CHEST Online Supplement

Prognosis for Spontaneous Resolution of OSA in Children

Ronald D. Chervin, MD; Susan S. Ellenberg, PhD; Xiaoling Hou, MS; Carole L. Marcus, MBBCh; Susan L. Garetz, MD; Eliot S. Katz, MD; Elise K. Hodges, PhD; Ron B. Mitchell, MD; Dwight T. Jones, MD; Raanan Arens, MD; Raouf Amin, MD; Susan Redline, MD; and Carol L. Rosen, MD, FCCP; for the Childhood Adenotonsillectomy Trial

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e-Appendix 1.

METHODS – ADDITIONAL DETAIL

Participants

The CHAT design has been published previously.[1,2] Institutional review board approvals were obtained at each site (Table 1), as was informed consent from caregivers, and assent from children aged ≥7 years. Children aged 5-9 years who generated data for the current analyses were recruited from pediatric sleep clinics and otolaryngology practices at 6 U.S. medical centers. Inclusion criteria included an obstructive apnea/hypopnea index (AHI) ≥2 events per hour of sleep, or an obstructive apnea index (OAI) ≥1, and candidacy for adenotonsillectomy for clinical purposes according to the subject's otolaryngologist. Exclusion criteria included AHI>30, OAI>20, oxygen saturation <90% for ≥2% of total sleep time, recurrent tonsillitis, a body mass index (BMI) z-score ≥3, or medication for Attention-Deficit/Hyperactivity Disorder (ADHD). Among 453 children randomized in CHAT, n=194 had complete follow-up, remained untreated surgically, and provided data for the current analyses.

Outcomes

Objective resolution of OSAS was defined as an AHI <2 and an OAI <1 on polysomnography at 7-month follow-up. Polysomnography followed standard guidelines, as did centralized scoring using pediatric criteria.[1-3] The AHI included obstructive apneas and all hypopneas, but not respiratory effort-related arousals. Resolution of OSAS symptoms was defined by scores on the caregiver-completed Pediatric Sleep Questionnaire Sleep-Related Breathing Disorder (PSQ-SRBD) scale. This well-validated[4,5] symptom inventory includes 22 items with "yes", "no", and "don't know" response formats: the total score (ranging from 0 to 1) is the number of positive responses divided by the number of items answered "yes" or "no". Items focus on snoring; other symptoms of obstructed breathing; observed apneas; ancillary symptoms such as mouth breathing; sleepiness; and behavioral symptoms. Component scores include a

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4-item sleepiness scale previously validated against the Multiple Sleep Latency Test,[6] a 4-item snoring scale, and a 6-item behavior scale, each scored analogously to the total PSQ-SRBD scale. Substantive resolution of OSAS symptoms was defined by a total PSQ-SRBD score ≥ 0.33 at baseline,[4] < 0.33 at 7-month follow-up, and at least 25% below baseline at follow-up.

Explanatory Variables

Variables tested for ability to predict spontaneous resolution of OSAS included demographic, history, physical examination, and polysomnographic findings. History data included several symptoms from the PSQ-SRBD scale; subscales described above; and the total score. Additional variables included caregiver report of allergies, nasal allergies more specifically, frequent colds or upper respiratory infections, asthma, frequent ear infections, Attention-Deficit Disorder or Attention-Deficit/Hyperactivity Disorder, use of nasal steroids, use of montelukast, or existence of a current smoker in the household. Global quality of life was assessed by the Pediatric Quality of Life Inventory (PedsQL) caregiver version as well as the child version; scores range from 0 to 100, with higher scores indicating better quality of life.[7,8] Behavior was assessed by the Conners' Rating Scale Revised: Long Version ADHD and hyperactivity T scores, which range from 0 to 100 (normative mean=50, SD=10).[9]

Physical examinations generated BMI z-scores,[2] waist circumference,[10] waist circumference percentiles,[11] and classification of tonsils into 4 size grades, subsequently dichotomized as less vs. more than 50% of the oropharyngeal cross-sectional area. The tongue and palatal position were classified as Friedman class I or II vs. class III or IV,[12] and also as Mallampati class I or II vs. III or IV.[13] Neck circumference (average of 3 measures) was assessed to the nearest 0.1 cm just below the thyroid prominence. Morning, resting systolic, and diastolic blood pressures were measured three times in the seated position, and blood was taken for assessment of C-reactive protein (CRP). Polysomnographic OSAS severity was assessed by the AHI, OAI, percent of sleep time with oxygen saturation below 92%, and minimum oxygen saturation.

Analyses

Univariate associations were tested using logistic regression models. Variables predictive ($p<0.05$) of either objective or symptom-based resolution of OSAS as the outcome were considered in two different forward stepwise logistic multiple regression models, with 2-fold cross validation, to assess for independent predictive value. The entry criterion was $p<0.20$ and explanatory variables were retained as long as they showed $p<0.10$. The only exception to this procedure occurred in the analysis that used objective resolution of OSAS as the outcome. As AHI and OAI were not independent of each other (a child

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with OAI <1 had to have an AHI > 2 to participate, and a child with an AHI < 2 had to have an OAI > 1), and AHI was the stronger predictor in univariate analysis, OAI was not entered in the multiple regression models. All calculations were performed using SAS version 9.2 (SAS Inc, Cary, IN). No adjustment was made for multiple comparisons.

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e-Table 1. Childhood Adenotonsillectomy (CHAT) institutional review board (IRB) committee names and protocol numbers.

Site Name	IRB Committee Names	IRB Protocol Numbers
University of Pennsylvania	University of Pennsylvania Institutional Review Board FWA 00004028	804695
Brigham & Women's Hospital	Partners Human Research Committee FWA # 00000484	2010-P-001079/1
University of Michigan Health System	Institutional Review Board (IRBMED) FWA # 00004969	HUM00006525
Children's Hospital of Philadelphia	The Committees for Protection of Human Subjects Institutional Review Boards FWA # 00000459	2006-7-4853
Cincinnati Children's Hospital Medical Center	Cincinnati Children's Hospital Medical Center Institutional Review Board FWA # 00002988	Study ID: 2008-0984
University Hospitals Case Medical Center	Institutional Review Board for Human Investigation FWA # 00003937	IRB 09-06-19
MetroHealth Medical Center	Metrohealth Institutional Review Board FWA # 00003938	IRB 07-01106
Saint Louis University	St. Louis University Institutional Review Board FWA # 00005304	15847
Montefiore Medical Center at Albert Einstein College of Medicine of Yeshiva University	Montefiore Medical Center Institutional Review Board FWA # 00002558	08-12-417
Children's Hospital Boston	Committee on Clinical Investigation at Children's Hospital Boston FWA # 00002071	09-01-0016

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