

## REVIEW ARTICLE

# Drug-induced Sleep Endoscopy

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## ABSTRACT

Obstructive sleep apnea (OSA) is a common disorder with significant associated morbidity. Though continuous positive airway pressure (CPAP) has been the treatment of choice, it has poor acceptability. Alternative therapies include surgery or oral appliances. A meticulous assessment of the airway is needed before these alternative therapies can be tailored to their specific needs. Drug-induced sleep endoscopy (DISE) provides a detailed visual description of the sites of upper airway obstruction and may conclusively lead to a better choice of therapy resulting in the wider use of this endoscopic examination in dedicated sleep centers. This review discusses the indication, procedure, and the controversies regarding DISE.

**Keywords:** Drug-induced sleep endoscopy, Endoscopy, Obstructive sleep apnea, Sedation.

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## INTRODUCTION

Obstructive sleep apnea is characterized by repetitive phases of complete (apnea) or partial (hypopnea) collapse of the upper airways during sleep, with resultant snoring, recurrent episodes of sleep interruption, hypoxemia and hypercapnia, along with swings in intrathoracic pressure and sympathetic surges. The health consequences of OSA are numerous. If left untreated, it is shown to be associated with increased cardiovascular events, excessive daytime sleepiness, cognitive dysfunction, impaired work performance, and decrements in health-related quality of life.<sup>1</sup> Obstructive sleep apnea is being increasingly recognized as an emerging important public health problem worldwide, including India.<sup>2</sup>

The gold standard treatment for OSA is CPAP, though its effectiveness is limited by the poor compliance due to low acceptability and poor tolerance.<sup>3,4</sup> Continuous positive airway pressure acts as a pneumatic splint,

which prevents airway collapse during sleep. Alternative options for treating OSA also intend to correct the areas of collapse in the upper airway; either permanently (via surgery) or only during sleep (using oral application therapy like mandibular advancement splints). Various surgical techniques, targeting selected sites of obstruction (including uvulopalatopharyngoplasty, expansion sphincter pharyngoplasty, tonsillectomy, tongue base surgery, and laser epiglottoplasty), have been described for the treatment of OSA.<sup>5</sup> The surgical techniques have 100% compliance and the effectiveness of the technique is critically dependent on the ideal selection of the patient. It is imperative for clinicians to realize that these surgical therapies need to be tailored specifically for each patient based on the anatomical defect identified, as there is no perfect surgery that will “fit all patients.”<sup>6</sup>

Airway assessment was earlier done in awake patients by clinical otorhinolaryngologic examination (awake endoscopy performed during tidal breathing and Müller’s maneuver) and cephalometry [using X-ray or computed tomography (CT)/magnetic resonance imaging (MRI)]. Although these techniques can identify the anatomic risk factors and provide an insight into the pathophysiology, these techniques performed in an awake patient are not always accurate in identifying the site(s) of obstruction. It has been observed that the structure of the airway can change dramatically between awake and asleep states, mostly due to alterations in muscle tone.<sup>7</sup>

A meticulous assessment of the three-dimensional anatomical topography of the obstructed airway during sleep is very important in planning the optimal treatment for an individual patient. This can be done using radiological techniques using dedicated imaging protocols performed during (drug-induced) sleep or by direct inspection of the airway during (drug-induced) sleep. Drug-induced sleep endoscopy is a dynamic, safe, and easy-to-perform technique that visualizes the anatomical sites, severity and configuration of the airway collapse, thereby guiding the design of a tailor-made treatment plan for the surgeon,<sup>8-10</sup> which may improve the perioperative outcomes.

