Drug-Induced Sleep Endoscopy in Persistent Pediatric Sleep-Disordered Breathing After Adenotonsillectomy

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Objectives: To demonstrate the feasibility of drug-induced sleep endoscopy (DISE) in the pediatric population and to examine DISE results in children with persistent sleep-disordered breathing (SDB) after tonsillectomy and adenoidectomy (T&A)

Design: Retrospective case series with medical chart review.

Setting: Tertiary pediatric medical center.

Patients: Thirteen pediatric subjects with persistent SDB after T&A are included in the study.

Intervention: Drug-induced sleep endoscopy was performed on all patients with documentation of all sites of persistent airway obstruction.

Results: Multilevel upper-airway obstruction was identified in the majority of patients, most commonly related to tongue base obstruction, adenoid regrowth, and/or inferior turbinate hypertrophy. There were no differences among the 4 subgroups.

Conclusions: Findings from DISE suggest that multiple factors contribute to airway obstruction in persistent SDB after T&A. Further research can address the extent to which directed surgical treatment can improve outcomes in these patients.


Pediatric obstructive sleep apnea (OSA) has been increasingly recognized as a significant disorder warranting further evaluation and management, given its association with daytime somnolence, behavioral problems, poor school performance, developmental delay, neurocognitive changes, pulmonary hypertension, and cor pulmonale.1-6 Obstructive sleep apnea is a disorder of breathing during sleep characterized by prolonged partial upper-airway obstruction and/or intermittent complete obstruction that disrupts normal ventilation during sleep.7 It has been estimated that OSA affects approximately 1% to 3% of all children.4-6,8

Sleep-disordered breathing (SDB) is a common entity in children and includes the continuum of sleep-related breathing disturbances, including OSA on the severe end of the spectrum, and is generally diagnosed clinically based on signs and symptoms.9 Sleep-disordered breathing has also been associated with decreased cognitive skills, decreased quality of life, behavior disturbances, and neurocognitive changes in children.3

Adenotonsillar hypertrophy is a major contributing factor to SDB in children, and tonsillectomy and adenoidectomy (T&A) has traditionally been considered to achieve resolution of SDB in approximately 80% to 90% of children.10-13 However, a more recent meta-analysis of 1079 subjects found that up to 33.7% of children may not experience resolution of SDB after T&A.14 The complexity of pediatric SDB is now more fully recognized, with multiple anatomical and systemic contributing factors. Certain patient populations, including obese individuals and those with specific comorbidities, such as trisomy 21 (Down) syndrome, cerebral palsy, and craniofacial abnormalities, may be particularly prone to persistence of SDB after T&A.10

Successful treatment of persistent SDB after T&A in the pediatric population remains challenging, given high rates of multilevel disease and the difficulty of obtaining a comprehensive airway examination. To develop a targeted and effective surgical treatment plan, airway evaluation is designed to characterize the pattern of upper-airway obstruction. Drug-induced sleep


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endoscopy (DISE) is a technique of upper-airway fiberoptic endoscopic examination during conditions of sedation and was first described as “sleep nasendoscopy” for adults with snoring or OSA by Croft and Pringle in 1991. In adults with OSA and without previous OSA surgery, DISE has been shown to be valid and reliable. Drug-induced sleep endoscopy in the pediatric population was first described in the English literature by Myatt and Beckenham in 2000. The objectives of this study were to demonstrate the feasibility of DISE in a pediatric population and to examine DISE findings in children with persistent SDB after T&A.

METHODS

This study included consecutive subjects with persistent SDB after prior T&A, who underwent DISE at the University of California, San Francisco, from June 2008 to September 2010. The presence of persistent SDB was determined either by polysomnography with an apnea-hypopnea index greater than 1 event per hour or by the continued presence of clinical signs or symptoms of SDB after T&A (frequent awakenings from sleep, loud snoring, pauses in breathing at night, and/or excessive daytime sleepiness). This study was approved by the University of California, San Francisco, Committee on Human Research.

All clinical information was obtained via retrospective medical chart review. Body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) was calculated from recorded height and weight on the date of DISE. Body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) was calculated from recorded height and weight on the date of DISE. The BMI percentile and Z-score for age and sex were determined.

