REVIEW ARTICLE

Drug-induced Sleep Videoendoscopy: Clinical Usefulness and Literature Review

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Abstract Fibreoptic examination of the pharynx under drug-induced sleep is a test that helps to detect the areas of vibration and collapse in patients with sleep-disordered breathing. This article is a review of the available literature on the subject, aimed at helping otolaryngologists to understand the procedure and to resolve some controversies surrounding it.

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KEYWORDS
Obstructive sleep apnoea; Diagnosis; Drug-induced sleep videoendoscopy; Review

PALABRAS CLAVE
Apnea obstructiva del sueño; Diagnóstico; Videoendoscopia del sueño inducido; Revisión

Exploración videoendoscópica con sueño inducido, utilidad clínica y revisión de la literatura

Resumen La exploración fibrosocópica de la faringe mediante sueño inducido es una prueba que ayuda a conocer las zonas de vibración y colapso de los pacientes con trastornos respiratorios del sueño. En este artículo se realiza una revisión de la literatura disponible sobre el tema para ayudar al otorrinolaringólogo a conocer la prueba y resolver algunas controversias existentes sobre el mismo.

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Introduction

Obstructive sleep apnoea syndrome (OSAS) affects from 2% to 4% of the adult population,1 involves serious repercussions on the daily life of patients, makes their quality of life worse due to excessive somnolence during the daytime and is also linked to a greater health expenditure and greater risk of premature death.2,3 There are many studies that show that treating these patients is cost-effective.4 The treatment of choice is nocturnal continuous positive airway pressure (CPAP), because it corrects the apnoeas and
hypopnoeas in spite of not knowing what the area(s) of obstruction are. However, patient compliance with this therapy can be low. In cases with low compliance or in those where CPAP is not indicated, surgery or other types of treatment (such as intraoral devices) can be appropriate.

However, in the latest Cochrane review of the literature on sleep apnoea surgery, the conclusion is reached that surgery cannot be recommended as treatment for non-selected OSAS patients. In a meta-analysis by Sher et al. global success of palate surgery was 40%. One of the arguments put forward to justify these poor results is poor patient selection. Imaging studies on the upper airway (UAW) using computed tomography (CT) and magnetic resonance (MR) have shown that the areas of obstruction are not the same in the patient awake and asleep. Consequently, when examining patients who are awake, it is possible that the collapsed areas found do not correspond to those of sleep.

In 1978, Borowiecki et al. published a fibroendoscopic study of the UAWs of patients with OSAS while they slept. The problem was that examining the UAW of a patient sleeping spontaneously was so difficult such that it was infeasible. To get around this problem, in 1991 it occurred to Croft and Pringle that it was possible to examine the UAW with an endoscope during sleep induced with midazolam. That was how drug induced sleep endoscopy (DISE) was born. If sleep is brought about pharmacologically, the patients can tolerate fibroendoscopy without waking up, an appropriate schedule during the work day can be carried out and the UAW can be visualised while the patient is asleep, which complements our examination of the patient awake. In addition, it makes it possible to carry manoeuvres to check on the usefulness of intraoral devices.

It is true that DISE offers the possibility of visualising the UAW of patients with sleep-disordered breathing (SDB), that is, both OSAS and simple snoring. However, there are doubts as to the usefulness of DISE. It has been argued that, as sleep is induced by using drugs, there is greater relaxation of the pharyngeal muscles than during natural sleep, making finding unreliable; the drugs could also alter normal UAW functioning during sleep, cancelling its normal reflexes. The examination time is not very long and cannot consequently represent an entire night’s sleep and the variety of respiratory episodes during the different sleep phases. In addition, as is true for the examination of a patient that is awake, results are contingent on the subjectivity of the otolaryngologist who observes the test. However, in the last few years various articles have been published detailing attempts to solve these controversies and to demonstrate the validity, reliability and safety of this diagnostic test.

