IMPACT OF UPPER AIRWAY SENSORY DYSFUNCTION ON RESPIRATORY EVENTS DURING SLEEP IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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ABSTRACT

Objective*: To assess the influence of upper airway sensory dysfunction on the respiratory events during sleep in patients with obstructive sleep apnea syndrome (OSAS).*

Methods*: Our study was performed over 30 patients with OSAS. The patients underwent a second night polisomnography (PSG) after bupivacaine application to uvula and soft palate and the outcomes of both PSG results were compared.*

Results*: In PSG-2, the mean Apnea-hypopnea index (AHI), AHI-supine, AHI-right lateral, AHI-REM and AHI-nonREM values were significantly higher than the same data acquired in PSG-1 ($p<0.001$, $p=0.001$, $p<0.001$, $p<0.001$, and $p=0.001$, respectively). In PSG-2, mean and minimum arterial O2 saturation were significantly lower compared to PSG-1 ($p=0.021$ and $p=0.039$, respectively). The correlation analysis of PSG-2 showed that AHI-nonREM and AHI-supine are more effected from the sensorial blockade.*

Conclusion*: Our study showed that, when the protective neuromuscular mechanism is removed by upper airway sensory blockage, the severity of OSAS increases. Upper airway sensorial blockade more influentially effects respiratory events in supine position and in non-REM phase.*

Key words*: Obstructive sleep apnea, oropharyngeal anesthesia, sensory function, polysomnography.*

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Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent upper airway (UA) obstruction episodes and blood oxygen desaturation during sleep[(1)]. In epidemiological studies conducted, the frequency of OSAS is cited as between 0.8 and 4 %[(1,2)]. It is known that there are sensorial mechanoreceptors in the UA that are sensitive to air pressure, airflow speeds, heat and muscle tone. A neuromuscular reflex arc is believed to exist between the afferent stimuli originating from these sensorial receptors and UA dilator muscle activity[(2,3)]. In some studies conducted in obstructive sleep apnea (OSA) patients while awake, palatal two point discrimination, tactile sense and heat sense were found to diminish significantly compared to healthy subjects[(2-5)]. In addition, numerous histopathological evidences show sensorial failure in UA of OSA patients[(6-10)].Whereas the role in OSA pathophysiology and outcomes for respiratory events played by the deficiency in UA sensory function is still unclear.

Bupivacaine is a long acting (mean 6-8 hours/effect duration) local anesthetic that performs specific sensory blockade and does not effect the motor function with executing 0.25% and not exceeding 25 mg dose ranges[(11-13)]. In our study, we have attempted to explore the impact of bupivacaine blockade of afferent sensorial nerve ends over soft palate and uvula,on respiratory events during sleep, in patients with OSA.

Materials and methods

Study Group: This prospective clinical study was carried out on 30 volunteer OSA patients at the Ankara Atatürk Chest Disease and Chest Surgery Training and Research Hospital, Sleep Disorders Laboratory after obtaining informed consent, with

the permission of Erciyes University Clinical Trials Ethics Committee. Patients with Apnea-Hypopnea Index in the range of 5-30, between the ages of 18 and 65 years and having a body mass index (BMI) below 30 were included in the study. Patients with chronic cardiovascular or neurologic diseases, diabetes mellitus, a history of allergic reaction in procedures with local anesthesia, a history of surgery due to OSAS and positive airway pressure (PAP) treatment, active UA infection or excessive retching reflex were excluded.

Soft palate sensorial blockade: Patients underwent a second night of polysomnography (PSG) within 7 days of the initial PSG. Before the second PSG, following the insertion of electrodes in the sleep laboratory, patients, in the sitting position, were injected in three points of the soft palate with 3 cc 0.25% bupivacaine (1 cc in each of the three points) with a 22 gauge dental injector (Figure 1). Following bupivacaine application, patients were sent to sleeping rooms for the second PSG.

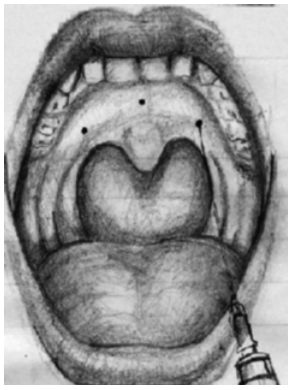

Figure 1: The points of bupivacaine injection before second night polysomnography.

