CHEST

Antiinflammatory Therapy Outcomes for Mild OSA in Children

Leila Kheirandish-Gozal, MD; Rakesh Bhattacharjee, MD; Hari P. R. Bandla, MD, FCCP; and David Gozal, MD, FCCP

BACKGROUND: OSA is highly prevalent in children and usually initially treated by adenotonsillectomy. Nonsurgical alternatives for mild OSA primarily consisting of antiinflammatory approaches have emerged, but their efficacy has not been extensively assessed.

METHODS: A retrospective review of clinically and polysomnographically diagnosed patients with OSA treated between 2007 and 2012 was performed to identify otherwise healthy children ages 2 to 14 years who fulfilled the criteria for mild OSA and who were treated with a combination of intranasal corticosteroid and oral montelukast (OM) for 12 weeks (ICS + OM). A subset of children continued OM treatment for 6 to 12 months.

RESULTS: A total of 3,071 children were diagnosed with OSA, of whom 836 fulfilled mild OSA criteria and 752 received ICS + OM. Overall, beneficial effects occurred in > 80% of the children, with nonadherence being documented in 61 children and adenotonsillectomy being ultimately performed in 12.3%. Follow-up polysomnography in a subset of 445 patients showed normalization of sleep findings in 62%, while 17.1% showed either no improvement or worsening of their OSA. Among the latter, older children (aged > 7 years; OR, 2.3; 95% CI, 1.43-4.13; $P < .001$) and obese children (BMI z-score > 1.65; OR: 6.3; 95% CI, 4.23-11.18; $P < .000001$) were significantly more likely to be nonresponders.

CONCLUSIONS: A combination of ICS + OM as initial treatment of mild OSA appears to provide an effective alternative to adenotonsillectomy, particularly in younger and nonobese children. These results support implementation of multicenter randomized trials to more definitively establish the role of ICS + OM treatment in pediatric OSA.

CHEST 2014; 146(1):88-95

Manuscript received September 25, 2013; revision accepted January 13, 2014; originally published Online First February 6, 2014.

ABBREVIATIONS: AHI = apnea-hypopnea index; ICS = intranasal corticosteroid; NPSG = nocturnal polysomnography; OM = oral montelukast; RCT = randomized controlled trial; Spo_2 = arterial oxygen saturation; T&A = adenotonsillectomy; TST = total sleep time

AFFILIATIONS: From the Section of Pediatric Sleep Medicine, Department of Pediatrics, Biological Sciences Division, Pritzker School of Medicine, The University of Chicago, Chicago, IL.

FUNDING/SUPPORT: Drs Kheirandish-Gozal and Gozal are supported by the US National Institutes of Health [Grants HL-65270, HL-086662, and HL-107160].

CORRESPONDENCE TO: David Gozal, MD, FCCP, Department of Pediatrics, Comer Children's Hospital, The University of Chicago 5721 S Maryland Ave, Chicago, IL 60637; e-mail: dgozal@peds.bsd.uchicago.edu

DOI: 10.1378/chest.13-2288

Since the initial description of OSA, this condition has emerged as being highly prevalent in children and as imposing potentially reversible neurocognitive, behavioral, cardiovascular, and metabolic morbidities.[1] Adenotonsillar hypertrophy has been recognized as the major pathophysiologic contributor to OSA in children and has been customarily managed by surgical removal of enlarged adenoids and tonsils with overall favorable results reported for moderate to severe OSA.[1-3] More recently, however, surgical adenotonsillectomy (T&A) for mild OSA has come under scrutiny,[1-3] particularly regarding the possibility that a significant proportion of the polysomnographic abnormalities associated with milder forms of OSA may not normalize after surgery, thereby prompting the need for development of nonsurgical therapeutic alternatives.[4] Based on such initial reports, preliminary evidence on the potential beneficial effects of oral montelukast (OM) and intranasal corticosteroids (ICSs) on improving breathing patterns during sleep in pediatric cases of mild OSA has emerged.[5-15] Furthermore, the biologic plausibility of the potential efficacy of these approaches has been substantiated,[16,17] raising the possibility that randomized controlled trials (RCTs) using antiinflammatory approaches would be justified for pediatric OSA. However, the effects of combined topical steroid and montelukast in mild OSA have not yet been explored.

