

Comparison of genioglossus muscle activity and efficiency of dexmedetomidine or propofol during drug-induced sleep endoscopy in patients with obstructive sleep apnea/hypopnea syndrome

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Abstract. – OBJECTIVE: The purpose of this study is to evaluate the haemodynamic and respiratory effects of dexmedetomidine vs. propofol in patients with OSAHS during the drug-induced sleep endoscopy (DISE), and analyze simultaneously the electromyography of genioglossus muscle.

PATIENTS AND METHODS: We conducted a study on 50 patients with OSAHS; patients were subjected to DISE with simultaneous polygraphic cardiorespiratory measurement and electromyography of genioglossus muscle. Patients undergoing DISE were divided in two groups: in Group A (19 M; 8 W) was administered propofol TCI and in Group B (16 M; 7 W) was administered dexmedetomidine TCI.

RESULTS: In Group A, a mean minimal SpO₂ decreasing of 3.7% ($p=0.000$) and a mean SpO₂ decreasing of 1.6% ($p=0.001$) was noticed, while there was an increase in BP20 of 14.8% ($p=0.000$) and HR20 of 11.1% ($p=0.000$). In Group B, it was showed a decreasing of mean minimal SpO₂ and mean SpO₂ values, about 1.8% ($p=0.000$) and 1.1% ($p=0.009$) respectively, while there was an increase of BP20 and HR20, about 8.7% ($p=0.000$) and 8% ($p=0.002$), respectively. Despite EMG activity comparing spontaneous sleep with propofol-DISE, there is a statistically significant change for the amplitude ($p=0.040$) and an increase of 7.01% for the area under the curve (AUC). Comparing spontaneous sleep with dexmedetomidine-DISE induced one, there is only an increase of 25.87% in the AUC.

CONCLUSIONS: A greater worsening of the cardio-respiratory basal values was noted after sleep induction with Propofol and same results were obtained confronting EMG of genioglossus muscle data.

Key Words

Obstructive sleep apnea hypopnea syndrome, Sleep-disordered breathing, Electromyography of genioglossus muscle, Drug-induced sleep endoscopy, Propofol, Dexmedetomidine.

Introduction

Obstructive Sleep Apnea Hypopnea Syndrome (OSAHS) is a common Sleep-Disordered Breathing (SDB) disease characterized by upper airway constriction and collapse during sleep. It presents intermittent hypoxia with resulting growth of reactive oxygen species/reactive nitrogen species and oxidative stress, which adversely affect the associated cardio/cerebrovascular disease in OSAHS¹⁻⁵. The underlying causes of OSAHS vary among patients^{6,7}. However, anatomically narrow and/or collapsible upper airways are the predominant causes of OSAHS^{6,8}. Its etiology is multifactorial, resulting from the interdependence of structurally vulnerable upper airway anatomy interacting with physiologic mechanism of ventilator instability during sleep. This inability to maintain the patency of the upper airway is attributable to the combination of sleep-related loss, also due to compensatory dilator muscle activity, and aerodynamic forces that can lead to closure⁹. These forces, resulting from the circulation of inspiratory airflow¹⁰ in anatomically predisposed airways, generate negative

intraluminal pressure and play an important role in the pathogenesis of OSAHS. Best muscles to study the upper airways are genioglossus muscles; they are a pair of fanshaped muscles found on either side of the tongue's midline extending from the mandible backward and upward and their function is to dilate the airway pharyngeal exerting a forward propulsion to the tongue. They follow a pattern of ElectroMyoGraphy activity of GenioGlossus muscle (EMGGG), which is typically part of the inspiratory phase. In obstructive sleep apnea, is prominent the evaluation of upper airway obstruction to reach site-specific treatment. Drug-Induced Sleep Endoscopy (DISE) is a diagnostic technique with which sleep is induced pharmacologically and the upper airways is evaluated by nasal endoscopy¹¹⁻¹⁴. It is the only exam that allows a three-dimensional and dynamic visualization of the site responsible for vibration and/or obstruction during apnea, hypopnea, flow limitation or snoring¹⁵. One of the important questions to answer is understanding which sedative drug used during the DISE is better to minimize the negative effects on breathing and muscle activity. Over the years, various sedatives were used to induce pharmacologically sleepiness such as: Propofol, Midazolam and Dexmedetomidine¹⁶. Midazolam used alone has been a while abandoned due to some disadvantages such as more difficulty to handle consequences in case of overdosing and longer hospital stay¹⁷. Propofol and Dexmedetomidine are two drugs proposed as alternatives. Both of them have shorter half-lives and reduced respiratory depression¹⁸⁻²¹. Propofol, with the development of Target-Controlled Infusion (TCI) technology, has increased the number of indications in clinical practice. Propofol-based TCI allows for the accurate control of sedation during DISE and results in an authentic reproduction of the sleep process²²⁻²⁴, but large use of Propofol can depress the hypoxic ventilatory response during conscious sedation^{20,21,25}.

