SLEEP-RELATED BREATHING DISORDERS FROM TOTS TO TEENS

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Introduction

"It is not at all uncommon to find children who suffer from … enlargements of the lymphoid (tonsillar) tissues of the nasopharynx and fauces, described by their parents and teachers as backwards and stupid. ... The fact, however, that children, the victims of nasal and pharyngeal obstructions, often suffer from headaches, especially when engaged in study, and frequently evince marked inability to fix their attention on their lessons or work for any length of time, has in recent years led many to suspect that these symptoms [are] in part a reflection of some evident hampering of the cerebral functions."

- *William Hill, B.Sc., M.B.Lond* (Hill 1889)

Obstructive Sleep Apnea

Astute clinical descriptions of obstructive sleep apnea (OSA) in children date from the era of Sir William Osler. (Osler 1892) Contemporary accounts began with Christian Guilleminault's report of eight children whose relatively severe airway obstruction during sleep was associated with headache, hypertension, and neurobehavioral disturbances. (Guilleminault, Eldridge et al. 1976)

Over the last 40 years, it has become clear that the pathophysiology of OSA is considerably different for children compared to adults. Children are more likely than adults to exhibit partial airway obstruction associated with arousals rather than episodic complete airway obstruction associated with substantial desaturations of SpO2. (Ward, Marcus et al. 1996) In contrast to the adult population, childhood OSA is more commonly associated with adenotonsillar hypertrophy compared to other risk factors such as obesity. Although OSA may occur at any point during childhood, it is most common between 2 and 8 years of age, when adenotonsillar size is largest relative to airway size. (Marcus 2001) Overall prevalence of OSA in the pediatric population is estimated to be about 2%.

Children with OSA usually exhibit some degree of noisy respiration during sleep, although this may differ from adult-style snoring. Mouth breathing, restlessness, and diaphoresis represent other common nocturnal symptoms. (Brouillette, Hanson et al. 1984) Daytime symptoms associated with childhood OSA are highly variable. Daytime somnolence is usually more subtle than is the case for adults with OSA. Excessive sleepiness is often only intermittently apparent during sedentary activities such as riding in an automobile. Inattention, hyperactivity, behavioral disturbances and impaired learning represent common but variable diurnal symptoms which are often misattributed to other causes. (O'Brien, Holbrook et al. 2003; O'Brien, Mervis et al. 2004; McNally, Shear et al. 2012)

Criteria for the diagnosis of OSA in children require the presence of at least one scorable obstructive event per hour of sleep during polysomnography (PSG) in combination with other clinical and PSG findings. (Anonymous 2014) Pediatric criteria differ from those used for adults due to ample scientific data documenting that children may experience clinically significant sequelae of OSA even when the frequency of obstructive respiratory disturbances during sleep is within the range of normal for the adult population (up to five per hour). (Rosen, D'Andrea et al. 1992)

Adenotonsillectomy represents the most commonly administered treatment for childhood OSA. The procedure is widely available and relatively safe, but does not always "cure" OSA in children, particularly when other modes of airway obstruction are present beyond adenotonsillar obstruction. In a large, randomized, multicenter trial assessing 379 children with OSA, PSG findings normalized for 79% of subjects treated with adenotonsillectomy compared to 46% of children receiving supportive care without surgery. (Marcus, Moore et al. 2013) Risk factors for persistence of OSA following adenotonsillectomy include young age, atypical anatomy of the upper airway (e.g. craniofacial disorders, cleft palate), and high severity of OSA preoperatively.

