnea. Similarly apneic episodes increase the negative intrathoracic pressure increasing the intra-abdominal pressure leading to a pressure gradient which is considered to be a culprit for developing GER.[4] Furthermore, children with obesity are at increased risk of both OSAS and GER. A study of 18 children with OSAS and tonsillar hypertrophy, who underwent overnight polysomnography with pH monitoring, revealed GER in 88.2% of patients.[5] Another study of 57 children with OSAS revealed that the reflux index was a significant risk factor for residual OSAS after AT.[6] A trial of 4–8 weeks of GER treatment with proton pump inhibitors in 21 children with OSAS showed mixed results. There was normalization of AHI in 3 children with mild OSAS, no change in AHI in 6 children with severe OSAS, and the remainder of children had some improvement in AHI.[2] In adults, treatment of OSAS with CPAP has been shown to improve GERD symptoms.[7] Studies of the effects of CPAP on children with GERD are lacking.

In conclusion, GER and OSAS coexist in children, but more research is needed to determine the exact relationship between OSAS and GER.

Allergic Rhinitis

Chronic nasal obstruction caused by allergic and non-allergic rhinitis is commonly seen in children

From the [a]Division of Pulmonary Medicine, The Children's Hospital of Philadelphia, Philadelphia, PA; and [b]Faculty of Medicine, National and Kapodistrian University of Athens, Athens, Greece.

Curr Probl Pediatr Adolesc Health Care 2016;46:7-10
1538-5442/$ - see front matter

http://dx.doi.org/10.1016/j.cppeds.2015.10.010

and has been associated with poor sleep quality, increased daytime fatigue, snoring, and OSAS.[8] Up to 40% of children in the United States are diagnosed with allergic rhinitis with a higher prevalence in boys.[9] Children tend to be more susceptible to seasonal allergies while perennial allergies are more common in adults. Allergic rhinitis has an early-phase and a late-phase response. The early phase is characterized by sneezing, rhinorrhea, and nasal congestion while tissue damage and nasal congestion predominate during the late phase. The inflammatory mediators are released during the late phase, therefore treatment with anti-inflammatory medications prior to the allergy season will modify the late phase response and will decrease nasal congestion.[9]

Nasal mucosal edema increases the nasal airway resistance and can cause mouth breathing during sleep. The negative intrathoracic pressure during inspiration necessary to overcome the increased nasal resistance during sleep can lead to pharyngeal airway collapse, producing obstructive events.[8,10] Furthermore, inflammatory mediators involved in the allergic response including tumor necrosis factor alpha, interleukin (IL) IL1β, IL4, IL10, and interferon gamma have been associated with sleep disruption.[11] PSG studies on patients with seasonal allergies have shown an increase in the number and length of obstructive apneas during the allergy season compared to periods when symptoms are absent.[12]

Management of allergic rhinitis symptoms with intranasal steroids has resulted in improvement in both AHI and in subjective daytime symptoms (fatigue, irritability, and energy).[12,13] Other treatment options include montelukast and combined therapy with montelukast and intranasal steroids.

Asthma

Asthma is a chronic inflammatory disease of the lower respiratory tract characterized by bronchial hyperreactivity and episodic, partially reversible lower airway obstruction.[14] Asthma ranks in the 3 most common chronic respiratory diseases of childhood,[15] with a prevalence of 9.3% in children 14 years of age and younger.[16] However, morbidity remains high despite evidence-based guidelines for evaluation and treatment. Studies have shown that asthma in children negatively affects school attendance, school performance,[17] and parents' work attendance.[18] Importantly, unaddressed co-morbidities, such as OSAS may lead to worse outcomes in asthmatic children.

OSAS is considered the most severe entity within the spectrum of sleep-disordered breathing (SDB) and it affects up to 3% of the general pediatric population.[19] Of note, the prevalence of OSAS seems to be increased among children with asthma compared to their peers without asthma.[20,21] Moreover, this increased risk of OSAS in asthmatic patients has been reported to correlate with poor asthma control and the need for high doses of inhaled or systemic corticosteroids.[22,23] There are indeed many survey-based studies reporting an association between OSAS and symptoms of asthma.[20,24–27] A recent systematic review investigating the association between asthma and SDB in children showed that SDB was significantly more frequent in children with asthma compared with non-asthmatics (23.9% vs. 16.7% respectively, $p < 0.0001$), and that children with asthma had a significantly higher risk for SDB with an odds ratio of 1.9.[28] However, only a few of these studies used polysomnography, which is the gold standard for the diagnosis of SDB.[29] The physiological and temporal relationships between both conditions should be addressed in further clinical trials, which should include not only subjective assessment of SDB and asthma but also include objective measures, such as polysomnography and spirometry, respectively.

Asthma and OSAS may have the same risk factors such as obesity,[30] allergic rhinitis,[31,32] gastroesophageal reflux, and low socioeconomic status,[19] therefore they may share common pathophysiologic mechanisms. This supports the "one-airway hypothesis," which suggests that upper airway pathology might influence the course of lower airway disease.[33,34] A plausible explanation is that the oxygen-free radicals, isoprostanes, and cysteinyl leukotrienes synthesized in the airway as a result of hypoxemia during obstructive episodes, act synergistically to increase bronchial hyper-responsiveness and reduce bronchial caliber in asthmatic individuals.[35] It seems, however, that the asthma–OSAS relationship is bidirectional. Asthma may contribute to OSAS with the following proposed mechanisms: (1) oxygen-free radicals released by the asthmatic airway upregulate the production of cysteinyl leukotrienes, which then induce a proliferative response in the lymphoid tissue, and thus may lead to adenotonsillar hypertrophy.[36,37] (2) Another explanation may involve a viral or other infectious agent that would modify the properties of the tissues across