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Drug-induced sleependoscopy – evaluation of a selection tool for treatment modalities for obstructive sleep apnoea

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Drug-induced sleep endoscopy – a review

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1. Abstract

Obstructive sleep apnoea (OSA) is a very common disorder with important day and nighttime symptoms and long-term effects on health. Different treatment modalities such as positive airway pressure (CPAP), oral appliance therapy using custom-made, titratable mandibular advancement devices (MADs), different types of surgery and positional therapy have been introduced over the years, with patient preference and adherence to therapy being key elements in improving treatment outcome. Several patient selection tools to improve treatment outcome have been introduced and evaluated over the years. Drug-induced sleep endoscopy (DISE) is a procedure that provides real-time upper airway evaluation of the sites of flutter and upper airway collapse. This review focuses on the indications and contraindications of DISE, methods of sedation and evaluation, add-on maneuvers and the results on patient selection and treatment outcome. A PICO approach was used to clarify the aims of this review. DISE has the advantage of being easily accessible in most ENT practices and being 3-dimensional, dynamic, site-specific, safe and is valuable in selecting patients for upper airway surgery and oral appliance therapy. There is a strong interest for further standardisation and exploration of the predictive value of this evolving technique.

2. Introduction

Obstructive sleep apnoea (OSA) is a very common sleep disorder characterised by repetitive upper airway collapse leading to disturbed sleep, decreased oxygen saturation levels and daytime symptoms such as excessive sleepiness [1-3]. Adequate treatment is essential to improve sleep quality and to reduce daytime symptoms, cardiovascular risks and social burden caused by reduced ability to work and traffic-related accidents [4]. Different treatment modalities such as positive airway pressure (PAP), oral appliance therapy using custom-made, titratable mandibular advancement devices (MADs), different types of surgery and positional therapy have been introduced over the years, with patient preference and adherence to therapy being key elements in improving treatment outcome [5,6]. Customised treatment planning is thus essential in matching treatment outcome with long-term adherence. For this purpose, several patient selection tools were introduced, with drug-induced sleep endoscopy (DISE) being a procedure introduced in 1991 that allows for a dynamic evaluation of the sites of flutter and collapse, using a flexible nasopharyngoscope to visualise the upper airway under sedation [7,8]. This review focuses on the indications and contraindications of DISE, methods of sedation and evaluation, add-on maneuvers and the results on patient selection and treatment outcome.

Translating the search into a PICO (Patient – Intervention- Comparison – Outcome) framework: this review focuses on patients with sleep-disordered breathing (P) in whom DISE (I) is performed to evaluate the applicability and outcomes (O) in terms of compliance, satisfaction and OSA severity of treatment by means of upper airway surgery, oral appliance therapy, positional therapy or other non-PAP therapies. Other upper airway imaging modalities can be considered as comparison (C).

A Pubmed/Medline search was performed with the following search terms: “drug induced sleep endoscopy”, “sleep endoscopy”, “sleep disordered breathing”, “obstructive sleep apnea”, ”adults”, without time limits and excluding the search results in other languages than English. The authors reviewed the results and included the articles that fitted the framework of this review and/or were considered of importance based on their expert opinion. An additional search based on the reference lists of these articles was also performed.

3. Results

Indications and contraindications

DISE can be performed in patients with sleep-disordered breathing in whom non-PAP therapy is considered as a primary treatment or in case of PAP or other non-PAP treatment failure or refusal

and in whom drug-induced sedation is allowed based on anesthesiologic evaluation. This evaluation can be based on the American Society of Anesthesiologists (ASA) score [9]. DISE can also be of additional value when assessing the underlying pathophysiology of OSA and incomplete response of treatment [6,10-13].

Absolute contraindications include ASA score 4, pregnancy, allergy to the sedative agent(s), and an expected extreme difficult airway. DISE may be contraindicated in patients with significant comorbidities, extreme severe OSA and/or severe obesity. This is not only based on assessment of anesthesiologic risks, but also on decreasing chances of successful non-PAP treatment in more severe OSA and/or obesity. However, case-specific necessity of upper airway assessment is to be considered.

Setting and sedation

DISE is most commonly performed in an outpatient setting, although an overnight stay may be indicated based on the patient's general condition or when concurrent surgery has been performed. DISE is performed with monitoring for oxygen saturation, cardiac rhythm and blood pressure and presence of resuscitation facilities are recommended, emphasising the need of anesthesiologic support, with the practical implementation hereof being country dependent. It is performed by an ENT surgeon in a semi-dark and silent (operating) room.

