World Journal of Otorhinolaryngology-Head and Neck Surgery (2021) 7, 221—227

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Review Article

Pediatric drug-induced sleep endoscopy: An updated review of the literature

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Available online 29 June 2021

KEYWORDS
Drug-induced sleep endoscopy;
Pediatric obstructive sleep apnea;
Adenotonsillectomy in children

Abstract The field of drug-induced sleep endoscopy (DISE) has grown considerably over the last 10∼15 years, to now include its use in pediatric patients. In this review article, we outline our approach to the use of this technology in Children with Airway Obstruction, most specifically in the management of children with airway obstruction and known or suspected adenotonsillar enlargement.

Introduction

Obstructive sleep apnea (OSA) has a prevalence of 1%∼4% for children in the United States.[1] Sequelae from pediatric OSA can include daytime somnolence, poor school performance, behavioral and neurocognitive problems, cardiovascular complications, enuresis, growth retardation,[2] and an overall significantly reduced quality of life.[3] Adenotonsillar hypertrophy has been widely recognized as the most significant contributor to OSA for otherwise healthy children.[2] The American Academy of Pediatrics considers adenotonsillectomy (AT) to be first-line treatment for pediatric OSA.[4] However, a recent meta-analysis reported residual obstructive symptoms in 33.7% of children post AT.[5] For patients with persistent obstructive symptoms following AT, overnight polysomnography (PSG) is often considered the next step in evaluation. While PSG findings are helpful in determining the presence and severity of OSA, they do not identify the specific location/anatomic cause of the obstruction. Awake flexible endoscopy can be useful in assessing for certain anatomic causes of obstruction including lingual tonsil hypertrophy and adenoid re-growth; however, these awake exams have not been shown to be representative of the patient's airway while asleep. An article by Lee et al reported that awake flexible endoscopy findings did not correlate to a similar scope with the patient asleep when assessing base of tongue collapse.[6] Chen et al[7] demonstrated that patterns of obstruction at the level of the lateral pharyngeal wall significantly differed in awake

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Peer review under responsibility of Chinese Medical Association.

Production and Hosting by Elsevier on behalf of KeAi

https://doi.org/10.1016/j.wjorl.2021.05.002

endoscopy compared to when the patient was asleep. The evolution of induced sleep endoscopy has allowed providers to assess anatomical sites causing airway obstruction exclusively during sleep.

Sleep endoscopy was initially pioneered by Croft and Pringle in 1989 and further developed in the 1990s.[8] It was named "drug-induced sleep endoscopy" (DISE) in 2005 by Kezirian and Hohenhorst.[2,9] The DISE technique involves an evaluation of the upper airway using a flexible endoscope while patients are in a pharmacologically induced sleep-like state. The scope is passed through the nares to examine the nasopharynx, oropharynx, larynx, and in some cases the trachea. The procedure has been shown to be safe, with test-retest reliability and moderate-substantial inter-rater reliability.[10] The goal of the DISE exam is to identify the site(s) of obstruction best to target surgically for the management of pediatric OSA. Controversy remains, however, as to how well DISE simulates physiologic sleep and, by extension, its utility in improving OSA.[11] DISE has classically been used to assess patients with persistent OSA after AT. More recently, DISE is being used for certain surgically naïve patients, further expanding the indications for and utility of DISE. DISE and its impact on treatment of pediatric OSA is a very active area of ongoing research.

The goal of this review article is to summarize the current literature on pediatric DISE, specifically examining the following areas of interest: indications for DISE, anesthetic protocols, comparison of DISE to other diagnostic modalities, DISE scoring systems, the use of DISE in surgically naïve patients, and DISE-directed surgical outcomes.

