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Review

Drug-induced sleep endoscopy: A new gold standard for evaluating OSAS? Part I: Technique

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ABSTRACT

Surgical results in obstructive sleep apnea syndrome (OSAS) vary greatly, whatever the surgical technique or site treated. Most authors agree that rigorous patient selection is logical and mandatory. Drug-induced sleep endoscopy (DISE) was introduced in 1991 and has been rediscovered and used extensively since the 2000s. It mimics sleep in order to observe the upper airway on flexible endoscopy. A review of the DISE literature was performed, and is reported in two parts. The present first part describes the technique: drugs, practical anesthesiologic and ENT modalities, reproducibility, and limitations.

1. Introduction

Obstructive sleep apnea syndrome (OSAS) affects 2–4% of adults in Western countries [1]. Continuous positive airway pressure (CPAP) is the gold-standard treatment in severe OSAS. In case of intolerance to CPAP or of moderate OSAS, alternative treatment, by surgery or dental appliance, is required, success depending on dynamic airway morphology during sleep.

Precise location of the obstruction site or sites (soft palate, lateral pharyngeal wall, tonsils, tongue base and/or epiglottis) is essential to achieving satisfactory success rates [2], but is hindered by the indeterminate number of sites and by the fact that exploration is performed in awake subjects. Several methods have been described: clinical examination by flexible endoscopy with or without Müller's maneuver [3], acoustic pharyngometry, or imaging by lateral cranial teleradiography, CT or MRI. All show limitations, particularly due to their not being performed during sleep.

Poor initial patient selection certainly goes some way to explaining the less-than-perfect results obtained with dental appliance and surgical techniques other than bimaxillary advancement which manages the upper airways globally.

The 2005 Cochrane Database Systematic Review of apnea surgery [2] stressed the need for research into tools to target obstruction sites. Dynamic airway study during sleep is a clinical challenge in OSAS.

Drug-induced sleep/sedation endoscopy (DISE) or video sleep nasendoscopy (VSE), first described by Croft and Pringle [4] in 1991, enables exploration during induced sleep. It is relatively quick and simple and can be performed on an outpatient basis, targeting possible obstruction sites [4].

The objective of the present article was to update applications of DISE in adults. The 1st part of the report describes the anesthetic drugs used and details the practical anesthesiologic and ENT modalities, reproducibility, and limitations.

2. drugs

Several anesthetic drugs may be used, alone or in association. Two are particularly widely described: midazolam (Hypnovel®), the first to be used in sleep endoscopy, and propofol (Diprivan®). Others, such as diazepam (Valium®) [5] and dexmedetomidine (alpha-2 agonist) [6,7], are also used, but less widely.

2.1. Pharmacologic properties

2.1.1. Midazolam

Midazolam is a benzodiazepine [8]. It activates chloride channels and induces neuronal depolarization. It enhances cerebral gamma aminobutyric acid (GABA) effects. Onset of action is 2–5 min after intravenous injection. It has the shortest half-life (1.5–3.5 hours) of all benzodiazepines. It is metabolized in the liver via CYP 3A4 isoenzyme and excreted via the kidneys. Given the presence of an active oxidation metabolite, accumulation is possible [9]. It has sedative anxiolytic and respiratory depression

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Table 1
Effects of midazolam diazepam on sleep and respiratory parameters.

	N Subj	AHI	BMI	Dose	Exam time (minutes)	Sleep stage	Respiratory parameters		
							S+	AHI	Sat
Diazepam									
Sadaoka et al. [5]	30 SAS 20 SN	20.1 (AI) ± 21.1	24.5 17.1–34.4	10.3 mg LA+	128	REM ↘	NM	AI ↗ during REM	Comp
Midazolam									
Quinn et al. [15]	54 SN	NM	NM	11.4 mg (5–18) VC			96.2%	NM	NM
Genta et al. [14]	15 OSA	38 ± 22	30 ± 4	2.4 mg (2–4.4) LA = 0	139	↗ N1	NM	NM	NM
Gregorio et al. [8]	25 OSA 15 N	13 (3–35)	28.8 ± 6.6	6.2 mg ± 3.8 LA = 0	41.5 ± 18.9	REM = 0	NM	Comp R = 0.67	Comp R = 0.77
Carrasco et al. [12]	14 OSA 2 SN	16.4 ± 17.2	26.9 ± 2.5	3.75 mg ± 1.4 LA = 0	11.9 ± 4.5	N2 N3 = 0 REM = 0	NM	AHI ↗	Sat ↘

