Increased Upper Airway Collapsibility in Children with Obstructive Sleep Apnea during Wakefulness

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Upper airway collapsibility (UAC) is increased in children with sleep-disordered breathing (SDB), but during wakefulness, active neural processes preserve upper airway patency, such that measurement of upper airway dynamics using acoustic pharyngometry may contribute to diagnostic accuracy in snoring children. Upper airway cross-sectional area obtained from acoustic pharyngometry measurements was assessed in 247 children referred for evaluation of suspected SDB and control subjects, before and after application of cetacaine 1% spray to the pharyngeal introitus under visual inspection. UAC was determined from the precentage change in cross-sectional area after topical anesthesia. UAC measurements were reproducible 1 week apart in both control subjects and patients with SDB ($p < 0.005$). A UAC less than or equal to -30% exhibited high sensitivity and specificity in identification of all children with obstructive apnea–hypopnea index greater than 5/hour total sleep time in a prospective initial sample of 54 children and in a subsequent *post hoc* sample of 94 snoring children. Thus, upper airway dynamic testing during wakefulness in response to a topical airway anesthetic may provide a useful clinical adjunct to the evaluation of snoring children, with more accurate identification of those children with SDB.

Keywords: sleep-disordered breathing; snoring; acoustic pharyngometry; topical anesthesia

Snoring, the cardinal symptom raising the suspicion of sleep-disordered breathing (SDB) in children, is highly prevalent in the general population, affecting approximately 11% of children aged 2–8 years (1–7). However, the ability of the physician to predict the presence of SDB by a careful history and physical examination is limited (8). Therefore, overnight polysomnography remains the definitive approach to diagnosis of SDB in snoring children but imposes a substantial burden to the child and family (9).

It is now firmly established that upper airway collapsibility (UAC) is markedly increased in either sleeping or anesthetized children with SDB (10, 11). Furthermore, upper airway measurements using acoustic pharyngometry in a large cohort of 203 children revealed significantly smaller cross-sectional areas (CSAs) of the upper airway at its narrowest point among children with snoring and SDB (12). However, these studies also revealed substantial overlap among the various degrees of SDB severity, thereby excluding this simple measurement as potentially valuable in the accurate diagnosis of SDB (12).

Acoustic pharyngometry is a noninvasive method that permits evaluation of the upper airway CSA as a function of the distance from the mouth during both wakefulness and sleep, is accurate and reproducible in both adults and children, and permits identification of the collapsible segment during obstructive events in adults with SDB (12–17). Furthermore, on application of topical anesthesia to the upper airway and thus removal of local reflexes that promote airway patency during wakefulness, adult patients with SDB will demonstrate substantial reductions in upper airway CSA and may even develop upper airway obstruction (18–25). We hypothesized that application of topical anesthesia to the upper airway and assessment of changes in CSA relative to baseline would permit identification of children with SDB because in the latter the magnitude of CSA reductions would be greater than in children with either primary snoring or in control subjects.

METHODS

Children aged 4 to 16 years, who were otherwise healthy, and who were referred to the Kosair Children's Hospital Sleep Medicine Center for evaluation of snoring were invited to participate in the study. In addition, healthy nonsnoring children were recruited from the community. None of the participants suffered from any known craniofacial disorder, was obese, or had undergone previous upper airway surgical procedures. The study was approved by the University of Louisville Human Research Committee, and parental informed consent and child assent, in the presence of a parent, were obtained.

Polysomnographic Assessment

A standard overnight multichannel polysomnographic evaluation was performed at the Sleep Medicine Center of Kosair Children's Hospital. Children were studied for up to 12 hours in a quiet, darkened room with an ambient temperature of 24°C in the company of one of their parents. All children were in bed with lights out between 9:00 and 9:30 P.M. and were awakened at 7:00 A.M. unless they awoke sooner. No drugs were used to induce sleep. The following parameters were measured: chest and abdominal wall movement by respiratory impedance or inductance plethysmography, heart rate by ECG, and air flow with a sidestream end-tidal capnograph, which also provided breath-by-breath assessment of end-tidal carbon dioxide levels ($P_{ET_{CO_2}}$; BCI SC-300; BCI, Menomonee Falls, WI) and a oronasal thermistor. Arterial oxygen saturation was assessed by pulse oximetry (Nellcor N 100; Nellcor Inc., Hayward, CA), with simultaneous recording of the pulse waveform. The bilateral electro-oculogram, eight channels of EEG, chin and anterior tibial EMG, and analog output from a body position sensor (Braebon Medical Corporation, Ogdensburg, NY) were also monitored. All measures were digitized using a commercially available polysomnography system (Stellate Systems, Montreal, PQ, Canada or Medcare, Buffalo, NY). Tracheal sound was monitored with a microphone sensor (Sleepmate, Midlothian, VA), and a digital time-synchronized video recording was performed.