Indications for DISE

As the role of DISE continues to be studied, indications for the procedure have expanded: ① persistent OSA after AT,② prior to AT for patient at high risk for persistent OSA (i.e. obesity, Down syndrome, craniofacial anomalies, neurologic impairment),③ significant symptoms of SDB or OSA with small tonsils and adenoids,④ occult or sleep-state dependent laryngomalacia,⑤ evaluation for candidacy for hypoglossal nerve stimulator procedure. The most well-studied indication for DISE is for a child with persistent OSA following AT. A 2016 systematic review revealed that at least one site of obstruction was identified in 100% of children who underwent DISE ($n = 162$).[2,12] Wilcox et al[2] in 2017 summarized studies using DISE to identify sites of obstruction in children with persistent OSA after AT; they found eight studies reporting that sites were identified in 89%∼100% of non-control patients. In 2017, Friedman et al[13] surveyed pediatric otolaryngologists; they found strong agreement from responders in performing DISE for such patients with residual OSA following AT regardless of comorbidities. Additionally, a plethora of recent literature has explored the role of DISE in surgically naïve patients. Studies have shown a benefit in performing DISE prior to AT in patients who have a relatively high risk of persistent OSA following AT, including those with obesity, Down syndrome, craniofacial anomalies, and neurologic impairment.[14–16] DISE in these patients can be useful in guiding management should residual disease persist following AT.[16] However, opponents of this algorithm argue that airway dynamics change significantly following AT, such that the results of the pre-procedure DISE are low yield as the airway dynamics will be greatly changed following AT.[13] Other situations where DISE can be helpful in surgically naïve patients include children with severe symptoms of sleep-disordered breathing (SDB) or those with OSA and small tonsils/adenoids on exam. Miller et al showed that small tonsils (1+) were not obstructive in most cases during DISE, and therefore additional sites of obstruction should be considered in lieu of proceeding with AT.[17] A study by Richter et al[18] highlighted the importance of identifying patients with sleep-state dependent laryngomalacia. This disease entity is difficult to identify on awake laryngoscopy alone.[19] In a meta-analysis by Camacho et al,[20] 48/62 (77.4%) of children diagnosed with sleep-state laryngomalacia had failed prior AT. Lastly, children who are being evaluated for hypoglossal nerve stimulator (HNS) treatment currently require DISE evaluation to be completed to determine candidacy for this procedure. Caloway et al[21] 2019 published data from 20 patients undergoing HNS in the current ongoing pediatric clinical trial. Circumferential collapse at the level of the velopharynx was considered a criterion for exclusion from the study.

Anesthetic protocols

In an ideal setting, the anesthetic for DISE should simulate a natural sleep state while allowing for spontaneous ventilation.[22] The anesthetic should not cause artificial respiratory depression, cardiovascular effects, or airway collapse beyond what is occurring in natural sleep. It should be repeatable, have a quick onset, be short in duration, and not result in excessive airway secretions.[23] While no medication or combination of medications meets all these criteria precisely, there is an extensive, ongoing effort to find a protocol that most closely aligns with these ideals.

During the DISE procedure, most children require some type of inhalational anesthetic agent before intravenous (IV) line insertion. Topical anesthetic of the nasal passage is avoided as it has been reported to potentially exaggerate findings associated with laryngomalacia, reduce upper airway reflexes, and impair the arousal response resulting in increased sleep apnea severity.[2,24] Also, decongestants are to be avoided to prevent altering the accuracy of the inferior turbinate evaluation.[24]

Beyond that, controversy remains as to which general anesthetic agent should be used. While nearly all anesthetics affect upper airway muscle tone to varying degrees, it is important to acknowledge that excessive sedation can produce an exaggeration of collapse and create false positives in the areas causing obstruction during sleep.[22,23] This highlights the importance of being mindful and intentional about the anesthetic protocol used for DISE. Currently, multiple anesthetic protocols have been proposed (Table 1), but none have been universally accepted. The most common anesthetic agents used in pediatric DISE are propofol, midazolam, dexmedetomidine (DEX), ketamine, and inhalational agents (i.e. sevoflurane).[23]

For adults, propofol is the anesthetic most frequently used for DISE and is titrated to a bispectral index between 50 and 75.[9] For pediatric DISE, propofol has historically

Table 1 Features of commonly used anesthetics for pediatric DISE.

Anesthetic agent	Features
Propofol	• Used for adult DISE • In pediatric DISE, criticized for its potential to cause excessive dose-dependent muscle relaxation and airway collapse
Midazolam	• A commonly used benzodiazepine • Causes central apnea and peripheral muscle relaxation
DEX	• It is a preferred medication for pediatric DISE due to its minimal effect on the airway • Studies have shown it to be less likely than propofol to cause upper airway obstruction • It replicates only non-REM sleep • It has been criticized for not providing adequate sedation as a single agent
Ketamine	• It has minimal to no effect on airway patency and minimal effects on central respiratory drive • Causes hypersalivation, which can make DISE more difficult
Inhalational agents	• Causes dose-dependent obstruction at various sites in the upper airway

DISE: drug-induced sleep endoscopy; DEX: dexmedetomidine; REM: rapid eye movement.

