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Pediatric Obstructive Sleep Apnea in High-Risk Populations: Clinical Implications

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Abstract

Certain common medical conditions are associated with a higher risk of pediatric obstructive sleep apnea (OSA). A lower threshold for screening is therefore indicated for such patient cohorts. In this article, we briefly discuss the high prevalence of OSA in children born prematurely, and in those with Down syndrome, craniofacial disorders, and neuromuscular disorders. Primary care providers should have an increased index of suspicion for OSA in these children, considering the neurocognitive disability that occurs in these high-risk groups when OSA is left untreated.

Pediatric obstructive sleep apnea (OSA) syndrome is defined as disordered breathing during sleep characterized by recurrent upper airway obstruction, intermittent nocturnal hypoxia, increased arousability, and potential hypoventilation. Untreated OSA is associated with behavioral problems, neurocognitive disabilities, poor school performance, hypertension, and failure to thrive.^{1,2} OSA is a relatively common disorder with a prevalence of 1% to 5% in children.³ Primary care providers should have an increased index of suspicion for OSA when there is a history of snoring, gasping, and pauses in breathing that may result in sudden arousals during sleep. However, there are children at high risk for OSA who may not present with these symptoms, and who deserve special attention as well as a low threshold for a sleep study referral. In this article, we describe a few of those groups, namely children who were born prematurely, those with Down syndrome or craniofacial disorders, and those with neuromuscular disorders.

PREMATURITY AND OSA

The prevalence of OSA in children born prematurely has become an increasing concern over the last few years.^{4,5} In one study, 9.6% of children age 5 to 12 years who were born preterm

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were diagnosed with OSA.⁴ In another study, parents reported that 21% of children age 8 to 11 years who were born prematurely are habitual snorers compared to 14% of children born full-term.⁵ One area of increasing concern is the specific neuro-cognitive problems that preterm children with sleep-disordered breathing (SDB) had compared to those without SDB. In fact, children born preterm with SDB had worse performance in cognitive and academic assessments than those children with SDB who were born full-term.⁶ Several reasons for the increased prevalence of OSA in children born premature have been proposed. One explanation is related to potentially abnormal development of the respiratory control centers, lungs, and airways. For example, lower airway obstruction secondary to subglottic stenosis, laryngomalacia, or tracheomalacia occurs at a higher incidence in children born prematurely secondary to early interventions and abnormal development.⁷ Another proposed explanation is the relatively lower rate of breast-feeding in preterm infants, as studies have shown that children who were breast-fed up to 5 months had less SDB severity.⁸ Breast-feeding may reduce the severity of SDB by two possible mechanisms: (1) the immunological protection provided by breast milk and (2) breast-feeding promotes healthy jaw formation and prevents anatomic issues that result in SDB.⁸ Furthermore, multiple gestation deliveries and chorioamnionitis are associated with an increased risk of OSA. The mechanism behind the link between chorioamnionitis and OSA is unclear, but may be related to increased exposure to inflammation in-utero. Given the strong correlation between OSA and inflammatory markers, the in-utero exposure to inflammation may contribute to the development of OSA.⁴ Thus, the increased risk of OSA in children born prematurely and the subsequent neurocognitive problems that ensue makes the diagnosis of OSA one that should not be missed. Unfortunately, it may be overlooked in this high-risk population. Thus, pediatricians need to screen children born prematurely for SDB and have a low threshold for referring them for a sleep study. Once SDB is diagnosed in these children, treatment will vary on severity, age, and cause of obstruction. In milder forms of OSA, a trial of nasal steroids may be beneficial. In more severe cases, removal of enlarged tonsils and adenoids is recommended. If nasal obstruction is present (eg, deviated septum from nasal intubation), surgical correction may be indicated. Continuous positive airway pressure therapy (CPAP) may be a consideration when OSA is severe enough and no surgical option is appropriate.