Sleep Variables

Sleep architecture was assessed by standard techniques (26). The apnea index was defined as the number of apneas per hour of total sleep time (TST). Central, obstructive, and mixed apneic events were counted. Obstructive apnea was defined as the absence of airflow with continued chest wall and abdominal movement for a duration of at least two breaths (27). Hypopneas were defined as a decrease in nasal flow greater

than or equal to 50% with a corresponding decrease in arterial oxygen saturation greater than or equal to 4% and/or arousal (28). The apnea–hypopnea index (AHI) was defined as the number of apneas and hypopneas per hour of TST. The obstructive apnea index was defined as the number of obstructive apneas per hour of TST. The mean oxygen saturation, as measured by pulse oximetry (arterial oxygen saturation), together with arterial oxygen saturation nadir, was determined. The mean and peak $P_{ET_{CO_2}}$ was determined. Because criteria for arousal have not yet been developed for children (29), arousals were defined as recommended by the American Sleep Disorders Association Task Force report (30) and included respiratory-related (occurring immediately after an apnea, hypopnea, or snoring), technician-induced, and spontaneous arousals. Arousals were expressed as the total number of arousals per hour of sleep time (arousal index). Periodic leg movements during sleep were scored if there were at least four movements of 0.5 to 5 seconds duration, and between 5 and 90 seconds apart. A periodic leg movement index greater than or equal to five per hour of sleep is generally considered as exceeding the normal range in children (31).

Pharyngometry Measurements

Pharyngometry data were collected either during the clinic visit or in the morning after the sleep study using the EccoVision Acoustic Pharyngometer (E. Benson Hood Laboratories, Pembroke, MA). This system has been used to measure pharyngeal CSA in adults (32–35) and more recently in children (12). Each measurement consists of a plot of CSA (expressed in square centimeters) as a function of the distance (in centimeters) from the mouth. Estimates of mean and minimal pharyngeal CSA are derived by the software. For each subject, two sets of data were obtained; namely, one after spraying of the pharyngeal cavity with saline under visual inspection and the other after topical anesthesia of the upper airway with cetacaine 1% (3 sprays/child). The oropharynx was anesthetized, with the goal of achieving loss of the gag reflex, as well as effective laryngeal anesthesia, as manifested by the subjective sensation of difficulty swallowing. All studies performed under anesthesia were completed within 30 minutes because of the short duration of action of cetacaine. However, children were instructed not to drink or eat for at least 4 hours after cetacaine administration. A baseline curve was obtained using nasal breathing. Subsequent measurements were obtained using oral breathing (nose clips were applied) at functional residual capacity. At least four curves were obtained and were considered valid if the CSA differed by 10% or less from one another. A well defined oral cavity segment between 0 and 5 cm, a distinct oropharyngeal segment, and no evidence of tongue occlusion or leak were also ascertained from the figures. For all children, a standard pediatric mouthpiece was used. Pre- and postcetacaine curves were compared in 0.2-cm increments along the anteroposterior axis, and the segment at which the pre–post change (expressed in %) was maximal was retained for analysis and defined as the UAC for that subject.