Dexmedetomidine, on the other hand, is a short-acting, highly potent, highly selective α_2 -adrenergic receptor agonist with unique properties of sedation and analgesia. The sedation induced by Dexmedetomidine parallels natural sleep and does not induce significant respiratory depression^{20,21,26}. In this study, we aim to compare the sedatives, haemodynamic and respiratory effects of Dexmedetomidine vs. Propofol in patients with OSAHS during the DISE, and analyze simultaneously the genioglossus muscle activity through the ElectroMyoGraphy (EMG).

Patients and Methods

Patient Selection

Our study was conducted on 50 patients (35 men; 15 women) in American Society of Anesthesiologists (ASA) status I-II, aged between 40-65 years old (mean age: 52.48 SD 6.78; 48 1.5 in men and 55.23 1.3 in women) and mean Body Mass Index (BMI) 27.87 0.57 kg/m². We have considered OSAHS diagnosed by polygraphic cardiorespiratory system with an Apnea-Hypopnea Index (AHI) score between $\geq 5 > 30$ events per hour (mean AHI 23.62, SD 4.27) and the obstruction sites screened by Drug-Induced Sleep Endoscopy (DISE) using the Nose Oropharynx Hypopharynx and Larynx (NOHL) classification²⁷. We excluded patients < 40 years old and older than 65 years, drug or alcohol abusers or those having history of chronic analgesic use, patients who known to have allergy against the study drugs, patients that would represent a higher risk for sedation (severe chronic obstructive pulmonary disease, previous acute myocardial infarction, decompensated congestive heart failure, and others), BMI > 30 kg/m² and patients with psychiatric disorders. All OSAHS patients underwent to polygraphic cardiorespiratory recording in spontaneous sleep. Subsequently these patients were subjected to DISE. EMGGG with simultaneous polygraphic cardiorespiratory measurement was instead carried out in 20 patients both in spontaneous sleep and during DISE. Patients undergoing the EMGGG were divided in two subgroups: subgroup A1 (6 M; 4 F) was administered Propofol (B. Braun Milan SpA, Milan, Italy) TCI and in subgroup B1 (7 M; 3 W) was administered dexmedetomidine (Orion Pharma S.r.l. Milan, Italy) TCI.

Sleep Study

The Polygraph System Embletta MPR System (Sapio Life S.r.l. Monza, Italy) (including Embletta MPR-PG and TX Proxy), according to the American Academy of Sleep Medicine standards (AASM 2012), allows monitoring of polygraph cardiorespiratory (level III). The Embletta MPR-PG can records the following channels: inducance plethysmography of the chest and abdomen, nasal cannula, pulse oximetry (oxygen saturation and heart rate), snoring through frequency environmental microphone, snoring derived by nasal cannula, thermistor oro-nasal, 1 DC input to acquire signals from external equipment, triaxial sensor integrated position, integrated actigraphy. The TX Proxy module allows the acquisition of

the signals coming from Embletta MPR-PG for their Real-time display. Embletta MPR-PG is connected via wireless to the TX Proxy, which transmits the information to the Personal Computer via LAN (Local Area Network). Both of these applications through the acquisition of a video signal (USB video card) can acquire and display Real-time the video of the sleep endoscopy (Figure 1). Apnea was defined as a significant decrease (>90%) in oronasal flow for at least 10 s. Hypopnea was defined as an airflow decrease of 30% of pre-event baseline for at least 10 s with $\geq 3\%$ oxygen desaturation from the baseline and/or an arousal. OSAHS severity was based on the Apnea and Hypopnea events/hour (AHI, Apnea/Hypopnea Index) and was graded as mild (AHI: 5 to 15 events/h), moderate (AHI: 15 to 30 events/h), or severe (AHI >30 events/h)²⁸.