DOWN SYNDROME AND OSA

Children with Down syndrome have an increased risk of OSA secondary to their craniofacial anatomy and generalized hypotonia. Classically, these children have midface hypoplasia, macro-glossia, glossoptosis, small airways, reduced upper airway tone, and obesity. All these factors increase their risk of inspiratory obstruction in the upper airway during sleep. The prevalence of OSA in children with Down syndrome is proposed to be between 30% and 80%.^{9–11} In a study by Marcus et al.¹⁰ in 1991, 53 children with Down syndrome underwent sleep studies. Of these 53, 100% had SDB, which included hypoventilation, OSA, and desaturations. OSA was present in 68% of children in which there was no clinical suspicion. In a more recent study¹² in the United Kingdom, 188 patients with Down syndrome underwent sleep studies. Of these, 14% had moderate to severe OSA and 59% had mild OSA.¹² When the impact of OSA on cognitive function and IQ was tested in a cohort of children with Down syndrome, those with OSA were found to have a decrease in

cognitive flexibility and lower verbal IQ.¹³ This makes the diagnosis and treatment of OSA in children with Down syndrome especially important due to their already lower cognitive reserve. Thus, if OSA is recognized and treated in the early years of cognitive development, this may result in enhanced cognition and quality of life. In addition, the OSA-induced neural insult and cognitive decline may increase their risk for Alzheimer's disease later in life.¹³ Finally, OSA and long-term intermittent hypoxemia may result in pulmonary hypertension and right-sided heart failure in this population. Because there is a poor correlation between parental reports and sleep study results, the American Academy of Pediatrics Committee on Genetics recommends that by age 4 years, all children with Down syndrome should have a sleep evaluation completed.¹⁴ Treatment of OSA in the Down syndrome population may depend on the age and severity of obstruction. If tonsils and adenoids are enlarged, removal may be beneficial. Weight loss may improve symptoms of OSA. Although CPAP may be challenging, some children and adolescents with Down syndrome do well with desensitization, family support, and an established routine.

CRANIOFACIAL DISORDERS AND OSA

Children with craniofacial disorders such as micrognathia and cleft lip/palate have an increased risk of OSA. Micrognathia increases the risk of OSA secondary to upper airway obstruction because the tongue is large relative to the mandibular structures and tends to prolapse backwards. The degree of midface and mandibular hypoplasia correlate with the degree of OSA. Children with cleft lip/palate can have an increased risk of OSA secondary to changes in the upper airway structure and possibly also secondary to nasal deformities. There is a significant improvement in OSA in these children after surgery.¹⁵ Children with isolated cleft palate may have significant OSA but the severity of OSA is much greater with palatal clefts in the context of Pierre Robin sequence.¹⁶ Pierre Robin sequence manifests as micrognathia, glossoptosis, airway obstruction, and often cleft palate. Airway obstruction in these children can be severe and the resultant OSA and intermittent hypoxia during the crucial time of cognitive development can result in a lower IQ.¹⁷ Treatment for this airway obstruction often necessitates a tracheostomy tube to bypass the obstructed upper airway until surgery to lengthen the mandible (mandibular distraction osteogenesis) can be performed. OSA improves significantly in infants with micrognathia after mandibular distraction osteogenesis.¹⁵ Thus, sleep studies should be performed in patients with craniofacial disorders to diagnose and treat OSA to optimize cognitive development.

OSA IN NEUROMUSCULAR DISORDERS

Respiratory muscle weakness in neuromuscular disorders first manifests as nocturnal hypoventilation. This eventually leads to disrupted sleep, early morning headaches, fatigue, and daytime sleepiness. Nocturnal hypoventilation often occurs prior to any daytime manifestations of respiratory decline. Duchenne Muscular dystrophy (DMD) is an X-linked disorder of the dystrophin gene that results in respiratory failure secondary to weakness of the diaphragm, intercostal muscles, and pharyngeal muscle weakness. As the respiratory muscles weaken, nocturnal hypoventilation occurs.¹⁸ It is important to diagnose this early to ensure adequate ventilation throughout the night and prevent the occurrence of daytime symptoms. All people with DMD will eventually develop SDB with nocturnal