Experimental Approach

In an initial stage, to ascertain reproducibility of the measurements and to verify the leading hypothesis that children with SDB have more collapsible upper airways during wakefulness using the UAC-derived pharyngometry procedure, both normal children and children with ob-

structive sleep apnea were studied. More specifically, 27 control children and 27 children with obstructive sleep apnea were compared. In addition, 15 control children and 15 children with obstructive sleep apnea were assessed twice, 1 week apart. Then, two large cohorts of snoring children were studied, namely 54 snoring children with varying degrees of SDB (Group 1), from which initial analyses allowed to define a UAC critical threshold value, and a second group of 94 snoring children (Group 2), in which the UAC cutoff value was tested. Finally, a group of 15 children with SDB who underwent surgical removal of adenotonsillar tissue (tonsillectomy and adenoidectomy [T&A]) were studied before and 10–12 weeks after surgery to assess changes in UAC and SDB severity. Thus, a total of 247 children participated in the study. It should be noted that in 14 more children (usually albeit not exclusively among the 5- or 6-year-old), reliable measurements were not possible due to problems with the mouthpiece or with intraindividual reproducibility of the CSA curves.

Statistical Analysis

Overnight polysomnographic studies were scored by one of the investigators (M.M.B.), who was unaware of the results of the pharyngometry measurements, the latter being analyzed by the other investigator (D.G.). The obstructive AHI, and percentage of TST with Sa_{O_2} higher than 90% were tabulated for each subject. SDB was defined as the presence of AHI greater than or equal to 5/hours of TST. Linear regression analysis and the Spearman coefficient of correlation, two-tailed student t tests, and receiver–operator curves were calculated from the UAC and the polysomnographic data. Data are presented as means $\pm$ SE, unless stated otherwise. A p value of less than 0.05 was considered as statistically significant.

RESULTS

The UAC was initially examined in 27 control children and 27 children with known SDB. The groups were matched for age (6.7 $\pm$ 0.2 years), sex (14:13, male:female), and ethnicity (10 African American and 17 white). Mean AHI for the control group was 0.6 $\pm$ 0.1/hour TST, whereas AHI was 16.3 $\pm$ 0.1/hour TST in SDB children (p < 0.0001). Mean CSA was 1.88 $\pm$ 0.27 cm² in control children and 1.67 $\pm$ 0.28 cm² in patients with SDB (p < 0.01). Similarly, the minimal CSA was 1.03 $\pm$ 0.17 cm² in control children and 0.95 $\pm$ 0.18 cm² in patients with SDB, respectively, (p < 0.04). Mean UAC in control children was −5.3 $\pm$ 1.9% compared with −40.7 $\pm$ 1.6% in SDB (p < 0.0001). Thus, upper airway is smaller, and UAC is markedly and significantly greater in children with SDB.

The reproducibility of the UAC measurements was further determined within 1 week in 15 control children (mean AHI: 0.4 $\pm$ 0.1; Figure 1) and in 15 children with SDB (mean AHI: 19.4 $\pm$ 3.3; Figure 1). There was a close agreement between the two tests for both CSA and UAC in either patients with SDB (coefficient of variation for CSA: 8.7 $\pm$ 1.8%; UAC: 13.4 $\pm$ 3.2%) or control children (coefficient of variation for CSA: 9.1 $\pm$ 1.7%; UAC: 14.2 $\pm$ 3.3%). Thus, CSA and UAC measurements yield
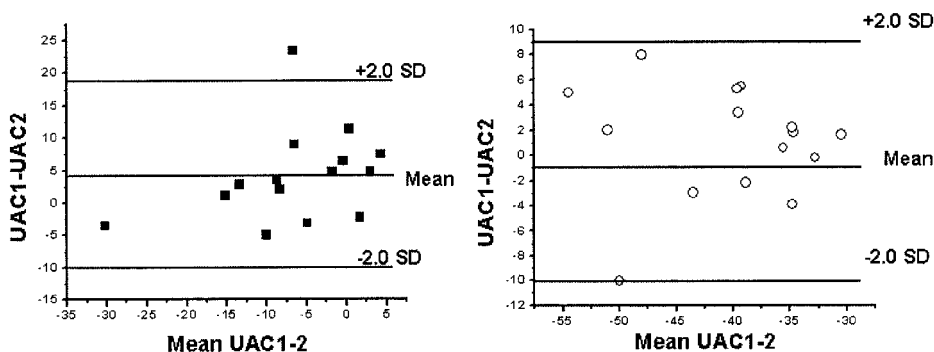

