Insights into Selected Aspects of Pediatric Sleep Medicine

Alex Gileles-Hillel[1], Mona F. Philby[1], and Gabrielle Lapping-Carr[2]

[1]Section of Pediatric Sleep Medicine and [2]Section of Pediatric Hematology-Oncology, Department of Pediatrics, Pritzker School of Medicine, Biological Sciences Division, The University of Chicago, Chicago, Illinois

Recommended Reading from the University of Chicago Fellows in Pediatric Sleep Medicine; David Gozal, M.D., Fellowship Faculty Mentor

Garetz SL, *et al.* Quality of Life and Obstructive Sleep Apnea Symptoms after Pediatric Adenotonsillectomy. *Pediatrics* (1)

Reviewed by Alex Gileles-Hillel

Health-related quality of life (QoL) assessments are a useful tool for evaluation of surgical and other interventions. QoL outcomes also dictate policy makers' decision-making and affect patient satisfaction. Obstructive sleep apnea (OSA) is a common condition in children and is associated with significantly reduced general health-related QoL (scores in the range of children with juvenile idiopathic arthritis) as well as reduced disease-specific QoL (2). Previous observational studies suggested that adenotonsillectomy (AT), the first-line treatment for pediatric OSA, results in improvements of QoL, but these studies have been hampered by not including a control group (i.e., a no-surgery group) and by lack of randomization (3).

To address this question more rigorously, Garetz and colleagues (1) analyzed data from the Childhood Adenotonsillectomy Trial (CHAT), a randomized, multicenter clinical trial. A total of 453 children, 5 to 9.9 years of age, with mild to moderate OSA were recruited from six centers and were randomly assigned to early AT (eAT) within 1 month of OSA diagnosis or to watchful waiting (WWSC). Generic health-related QoL was evaluated with the Pediatric Quality of Life (PedsQL) inventory comprising physical, emotional, social, and academic domains, and disease-specific QoL was assessed with the OSA-18 instrument, looking at five different domains: sleep disturbance, physical suffering, emotional distress, daytime problems, and caregiver concerns (1). In addition, OSA severity was ranked on a Sleep-Related Breathing Disorder (SRDB) scale of the Pediatric Sleep Questionnaire (PSQ).

At baseline, the eAT and WWSC groups were similar. At follow-up, the eAT group showed greater improvements in most QoL indices and in all OSA-18 domains when compared with the WWSC group. Improvements in PedsQL were most pronounced in the academic and physical performance domains ($P < 0.01$), with no differences across domains in the OSA-18 outcomes ($P \leqslant 0.01$). Similarly, PSQ-SRDB score improvements were all substantially higher in the eAT group ($P < 0.01$). Weight changes did not appear to affect the magnitude of changes in eAT ($P > 0.05$ for all). However, African-American children were more likely to report smaller improvements but only in the PSQ-SRDB scores. Notably, improvements in QoL were noted in the initial CHAT outcomes report, but this report did not elaborate further on such initial findings (4). Improvement in PSG indices was associated with QoL and symptomatic improvement but explained only a small portion of the variance across QoL scores.

The main limitation of the current study is the possibility of placebo effect in the surgical intervention, and such differences could potentially wane over time. It would also have been desirable to assess which of the components of QoL tools provide a better predictive assessment of the AT outcomes. Nonetheless, this randomized clinical trial provides robust support for considering QoL outcomes as an adjunct measure of AT efficacy in addition to the traditional PSG. This is particularly important among children with OSA with mild to moderate severity in whom equipoise on the most appropriate treatment modality may not always be apparent. ■

References

1. Garetz SL, Mitchell RB, Parker PD, Moore RH, Rosen CL, Giordani B, Muzumdar H, Paruthi S, Elden L, Willging P, *et al*. Quality of life and obstructive sleep apnea symptoms after pediatric adenotonsillectomy. *Pediatrics* 2015;135: e477–e486.
2. Crabtree VM, Varni JW, Gozal D. Health-related quality of life and depressive symptoms in children with suspected sleep-disordered breathing. *Sleep* 2004;27:1131–1138.
3. Baldassari CM, Mitchell RB, Schubert C, Rudnick EF. Pediatric obstructive sleep apnea and quality of life: a meta-analysis. *Otolaryngol Head Neck Surg* 2008;138:265–273.
4. Marcus CL, Moore RH, Rosen CL, Giordani B, Garetz SL, Taylor HG, Mitchell RB, Amin R, Katz ES, Arens R, *et al*.; Childhood Adenotonsillectomy Trial (CHAT). A randomized trial of adenotonsillectomy for childhood sleep apnea. *N Engl J Med* 2013; 368:2366–2376.