been criticized for its potential to cause excessive dose-dependent muscle relaxation and airway collapse; however, in 2020, Kirkham et al[16] retrospectively compared DISE findings for children sedated with propofol versus DEX and did not find a significant difference in the degree of upper airway obstruction. Midazolam is a commonly used benzodiazepine for DISE but may cause both central apnea and peripheral muscle relaxation and obstruction.[23] DEX is currently considered the preferred medication for pediatric DISE due to its minimal effect on the airway. Unfortunately, it replicates only non—rapid eye movement (REM) sleep and has been criticized for not providing adequate sedation as a single agent.[25,26] Ketamine has minimal to no effect on the airway patency and minimal effects on central respiratory drive. However, ketamine does cause hypersalivation which can make DISE more difficult. Lastly, inhalational agents cause dose-dependent obstruction at various sites in the upper airway.[22]

Differences in anesthetic protocols make direct comparison of DISE results difficult. For example, a head-to-head comparison of propofol and DEX showed significant differences in upper airway scoring with DISE.[27] A universally accepted anesthesia protocol is critically important but still not agreed upon as of the date of the publication of this manuscript.

Comparison of DISE to alternative diagnostic modalities

DISE has several advantages, including the ability to obtain a three-dimensional view of the airway and to concurrently offer surgical intervention in the same operative setting. Allowing for concurrent surgical intervention limits the need for multiple anesthetics and is more convenient for the families. One limitation of DISE is the ability to assess only one site of obstruction at a time.[2] A second disadvantage is the scope's presence in the airway during the exam; some argue that the scope itself can stent open the airway during the exam, thereby changing the obstructive pattern.[28] Despite these limitations, many providers and families feel the benefits outweigh these disadvantages and consider pairing the diagnostic DISE with a plan for therapeutic intervention in the same operative setting.[2,13]

In addition to DISE, several other modalities have been used to identify sites of obstruction for pediatric patients with OSA (Table 2). Cine magnetic resonance imaging (MR) is a procedure completed with the child sedated while spontaneously ventilated. The main advantage of cine MR is the ability to assess multiple levels of obstruction simultaneously; some feel this ability provides a better overall assessment of the airway.[2] In contrast to DISE, MR allows

Table 2 Summary of advantages and disadvantages for imaging modalities assessing for sites of obstruction for patients with OSA.

Items	Advantages	Disadvantages
DISE	Can perform surgical interventions at the same time, 3-D view	Visualize one site at a time, scope stents the airway, difficult for OR planning
Cine MR	Image multiple sites simultaneously, distinguish lingual tonsils from BOT	Expensive, requires second anesthetic to perform surgical interventions
MLB	Evaluate for SAL	Low yield without specific comorbidities
CT	3D reconstructions, can do without sedation	Radiation exposure
Cephalometrics	Availability of plain film imaging	Unknown sensitivity and specificity
Lateral neck films	Availability of plain film imaging	Patient is awake, sitting upright

OR: operating room; MR: magnetic resonance imaging; BOT: base of tongue; MLB: microlaryngoscopy/bronchoscopy; SAL: synchronous airway lesions; CT: computerized tomography.

visualization of the obstruction without instruments in the airway. Cine MR is also felt to be superior in its ability to assess for glossoptosis and to distinguish lingual tonsillar hypertrophy from base of tongue obstruction.[29] The main disadvantages of cine MR are the expense of the study and the fact that surgical interventions would need to be completed in a separate setting.[29] Interestingly, results for DISE and cine MR exams have not been found to specifically correlate; Clark et al in 2017 evaluated 15 children with OSA using DISE and cine MR and found discrepancies in the diagnostic results in 33% of the patients.[30] Most of these diagnostic differences were attributed to the fact that the DISE exam found additional sites of obstruction that were not identified on MR.

Some providers perform tracheoscopy or microlaryngoscopy/bronchoscopy (MLB) at the same time as DISE to assess for synchronous airway lesions below the level of the glottis. A survey of pediatric otolaryngology providers in 2016 reported that 30% examine trachea/bronchi during DISE.[13] Bliss et al[31] found that only 5% of patients undergoing DISE had a synchronous airway lesion (SAL) identified with MLB and only a few of these required surgical correction. Their study concluded that in most cases concurrent MLB with DISE is unnecessary but may be considered when there is a history of intubation, prematurity, or other genetic, neurologic, or craniofacial comorbidities. Additionally, they highlight that the improved optics of the distal chip fiberoptic scopes used for DISE allow for easier visualization of the subglottis and may be able to identify patients who would benefit from further MLB evaluation.[31]

A study by Quinlan et al[32] highlighted new computed tomography (CT) technology allowing for "dynamic 3-dimensional CT" imaging of the upper airway that does not require sedation. CT may be less favorable in pediatric patients, however, due to radiation exposure. Other reports have been published using cephalometrics and lateral neck films to identify sites of airway obstruction.[33] Cephalometrics can use known measurements and ratios to determine areas of narrowing and possible obstruction. However, no known published studies identify the sensitivity and specificity of these calculated ratios.[32] Lateral neck radiographs are widely available with relatively low cost, but the ability to identify obstruction may be limited by the 2-dimensional result, as well as the fact that the patient is sitting upright and is awake.