Figure 1. Bland–Altman scatterplots of upper airway collapsibility (UAC) measurements conducted 1 week apart in control children (*left panel*) and children with polysomnographically diagnosed sleep-disordered breathing (SDB). The SD of the differences was 8.0 and 4.5% for control children and patients with SDB, respectively.
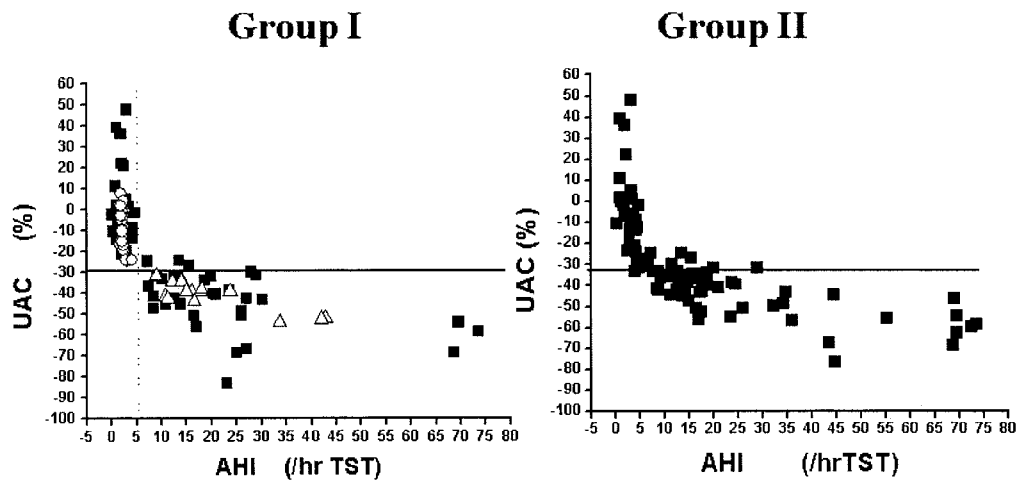
Group I   Group II

Figure 2. (*Left panel*) Scatterplots of UAC measurements plotted against obstructive apnea–hypopnea index (AHI) in 15 control children (*open circles*), 15 children with known SDB (*open triangles*), and 54 children referred for evaluation of snoring (*closed squares*). SDB is defined as AHI greater than or equal to 5/hour total sleep time (TST) (*vertical dotted line*). Receiver–operator curve analysis allowed for development of a UAC cutoff value set at less than or equal to 30% (*horizontal line*). (*Right panel*) Scatterplot of UAC measurements plotted against obstructive AHI in 94 children referred for evaluation of snoring (*closed squares*). SDB is defined as AHI greater than or equal to 5/hour TST (*vertical dotted line*). Receiver–operator curve analysis allowed for development of a UAC cutoff value set at less than or equal to 30% (*horizontal line*).

similar information on two separate occasions and display a coefficient of repeatability of 16% in control subjects and 9% in patients with SDB. It should be emphasized that the site corresponding to the maximal change in CSA after topical anesthesia varied from child to child along the anteroposterior axis but was consistently the same in any given child.

To examine the potential value of UAC determinations in the prediction of SDB in children, an initial cohort of 54 snoring children was assessed (Figure 2A). Their demographic and polysomnographic characteristics are shown in Table 1. Receiver–operator analysis revealed that a UAC of less than or equal to -30% was the optimal cutoff value and was associated with a sensitivity of 93.3% and a specificity of 100% in identifying SDB from primary snoring. Of note, all the control children (*open circles*, Figure 2, *left panel*) or the SDB children (*open triangles* in Figure 2, *left panel*) included above would also have been correctly identified.

To assess the value of a cutoff UAC less than or equal to -30%, a second group of 94 snoring children was prospectively tested (Figure 2, *right panel*). In this group, the UAC cutoff value achieved a sensitivity of 90.9% and a specificity of 88.4% (Figure 2) in differentiating between primary snoring and SDB.