Continuous positive airway pressure (CPAP) is also considered a first line treatment for OSA in children. It is used most commonly for children who are not candidates for adenotonsillectomy, or whose OSA persists despite adenotonsillectomy. Although this treatment is considered both safe and effective, it is sometimes not feasible for use in young children or those with significant neurological or developmental disabilities. Many children achieve successful long term compliance with CPAP, particularly those who understand the need for treatment and perceive clear clinical benefit. (Massa, Gonsalez et al. 2002; O'Donnell, Bjornson et al. 2006; Beebe and Byars 2011; DiFeo, Meltzer et al. 2012) Consistent use may be associated with improvements in a variety of neurocognitive measures. (Marcus, Radcliffe et al. 2012)

Sleep-related Breathing Disorders Associated with Specific Genetic and Neurological Disorders
It is estimated that over one third of children with Down syndrome (Trisomy 21) may have OSA.(de Miguel-Diez, Villa-Asensi et al. 2003; Ng, Hui et al. 2006) It is postulated that this increased risk may be related to multiple factors including hypotonia, macroglossia, and sometimes obesity.

OSA is also common among children with Prader-Willi syndrome (PWS), another condition associated with hypotonia, developmental disability, and propensity toward obesity. In one Australian cohort, OSA was identified in 44% of subjects referred for PSG screening prior to planned initiation of growth hormone therapy. (Vandeleur, Davey et al. 2013) Limited data suggest that growth hormone supplementation may be associated with added risk for OSA in some children with PWS, so careful monitoring for sleep-related breathing disorders has been recommended for children receiving this treatment. (Berini, Spica Russotto et al. 2013; Deal, Tony et al. 2013)

A variety of craniofacial disorders are associated with increased risk for childhood OSA, including conditions associated with maxillary or mandibular hypoplasia (e.g. Crouzon syndrome, Pierre Robin Syndrome, hemifacial macrosomia), skeletal dysplasias associated with substantial craniofacial anomalies (e.g. Achondroplasia, Klippel-Feil syndrome), and conditions associated with cleft palate. (Cielo and Marcus 2015) The specific nature of the underlying craniofacial disorder often impacts treatment. For example, children with surgically repaired cleft palate are less likely to undergo adenoidectomy for treatment of OSA due to increased risk for hypernasality as a side effect.

Muscular dystrophies may be associated with increased risk for forms of sleep-disordered breathing which include sleep-related hypoventilation, defined as more than 25% of total sleep time spent with CO_2 levels exceeding 50 mm Hg. (Anonymous 2014) In one retrospective series of boys with X-linked Duchenne muscular dystrophy, 63% had OSA and17% had hypoventilation. (Sawnani, Thampratankul et al. 2015) Children with congenital myopathies and mitochondrial disorders experience similar risks for hypoventilation. Sleep-related hypoventilation associated with underlying neuromuscular disorders usually requires positive pressure ventilation therapy during sleep for optimal management.

Chiari malformations in children may be associated with central sleep apnea (CSA) or sleep-related hypoventilation, sometimes in combination with OSA. (Rabec, Laurent et al. 1998) When sleep-disordered breathing does not resolve following decompression procedures, optimal treatment depends on the type(s) of residual respiratory disturbance present. Central sleep apnea may respond to PAP therapy, low-flow oxygen by nasal cannula, or respiratory stimulants such as acetazolamide. Hypoventilation may worsen with oxygen therapy, but improve with positive pressure ventilation or respiratory stimulants. (Milerad, Lagercrantz et al. 1992)

Central congenital hypoventilation syndrome (CCHS) is characterized by profound alveolar hypoventilation which occurs primarily or exclusively during sleep. Although initial clinical descriptions of the condition date from 1970, associated mutations involving the Paired-Like Homeobox 2B (PHOX2B) gene were identified beginning in 2003. (Mellins, Balfour et al. 1970; Amiel, Laudier et al. 2003; Sasaki, Kanai et al. 2003) The condition is currently classified as a neurocristopathy which also affects the autonomic nervous system and is associated with increased risk for Hirschsprung disease and neural crest tumors. (Weese-Mayer, Rand et al. 2017) Early diagnosis of the condition is essential, as most affected patients require assisted ventilation during sleep, and some require 24-hour ventilatory support.

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