Validity of Drug Induced Sleep Endoscopy

To demonstrate the validity of DISE, we have to respond to the question of whether it represents normal sleep. There are several articles that have attempted to answer this question. In 1996 Sadaoka et al. induced sleep with diazepam a 50 patients with SDB for 3h. These patients were monitored in the same way as in the habitual polysomnography (PSG) and the researchers compared their sedation findings with the nocturnal PSG that was carried out that same week. There were no significant differences in the apnoea index or in the minimum oxygen saturation between natural sleep and induced sleep. As for the stages of sleep, they found no differences in non-rapid eye movement NREM sleep, while REM sleep was decreased or absent. In 2010 Rabelo et al. published a study in which they demonstrated the validity of a sedation technique using a pump, Target Control Infusion (TCI), with propofol. They were able to reproduce snoring in the 11 patients with OSAS, but not in any of the four control subjects and the apnoea-hypopnoea index (AHI) was equivalent in both natural sleep and induced. However, minimum saturation was lower with propofol. As for sleep patterns, they found an absence of REM stage and an increase in deep sleep (N3 stage). Patient sedation lasted from 90 to 120 min. These authors concluded that DISE is a good method for studying patients with OSAS given that it did not change the respiratory sleep parameters.

Other authors have studied the pharyngeal critical closing pressure (Pcrit) of patients with OSAS and without disease, using sleep induced with various drugs. We briefly summarise the concept of Pcrit: the difference between the collapsing and dilating forces of the UAW are known as transmural pressure (TMP) and Pcrit is the value of TMP at which the UAW collapses and its breath flow ceases; it is consequently an index of UAW collapsibility. Pcrit can be calculated with the help of a CPAP, and corresponds to the pressure applied in the nostrils below or above which the flow ends or the UAW opens, respectively. The resistance reflects the degree of UAW narrowness above the area collapsed. All these researchers came to the conclusion that Pcrit is equivalent to that of natural sleep in NREM stage. We will now discuss these studies in greater detail.

Genta et al. studied 15 patients with OSAS that they sedated with midazolam for more than 2 h, comparing the results with those obtaining using basal PSG. They found that Pcrit was equivalent with both natural and induced sleep at low doses of midazolam; likewise, sleep patterns were also equivalent, reproducing all the sleep stages, including REM. The conclusion they reached was that induced sleep was a state similar to natural sleep and, consequently, it was useful for studying patients with OSAS. Ayuse et al. also studied the Pcrit of disease-free subjects sedated with midazolam, finding that it was equivalent to natural NREM stage sleep. One particularity of this study was that, with the help of intraoral devices made for each patient, they were able to assess the effect of different degrees of buccal opening. This allowed them to verify that, even in disease-free subjects, Pcrit is higher when sleeping with the mouth open and that the UAW is obstructed when the mouth is open to its maximum. Hillman et al. studied Pcrit and the muscle tone of the genioglossus in patients sedated using with a propofol TCI pump. They discovered that, at low doses of propofol, both Pcrit and muscle tone remained the same and that both parameters fall at the moment of loss of consciousness, just as happens in natural sleep. The dose of propofol at which consciousness was lost varied from one individual to another and, in addition, the Pcrit was equal to that of natural NREM sleep.

The Pcrit studied in these articles is a statistical measure that tells us about collapsibility (the greater the Pcrit, the more collapsible the UAW), but it yields no information about the activity of the pharyngeal muscles. To ascertain this, studies that assess both passive and active Pcrit are
needed. A CPAP is used so that the patient falls asleep; as there is no collapse, the muscles relax and remain inactive, so passive Pcrit can be calculated. To calculate the active value, the use of the CPAP is stopped, with the muscles then becoming active, and how they work can then be ascertained indirectly. The authors who studied these physiological aspects with the patients under sedation reached the conclusion that muscle activity of the UAW is unchanged and that the mechanisms that keep the UAW permeable remain intact during sedation with propofol.18

Another way to compare natural sleep and that induced by drugs is using the bispectral index (BIS), a system of EEG monitoring that gives us an index of how deep the anaesthesia is. The levels of BIS at which consciousness is lost vary from one individual to another, but they are approximately 70–50.17 Researchers who compared BIS levels using both sedation and natural sleep concluded that they are equivalent.19,20 In addition, Abdullah et al.20 studied the activity of the genioglossus and checked, by means of PSG, the depth of sleep reached during the performance of a normal diagnostic DISE (which generally lasts some 15–20 min). Those authors found that muscle activity was unchanged by the sedation, and that it was equivalent to that of natural sleep in the same sleep stages. In 15 min of sedation with midazolam, the sleep stages of N1 and N2 were reached; although this may seem slight, but patients with OSAS spent from 63% to 79% of the time sleeping at night in these stages. Consequently, it seems that DISE represents natural sleep in the NREM stage.