UAC measurements and overnight polysomnography were repeated within 10 to 12 weeks after T&A in 15 children with SDB (Figure 3). In all but two children, AHI decreased to below 5/hour of TST (Figure 3; p < 0.001 vs. presurgery). In 10 of the SDB children, UAC was improved, and the values after T&A were similar to that in control children (p, not significant vs. control children; pre- vs. postsurgery: p < 0.01). In these children, mean CSA values were 1.64 ± 0.29 cm^2 preoperatively and 1.97 ± 0.34 cm^2 after T&A (p < 0.01). However, in the remaining five children, despite resolution of SDB after T&A, UAC values remained within the cutoff threshold (Figure 3). In these children, mean CSA were 1.66 ± 0.30 cm^2 preoperatively and 1.75 ± 0.34 cm^2 postoperatively (p is not significant). There were no statistical differences in the demographic or polysomnographic characteristics between these children.

DISCUSSION

This study shows that acoustic pharyngometric measurements of the upper airway before and after topical anesthesia provide

a reproducible measure of UAC in awake children. Furthermore, a cutoff value derived from the differences in CSA before and after topical anesthesia predicts, with high sensitivity and specificity, the number of children who have SDB. Furthermore, measurements of UAC after surgical removal of tonsils and adenoids in children with SDB show normalization of upper airway dynamics in approximately two-thirds of the children, whereas in the remaining one-third increased UAC remains

TABLE 1. DEMOGRAPHIC AND POLYSOMNOGRAPHIC FINDINGS IN TWO GROUPS OF SNORING CHILDREN WHO UNDERWENT UPPER AIRWAY COLLAPSIBILITY MEASUREMENTS

	Group 1 (n = 54)	Group 2 (n = 94)
Mean age (range), yr	6.6 ± 3.5 (4.8–14.5)	6.7 ± 4.4 (4.5–15.8)
Male sex, n (%)	28 (52)	18 (55)
Ethnicity, n (%)		
African American	24 (44)	41 (43)
White non-Hispanic	25 (46)	47 (50)
Other	6 (11)	6 (6)
Sleep efficiency, %	89.2 ± 7.3	90.7 ± 7.8
Sleep latency, min	22.2 ± 17.3	21.0 ± 16.8
REM latency, min	125.4 ± 32.2	124.5 ± 34.3
SWS, %TST	26.6 ± 5.3	27.1 ± 5.3
REM, %TST	18.4 ± 4.6	17.1 ± 4.4
Spontaneous arousal index	6.8 ± 3.4	7.3 ± 2.4
Respiratory arousal index	4.7 ± 3.3	3.9 ± 0.4
Total arousal index	24.0 ± 3.8	22.4 ± 2.8
PLM index with arousal, per hour TST	0.3 ± 0.4	0.2 ± 0.2
PLM index in sleep, per hour TST	2.9 ± 2.7	2.6 ± 2.4
PLM index total, per hour TST	3.2 ± 3.3	2.7 ± 2.5
AHI, per hour TST	17.8 ± 4.3	17.5 ± 3.3
AI, per hour TST	3.7 ± 0.9	3.5 ± 0.6
Mean Sp$_{O_2}$	94.8 ± 2.6	94.9 ± 1.9
Sp$_{O_2}$ nadir	63.1 ± 8.8	64.5 ± 5.6

Definition of abbreviations: AHI = apnea–hypopnea index; AI = apnea index; PLM = periodic leg movements; Sp$_{O_2}$ = arterial oxygen saturation; SWS = slow wave sleep; TST = total sleep time.
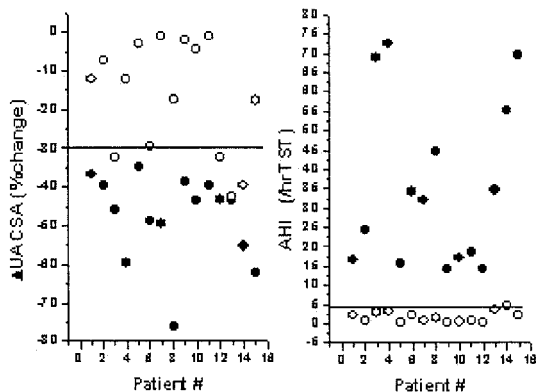
Figure 3. Scatterplot of UAC measurements (*left panel*) and obstructive AHI (*right panel*) in 15 children with SDB before (*closed circles*) and 10–12 weeks after (*open circles*) undergoing adenotonsillectomy. Improvements in UAC occurred in all but 1 child (Patient 13) whereas 10 patients normalized their UAC values, the remaining 5 continued to exhibit UAC measurements beyond the cutoff value less than or equal to 30% (*horizontal line*). SDB is defined as AHI greater than or equal to 5/hour TST (*horizontal line*).

despite marked improvements and/or normalization of their respiratory patterns during sleep.