DISE Protocol

Once a sufficient sedation was reached with Propofol or Dexmedetomidine, obtaining Bispectral Index Score (BIS™ monitoring, Medtronic Parkway, MN, USA) level between 50 and 70, we proceed with the DISE. To perform the DISE, we used a nasofibroscope of 4 mm, an Olympus (Tokyo, Japan) light source and camera. The flexible endoscope was introduced into the nasal cavity providing sequentially a detailed visualization of the nasopharynx, the retropalatal region, the oropharynx, the palatine veil, tongue base and epiglottis. Propofol was administered to group A with a brain concentration of 2.0 ng/mL, which was increased by 0.3 ng/mL every 2 minutes^{17,19}. Dexmedetomidine was administered to group B

at a dose of 1 ng/kg for 10 minutes, followed by a dexmedetomidine infusion at a rate of 1 ng/kg/hour^{29,30}. The blood concentration of propofol or dexmedetomidine was increased incrementally every 2 minutes until the desired depth of sleep was reached. Heart Rate (HR), Blood pressure (BP), Peripheral Oxygen Saturation (SpO₂), Ramsey Sedation Scores (RSS) to evaluate precisely the level of consciousness during titration of sedative medications, and BIS values were recorded when the patients arrived to the recovery room (Time 0: T0) at 5 minute intervals. Sufficient sedation was determined as the duration between the initiation of the drug infusion and the time the time when RSS:4 and BIS <75 (light sleep: 65 to 75; deep sleep: 50 to 60)^{31,32} values were obtained. Patients were evaluated in the drug-induced sleep state for approximately 10 to 15 minutes. The DISE findings were characterized using the NOHL classification²⁷, which evaluates grade and patterns of upper airways collapse.

Electromyography of Genioglossus Muscle

Electromyography of genioglossus muscle begins with a standardized local anaesthesia with lidocaine spray (Ogna and Figli S.r.l.-Muggiò-Monza Brianza, Italy); then, after 1 min, the needle is inserted into the right edge of the anterior third of the tongue to a depth of about 20 mm and fixed manually by reining. Patients need to anteflect their head, not to swallow and leave their mouth open during the procedure (saliva running out is wiped away.) To assess spontaneous activity, subjects need to attempt retracting the tongue.

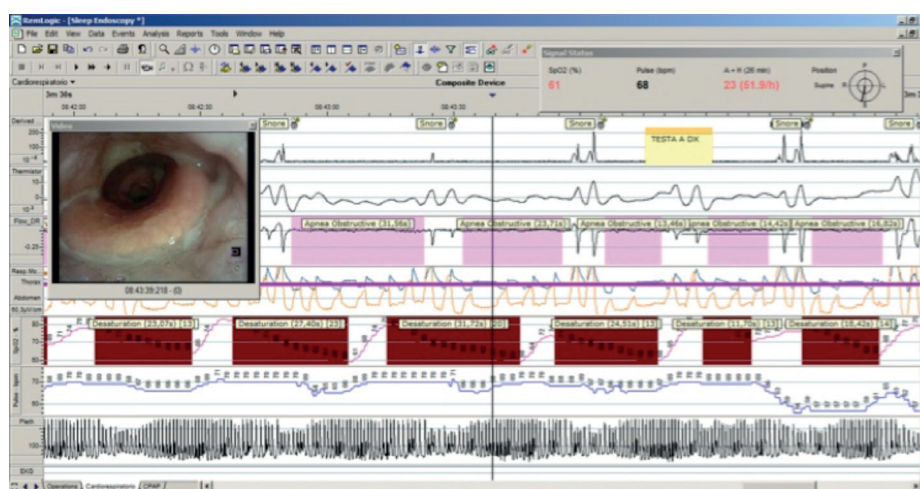


Figure 1. Sleep endoscopy paired to the polygraphic track.