Reliability of Drug Induced Sleep Endoscopy

To demonstrate the reliability of DISE, other studies have been carried out. Berry et al.21 showed the reliability of sedation with propofol TCI pump, being able to reproduce snoring in all of the patients who had snoring problems but in none of the controls. Rodriguez-Bruno et al.22 and Kezirian et al.23 found that the agreement observed by different observers was good, especially in the area at the base of the tongue and supraglottis; there was also good reproducibility of the findings in successive DISE. Gillespie et al.24 also observed good levels of agreement among the various observers. These studies make it clear that the subjectivity of the test is not significant.

Not all authors agree that the reliability of DISE is good. Badawey et al.25 were unable to reproduce snoring in 10% of their patients. They also suggested that DISE not be used in patients with simple snoring disorder, because all of their patients improved after velum surgery. This fact is unsurprising, given that all the patients in their study showed vibration in the area of the velum, although some patients also presented other areas of vibration. Likewise, Marais26 advises against using DISE because, when using propofol, snoring was not reproduced in almost 20% of the snorers, while it was reproduced in 45.3% of the patients that were theoretically not snorers. However, the patients used as controls lacked any type of sleep study that could have confirmed that they were in fact not snorers. Blumen et al.27 studied the partners of snorers and had to exclude 30% of them because they were snorers even though their partners did not know it. There could also have been undiagnosed snorers in the control group from the Marais study. In addition, in that article the technique of propofol sedation was not specified, so we do not know if it was a technique using boluses or a TCI pump. This distinction is important: DeVito et al.28 compared the two ways of administering the drug in DISE use and found that the TCI technique was more reliable, reproducing snoring in all of their patients and obtaining sedation levels that were lighter and more stable, as measured by BIS and by blood saturation. With the technique of propofol boluses, although less time was necessary for performing DISE, they did not manage to reproduce snoring in all their patients; in addition, sedation was sometimes too deep and in others too light, which made it necessary to administer another bolus, thus making the pharyngeal findings much less reliable.

The studies in which analysis of the sound of snoring obtained with sedation is compared with sleep induced in patients with simple snoring reveal that there are some differences between them. Agrawal et al.29 found that, although in general there was good agreement in the areas of vibration, in some patients there was an increase in the vibration at the base of the tongue. Jones et al.30 found that, even at small doses of propofol, there were changes in the characteristics of the snoring: it was stronger with sedation than with natural sleep.

Safety of Drug Induced Sleep Endoscopy

Safety of the test is an important point to bear in mind. There are authors who have performed more than 7000 tests without complications.31 Likewise, in cases of childhood OSAS DISE can be performed safely to ascertain the areas of collapse that cause the apnoeas.32-37 Although it is not necessary to carry out the test in the operating theatre, the place chosen has to be equipped with resuscitation devices and with a complete monitoring unit. It should be remembered that these patients, some of them cases of severe OSAS, have a significant risk potential and an airway of difficult intubation.

Usefulness of Drug Induced Sleep Endoscopy and Classifications

Diagnostic tests serve to confirm or rule out a finding that oblige us to change our therapeutic attitude. It would not make sense to perform DISE if it did not provide any further information than the examinations carried out with the patient awake. Consequently, we have to find out whether there are any differences between examining the patient awake and under induced sleep. All the authors who have compared their finding have concluded that there are differences in the findings obtained from the two examinations.37-44 Almost all of the authors found that collapse is multilevel in the majority of the patients (Table 1). The great disparity among the percent of collapse is due to the great heterogeneity of the samples in the various studies; although most of the studies were performed using patients with OSAS, some studies have a high percentage of patients with simple snoring, while there are also differences in the severity of the patients. In spite of the fact that there are patients with slight OSAS and multiple
areas of collapse, generally the more serious the apnoea, the more areas of collapse. However, it is also true that there are patients with severe OSAS and a single area of collapse.

In addition, performing DISE modified the therapeutic indication of the patients. Eichler et al. observed that, bearing the surgical possibilities in mind, using DISE modified the treatment options in 63.9% of the cases. In the study by Gillespie et al., surgical indications changed in 62% of the patients. Such modifications in the surgical indications are due to, among other things, the fact that DISE is capable of diagnosing epiglottic collapse and that this collapse is impossible to diagnose with the patient awake, except for some cases of floppy epiglottis. Likewise, surgical techniques to use in the velum and in the base of the tongue are modified, both to be suggested and to be advised against. If we also take into consideration the use of mandibular advancement devices (MADs) in the treatment of these patients, the changes in treatment indications ascend to 78.4%. Vroegop observed that patients that, after DISE, were considered good candidates for MAD had a greater probability of success with the treatment than those that were not, with an odds ratio of 4.96 ($P=0.002$).