DISE scoring systems

An ideal scoring system would be standardized, validated, and universally accepted. A standardized scoring system would allow for objective outcome analysis after DISE between clinicians, institutions, and studies.[2] Currently, there are several published scoring systems for DISE, but no consensus yet among providers.[13] A review by Amos et al[34] found that among 44 DISE studies, 21 different scoring systems were used. A study by Tejan et al[35] used six different scoring systems on the same subset of surgically naïve pediatric patients undergoing DISE and concluded that all of the scoring systems lacked standardization of anatomic sites and rating scales. The six most common scoring systems used for pediatric DISE are summarized in Table 3. Each system is unique and varies by the anatomic sites, quantification, and characterization of airway obstruction. The VOTE system has been the most widely studied and is used in both adults and pediatric patients.[36] This system is criticized for pediatric DISE due to its omission of the nasopharyngeal and supraglottic sites. The Chan scoring system, published in 2014,[37] documents the percentage of obstruction at all sites other than lingual tonsils, which are described as present or absent. This system is similar to VOTE but includes the nasal, nasopharynx, and supraglottic sites. The Sleep Endoscopy Rating Scale (SERS) and the Bachar grading system evaluate similar sites but add an overall total score of upper airway

Table 3 Commonly used scoring systems for pediatric drug-induced sleep endoscopy.

Scoring system	Details
VOTE	• Most studied • Used in children and adults • Concise and easy to use • Evaluates: velum, oropharynx, tongue base, epiglottis • Criticized in children because it omits the nasopharynx and supraglottis
Chan	• Evaluates: nose, adenoid, velum, oropharynx/LPW, tongue base, lingual tonsils, epiglottis and supraglottis • Notes whether a jaw thrust or oral airway was required
SERS	• Evaluates: nose, nasopharynx, velum, oropharynx/LPW, hypopharynx, larynx • Uses an overall score for upper airway obstruction
Bachar	• Evaluates: nose, nasopharynx, palate and tonsils, tongue base, hypopharynx, and larynx • Uses an overall score for upper airway obstruction
Boudewyns	• Evaluates: adenoids, tonsils, tongue base, palate, epiglottis, and supraglottis • Describes if obstruction is fixed or dynamic • Allows for generalized impression of hypotonia present or absent
Fishman	• Evaluates: nose, nasopharynx, lateral walls, tongue base, supraglottis • Rates the degree of obstruction at several levels • Includes the quality of exam and the level of confidence in the findings

LPW: lateral pharyngeal wall.

obstruction.[38,39] The Boudewyns scoring system uniquely characterizes the obstruction as fixed or dynamic and also allows for a generalized impression as to whether hypotonia is present or absent.[40] The Fishman system evaluates the degree of obstruction at several sites but also factors in the quality of the exam, the confidence in the findings, and the severity of OSA, and asks the provider to determine the primary site of obstruction at the end of the exam.[41] More recently, Williamson et al[42] published another scoring system that evaluates obstruction at more sites than any of the six above systems: nasal airway, adenoid, palate, tonsils and lateral pharyngeal wall, tongue base, lingual tonsils, vallecula, epiglottis, aryepiglottic folds, and arytenoids. Currently, the use of multiple DISE scoring systems has created a lack of uniformity in how DISE is reported and studied. The need for a single universally agreed upon scoring system for DISE is imperative to move the field of pediatric sleep surgery forward.[2]