## HISTORY OF DISE

The direct visualization of the airway during sleep was only possible after the advent of the flexible endoscope. Borowiecki et al<sup>11</sup> had used endoscopy to study 10 patients with OSA in natural sleep and suggested that the structures

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involved in production of airway obstruction are the muscles of velopharyngeal sphincter and tongue. A few years later, Rojewski et al<sup>12</sup> used polysomnography (PSG) to monitor the natural sleep state along with synchronous video recording of the upper airway. Almost a decade later, Croft et al<sup>13</sup> described the technique of sleep nasoendoscopy, where sleep was induced using sedatives and the site of obstruction was identified. These studies provided the conceptual and methodological framework of DISE. However, the published literature on this technique remained scant till the past two decades.<sup>14</sup>

## Indications

A detailed evaluation of the level(s), degree, and patterns of obstruction in a patient of OSA would lead to better selection of surgical techniques and subsequently lead to better treatment outcomes.<sup>15</sup> It is specially indicated in patients with OSA in whom non-CPAP therapy is considered or those who are intolerant to/have failed CPAP therapy.<sup>8,16</sup> It will also be helpful in assessing patients who have responded suboptimally to previous surgical interventions/oral appliances used for the treatment of OSA and help in identifying the site of residual obstruction.<sup>17,18</sup>

Another potential use of DISE is while titrating CPAP.<sup>19</sup> Drug-induced sleep endoscopy performed during CPAP therapy has shown that the pattern and degree of airway expansion after CPAP differ in accordance with the obstruction site—there is a tendency for persistent closing in cases of anteroposterior obstruction *vs* cases of lateral obstruction in the CPAP titration.<sup>20</sup> This suggests that the expansion of the lateral pharyngeal walls is mediating the effects of CPAP; however, in patients with significant obstruction at the level of the tongue and soft palate, either a CPAP titration or a non-CPAP modality may need to be used.

## Contraindication

Drug-induced sleep endoscopy should never be performed in patients with unacceptable anesthetic risk profile (American Society of Anesthesiologists 4). It should also be avoided during pregnancy, and in patients with an allergy to the anesthetic drugs.

## MATERIALS AND METHODS

### Preprocedure Evaluation

A European panel of experts had formed a consensus for many aspects of the DISE technique in 2014.<sup>14</sup> A sleep study should be done prior to the DISE to assess the severity of OSA and to evaluate for the position of the body at which the sleep apnea is worse. A detailed clinical and endoscopic awake upper airway examination should be

done before proceeding to a sleep-induced endoscopy. A pre-sedation assessment should also be an integral part of the preprocedure evaluation.

## Drugs used

### *Local Anesthesia, Nasal Decongestants, Other Medications*

Often, nasal decongestion, nasal local anesthesia, and antisecretory drugs are described as preparatory measures. However, the European position paper on DISE does not recommend the use of atropine infusion and the use of local anesthesia prior to inserting the endoscope.<sup>14</sup> Although the use of atropine and decongestants may reduce the secretions and improve visibility, the same can be achieved by suctioning. Also, because of lack of knowledge about the impact of these drugs on sleep physiology and the changes it may cause on the cardiovascular system, it is advisable to avoid using these drugs. Similarly, though local anesthetics may reduce nasal irritation and increase the ease of scope insertion, it can at the same time, influence the pharyngeal muscle tone and impact the resistance of the upper airway. Hence, even the routine use of local anesthetics is discouraged.<sup>14</sup>

### *Sedative Drugs*

The sedative drug is selected based on its ability to allow an easy titration of the dose to the desired effect, closely mimic the natural physiological sleep and have a suitable duration for the procedure to be carried out. A recent review demonstrated relatively few investigations seeking to characterize the neuropharmacologic suitability of DISE agents. The common sedatives that are used for DISE include midazolam/propofol or a combination of the two.<sup>14</sup>

The other common drug is dexmedetomidine.<sup>21</sup> Compared with propofol and midazolam, dexmedetomidine's mechanism of action appears most likely to replicate a natural sleep<sup>22</sup> and provide greater hemodynamic stability and less respiratory depression.<sup>23</sup> However, more studies are required for assessing the effect of drugs on critical closing pressure and pharyngeal muscle tone (using genioglossus electrode electromyography), which have an impact on the upper airway collapsibility. This will allow in selecting the best drug (or drug combination) for DISE.