Polysomnography

All patients were advised to keep their ordinary standard activities and to give up alcohol and sedative drugs in the test day. Standard entire night polysomnographic examinations in all patients applied using Compudemics Voyager Digital Imaging. Polysomnography were encompassing of electrocardiogram, four electroencephalography channels, bipolar surface electromyograms for submental and anterior tibial muscles and position sensors recording body positions and motions. Nasal and oral airway measurements, pulse oximeter, a tracheal microphone, thoracic and abdominal respiratory efforts and synchronical video were used to respiratory monitoring. Apnea was defined as a complete cessation of airflow for at least 10 s. Hypopnea was defined as a decrease in airflow of at least 50 %, accompanied by 4 % desaturation and a reduction in chest wall movement and/or arousal. AHI was defined as the number of apneas and hypopneas per hour of sleep. Sleep staging was performed according to the standard criteria set by the American Academy of Sleep Medicine (Mild OSAS: AHI=5-15, Moderate OSAS: AHI=15-30, Severe OSAS:AHI>30)[14].

Statistical analysis

Polisomnographic data were compared from the first and second polisomnographies (PSG-1 and PSG-2). Apart from definitive statistical methods in the evaluation of data (mean values and standard deviation), distributions were also derived. In the comparisons of both PSGs, Wilcoxon sign test was applied. In both cohort comparisons, Mann-Whitney U test was used. In the test of variables, Pearson correlation analysis was implemented. A significance level of 0.05 was used.

Results

Mean age of the 30 patients was 48.2. 18 patients were male and 12 were female. Mean body mass index was 25.1. When the polisomnographic data were compared from the first and second polisomnographies, total sleep time was found to be significantly low in the second tests ($p=0.016$). There was no significant difference between the two tests in terms of sleep efficiency and REM ratio (REM phase sleep time/complete sleep time) ($p=0.29$. $p=0.751$, respectively).

In PSG-2, the mean AHI, AHI-supine, AHI-right lateral, AHI-REM and AHI-nonREM values were significantly high compared to PSG-1 ($p<0.001$, $p=0.001$, $p<0.001$, $p<0.001$, and $p=0.001$, respectively). Average PSG-1 and PSG-2 values compared with respect to sleep positions and sleep phases are presented in table 1.

A significant increase was found in PSG-2 in terms of total hypopnea and mixed apnea numbers ($p<0.001$, $p=0.006$, respectively). However, total apnea, central apnea and obstructive apnea numbers did not increase significantly ($p=0.214$, $p=0.229$, $p=0.319$, respectively). Mean apnea durations and longest apnea durations were significantly higher in PSG-2 ($p=0.022$ and $p=0.034$, respectively). The correlation analysis of PSG-2 in terms of sleep phase and sleep position shown that AHI- nonREM and AHI-supine are more effected from the sensori-

al blockade (table 2). In PSG-2, mean and minimum arterial O2 saturation were significantly lower compared to PSG-1 (p=0.021 and p=0.039, respectively).

	n	Mean ± SD	Min.	Max.	Median	z	p
AHI-1	30	15,8 ± 7,3	1,0	32,0	15,6	-4,1	0,000*
AHI-2	30	31,8 ± 17,3	4,8	67,7	30,6		
AHI- left 1	30	9,5 ± 23,3	0,0	120,0	0,0	-1,0	0,338
AHI- left 2	30	11,6 ± 18,4	0,0	90,0	4,1		
AHI- right 1	30	7,5 ± 8,4	0,0	23,7	5,5	-3,6	0,000*
AHI- right 2	30	20,1 ± 14,5	0,0	62,3	18,6		
AHI- supine 1	30	15,6 ± 12,1	0,0	36,3	16,6	-3,5	0,001*
AHI- supine 2	30	36,9 ± 27,2	0,0	84,3	42,6		
AHI- prone 1	30	5,3 ± 7,5	0,0	20,0	0,0	-0,4	0,670
AHI- prone 2	30	7,5 ± 15,3	0,0	46,0	0,0		
AHI-REM 1	30	22,5 ± 13,5	0,0	47,6	23,9	-3,8	0,000*
AHI-REM 2	30	47,0 ± 33,8	0,0	120,0	36,0		
AHI- nonREM 1	30	13,9 ± 7,4	0,4	26,1	13,8	-3,3	0,001*
AHI-nonREM 2	30	25,0 ± 16,6	3,3	67,3	21,0		