hypoventilation.¹⁹ Snoring may not be noted, but other symptoms may exist including sleep disruption, nonrefreshing sleep, and daytime sleepiness. American Thoracic Society guidelines recommend a regular review of the sleep history.²⁰ When these patients become wheelchair dependent, one should consider performing a polysomnogram annually. Once clinically significant SDB with hypoventilation is identified, initiation of noninvasive positive pressure ventilation is indicated.²⁰ A tracheotomy with ventilation may be considered with advancing muscle weakness and associated hypoventilation that progresses beyond the nighttime.²⁰ Pompe disease is another neuromuscular disease that results in OSA and central sleep apnea.²¹ It occurs secondary to a deficiency of acid alpha glucosidase—an enzyme necessary to degrade lysosomal glycogen. The increased lysosomal glycogen accumulation in the respiratory muscles and motor neurons results in progressive respiratory muscle weakness and eventually respiratory failure.^{22,23} In addition, patients with Pompe disease have macroglossia, glossoptosis, and weak floppy upper airways, which result in a smaller upper airway and a predisposition to obstruct at night during inspiration. These patients also have central sleep apnea, presumably secondary to involvement of their respiratory rhythm generators.²⁴ Similarly, a high prevalence of OSA is found in other lysosomal storage disorders, namely the mucopolysaccharidoses.²⁵ Thus, a regular review of sleep history and a sleep evaluation should be considered in lysosomal storage and neuromuscular disorders, and a formal sleep evaluation should be completed if there is suspicion for upper airway obstruction or neuro-muscular weakness.

REFERENCES

1. Scullin MH, Ornelas C, Montgomery-Downs HE. Risk for sleep-disordered breathing and home and classroom behavior in Hispanic preschoolers. *Behav Sleep Med*. 2011;9(3):194–207. doi: 10.1080/15402002.2011.583907. [PubMed: 21722014]
2. Kang KT, Chiu SN, Weng WC, Lee PL, Hsu WC. Comparisons of office and 24-hour ambulatory blood pressure monitoring in children with obstructive sleep apnea. *J Pediatr*. 2017;182:177–183.e2. doi: 10.1016/j.jpeds.2016.11.032. [PubMed: 27939257]
3. Marcus CL, Brooks LJ, Draper KA, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics*. 2012;130(3):e714–755. doi: 10.1542/peds.2012-1672. [PubMed: 22926176]
4. Tapia IE, Shults J, Doyle LW, et al. Perinatal risk factors associated with the obstructive sleep apnea syndrome in school-aged children born preterm. *Sleep*. 2016;39(4):737–742. doi: 10.5665/sleep.5618. [PubMed: 26446117]
5. Rosen CL, Larkin EK, Kirchner HL, et al. Prevalence and risk factors for sleep-disordered breathing in 8- to 11-year-old children: association with race and prematurity. *J Pediatr*. 2003;142(4):383–389. [PubMed: 12712055]
6. Emancipator JL, Storfer-Isser A, Taylor HG, et al. Variation of cognition and achievement with sleep-disordered breathing in full-term and preterm children. *Arch Pediatr Adolesc Med*. 2006;160(2):203–210. doi: 10.1001/archpedi.160.2.203. [PubMed: 16461879]
7. Amin RS, Rutter MJ. Airway disease and management in bronchopulmonary dysplasia. *Clin Perinatol*. 2015;42(4):857–870. doi: 10.1016/j.clp.2015.08.011. [PubMed: 26593083]
8. Montgomery-Downs HE, Crabtree VM, Sans Capdevila O, Gozal D. Infant-feeding methods and childhood sleep-disordered breathing. *Pediatrics*. 2007;120(5):1030–1035. doi: 10.1542/peds.2007-0722. [PubMed: 17974740]
9. Shott SR, Amin R, Chini B, Heubi C, Hotze S, Akers R. Obstructive sleep apnea: should all children with Down syndrome be tested? *Arch Otolaryngol Head Neck Surg*. 2006;132(4):432–436. doi: 10.1001/archotol.132.4.432. [PubMed: 16618913]