DISE for surgically naïve patients

Traditionally, DISE has been used to assess the airway of children who had persistent OSA following AT. However, recent studies have shown utility in performing DISE on surgically naïve patients prior to AT. Gazzaz et al showed DISE affected decision-making in surgically naïve patients with snoring and SDB in up to 35% of children. Additionally, an alternate diagnosis or surgical target was identified by DISE in 54% of the patients.[43] Chen et al[7] reported DISE findings for patients with OSA and small tonsils and concluded that DISE was an effective way to determine the necessity of tonsillectomy. Miller et al reported that for surgically naïve patients with OSA and small non-obstructive tonsils, DISE was useful in identifying other sites of obstruction. The supraglottis was the most common site of obstruction found and supraglottoplasty was the most common procedure performed for this patient cohort.[17] Kirkham et al reported 62 surgically naïve patients with OSA who were considered high risk for having persistence after traditional AT. These patients underwent DISE prior to any surgical intervention. Based on the DISE findings, 42% underwent AT, while 58% underwent treatment other than AT, including 18% who had multilevel surgery.[16] This study demonstrates the ability of DISE to change the surgical management for pediatric patients with OSA who are surgically naïve. With this knowledge, the question then becomes whether DISE should be completed on all children prior to AT. Collu et al[44] aimed to identify specific subgroups of patients for whom DISE should specifically be considered. They concluded that DISE is not as useful for "conventional" or classic cases. In this study, "conventional" patients were those with mild to moderate OSA and larger tonsils; DISE changed the plan in only 4.5% of the patients.

The ability of DISE to change management and DISE-directed surgical outcomes

Multiple studies have attested to the ability of DISE to change patient management, supporting it as a useful tool in the management of pediatric OSA. A prospective study by Hybaskova et al followed 51 pediatric patients with PSG-confirmed OSA. Based on history, physical exam, and PSG findings, a therapeutic plan was designed prior to DISE. Once DISE was performed, the surgical plan was changed in 60.8% of the patients based on the DISE findings.[45] A recent systematic review of pediatric patients with OSA by Saniasiaya et al[8] reported that DISE findings caused a change in the surgical plan for 30% of the patients. Similarly, Blanc et al[46] reported 31 patients with OSA/hypopnea syndrome and found that DISE caused a change in surgical treatment of obstruction sites in 45% of the patients.

Using DISE to guide surgical decision making is described as DISE-directed surgery.[47] Several investigators have examined DISE-directed surgical outcomes in children using standard objective criteria. Wootten et al assessed 26 patients retrospectively who had persistent OSA after AT. These patients underwent DISE with DISE-directed surgical interventions performed in the same setting. The study reported that 92% of patients experienced subjective improvement in symptoms as well as a decrease in mean obstructive apnea-hypopnea index (OAHI) from 7.0 ± 5.8 events per hour to 3.6 ± 1.8 events per hour. Only one patient had complete normalization of the OAHI, and the study failed to show a statistically significant difference in the pre- and post-operatively OAHI.[47] A recent systematic review and meta-analysis by Socarras et al demonstrated that DISE-directed surgeries led to significant mean reductions in OAHI in children with persistent OSA following AT. However, the authors noted that complete resolution of the OSA is rarely observed even with DISE-directed surgery. The study highlights that factors such as medical co-morbidities and severe baseline OSA may contribute further to persistent disease.[28] A study by He et al reported 56 pediatric patients with either persistent OSA following AT or infant OSA. These patients underwent DISE-directed surgery and had significant improvement in both OAHI and oxygen saturation nadir. The most commonly performed surgical procedures were adenoidectomy (48%), supraglottoplasty (38%), tonsillectomy (27%), lingual tonsillectomy (13%), nasal surgery (11%), pharyngoplasty (7%), and partial midline glossectomy (7%). The study found that DISE-directed surgery had better results for children with a lower AHI at baseline.[48] Esteller et al[49] showed that DISE-directed surgery led to significant improvement of OAHI in 20 otherwise healthy patients with prior AT. For surgically naïve patients, DISE-directed surgery has also been shown to decrease OAHI. Kirkham et al[5] examined 62 surgically naïve children at high risk for persistent OSA and found significant reductions in OAHI and improvement in oxygen nadir following DISE directed intervention. As more DISE-directed data become available in the future, the specific role of DISE-directed surgery may become more apparent.

Future directions

In a recent publication by Bergeron et al,[50] the authors described their institutional experience in performing DISE in the MR induction room compared to DISE completed in the traditional operating room. No major complications occurred, and total time of procedure was similar. There was a significant cost reduction when DISE was performed in the MR induction room. The downside remained that surgical interventions could not be incorporated in the MR setting.

Conclusion

DISE is helpful in its ability to guide the surgical management of pediatric patients with SDB and OSA. Its utility has been shown in managing patients with OSA who have already had AT as well as in certain surgically naïve patients. The field of pediatric sleep surgery ultimately needs a universally agreed upon anesthetic protocol and scoring system for DISE.

Declaration of competing interest

None.

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Edited by Li-Shi Yang