"Overweight" was defined as a BMI of the 85th to lower than the 95th percentile, and “obese” was defined as a BMI at or higher than the 95th percentile, according to guidelines of the Centers for Disease Control and Prevention.

All subjects underwent DISE performed by a pediatric otolaryngologist (A.K.M. or K.W.R.) in the operating room. Subjects were positioned on the operating table in the supine position, with standard cardiopulmonary anesthetic monitoring by a pediatric anesthesiologist, including pulse oximetry and 3-lead electrocardiography. No topical anesthetic or vasoconstrictor was used. After initial induction of anesthesia with inhaled sevoflurane to allow sedation for placement of an intravenous (total inhalation time of approximately 2-5 minutes), an intravenous infusion of propofol was given (loading dose of 1 mg/kg, followed by 200-300 µg/kg/min). Spontaneous respiration was maintained throughout, and the target depth of sedation was the absence of a response to verbal stimulation in a normal voice, similar to a Modified Ramsay Score of 5 or Observer’s Assessment of Alertness/Sedation Score of 2 to 3 that has been described in adults. Once the target depth of sedation was achieved, the upper airway was examined using a 2.7-mm flexible fiberoptic endoscope. Extreme care was taken to avoid oversedation and any interventions such as mask ventilation, the placement of an oral airway, or jaw thrust that would alter airway anatomy.

The level of obstruction was determined at the time of DISE by the operating pediatric otolaryngologist. The previously described VOTE (velum, oropharyngeal lateral walls, tongue base, and/or epiglottis) criteria was used to document the level of obstruction. Configuration of obstruction at these regions was not included in this study. A subject was determined to have obstruction at a specific level if the subject met VOTE criteria for category 1 (partial obstruction) or category 2 (complete obstruction) at that level. We also included 3 additional locations of obstruction in the pediatric population that are not incorporated in the VOTE classification: inferior turbinate hypertrophy, adenoid regrowth, and laryngomalacia. Inferior turbinate hypertrophy was diagnosed if the inferior turbinates obstructed greater than 50% of the nasal cavity. Adenoid regrowth was diagnosed if the adenoid pad obstructed greater than 25% of the nasopharynx. Laryngomalacia was diagnosed if redundant mucosa was identified overlying the arytenoids with prolapse into the glottis on inspiration.

Fisher exact tests were used to compare DISE findings across the 4 subgroups: subjects with cerebral palsy; subjects with trisomy 21 syndrome, overweight or obese subjects, and otherwise healthy subjects. P < .05 was considered statistically significant. This was a convenience sample, without data to establish an appropriate sample size a priori.

RESULTS

Thirteen subjects underwent DISE. Baseline demographic and polysomnography data are presented in Table 1. Mean (SD) age was 7.8 (3.3) years (range, 3-15 years), and most (10 of 13 [77%]) were male. Seven