Furthermore, subjects were told to protrude the tongue until single recordings could be differentiated, to record latency, amplitude and area under the curve (AUC), the needle was withdrawn for at least 2-3 mm between the two sites. Next, subjects were told to press the tongue to the left against the investigator's index finger to increase force continuously from zero to maximum within about 10 s. The EMGs were recorded via standard concentric needle electrodes (length 25 or 50 mm, recording surface: 0.07 mm²) by means of a commercially available EMG recorder (Dantec™ Keypoint, Alpine Biomed ApS-Skovlunde, Denmark).

Statistical Analysis

Continuous variables are summarized as mean \pm SD. Categorical variables are summarized as frequencies and percentages. Variables were compared between patients with propofol-DISE and dexmedetomidine – DISE by independent *t*-test. A *p*-value < 0.05 was considered statistically significant.

Results

There is no statistical difference between the two groups data (Table I) within the basal activity (spontaneous sleep) and in the obstruction sites (Table II). The group A had nose, oropharynx, hypopharynx and larynx obstruction in 48.1%, 62.9%, 88.8% and 25.9%, respectively; the group B had the same sites of obstruction in 34.7%, 82.6%, 86.9% and 21.7%, respectively (Figure 2). Despite EMG activity, comparing spontaneous sleep with propofol-induced sleep in subgroup A1, there is a statistically significant

change only for the amplitude ($p=0.040$), but not for latency (Table III); an increase of 7.01% was observed for the (AUC). In subgroup B1 there aren't statistically significant alterations comparing spontaneous sleep with Dexmedetomidine induced one, but only an increase of 25.87% in the AUC (Table IV). After Propofol administration, it was noticed an evident worsening of respiratory values (minimal SpO₂ and mean SpO₂), blood pressure and heart rate statistically significant (Figure 3). In Group A, after sleep induction with Propofol, a mean minimal SpO₂ decreasing of 3.7% ($p=0.000$) and a mean SpO₂ decreasing of 1.6% ($p=0.001$) was noticed, while there was an increase in BP20 14.8% ($p=0.000$) and HR20 11.1% ($p=0.000$) values. Group B, on the other hand, after administration of Dexmedetomidine for sleep induction, showed a decreasing of mean minimal SpO₂ and mean SpO₂ values, about 1.8% ($p=0.000$) and about 1.1% ($p=0.009$) respectively, while there was an increase of BP20 e HR20, about 8.7% ($p=0.000$) and 8% ($p=0.002$), respectively.

Discussion

Over the past years there were many debates about which was the best sedative to perform the sleep endoscopy. Some studies^{20,29,30,33} have compared the two drugs (Propofol and Dexmedetomidine) relying on the sedative, hemodynamic and respiratory effects, but none of these one compared the drugs according to the muscle responsiveness. Most of the reseraches^{21,34} identified dexmedetomidine as a pharmacological agent more stable and secure based upon cardiopulmonary status.

Table I. Baseline characteristics of obstructive sleep apnea patients who underwent drug-induced sleep endoscopy by drug (N = 50).

Characteristic	Group A (n = 27)	Group B (n = 23)	<i>p</i> -value
Male n (%)	19 (70.3%)	16 (69%)	
Female n (%)	8 (29.7%)	7 (31%)	
Age	52.14 \pm 7.2	52.34 \pm 6.09	0.9170
Body mass index, kg/m ²	27.31 \pm 1.35 [23.9-29.6]	26.99 \pm 1.27 [24.7-29.2]	0.3926
ODI, events/h	22.02 \pm 4 [15-28]	23.21 \pm 4.55 [15-30]	0.3329
AHI, events/h	23.28 \pm 4.2 [16.7-29]	24.01 \pm 4.42 [16.2- 29.6]	0.5498
Nadir SaO ₂ , %	86.84 \pm 1.55 [84-90.1]	87.01 \pm 1.28 [84.6-89]	0.6880
T < 90%	5.39 \pm 2.15 [2.4-10.9]	6.17 \pm 2.18 [2.6-10.9]	0.2123
Mean oxygen saturation	95.84 \pm 1.33	95.95 \pm 1.39	0.7743

AHI: apnea-hypopnea index; ODI: oxygen desaturation index; Nadir SaO₂: minimal oxygen saturation; T < 90% = percentage of the total time with oxygen saturation level < 90%; mean oxygen saturation. *Values are given as mean \pm SD [range] or number (%) of subjects.