10. Marcus CL, Keens TG, Bautista DB, von Pechmann WS, Ward SL. Obstructive sleep apnea in children with Down syndrome. *Pediatrics*. 1991;88(1):132–139. [PubMed: 1829151]
11. Levanon A, Tarasiuk A, Tal A. Sleep characteristics in children with Down syndrome. *J Pediatr*. 1999;134(6):755–760. [PubMed: 10356146]
12. Hill CM, Evans HJ, Elphick H, et al. Prevalence and predictors of obstructive sleep apnoea in young children with Down syndrome. *Sleep Med*. 2016;27–28:99–106. doi: 10.1016/j.sleep.2016.10.001.
13. Breslin J, Spano G, Bootzin R, Anand P, Nadel L, Edgin J. Obstructive sleep apnea syndrome and cognition in Down syndrome. *Dev Med Child Neurol*. 2014;56(7):657–664. doi: 10.1111/dmcn.12376. [PubMed: 24471822]
14. McCandless SE; Committee on Genetics. Clinical report-health supervision for children with Prader-Willi syndrome. *Pediatrics*. 2011;127(1):195–204. doi: 10.1542/peds.2010-2820. [PubMed: 21187304]
15. Cielo CM, Taylor JA, Vossough A, et al. Evolution of obstructive sleep apnea in infants with cleft palate and micrognathia. *J Clin Sleep Med*. 2016;12(7):979–987. doi: 10.5664/jcsm.5930. [PubMed: 27092700]
16. MacLean JE, Fitzsimons D, Fitzgerald DA, Waters KA. The spectrum of sleep-disordered breathing symptoms and respiratory events in infants with cleft lip and/or palate. *Arch Dis Child*. 2012;97(12):1058–1063. doi: 10.1136/archdischild-2012-302104. [PubMed: 23042804]
17. Kapp-Simon KA, Krueckeberg S. Mental development in infants with cleft lip and/or palate. *Cleft Palate Craniofac J*. 2000;37(1):65–70. doi: 10.1597/1545-1569(2000)037<0065:MDIWC>2.3.CO;2. [PubMed: 10670892]
18. Sawanani H, Thampratankul L, Szczesniak RD, Fenchel MC, Simakajornboon N. Sleep disordered breathing in young boys with Duchenne muscular dystrophy. *J Pediatr*. 2015;166(3):640–5.e1. doi: 10.1016/j.jpeds.2014.12.006. [PubMed: 25722267]
19. Hukins CA, Hillman DR. Daytime predictors of sleep hypoventilation in Duchenne muscular dystrophy. *Am J Respir Crit Care Med*. 2000;161(1):166–170. doi: 10.1164/ajrcrm.161.1.9901057. [PubMed: 10619815]
20. Finder JD, Birnkrant D, Carl J, et al. Respiratory care of the patient with Duchenne muscular dystrophy: ATS consensus statement. *Am J Respir Crit Care Med*. 2004;170(4):456–465. doi: 10.1164/rccm.200307-885ST. [PubMed: 15302625]
21. Mellies U, Ragette R, Schwake C, Baethmann M, Voit T, Teschler H. Sleep-disordered breathing and respiratory failure in acid maltase deficiency. *Neurology*. 2001;57(7):1290–1295. [PubMed: 11591850]
22. Fuller DD, ElMallah MK, Smith BK, Corti M, Lawson LA, Falk DJ, et al. The respiratory neuromuscular system in Pompe disease. *Respir Physiol Neurobiol*. 2013;189(2):241–249. doi: 10.1016/j.resp.2013.06.007. [PubMed: 23797185]
23. Turner SM, Hoyt AK, ElMallah MK, Falk DJ, Byrne BJ, Fuller DD. Neuropathology in respiratory-related motoneurons in young Pompe (Gaa^{-/-}) mice. *Respir Physiol Neurobiol*. 2016;227:48–55. doi: 10.1016/j.resp.2016.02.007. [PubMed: 26921786]
24. ElMallah MK, Pagliardini S, Turner SM, et al. Stimulation of respiratory motor output and ventilation in a murine model of Pompe disease by ampakines. *Am J Respir Cell Mol Biol*. 2015;53(3):326–335. doi: 10.1165/rcmb.2014-0374OC. [PubMed: 25569118]
25. Moreira GA, Kyosen SO, Patti CL, Martins AM, Tufik S. Prevalence of obstructive sleep apnea in patients with mucopolysaccharidosis types I, II, and VI in a reference center. *Sleep Breath*. 2014;18(4):791–797. doi: 10.1007/s11325-014-0944-6. [PubMed: 24705807]