Table 1: Comparison of mean apnea-hypopnea index (AHI) in terms of sleep phases and sleep positions among the two sleep studies (AHI-REM, AHI-nonREM: mean apnea-hypopnea index in the REM and nonREM phases of the sleep; AHI-supine, prone, left and right: mean apnea-hypopnea index in the diffirent sleep positions, *statistically significant).

Pearson Correlation Test		
		AHI1-AHI2
AHI-REM1 - AHI-REM2	R	0,685
	p	0,090
	N	30
AHI-nonREM1 - AHI-nonREM2	r	0,716
	p	0,000*
	N	30
AHI-supine1 - AHI-supine2	r	0,586
	p	0,001*
	N	30
AHI-left 1 - AHI-left 2	r	0,315
	p	0,090
	N	30
AHI-right 1 - AHI-right 2	r	0,563
	p	0,001
	N	30
AHI-prone 1 - AHI-prone 2	r	0,381
	p	0,038
	N	30

Table 2: Correlation of apnea-hypopnea index differentiation in the two sleep studies with sleep phase and position (AHI-REM, AHI-nonREM: mean apnea-hypopnea index in the REM and nonREM phases of the sleep; AHI-supine, prone, left and right: mean apnea-hypopnea index in the different sleep positions, *statistically significant)

Discussion

Numerous studies have mentioned the role of UA sensory dysfunction in OSA pathophysiology[2-17]. Our study was organized to determine the effect of palatal sensory dysfunction on respiratory events during sleep in patients with OSA in a homogenous group with respect to age, gender, BMI and AHI. In the second polysomnography, which was performed after the bupivacaine injection, the total sleep time decreased significantly. We think that this result is due to the patients' sensation of disturbance related to local and hesitation feeling in throat. However, the insignificant variation between sleep efficiency and REM ratios in our study enabled us to compare respiratory parameter variations in both tests more reliably. Our findings reveal the fact that soft palate and uvula sensory blockade without motor blockade reinforced airway collapse during sleep.

Disrupted UA sensory function in OSA cases has been investigated in numerous studies. Larsson et al.[17] reported defects in the oropharynx's heat sensitivity and Sunnergren et al.[18] in the soft palate's cold sense perception in patients with OSAS. Kimoffet al.[2] and Guilleminaut et al.[3] determined remarkable defects in palatal two points discriminations in OSAS patients.These studies affirm the fact that deformation in vibration related to snoring or deformations in UA features may lead to sensory neuropathy. There are also histopathological evidences that show UA sensory dysfunction in OSAS[6-9].

Friberget al.[6] showed mucosal neurogenic disease and an increase of variable nerve ends in mucosal epithelium in oropharyngeal mucosal biopsy of OSA patients. Woodson et al.[7] diagnosed focal degeneration in myelin threads in OSAS patients in the investigation of uvulopalatopharyngoplasty specimens with electron microscopy. Those lesions are held responsible for the delay of arousal response to apnea in OSAS. Many authors think that snoring is responsible for those histologic modifications. Furthermore, some data proves that there are apnea termination enabling soft palatal mucosal sensor receptors exist[6-8,19]. Axon degeneration in afferent neurons and deregulation in segmental demyelination may lead to impulse transmittance and related sensory failure.

In our study, sensory failure led to similar outcomes, and the intensity of the disease revealed significant expansion. In some studies, sensory failure that did not show any variation in snoring or OSAS

patients and that loss failing to show any correlation with apnea intensity, make us think that palatal mucosa sensory failure is encountered in the early phase and may be held responsible for obstructions[8-10]. UA's destruction of the mucosal sense may be an early response to sleep obstruction progression, because of neural damage in apneas or vibration related edema. In awake OSAS patients, air flow in UA respiratory stimulants and negative pressure feedback alleviations hasled to great and quick lowering of pharyngeal dilatator muscle activation and imaged by tonic and phasic genioglossus electromyography[20-21]. This leads to the fact that local airway stimulants may activate dilatators pharyngeal muscle.