Despite the fact that there are authors that believe that DISE is not useful to improve velum surgery results, other groups with extensive experience with the technique have published, selecting patients with DISE, their cure rates are much higher than those of the meta-analysis of Sher et al.; Hessel and de Vries successfully treated 69% of the patients on which they performed uvulopalatoplasty, the success criterion being AH1<15 with a reduction of 50%. However, they did not perform PSG after surgery because the significant subjective improvement of the patient made either the ORL specialist or the patient refuse to carry out the test. Chisholm and Kotecha successfully treated 90% of the patients on which they performed uvulopalatoplasty using laser, with and without tonsillectomy. In their case, one of the criteria for success was AH1<20 with a reduction of 50% of the previous AH1. All the patients had PSGs from 4 to 36 months after surgery. It is noteworthy that this group obtained higher success rates in the patients with OSAS than in the patients with simple snoring (in which they had a long-term success rate of 55%). The justification for this difference is, firstly, because the criteria of inclusion in laser surgery on the velum of this patient group were less strict, operating on patients that presented other areas of vibration in addition to that of the palate and, secondly, because the method for assessing success was completely subjective through a telephone survey.

In 2012 there were two published articles that attempted to help to rule out for phase I surgery patients that theoretically are not good candidates according to DISE findings. The first article reported that severe collapse of the lateral pharyngeal walls at the level of the base of the tongue or a supraglottic collapse was an indicator of failure of phase I surgery. The second report indicated that complete circular collapse circular in the velum and complete anteroposterior collapse of the base of the tongue were indicators of surgical failure. Another author had previously published that patients with collapse circular in velum did not respond well to uvulopalatoplasty, while those with an anteroposterior collapse did indeed respond well. It is evident that further investigation in this aspect is necessary to avoid operations, not risk-free, on patients on which it is presupposed that such surgery is not going to benefit. However, to be able to do so, a common classification for describing the findings is needed, so that we all speak the same language in referring to the same type of collapse. At the moment there are at least six classifications published, which can be seen in Table 2.

There are also studies published in which DISE is used for titration of CPAP. The pressures needed to keep the UAW open and eliminate the apnoeas were the same as with conventional titration using PSG, with the advantage of being performed more quickly.

### Table 1 Single-Area or Multi-Level Collapse in Various Studies Published.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>No.</th>
<th>Type of patients</th>
<th>Single-level obstruction (%)</th>
<th>Multi-level obstruction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdullah, 2003</td>
<td>93</td>
<td>OSAS</td>
<td>14.61</td>
<td>85.39</td>
</tr>
<tr>
<td>Bachar, 2008</td>
<td>43</td>
<td>OSAS</td>
<td>28</td>
<td>72</td>
</tr>
<tr>
<td>Carrasco, 2005</td>
<td>51</td>
<td>SDB</td>
<td>41.2</td>
<td>58.3</td>
</tr>
<tr>
<td>Hessel, 2002</td>
<td>340</td>
<td>SDB</td>
<td>35</td>
<td>65</td>
</tr>
<tr>
<td>Hamans, 2010</td>
<td>70</td>
<td>OSAS</td>
<td>61.4</td>
<td>32.9</td>
</tr>
<tr>
<td>Kezirian, 2010</td>
<td>108</td>
<td>OSAS</td>
<td>21</td>
<td>79</td>
</tr>
<tr>
<td>Kotecha, 2007</td>
<td>2485</td>
<td>SDB</td>
<td>41</td>
<td>57.7</td>
</tr>
<tr>
<td>Marais, 1998</td>
<td>205</td>
<td>SS</td>
<td>92.2</td>
<td>7.8</td>
</tr>
<tr>
<td>Pringle, 1991</td>
<td>50</td>
<td>SDB</td>
<td>54</td>
<td>46</td>
</tr>
<tr>
<td>Quinn, 1995</td>
<td>50</td>
<td>SS</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>Rabelo, 2013</td>
<td>46</td>
<td>SDB</td>
<td>47.83</td>
<td>52.17</td>
</tr>
<tr>
<td>Saunders, 2004</td>
<td>35</td>
<td>SDB</td>
<td>57.15</td>
<td>42.85</td>
</tr>
<tr>
<td>Steinhart, 2000</td>
<td>324</td>
<td>SDB</td>
<td>58</td>
<td>42</td>
</tr>
<tr>
<td>Ulualp, 2013</td>
<td>82</td>
<td>OSAS</td>
<td>71</td>
<td>29</td>
</tr>
</tbody>
</table>