Titration of the amount of drug to be administered is another important aspect. The drugs can be administered as a bolus or an infusion. A target-controlled infusion has been recommended as an effective drug delivery system.<sup>24,25</sup> Electroencephalography-derived parameters, such as bispectral index (BIS) can be used to assess the depth of sedation and anesthesia.<sup>26,27</sup> If BIS is available,

the sedatives are administered to BIS levels between 50 and 70; this correlates best with the appropriate level of sedation for the DISE procedure. The advantage of this technique is the reproducibility of the protocol even for heterogeneous groups of patients. In addition, the gradual controlled and standardized increase of the plasma level of the drug with real-time control of the BIS index leads to a precisely controllable depth of sedation.<sup>25</sup>

### Patient Positioning

Traditionally, the DISE is performed in the position where the OSA is most severe—this is usually the supine position but the preprocedure PSG may identify a different position. It is advisable to perform the study in both the supine and lateral positions as differences in position have been shown to have an impact on the upper airway collapse.<sup>28</sup> This allows the clinician to see what impact positional therapy may have in alleviating the apneas/hypopneas.

### Procedure

The procedure should ideally be performed in a silent and dark room where facilities for monitoring and resuscitation are easily available. It is essential to have equipment for cardiorespiratory monitoring while administering sedative drugs. In addition, it is desirable to have simultaneous polygraphic monitoring<sup>12,29</sup> along with equipment for assessing the depth of sedation (e.g., BIS).<sup>25</sup> It would be advantageous to have facilities to record the endoscopic finding for review at a later time, especially prior to a planned surgical intervention.

The team performing DISE should comprise of at least three people—one to perform the procedure, a second person (an anesthetist or an appropriately clinically trained individual) to administer and monitor the patient, and a third person in case any emergency arises.

The thinnest size flexible endoscope available should be used for DISE. During the procedure, the endoscope is gradually advanced into the airway and the airway is inspected. The nasal route is usually used, though occasionally, an additional oral examination may also be carried out if the patient is sleeping with the mouth open. The procedure should include observing at least two or more cycles (i.e., a complete and stable sequence of snoring–obstructing hypo/apnea–oxygen desaturation–breathing) for each segment of the airway (from nasopharynx to hypopharynx and larynx). At times, the administration of sedatives (especially when using a combination/a bolus technique of delivering the drug) may cause an exaggerated early response and it is advisable to wait for some cycles before beginning the examination.

Another interesting application of DISE is to see if the mandibular advancement devices could be completely therapeutic for a patient. Drug-induced sleep endoscopy provides the clinician an opportunity to assess the airway with the oral appliance *in situ*. The European expert panel recommends starting the sedation process with the oral appliance *in situ* and after the assessment with the appliance, to remove it and reassess in order to avoid arousals.<sup>14</sup> Some authors have tried using simulation bite in maximal comfortable protrusion of the mandible performed during DISE to predict the utility of the mandibular advancement devices in treating the OSA.<sup>30-32</sup>

A major limitation in advancing the use of DISE has been the multiplicity and, in many cases, the complexity of classification systems that prevent the comparison of results across studies and centers. The European position paper recommends that while reporting the findings, it is imperative that the endoscopist reports three features—the level (and/or structures), the severity (degree of obstruction), and the configuration (anteroposterior, lateral, and concentric) of the obstruction. Different authors have described the levels differently; some using levels, some describing the structures while others prefer a hybrid of the two. Multiple systems for reporting the finding of DISE have been proposed.