Sedation can be induced with several drug regimens, with midazolam and propofol being the most widely used drugs, either as a single agent or combined, and alternatively, a combination of these medicines with other drugs such as remifentanil or ketamine has been described [6,7]. Midazolam is considered well effective for induction of sleep and as background sedation, while propofol, with its rapid onset of action and recovery, can be used for fine-tuning [14]. A target-controlled infusion (TCI) system for the administration of propofol provides an objective (computer-controlled), reproducible and measured state of sedation, improving stability and accuracy of sedation [14-17]. Propofol is furthermore known to significantly change sleep microarchitecture, with cardinal respiratory parameters [apnoea-hypopnoea index (AHI) and mean SaO2] remaining unaffected, but providing a state mimicking the critical closing pressure [18]. Possible benefits to the combination of midazolam followed by propofol have been reported to include midazolam's anxiolytic effects, as well as a theoretical synergistic effect with propofol. However, it remains unclear as to whether the use of midazolam actually reduces the required propofol dose [19,20].

Recent research suggested that additional use of remifentanil, a short-acting synthetic opioid analgesic drug, reduces the target concentration of propofol, while the time needed for sufficient

sedation was significantly shorter. It was also reported that the cough reflex was reduced, although it was associated with a higher incidence of oxygen desaturation [21,22].

An alternative to propofol and/or midazolam can be dexmedetomidine, a selective α2-receptoragonist that inhibits the locus coeruleus, a predominantly noradrenergic nucleus in the brain stem that induces a sedative effect. A study on comparing propofol with dexmedetomidine concluded that dexmedetomidine provides a more stable profile based upon cardiopulmonary status. However, propofol for its part has a quicker onset and a shorter half-life [23]. Compared to propofol and midazolam, dexmedetomidine's mechanism of action appears most likely to induce natural sleep pathways [20]. Dexmedetomidine did not have dose-dependent effects when evaluated using cine-magnetic resonance imaging, unlike sevoflurane, isoflurane, and propofol, and caused less dynamic collapse than propofol. It also shows a lesser degree of airway collapse and higher oxygen saturation levels at greater sedation depth during DISE [24,25]. Further studies of its effect on upper airway collapsibility (critical closing pressure) and pharyngeal muscle tone (genioglossus electrode electromyography) are needed [20].

To control the depth and stability of sedation, electroencephalogram (EEG)-derived indices can be applied, such as bispectral (BIS) index systems, spectral entropy, and qCON monitor [26,27]. The use of BIS can be interesting in particular in study settings where strong intraindividual differences in depth of sedation are to be avoided [28]. When assessing the effects of the sedative agents, no relevant changes in main respiratory parameters such as AHI were detected, while literature revealed an abolishment of rapid eye movement (REM) sleep [29,30]. The DISE examiner must be aware of the possible pitfall of over-inducing muscle relaxation, which could lead to artefactual worsening of upper airway collapse [31].

Evaluation and inter- and intrarater variability

The regions of the upper airway that can be investigated using DISE are the following: the velum/palate, pharynx, tongue base and the epiglottis. The degree of collapse can be reported as complete, partial, or none or (semi-)quantitative and the pattern of the obstruction as being circular/concentric, anteroposterior, or lateral. Different scoring systems have been introduced over the years, each with their own anatomical accents, grading of collapse and in- and exclusion of collapse types [8,30,32-49]. The working group of the European Position Paper reached consensus on the fact that a scoring and classification system should include the following features: level (and/or structure), degree (severity) and configuration (pattern, direction) of narrowing and obstruction [6,37].

As for inter- and intrarater variability in assessing upper airway collapse during DISE, studies with different set-up specifically on this subtopic have been published, ranging from larger groups of observers rating a smaller set of DISE videos to a set-up with less observers but larger DISE video sets [47,50-52]. In general, interrater reliability of DISE is moderate to substantial, and higher agreement has been found among experienced ENT surgeons, although site-specific results differ, with the most recent report showing a negative impact of less experience on the identification of tongue-base obstructions [41,47,51,53,54]. Most results suggest that experience in performing DISE is necessary to obtain reliable observations. The test-retest reliability of DISE appears to be good [55] .