(Received in original form February 10, 2015; accepted in final form March 12, 2015)

Correspondence and requests for reprints should be addressed to David Gozal, M.D., Department of Pediatrics, University of Chicago, Chicago, IL 60637. E-mail: dgozal@uchicago.edu

Am J Respir Crit Care Med Vol 191, Iss 12, pp 1459–1461, Jun 15, 2015

DOI: 10.1164/rccm.201502-0279RR
Internet address: www.atsjournals.org

Rosen CL, *et al.* Obstructive Sleep Apnea and Sickle Cell Anemia. *Pediatrics* (5)

Reviewed by Gabrielle Lapping-Carr

End-organ damage in sickle cell disease (SCD) is mediated by a complex constellation of processes, such as endothelial damage, hemolysis, inflammation, and ischemia-reperfusion injury. Obstructive sleep apnea syndrome (OSAS) is of particular concern in SCD owing to the additive or potentially synergistic impact of increased nighttime hypoxia as well as OSAS's intrinsic associations with similar end-organ targets as those affecting SCD (6). Before the article by Rosen and colleagues (5), wide ranges were reported in the prevalence of OSAS among patients with SCD, ranging from 10 to 79%, and it was unclear whether standard OSAS risk factors are also applicable in patients with SCD (7, 8).

To address these issues, Rosen and colleagues reported the baseline results of the Sleep and Asthma Cohort (SAC) study (5). This study consisted of a large, prospective, multiinstitutional analysis of patients with SCD who were enrolled irrespective of potential risk of OSAS. They enrolled a total of 283 patients who were either homozygous for the sickle cell variant or compound heterozygotes with β^0-thalassemia, and 260 completed a successful polysomnography. Using obstructive apnea–hypopnea index (OAHI) scores of $\geqslant$1 and $\geqslant$5 per hour of total sleep time (TST), the prevalence rates of OSAS were 41 and 10%, respectively, as compared with 1 to 4% in children in the general population. Interestingly, although lower waking Sp_{O_2} was associated with greater OAHI values, higher body mass index and elevated blood pressure were not. It would be important to examine in future studies whether the lower waking Sp_{O_2} prompted the occurrence of higher OAHI because of increased 3% Sp_{O_2} drops in the context of being in the steeper portion of the hemoglobin dissociation curve. Other typical risk factors for OSAS, such as allergic conditions and tobacco exposure, were also not associated with increasing OAHI. Two models were further evaluated by multivariate analyses using OAHI $\geqslant$ 1 per hour of TST or OAHI $\geqslant$ 5 per hour of TST and compared with no-OSAS. The higher OAHI cutoff proved a better screening test with a positive predictive value of 0.32 and a negative predictive value of 0.99. This model ultimately included only two variables that were identified as being significantly and independently associated with OSAS status: habitual snoring (odds ratio, 16.93; 95% confidence interval, 4.98–57.5; $P < 0.001$) and waking $Sp_{O_2} \leqslant 96\%$ (odds ratio, 5.51; 95% confidence interval, 1.63–18.61; $P = 0.006$).

In summary, Rosen and colleagues provide useful insights indicating that OSAS in SCD needs to be viewed as a singular entity with different risk factor constructs from those traditionally encountered among OSAS in patients without SCD. In addition, this study represents the largest report of OSAS in SCD and provides strong evidence on the presence of an increased prevalence of OSAS in SCD. The next critical steps should include prospective multicenter testing of the proposed model, delineation of outcomes using treatment randomization, and improved understanding of the temporal trajectories of OSAS in patients with SCD. ■

References

5. Rosen CL, Debaun MR, Strunk RC, Redline S, Seicean S, Craven DI, Gavlak JCD, Wilkey O, Inusa B, Roberts I, *et al*. Obstructive sleep apnea and sickle cell anemia. *Pediatrics* 2014;134:273–281.
6. Gileles-Hillel A, Kheirandish-Gozal L, Gozal D. Hemoglobinopathies and sleep: the road less traveled. *Sleep Med Rev* 2015;24C:57–70.
7. Kaleyias J, Mostofi N, Grant M, Coleman C, Luck L, Dampier C, Kothare SV. Severity of obstructive sleep apnea in children with sickle cell disease. *J Pediatr Hematol Oncol* 2008;30:659–665.
8. Salles C, Ramos RTT, Daltro C, Nascimento VM, Matos MA. Association between adenotonsillar hypertrophy, tonsillitis and painful crises in sickle cell disease. *J Pediatr (Rio J)* 2009;85:249–253.