There have been few studies with small study groups investigating the impact of upper airway anesthesia on the sleep disorder, and there is no recent study on this subject[11-15]. Topical anesthesia was preferred in these limited studies (bupivacaine+lidocaine gargle and spray forms). In those forms, applied anesthetics fail to create the desired sensory blockage, and their effects are restrained to the initial hours of sleep. In this case it causes failures in measuring the sensory blockage outcome over the REM phase, which is dominant, especially in the latest phases of sleep. In topical anesthesia, applied by gargle and spray forms, only mucosal receptors are blocked while sensory fiber, lying between submucosal and muscle fiber are not blocked.

In our study, bupivacaine, which is the drug effective for the longest period, is selected, and specific sensory blockage executing 0.25% and not exceeding 25 mg dose ranges are preferred, which does not effect motor function[11-13]. Deegan et al.(15) performed a second PSG on 6 OSAS patients following topical oropharyngeal anesthesia (TOPA), and the mean AHI increased from 21.2 to 25.2. This difference was not significant. This result may be because of the small study group and the use of topical anesthesia. Mc Nicholas et al.[22] applied a control PSG, a PSG with nasal topical anesthesia, and TOPA, carried out three nights on healthy individuals. They reported no significant difference between the PSG outcomes of the nasal topical anesthesia and control PSG; however, there was a significant increase in the severity of OSAS in the TOPA group. They also reported that the disease in the REM phase was more influenced by sensory anesthesia, but they failed to evidence the mechanisms further to its possible cause.

In our study, AHI-nonREM was found to be much more influenced by sensory nerve blockage compared to AHI-REM. This finding may be explained by partial paralysis emerging in the REM phase respiratory muscles leading to alleviation in reflex dilatators muscle response to apnea and hypopneas. Furthermore, they diagnosed that the effects of TOPA is contained to a few hours of sleep, so that in the first half of the sleep study, apnea/hypopnea intensification is more remarkable. DeWeese et al.[23] demonstrated increased inspiratory flow rates after TOPA during the sleep non-REM phase. In our study, having non-REM phase much more influenced from UA sensory blockage supports the validity of methods conducted by DeWeese et al. In wakefulness, failure of sensory blockage, causing the same outcomes, refers to the fact that during the wakeful phase, impact of local mechanoreceptors on stabilization of pharynx remains minimal. Chadwick et al.[19] reported a significant increase in AHI and desaturation indexes during second PSGs following TOPA on 8 non-apnea patients. Their findings are parallel with our results, which indicate that UA sensory anesthesia postpones apnea end arousals elongates apnea duration, and in response to negative pressure, destructs the emerging genioslossus dilatator response.

A limitation of our study is the lack of a control group by the injection of saline. However, we think that a PSG with saline injection to the soft palate may influence the PSG-1 results at a low degree, related to local and hesitation feeling in throat. We think that UA sensory afferent data not only prevents apnea formation but is also seen to have a role in the course of ending formed hypopnea and apneas. At the same time, the only mechanism ending apnea formation is not neuromuscular reflex. During apnea, formed hypoxemia and hypercapnia have also important effects. In our study, diagnosing a significant increase in oxygen desaturation index motivates us to consider the fact that the initial mechanism in ending apneas is the neuromuscular reflex. Hypoxemia and hypercapnia, when reached to a certain level, secondary central mechanism creates its effect[24]. In addition to this, our study showed that supine position is more effected by sensory blockade, and intensification, with regard to intensity and duration, in supine position seems more significant compared to other sleep positions.

Conclusion

Our study showed that, when the protective neuromuscular mechanism is eliminated by upper airway sensory blockage, the severity of OSA increases. UA sensorial blockade more influentially effects respiratory events in supine position and in non-REM phase. Further studies are required to show whether sensory neuropathy is a cause or a result in patients with OSA.

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