No.: number of patients included in the study; OSAS: obstructive sleep apnoea syndrome; SDB: sleep-disordered breathing; SS: simple snorers.

* Study carried out on paediatric patients.
Table 2. DISE Classifications Published to Date.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Classification</th>
</tr>
</thead>
</table>
| Pringle, 1993 | Grade 1: simple snoring  
Grade 2: obstruction only in vellum  
Grade 3: obstruction in vellum + intermittent obstruction only on inspiration in hypopharynx  
Grade 4: obstruction in vellum + complete collapse of the entire respiratory cycle in hypopharynx (generally circular)  
Grade 5: hypopharyngeal collapse, generally from anteroposterior displacement of the tongue |
| Camilleri, 1995 | Grade 1: palatal snoring  
Grade 2: mixed snoring  
Grade 3: base of the tongue snoring |
| Vicini, 2007, 2012 | Area  
Nose | Oropharynx  
AP, C and L are added based on the morphology of the collapse  
Hyopharynx  
AP, C and L are added based on the morphology of the collapse  
Larynx  
A: Supraglottis  
B: Glottis |
| 0%-25% | 1 | 1 |
| 25%-50% | 2 | 2 |
| 50%-75% | 3 | 3 |
| 75%-100% | 4 | 4 |
| Kezirian, 2011 | Structure  
Degree  
Configuration  
0: No collapse  
1: Partial collapse or vibration  
2: Complete collapse  
x: not visualised  
AP  
Lateral  
Circular |
| Vellum  
Lateral pharyngeal walls  
Base of the tongue  
Epiglottis |
| Bachar, 2012 | Area  
No collapse  
Partial collapse  
Complete collapse  
The collapse found in each area is marked and the indexes are added together, giving a number |
| Nose+nasopharynx | 0 | 1 | 2 |
| Palate (including tonsils) | 0 | 1 | 2 |
| Base of the tongue | 0 | 1 | 2 |
| Larynx | 0 | 1 | 2 |
| Hypopharynx (LPW) | 0 | 1 | 2 |
| Gillespie, 2013 | Degree  
DISE Index  
AP Palate  
Hyopharynx  
Larynx  
Tonsils  
Base of the tongue  
Epiglottis |
| 0 | 1 | 2 | 3 | 4 |

AP, anteroposterior; C, circular or concentric; L, lateral; LPW, lateral pharyngeal walls; +, nose oropharynx hypopharynx and larynx (NOHL) classification, in which the degree of obstruction in each area is recorded along with its morphology and we have a TNM type composition.

\(^a\) VOTE Classification: the lateral pharyngeal walls refer to the level of the tonsillar area and include the tonsils if present.
Indications for Drug Induced Sleep Endoscopy

Bearing in mind for all the studies that we have discussed, we feel that DISE is a test that is useful for the diagnosis of patients with SDB. The test is unsuited for the diagnosis of the severity of the OSAS, but it provides us with a vision of the UAW that helps us to make the therapeutic decisions required for each patient.

We feel that it is useful and, consequently, that it would be indicated in the following cases:

- Patients with moderate or severe OSAS without morbid obesity, who cannot tolerate CPAP as the diagnostic test before appropriate surgical indication or MAD.
- Patients with mild OSAS or simple snoring with MAD or in which surgical treatment is indicated.
- Patients with OSAS that have not responded to surgical treatment.
- Children with residual obstructive sleep apnoea after adenotonsillectomy.

Contraindications for DISE would be:

- Allergy to the components of propofol (especially soy or eggs) or of midazolam.
- High surgical risk (American Society of Anesthesiologist risk score>3).

Patients who need to be treated with CPAP, weight loss or positional therapy do not need to have DISE, given that knowing the areas of obstruction is not important in these methods of treatment.

Conflict of Interests

The authors have no conflicts of interest to declare.

References