The VOTE system is a commonly used system for describing the findings.<sup>33</sup> It looks for obstruction at the level of the velum, lateral walls of the oropharynx, tongue base, and epiglottis. For reporting the severity, the VOTE system uses the only three degrees of severity—none, partial, and complete obstruction. The simplicity of this grading system allows for good interrater agreement.<sup>34</sup>

Another system used is the NOHL classification (which reports obstruction at the level of the nose, oropharynx, hypopharynx, and the larynx) where the grading is done as ranging from 0 to 25%, 25 to 50%, 50 to 75%, and 75 to 100%.<sup>35</sup> The concentric shape of the hypopharynx in the NOHL classification is composed of the lateral movement of the pharynx and the anteroposterior tongue base. In the VOTE classification, these two sites are evaluated separately. There is a paucity of studies which compare the reporting systems to see which would be an ideal method. A prospective study comparing the VOTE and the NOHL system has concluded that the VOTE classification was more comprehensive in the analysis of the epiglottis and pharynx by DISE and the relationship between OSA severity and number of affected sites was also established by VOTE.<sup>36</sup>

### Alternatives

Some authors have questioned the validity of DISE; the use of drugs may not necessarily mirror the changes

during natural sleep. Also, the position of the patient during the examination is well known to impact the findings. One of the alternatives to using drugs is doing the procedure during natural sleep.<sup>11</sup> However, this has its own set of problems; a long tedious process which may not at times be completely performed due to frequent arousals while maneuvering the endoscope.

Yet another alternative, which avoids the use of the endoscope, requires the use of radiological techniques like sleep video fluoroscopy and dynamic CT/MRI.<sup>37,38</sup> However, these techniques carry the risk of radiation and often are expensive.

An innovative technique to study upper airway obstructions is the use of channel catheters to measure the change of pressure in airway at sleep apnea episodes—tracking the change of inspiratory pressures at the different level of the upper airway and the esophagus.<sup>39</sup> This can be performed during natural sleep and also allows for a longer evaluation. However, the accuracy of the results requires that the catheter does not migrate and the placement of the catheter should not disturb sleep.

Another novel technique is acoustic reflectometry, which uses the principle that sound reflects differently by the cross-sectional area of the airway space because of the impedance change.<sup>40</sup> This method has several advantages. It is inexpensive, noninvasive, easy to perform, does not disturb sleep, can evaluate multiple apnea events with simultaneous recording of PSG without any radiation exposure. However, there are certain limitations including its dependency on the patient's position and inability to pinpoint the exact site and severity of obstruction, because of which it is not routinely performed.

## CONTROVERSIES

The last decade has witnessed a growing interest in DISE and an increasing number of publications on this technique. However, there are several grey areas and significant debate regarding DISE. Natural sleep is very heterogeneous—with varying tone of the airway muscles during different stages of sleep and with the airway anatomy changing with the position of the patient. Drug-induced sleep endoscopy allows only a relatively brief evaluation compared with 6 to 8 hours of natural sleep. A consensus is needed on the depth of sedation (and its monitoring) so that the airway architecture assessed during the procedure closely replicates that during natural physiological sleep. The drugs selected for premedication and inducing sleep need to be selected so that they have a minimal impact on the airway tone and the upper airway collapse.

The role of DISE in the surgical management of OSA needs to be further explored; especially whether certain DISE findings are related to treatment advice and outcomes. Drug-induced sleep endoscopy is an objective method for visualizing upper airway obstruction. The classification and assessment of clinical findings based on DISE is highly subjective due to the increasing number of DISE classification systems. A universally accepted objective DISE assessment is needed to allow the results to be effectively communicated and compared between groups. Further research is also needed to link the different grading systems with outcome data in order to ascertain the best grading and treatment for OSA.

## CONCLUSION

Drug-induced sleep endoscopy allows direct visual evaluation of the airway and identifies areas of collapse; thereby influencing decision regarding the selection of surgical techniques or the usefulness of oral appliances in treating OSA. However, the sedation used, the protocol for performing and reporting of DISE requires refinement and universal consensus in order to ensure its appropriate and adequate use in OSA patients. This technique has the potential to revolutionize the diagnosis of OSA and has been envisaged to be the gold standard test for planning the treatment of OSA.

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