Table 1. Demographics and Polysomnography Results for All Subjects

<table>
<thead>
<tr>
<th>Subject, No./Sex/Age, y</th>
<th>Race/Ethnicity</th>
<th>Comorbidity</th>
<th>BMI</th>
<th>BMI Percentile</th>
<th>BMI, Z-Score</th>
<th>Pre-DISE AHI, Events/h</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/4</td>
<td>White</td>
<td>None</td>
<td>16.0</td>
<td>70.4</td>
<td>0.5</td>
<td>1.5</td>
</tr>
<tr>
<td>2/M/8</td>
<td>White</td>
<td>None</td>
<td>17.9</td>
<td>84.2</td>
<td>1.0</td>
<td>3.6</td>
</tr>
<tr>
<td>3/F/8</td>
<td>White</td>
<td>Obese</td>
<td>24.2</td>
<td>98.6</td>
<td>2.2</td>
<td>4.7</td>
</tr>
<tr>
<td>4/M/3</td>
<td>White</td>
<td>Overweight</td>
<td>17.8</td>
<td>91.5</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>5/M/8</td>
<td>Black</td>
<td>Overweight</td>
<td>19.7</td>
<td>93.9</td>
<td>1.6</td>
<td>4.0</td>
</tr>
<tr>
<td>6/M/12</td>
<td>Hispanic</td>
<td>Cerebral palsy</td>
<td>15.2</td>
<td>7.4</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>7/M/9</td>
<td>White</td>
<td>Cerebral palsy</td>
<td>18.1</td>
<td>80.4</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>8/M/4</td>
<td>Hispanic</td>
<td>Cerebral palsy</td>
<td>15.1</td>
<td>30.9</td>
<td>0.5</td>
<td>8.5</td>
</tr>
<tr>
<td>9/M/8</td>
<td>Hispanic</td>
<td>Trisomy 21 syndrome</td>
<td>16.9</td>
<td>73.2</td>
<td>0.6</td>
<td>16.6</td>
</tr>
<tr>
<td>10/F/6</td>
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<td>Trisomy 21 syndrome</td>
<td>16.3</td>
<td>74.4</td>
<td>0.7</td>
<td>23.5</td>
</tr>
<tr>
<td>11/M/10</td>
<td>Black</td>
<td>Trisomy 21 syndrome/obese</td>
<td>35.0</td>
<td>99.3</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>12/M/10</td>
<td>White</td>
<td>Trisomy 21 syndrome/overweight</td>
<td>20.9</td>
<td>91.9</td>
<td>1.4</td>
<td>4.1</td>
</tr>
<tr>
<td>13/F/6</td>
<td>White</td>
<td>Trisomy 21 syndrome/overweight</td>
<td>18.0</td>
<td>93.2</td>
<td>1.5</td>
<td>4.6</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td>19.3</td>
<td>76.1</td>
<td>0.9</td>
<td>7.9 (7.3)</td>
</tr>
</tbody>
</table>

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DISE, drug-induced sleep endoscopy.
jects (54%) were white, 4 (31%) were Hispanic, and 2 (15%) were African American. No patients had undergone prior inferior turbinate reduction procedures. The majority (85%) of subjects had 1 of the following co-morbidities: cerebral palsy, trisomy 21 syndrome, or overweight or obesity. Eight subjects (62%) previously failed a trial of continuous positive airway pressure (CPAP) because of young age and/or comorbidities. Nine subjects (69%) previously failed a 3-month trial of nasal steroid spray. A 3-month trial of oral leukotriene inhibitor failed in 6 subjects (46%).

Nine subjects (69%) underwent pre-DISE (post-T&A) polysomnography with a mean (SD) apnea-hypopnea index of 7.9 (7.3). The remaining four (31%) were diagnosed as having SDB based on symptoms, including frequent awakenings from sleep, loud snoring, pauses in breathing at night, and/or excessive daytime sleepiness.

All subjects tolerated DISE, and there were no complications. Based on DISE findings (Table 2), multi-level obstruction occurred in all subjects except 2 subjects with obstruction located at the tongue base only. The mean (SD) number of obstructive pathologic conditions per subject was 2.8 (1.6). Tongue base obstruction was the most common diagnosis and was present in 11 subjects (85%). This was followed by adenoid regrowth (69%) and inferior turbinate hypertrophy (54%). All subjects underwent surgical intervention based on DISE findings. Eight subjects (62%) had these procedures completed during the same anesthetic as the DISE procedure. The remaining 5 subjects (31%) were scheduled for these additional procedures at a later date.

The previously described VOTE classification system was used to describe obstruction at the velum, oropharyngeal lateral walls, tongue base, and/or epiglottis. Both subjects with documented obstruction at the oropharyngeal lateral wall position had obstruction due to tonsillar regrowth without evidence of significant contribution from adjacent lateral wall tissues. Of the 11 subjects, 10 (91%) with documented obstruction at the tongue base region had lingual tonsillar hypertrophy as the primary cause of obstruction.

Table 3 presents the subgroups and the contribution of specific structures to airway obstruction during DISE. All 3 subjects with cerebral palsy had tongue base obstruction and adenoid regrowth. Oropharyngeal lateral wall obstruction (tonsillar regrowth) was most common in the overweight or obese group (33%) who also had a significant amount of adenoid regrowth (67%). Fisher exact test results showed that there was no association between subgroups and the contribution of specific structures to obstruction during DISE in this sample (all P > .05).

This study examined DISE findings of pediatric patients with persistent SDB after T&A. Multiple factors contributed to persistent SDB during DISE, especially tongue base obstruction.
obstruction, primarily due to lingual tonsillar hypertrophy, adenoid regrowth, and inferior turbinate hypertrophy.