Before we address the potential significance of our findings, some technical issues deserve comment. First, the quality and signal-to-noise ratio of the acoustic signal is highly dependent on the size and characteristics of the mouthpiece (12). We employed the smallest mouthpiece provided by the manufacturer and did not attempt to optimize this component of the test. It is possible that improved CSA curves across the anteroposterior axis may be obtained after optimization of the mouthpiece size, and that this may allow for better and operator-free analysis of individual UAC values. Second, the determination of UAC varied from child to child along the anteroposterior axis. This was not unexpected considering that the more collapsible segment leading to the narrowest point in the airway is not consistently located in the same region of the upper airway but rather varies from child to child (36, 37). Third, although relatively straightforward and simple, the maneuvers required for UAC measurements require full cooperation of the child and probably preclude such testing in very young children or in children who cannot cooperate for other reasons. Fourth, topical application of anesthetics is associated with a short yet significant period of discomfort, whereby the onset of action of the topical anesthetic induces a "burning" aversive sensation and is followed by pooling of saliva in the oral cavity, which potentially can contaminate the quality of the acoustic signals. Fifth, we selected otherwise healthy children whose snoring was primarily attributable to enlarged lymphadenoid tissue in the upper airway and therefore excluded children with craniofacial syndromes, morbid obesity, or neuromuscular disorders, and cannot extrapolate our findings to these patient groups. Finally, precautions aiming to prevent potential aspiration or any other complication resulting from the temporary anesthesia of the upper airway should be routinely instituted.

The decreases in CSA in waking children with SDB after application of topical anesthesia confirm previous findings by Marcus and coworkers (11) and Isono and coworkers (10) regarding the increased collapsibility of the upper airway in these patients. Furthermore, our findings strongly suggest that similar to adult patients with SDB (38), topical receptor mechanisms in the nasopharynx are tonically active during wakefulness in

SDB, underlie critical inputs to the augmentation of dilator muscle activity, and thereby preserve airway patency during waking. This important mechanism for the preservation of upper airway patency can therefore be used for reliable discrimination between children with primary snoring and those with SDB and improve the diagnostic accuracy of the latter when added to a careful medical history and physical examination. Indeed, because of the poor yield of clinical assessment alone (8, 39, 40), multiple approaches have been attempted to simplify the diagnostic algorithm of SDB in children and obviate the need for laboratory-based polysomnography. Examples include nighttime sound and video recordings, overnight oximetry, and simplified multichannel recordings in the home (38, 41–47). We now suggest that a simple noninvasive test performed during the outpatient evaluation of a snoring child affords improved accuracy to the diagnosis of SDB in snoring children and would benefit from prospective evaluation at additional pediatric sleep centers for confirmation purposes.

The discrepant changes in UAC measurements in those children who underwent T&A are particularly intriguing and suggest that in the majority of pediatric patients with SDB, the anatomic effects imposed by the hypertrophy of lymphatic tissue in the airway are the major determinants of increased UAC. This is in line with the overall anticipated outcomes after T&A (48) and also concurs with the overall proposed mechanisms underlying UAC in children (49). In contrast, in approximately one-third of the patients, removal of hypertrophic lymphatic tissue resulted in marked amelioration of the polysomnographic abnormalities but did not appear to modify the dependency on topical dilator mechanisms during wakefulness, as evidenced from the continuing UAC measurements at values less than or equal to −30%. We suggest that these children may correspond to the group that has inherently increased UAC and therefore be at higher risk for recurrence of SDB later in life (50). However, it is possible that these children may demonstrate improvement in their UAC at later time points, such that 10–12 week recovery period may be insufficient for normalization of their UAC responses.

In summary, maintenance of a patent upper airway during wakefulness in children with SDB requires tonic activation of topical mechanisms that lead to activation of the upper dilator muscles. Abolition of these mechanisms by topical anesthesia reliably differentiates between children with primary snoring and those with SDB.

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