Bhattacharjee R, *et al.* Association of Adenotonsillectomy with Asthma Outcomes in Children: A Longitudinal Database Analysis. *PLoS Med* (9)

Reviewed by Mona F. Philby

Asthma and obstructive sleep apnea (OSA) are common childhood conditions, are characterized by the presence of chronic inflammatory processes in the airways, and lead to significant end-organ morbidities and to elevated annual healthcare costs.

The prevalence of childhood asthma has been steadily rising worldwide and is currently recognized as the third most frequent cause of hospitalization, exceeded only by pneumonia and injuries in children (10). According to the National Health Interview Survey 2011, an estimated 39.5 million people (12.9%), including 10.5 million (14.0%) children in the United States alone, have been diagnosed with asthma during the course of their lifetime. Of these, 18.9 million (8.2%) adults and 7.1 million (9.5%) children still suffer from this disease.

OSA is characterized by recurrently increased upper airway resistance or obstruction during sleep leading to intermittent hypoxemia and hypercapnia and to sleep fragmentation. OSA affects 1 to 4% of the pediatric population, and adenotonsillectomy (AT) constitutes the first line of treatment. OSA and asthma are increasingly being recognized as potentially overlapping conditions, whereby the presence of one may adversely affect the other. In adults, an increased prevalence of OSA was reported in patients with poorly controlled asthma (11, 12) and vice versa (13). Furthermore, a small, prospective, uncontrolled study showed that treatment of OSA in children with poorly controlled asthma markedly ameliorated their symptoms (14), and the aforementioned CHAT study would also indicate similar outcomes (4). Indeed, Marcus and colleagues (4) reported that 18 asthmatic events took place among 203 children in the delayed treatment group compared with 3 asthmatic events among 194 children in the early AT group ($P < 0.002$).

Bhattacharjee and colleagues (9) gathered pertinent information using the MarketScan database between 2003 and 2010, identified 13,506 children with asthma who underwent AT, and examined their asthma control for the period covering 1 year before and 1 year after the AT surgery while using 27,012 age-, sex-, and ethnicity-matched children with asthma who did not undergo AT. Significant reductions in the occurrence of acute asthma exacerbations or acute status asthmaticus, the primary outcome of the study, emerged ($P < 0.0001$). Additionally, AT

resulted in significant reduction in asthma prescription refills, including bronchodilators, leukotriene receptor antagonists, and corticosteroids (inhaled or systemic), all of which are indicative of meaningful improvements in asthma control. Such changes in children with pre- and post-AT asthma were not detectable in the children with asthma who did not undergo AT.

The retrospective, observational nature of this study precludes definitive conclusions but does lend support to the concept that adenotonsillar hypertrophy likely associated with OSA may act as a modulator of asthma severity. A randomized controlled trial aimed at studying the effects of body mass index, tonsillar size, and underlying indications for AT should likely provide more factual insights into the causal relationships between OSA treatment with AT and improved asthma control in children. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

References

9. Bhattacharjee R, Choi BH, Gozal D, Mokhlesi B. Association of adenotonsillectomy with asthma outcomes in children: a longitudinal database analysis. *PLoS Med* 2014;11:e1001753.
10. Ding G, Ji R, Bao Y. Risk and protective factors for the development of childhood asthma. *Paediatr Respir Rev* 2015;16:133–139.
11. Yigla M, Tov N, Solomonov A, Rubin AH, Harlev D. Difficult-to-control asthma and obstructive sleep apnea. *J Asthma* 2003;40:865–871.
12. Teodorescu M, Consens FB, Bria WF, Coffey MJ, McMorris MS, Weatherwax KJ, Palmisano J, Senger CM, Ye Y, Kalbfleisch JD, *et al*. Predictors of habitual snoring and obstructive sleep apnea risk in patients with asthma. *Chest* 2009;135:1125–1132.
13. Teodorescu M, Barnet JH, Hagen EW, Palta M, Young TB, Peppard PE. Association between asthma and risk of developing obstructive sleep apnea. *JAMA* 2015;313:156–164.
14. Kheirandish-Gozal L, Dayyat EA, Eid NS, Morton RL, Gozal D. Obstructive sleep apnea in poorly controlled asthmatic children: effect of adenotonsillectomy. *Pediatr Pulmonol* 2011;46:913–918.