Position, manoeuvres and use of devices during the procedure

DISE is usually performed in supine position in the baseline setting, meanwhile taking into account the patient's sleeping habits at home. Research on positional OSA and DISE showed that changes in position during DISE may provide additional information about the presence of positional OSA and the accompanying upper airway behaviour, with the specific finding that rotating the head results in similar upper airway findings as turning both head and trunk in a lateral position [45,56-59].

Furthermore, intraoral (titratable) devices and mimicking manoeuvres can be applied during DISE. It was demonstrated that mimicking mandibular protrusion can be indicative of treatment outcome with MADs [60,61]. However, the use of a simulation bite is to be considered superior, as this specifically takes into account the maximal comfortable mandibular protrusion the patient is able to tolerate, as well as the thickness of the oral device [62,63]. In addition, both jaw thrust (Esmarch) and chin-lift manoeuvres can be disturbing stimuli, potentially causing arousals resulting in awakening of the patient. Recent research showed the feasibility of a remotely controlled mandibular positioner (RCMP) for the determination of the effective target protrusive position (ETPP) [64,65].

DISE can also be performed with active therapy such as MRA or PAP, to assess (residual) upper airway collapse and/or snoring and to be able to determine additional treatment options [13,66,67].

Treatment outcome

DISE has an additional value in optimizing patient selection for surgical upper airway interventions and can also be helpful in selecting patients for MAD treatment [60,61,68-70]. For this purpose, several perioperative manoeuvres were introduced, as described above. It was demonstrated that DISE has a relevant influence on recommendations for treatment location when compared to awake assessment including endoscopic examination, in particular when considering MAD treatment or tongue base interventions [41,71-73]. The role of DISE for patient selection for maxillomandibular

advancement (MMA) surgery has also been described, with AHI and oxygen desaturation index (ODI) improvement after MMA being best correlated with increased lateral pharyngeal wall stability [74].

DISE could modify surgical treatment options and procedures in 50% of OSA patients, but the available published studies lack evidence on the association between this impact and surgical outcomes [75]. However, patient selection based on site-specific upper airway behaviour has been shown of value in improving treatment outcome [76-82]. More specifically, a complete circular collapse at the level of the palate (Figure 1) can be associated with less favourable surgical outcomes for upper airway stimulation therapy, although a recent report showed similar improvement in patients with isolated retropalatal collapse as compared to other types of collapse with regard to AHI [78,83]. A recent multicentre study showed surgical response was associated with tonsil size and body mass index (inversely), and oropharyngeal lateral wall-related obstruction was associated with poorer surgical outcomes, as complete tongue-related obstruction was associated with a lower odds of surgical response in moderate to severe OSA. Surgical outcomes were not clearly associated with the degree and configuration of velum-related obstruction or the degree of epiglottis-related obstruction [53]. It must be mentioned that comparison of study results from different sleep centres across the world is challenging, as standardisation for DISE is lacking [26].

4. Discussion/Conclusion

In this review, an overview of the essentials on DISE is given, with a specific focus on recent highlights in literature on this topic.

In guiding OSA patients towards an optimised (non-PAP) treatment (patient in PICO framework), clinicians can combine patient preference and characteristics such as awake upper airway evaluation, body mass index (BMI), AHI and medical comorbidities with the most appropriate treatment suggestion(s) based on individual DISE findings, taking into account the above-mentioned associations of DISE findings with treatment outcome and applying these to counsel patients on the expectations of treatment outcome (outcome in PICO framework).