N Subj: number of subjects; SN: snorer; OSA: obstructive sleep apnea; N: normal subject without S/OSA; AHI: apnea-hypopnea index; NM: not measured/mentioned; AI: apnea index; BMI: body-mass index; VC: nasal vasoconstrictor; LA: local nasal anesthesia; N1: sleep; N2: sleep; N3: slow wave sleep; REM: rapid eye-movement sleep; S+: snoring; Sat: blood-oxygen saturation; Min: minimum; Comp: comparable; R: correlation coefficient.

effects. Antagonists exist: notably, flumazenil (Anexate®), which counters the induced respiratory depression and sedation within 1 minute [3].

2.1.2. Propofol

Propofol interacts with the GABA-A benzodiazepine receptor complex [10]. It enhances GABAergic GABA-A receptor action, inhibiting the GABA neurotransmitter. Interaction with GABA-A benzodiazepine receptors also inhibits acetylcholine action, either directly by reduced cholinergic neuron discharge frequency in the frontal cortex and hippocampus, or indirectly by enhancing serotonin action; these regions are more active during arousal and REM sleep [11]. Action onset is almost immediate (< 1 minute) after intravenous injection. Elimination half-life is short: 45–55 minutes. It is metabolized in the liver into an inactive metabolite; there is thus no accumulation. It is excreted in the urine. It has a central respiratory depression effect, induces amnesia, although less than with benzodiazepines, inhibits the swallowing reflex [12] and induces sneezing [13] and low blood pressure. There are no antagonists.

2.2. Action on sleep and respiratory parameters

2.2.1. Midazolam

Various studies compared the macrostructure of natural and midazolam-induced sleep, with conflicting results. Genta et al. [14], studying sleep architecture in apneic patients, found comparable proportions of stages except for stage N1, which was slightly increased under midazolam. Abdullah et al. [3] found a very low rate of REM sleep, whereas Gregorio et al. [8] found none at all under midazolam. The difference may be related to injected dose, as very low-dose midazolam induces sleep comparable to natural patterns, if the polysomnography (PSG) readings were correct.

Comparison of respiratory events gave more consistent results, with good correlation for apnea-hypopnea index (AHI) and minimum oxygen saturation between induced and natural sleep [8]. Quinn et al. reported snoring in induced sleep in almost all snorers [15].

2.2.2. Propofol

Propofol induces sleep equivalent to slow wave sleep (N3) in normal subjects [16] at a target concentration of 1.54 ± 0.23 μg/mL. Rabelo et al. [11,17] compared 1 night's natural sleep, a nap and a propofol-induced sleep of 90–120 minutes in apnea patients and controls. Sleep architecture in the full night's sleep was comparable to that for the natural nap, whereas propofol-induced sleep showed significantly reduced N1 and increased N3 stages, with absence of REM sleep. Regarding respiratory events, AHI and mean oxygen saturation were comparable in induced sleep; only minimum oxygen saturation was lower. Snoring is found in 81.9–100% of snorers and apnea patients [11,15,17–21]. In control subjects, responses vary but most show no snoring in induced sleep [11,17,21]; only Marais reported snoring in induced sleep in baseline non-snorers [18]. All data are exposed in Tables 1 and 2.

2.2.3. Midazolam and propofol in association

There are few studies dedicated to sleep architecture and respiratory parameters in associated midazolam and propofol. Bachar et al. [22] reported that depth of sleep assessed on Bispectral Index Score (BIS) was comparable between natural and induced sleep in snorers and mild OSAS patients.

2.3. Action on pharyngeal muscles and critical closing pressure

The pharyngeal dilator muscles protect the upper airway against collapse induced by the diaphragm, keeping it open by lowering critical closure pressure.

2.3.1. Midazolam

Muscle response to increased airflow resistance under midazolam is conserved in normal subjects [23]. In OSAS patients, critical closing pressure is not higher with Midazolam than in physiological sleep (respectively, −0.97 ± 3.21 versus −0.82 ± −3.44 cm H_2O [$P = 0.663$]) [14] if injection is slow and low dose (mean, 1 mg; range, 0.6–1.2 mg). This was confirmed by Civelek et al., who demonstrated that the pressure generated by the CPAP required to resolve obstruction during 1 night's manual titration was comparable to CPAP titration during sleep endoscopy (8.37 ± 3.84 versus 9.93 ± 4.77 cm H_2O) [24].