Here we report on the retrospective assessment of our clinical experience in a large cohort of patients diagnosed with mild OSA with polysomnography who were treated with a combination of ICS + OM for $\geq$ 12 weeks, followed by either no further treatment or by continued OM therapy for an additional 6 to 12 months.

Materials and Methods

Patients

This retrospective review study of our clinical experience was approved by the institutional human study review committees of the University of Louisville (protocol number 474.99) and the University of Chicago (protocol numbers 09-008-A and 10-615-A). The population for the study was identified by screening charts from the Sleep Center medical records at Kosair Children's Hospital in Louisville, Kentucky, for the time period from January 2007 until December 2008; St. Mary Women and Children's Hospital, Evansville, Indiana, from January 2007 until December 2012; and Comer Children's Hospital at the University of Chicago, Chicago, Illinois, from January 2011 until December 2012. The charts of children aged 2 to 14 years who were referred by their primary care pediatricians or pediatric otolaryngologists and underwent overnight sleep studies for suspected OSA were identified. Exclusion criteria were as follows: past T&A, genetic disorders, neuromuscular diseases, craniofacial abnormalities, or current treatment with medications such as corticosteroids (either oral, inhaled, or intranasal) or OM.

The period covered by this retrospective review corresponded to the implementation of a standard clinical management protocol whereby children with OSA and obstructive apnea-hypopnea index (AHI) $>$ 5.0/h of total sleep time (TST) were referred for surgical T&A or occasionally for CPAP therapy, while those with obstructive AHI $>$ 1.0/h TST but $<$ 5.0/h TST were initially recommended treatment with ICS + OM, following which a second overnight sleep study was performed to assess clinical response to therapy. Children with an obstructive AHI $<$ 1.0/h TST were considered to have primary snoring and did not receive treatment.

For children receiving ICS + OM, nonadherence was considered to be present if they received $<$ 3 weeks of any of the two medications as indicated by the parents or based on the absence of prescription refills. Otherwise, if the second nocturnal polysomnography (NPSG) documented improvement, OM was usually continued for up to 12 months. If no changes or worsening of the NPSG results occurred, then T&A was recommended. A third NPSG was conducted after 6 to 12 months of OM, and based on the findings (ie, worsening OSA, persistent mild OSA, or normal NPSG results), T&A, OM, or no treatment were recommended, respectively (Fig 1).

In addition to demographic information including age, sex, and ethnicity, height and weight were extracted from all the charts. Tonsil size derived from a score of 0 (no tonsils present) to 4 (kissing tonsils),[18] Mallampati score (Likert scale range, 1-4),[19] and adenoid size as estimated from lateral neck radiographs based on the degree of choanal obstruction on a Likert scale range, 1 to 4 (4: 75% to 100%; 3: 50% to 75%; 2: 25% to 50%; and 1: 0% to 25%) were tabulated when available, as previously described.[20,21]

BMI z-Score Calculation

Height and weight were recorded when each child arrived for NPSG. BMI *z*-score was calculated using an online BMI *z*-score calculator provided by the US Centers for Disease Control and Prevention.[22] Children with BMI *z*-score values $>$ 1.67 were considered obese.[23]

Overnight Sleep Study

An NPSG was performed in the laboratory in the presence of a trained polysomnographic technologist at each sleep center using the computerized clinical-data-acquisition system in use at that site. Briefly, the bilateral electrooculogram, eight channels of EEG, chin and anterior tibial electromyograms, tracheal sounds, and analog output from a body position sensor were monitored, along with chest and abdominal wall movement, ECG, and airflow using nasal pressure catheter, end-tidal capnography, and an oronasal thermistor. Arterial oxygen saturation (Spo_2) was assessed by pulse oximetry with simultaneous recording of the pulse waveform. In addition, a digital time-synchronized video recording was performed.

After removal of movement and technical artifacts, the studies were scored according to standard criteria as defined by the American Academy of Sleep Medicine in 2007, with all scoring technologists being supervised by one of the authors to ensure consistency across centers.[24] The proportion of time spent in each sleep stage was expressed as percentage of TST (%TST). Central, obstructive, and mixed apneic events were counted, and hypopneas were assessed. Obstructive apnea was defined as the absence of airflow with continued chest wall and abdominal movement for duration of at least two breaths. Hypopneas were defined