Table II. Classification NOHL. NOHL Classification findings of upper airway obstruction in propofol and dexmedetomidine-Based drug-induced sleep endoscopies.

Obstruction sites	Propofol - DISE (n = 27)							Dexmedetomidine - DISE (n = 23)							p-value		
	Degree ^a				Pattern ^b			Degree ^a				Pattern ^b					
	1	2	3	4	AP	Tr	C	1	2	3	4	AP	Tr	C			
Nose	2 (7.4)	9 (33.3)	2 (7.4)					5 (21.7)	3 (13)								0.609
Oropharynx		4 (14.8)	8 (29.6)	5 (18.5)	10 (37)	3 (11.1)	4 (14.8)		7 (30.4)	9 (39.1)	3 (13)	8 (34.7)	5 (21.7)	6 (26)			0.854
Hypopharynx	2 (7.4)	6 (22.2)	10 (37)	6 (22.2)	12 (44.4)	5 (18.5)	7 (26)		5 (21.7)	12 (52.1)	3 (13)	10 (43.4)	4 (17.3)	6 (26)			0.752
Larynx ^c	-		20 (74)					-		18 (78.3)							
	+		7 (26)					+		5 (21.7)							
Palatine tonsillar hypertrophy grade ^d	-		10 (37)					-		13 (56.5)							
	+		17 (63)					+		10 (43.5)							

^aDegree of obstruction: 1: 0–25% / 2: 25–50% / 3: 50–75% / 4: 75–100%
^bConfiguration: anteroposterior (AP); Transversal (Tr); Concentric (C)
^cLarynx Obstruction: Absent (-) or Present (+)
^dPalatine tonsillar hypertrophy grade III e IV: Absent (-) or Present (+)

Due to greater obstruction leading to worsening apneas, hypopneas and oxygen desaturation, some studies present a compelling argument for its use during DISE and this observation may be more precise about the airway obstruction that occurs during sleep. In our study we have noticed heart rate and respiratory rate worsening both with propofol and dexmedetomidine compared to basal data; nevertheless, this worsening was more evident after Propofol sedation. The same results were obtained confronting EMG data before and

after administration with both pharmacologic agents. Comparing EMG data and cardio-respiratory data with DISE gives these results: during DISE with sleep pharmacological induction by propofol and dexmedetomidine we have noticed respiratory depression (oxygen average saturation decrease, minimum oxygen level decrease) and both frequency and heart pressure alteration; moreover appeared a simultaneous EMG activity reduction in genioglossus muscle, although it was more evident after propofol administration.

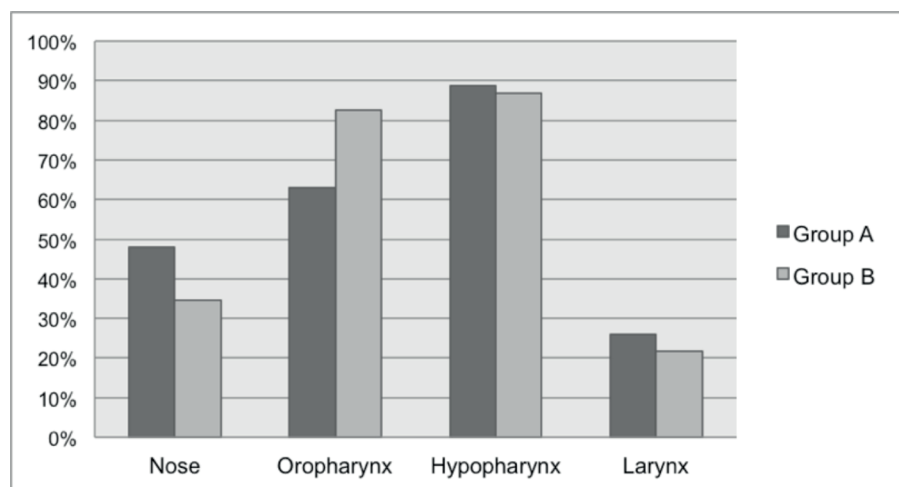


Figure 2. Percentages of obstruction sites during propofol - DISE and dexmedetomidine - DISE.