Successful treatment of persistent SDB after T&A in the pediatric population is challenging, given the high rates of multilevel disease and the difficulty of obtaining a comprehensive airway examination. Airway evaluations include direct visualization of the upper airway using a flexible fiberoptic endoscope, which can be performed during wakefulness, sleep, or sedation.\textsuperscript{26,27} Awake endoscopy can be difficult to perform in the pediatric population, especially in developmental delay. Endoscopy findings during wakefulness may differ markedly from sleep because of differences in muscle tone, airway reflexes, and other changes that occur with sleep.\textsuperscript{27}

Myatt et al\textsuperscript{10} published a series of pediatric DISE in 2000. This study included pediatric subjects with complex airway obstruction, although most had not undergone prior T&A. The results suggested that the most common cause of obstruction was tongue base collapse, which was present in 30% of the subjects, followed by velopharyngeal and tonsillar obstruction, both present in 20% of subjects. The authors also found that DISE results corresponded with a blinded review of recorded awake flexible endoscopy performed in clinic. In comparison, our study found tongue base obstruction to be more prevalent at 85% and velum and tonsillar obstruction to be similar but slightly less common at 15% for each category. Truong et al\textsuperscript{39} recently published a series of pediatric patients with OSA who underwent DISE. In this study, 51% of subjects had persistent OSA despite prior T&A. For these subjects, the study found that common sites of persistent obstruction included the adenoid pad, lingual tonsils, and laryngomalacia.\textsuperscript{28}

Several other evaluation techniques have been developed or applied in children to characterize the pattern of upper-airway obstruction, including pharyngeal pressure catheters,\textsuperscript{29} cinefluoroscopy,\textsuperscript{30} cine computed tomography,\textsuperscript{31} and cine magnetic resonance imaging (MRI).\textsuperscript{32} Each method has associated risks and benefits, but most have never been used to examine pediatric subjects with persistent SDB after T&A.

Donnelly et al\textsuperscript{33} used cine MRI to examine 27 pediatric subjects with trisomy 21 syndrome with persistent OSA after T&A.\textsuperscript{33} We found similar rates of adenoid regrowth (69% in the present study vs 63% in their study) but higher rates of lingual tonsill hypertrophy (77% vs 30%).\textsuperscript{33} Cine MRI similarly requires intravenous sedation without intubation, performed during an MRI, which may be more or less desirable than sedation in an operating room.

It is known that results of T&A in children with trisomy 21 syndrome, cerebral palsy, obesity, and craniofacial abnormalities are less successful than in children without these comorbidities.\textsuperscript{33-35} We did not see systematic differences in the contributions of specific factors to airway obstruction, but this may have been related to small sample sizes, particularly when divided among the subgroups.

Approximately 30% to 60% of children with trisomy 21 syndrome develop OSA due to multiple factors, including midface and mandibular hypoplasia, macroglosia, glossoptosis, narrow nasopharynx, generalized hypotonia, and a tendency toward obesity.\textsuperscript{3,33} In addition, 30% to 50% of patients with trisomy 21 syndrome who are treated with T&A develop persistent or recurrent OSA.\textsuperscript{33,34} Prior reports have indicated that lingual tonsillar hypertrophy is common in the population with trisomy 21 syndrome.\textsuperscript{11,35} In our study, all subjects with trisomy 21 syndrome were found to have tongue base obstruction as a likely contributing factor to persistent SDB on DISE examination.

Children with cerebral palsy also have a much higher incidence of OSA and SDB than age-matched controls when investigated with polysomnography.\textsuperscript{35} This is thought to be due to central apneas, poor gag reflex, salivary pooling, and hypotonia of the pharynx leading to collapse of the pharynx during sleep, especially at the level of the tongue base.\textsuperscript{10,35} Our study found that all subjects with cerebral palsy had tongue base obstruction and adenoid regrowth.