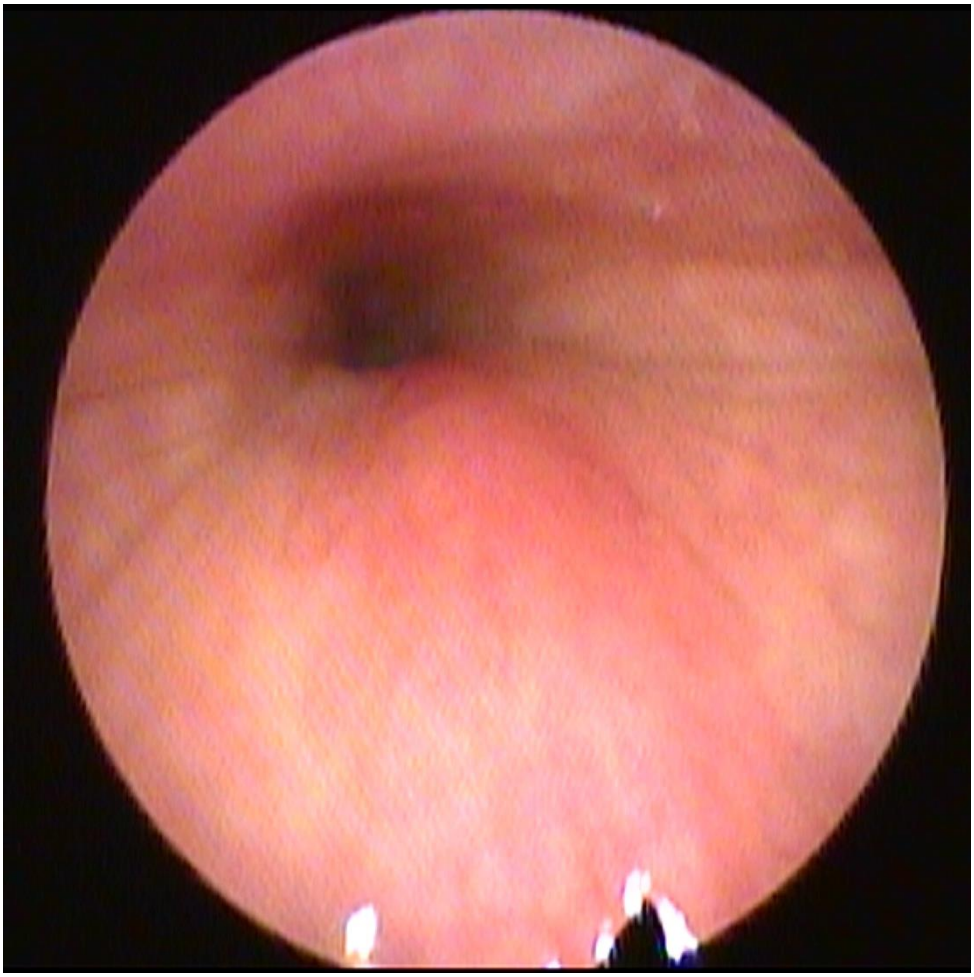
There is a strong interest for further standardization of the scoring and exploration of the predictive value of this evolving technique. DISE (intervention in PICO framework) has the advantage of being easily accessible in most ENT practices, and being 3-dimensional, dynamic, site-specific, safe and without disadvantages such as radiation and costs that come with imaging such as computer tomography (CT) or magnetic resonance image (MRI) scan (comparison in PICO framework), respectively. However, the ENT surgeon performing DISE must bear in mind that DISE is a snapshot of the upper airway during a drug-induced episode of sedation mimicking natural sleep, and, therefore,

administration of drugs should be kept to a minimum, including the avoidance of decongestants, anti-secretory drugs or others [6]. As for the general drug regimen for DISE, the evaluation of the role of dexmedetomidine should be further clarified, to balance the (dis)advantages of dexmedetomidine (pro: more stable sedation based on cardiorespiratory parameters; con: possible inadequate upper airway collapse, less reliable in achieving adequate sedation) and those of propofol (pro: more reliable in achieving target depth of sedation, faster onset of action and shorter half-life; con: causes more respiratory depression, higher risk of more severe airway obstruction requiring intervention).

Efforts towards a universal standardised scoring system applied in sleep centres where DISE is performed on a regular basis are made, but have not resulted in a world-wide consensus yet [37]. There also remains an urgent need for controlled prospective studies to consolidate the role of DISE and temper any uncritically use in institutions that rely on positive reimbursement criteria.

Once these research goals are properly addressed, comparison of results on patient selection and treatment outcome will be easier, ideally adding to an improved standard of care for OSA patients who are eligible for non-PAP treatment.

Figure 1



Complete circular collapse at the level of the palate

5. Appendix

N/A

6. Supplementary Material

N/A

7. Statements

7.1. Acknowledgement

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7.2. Statement of Ethics

The authors have no ethical conflicts to disclose.

7.3. Disclosure Statement

Any financial interests (stocks, patents, employment, honoraria, or royalties) or nonfinancial relationships (political, personal, or professional) that may be interpreted as having influenced the writing of the manuscript must be declared in the Disclosure Statement.

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after submission, an explanation and a signed statement of agreement confirming the requested change are required from all the initially listed authors and from the author to be removed or added.

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All authors contributed substantially and fulfilled the following criteria:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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