Table III. EMGGG activity of subgroup A1 in spontaneous sleep vs. propofol during DISE.

Parameters		Spontaneous sleep	Propofol	<i>t</i>	<i>p</i> -value
Latency (ms)	Lat 1	124	122	0.037	0.9721
	Lat 1-2	1404	1442		
	Lat 2	1528	1564		
Amplitude (µV)	Amp 1	44.2	2.81	2.997	0.040
	Amp 1-2	31.3	0.37		
	Amp 2	12.9	3.17		
AUC (µVms)	Area 1-2	2.1535	1511		

Table IV. EMGGG activity of subgroup B1 in spontaneous sleep vs. dexmedetomidine during DISE.

Parameters		Spontaneous sleep	Dexmedetomidine	<i>t</i>	<i>p</i> -value
Latency (ms)	Lat 1	4200	11800	0.0261	0.980
	Lat 1-2	149800	139600		
	Lat 2	154000	151400		
Amplitude (µV)	Amp 1	104	14.0	1.7184	0.160
	Amp 1-2	5.00	7.08		
	Amp 2	10.9	21.1		
AUC (µVms)	Area 1-2	42046	10880		

After Dexmedetodine administration we expected bradycardia due to a decrease in noradrenaline release, a decrease in centrally mediated sympathetic tone, and an increase in vagal activity³⁵. However, as observed by Arain et al³⁶, Al-Mustafa et al³⁷ and Mahmoud et al³⁸, dexmedetomidine could have rebound effect with the postsynaptic vascular smooth muscle to cause vasoconstriction and it is possible that the sympathoinhibitory effects of dexmedetomidine were slightly opposed by direct α -2 mediated vasoconstriction.

Conclusions

Both dexmedetomidine and propofol have their advantages during DISE. While generally dexmedetomidine is preferred because it provides a more stable profile based upon cardiopulmonary status, propofol for its part has a quicker onset and a shorter half-life. Based on the premise that this is a pilot study, there are significant limits. One of the limits about this study is not administering both groups with both sedative, but execut-

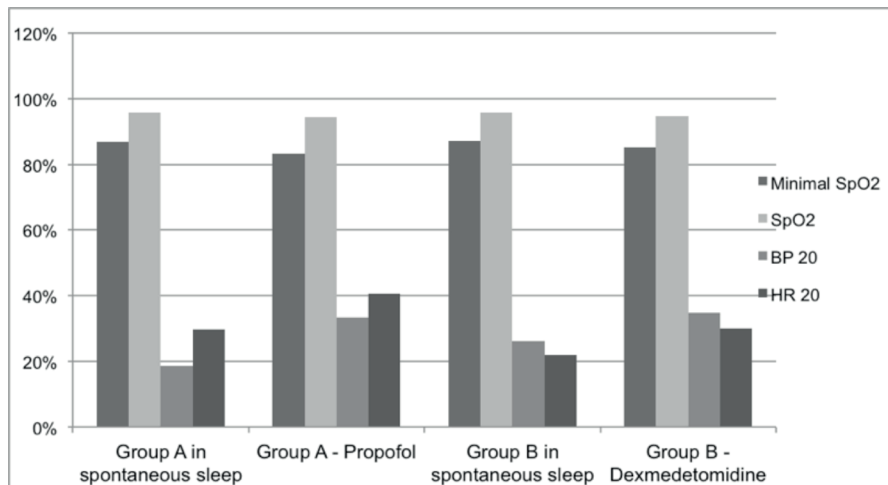


Figure 3. Cardio respiratory values in group A and group B before and after sedation.

ing EMGGG to all patients in spontaneous sleep before DISE results in objective data to compare about real action of these sedatives. Another limit is the modest number of subjects administrated with EMGGG, so is auspicious to increase this number in future studies.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Conflict of Interests

The authors declare that they have no conflict of interest.

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