Overweight and obesity is also a risk factor for OSA, and approximately one-third of obese children have comorbid OSA.\textsuperscript{36,37} The prevalence of obesity in children has increased dramatically over the past 2 decades, and recent estimates suggest that 33% of children in the United States are overweight and 17% are obese.\textsuperscript{38} The etiology of OSA in obese children is thought to be secondary to adipose tissue deposited around the pharynx or subcutaneous tissue of the neck leads to compression of the pharynx and reduction in its cross-sectional area.\textsuperscript{36,37} A recent meta-analysis showed that T&A significantly reduces severity of OSA in obese children but is rarely curative with 75% to 88% of obese children with evidence of persistent OSA.\textsuperscript{36} If the number of obese and overweight children continues to grow, the rates of persistent SDB will also rise. Our study found that obese and overweight subjects were most likely to have tongue base obstruction and adenoid regrowth on DISE.

Drug-induced sleep endoscopy may be especially useful for children with persistent SDB after T&A because it may identify the anatomical structures that contribute to obstruction and enable tailored surgical treatment. A number of treatments beyond T&A have been reported for pediatric SDB, including removal of recurrent adenoid and tonsil tissue,\textsuperscript{35} turbinoplasty,\textsuperscript{39} septoplasty,\textsuperscript{39} lingual tonsillectomy,\textsuperscript{39} tongue reduction surgery,\textsuperscript{39} genioglossus advancement,\textsuperscript{40} hyoid suspension,\textsuperscript{41} uvulopalatopharyngoplasty,\textsuperscript{41} maxillary expansion/advancement,\textsuperscript{42} mandibular advancement,\textsuperscript{39} and supraglottoplasty.\textsuperscript{43,44} Recent articles have described the entity of “late-onset” or “occult” laryngomalacia as the cause of OSA with a significant improvement in sleep study results after supraglottoplasty.\textsuperscript{43,44} Drug-induced sleep endoscopy and other evaluation techniques may enhance the selection from among these treatments and others. A combined approach of DISE followed by surgery for persistent SDB performed under the same anesthetic is often preferred by families to avoid multiple general anesthetics. Although, we have found that the combined approach can make for challenging preoperative discussions with a multitude of surgical interventions needing to be discussed without knowing which may be ultimately required.
Several challenges are associated with DISE, such as optimizing the balance of anesthesia to induce sleep without inducing significant airway obstruction. The child must be sufficiently sedated to tolerate the procedure but must be breathing spontaneously without central apneas. Therefore, we recommend that pediatric DISE only be performed where personnel with appropriate experience and equipment for difficult airway management are available. Although, to our knowledge, this is the largest study of its kind, the statistical analysis of the comorbidity subgroups in this study is limited in terms of power owing to the small number of subjects in each subgroup. Larger and more detailed investigations are needed to adequately assess differences within subgroups, including age, sex, race/ethnicity, and comorbidities. Another limitation of this study is that DISE has been validated in the adult population but has not been validated in the pediatric population. Future research, ideally with large prospective cohorts, will enable evaluation surgical interventions based on DISE findings and will assess outcomes of these procedures with preoperative and postoperative polysomnography.

Our study is in agreement with prior studies in that patients with comorbidities such as cerebral palsy, trisomy 21 syndrome, and obesity have an increased likelihood of developing persistent SDB. This study has shown that multilevel disease is common in persistent SDB and may explain the need for multiple additional surgical interventions.

In conclusion, DISE is a tool for diagnosing multilevel airway obstruction in adults and is now being used in the pediatric population. Using this technique, we were able to identify sites of obstruction in pediatric subjects with persistent SDB after T&A. Multilevel obstruction was identified in the majority of subjects. The most common sites of persistent obstruction were tongue base obstruction, adenoid regrowth, and inferior turbinate hypertrophy. Further studies are needed to assess adjuvant surgical procedures based on DISE findings and to assess their long-term effectiveness in treatment of pediatric persistent SDB.

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Author Contributions: Dr Durr had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Durr, Meyer, and Rosbe. Acquisition of data: Durr, Meyer, and Rosbe. Analysis and interpretation of data: Durr, Meyer, Kezirian, and Rosbe. Drafting of the manuscript: Durr. Critical revision of the manuscript for important intellectual content: Meyer, Kezirian, and Rosbe. Statistical analysis: Durr and Kezirian. Obtained funding: Durr. Administrative, technical, and material support: Durr and Meyer. Study supervision: Meyer and Rosbe.

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REFERENCES


