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Original Article

Factors associated with the required level of positive airway pressure in patients with obstructive sleep apnea syndrome

Suleyman Emre Karakurt, Kursat Murat Ozcan, Muge Ozcan, Mehmet Fatih Karakus, Serdar Ensari, Haci Huseyin Dere

Clinic of Otorhinolaryngology, Ankara Numune Training and Research Hospital, Ankara, Turkey

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Abstract

Aim: To investigate the factors associated with the required level of positive airway pressure as determined by continuous positive airway pressure titration in patients with obstructive sleep apnea syndrome (OSAS).

Materials and Methods: A total of 87 OSAS patients were included in the study. The patients were assigned to two groups (low-pressure and high-pressure) based on the positive airway pressure level they required. The groups were compared with respect to baseline clinical characteristics, Muller maneuver findings and polysomnography findings.

Results: There were 54 patients in the low-pressure group and 33 patients in the high-pressure group. No significant differences were found between low-pressure and high-pressure groups in terms of mean age, mean body mass index and gender distribution ($p>0.05$). A statistically significant higher rate of two level obstruction was found in the high-pressure group than in the low-pressure group ($p=0.004$). Comparison of the groups with respect to polysomnography findings showed mean apnea-hypopnea index (AHI) values of 42.88±26.63 and 54.16±31.29, mean rapid eye movement (REM)-AHI values of 37.38±30.72 and 58.21±26.09 and mean supine-AHI values of 66.04±32.98 and 64.03±31.15 in the low-pressure group versus high-pressure group, respectively. The mean AHI and supine-AHI values were not significantly different between the groups ($p>0.05$) but the high-pressure group showed a significantly greater mean REM-AHI in comparison to low-pressure group ($p=0.002$).

Conclusion: The number of obstruction levels determined by Muller maneuver and REM-AHI appear to be the prominent factors affecting the positive airway pressure level required in OSAS patients.

Keywords: CPAP ventilation; polysomnography; sleep apnea

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a disorder characterized by repeated episodes of partial or complete obstruction of upper airway during sleep (1). OSAS has a multifactorial etiology and a prevalence of 2-4% among males and 1-2% among females (2). Snoring, daytime sleepiness and impaired cognitive performance are only a few clinical symptoms that results in diminished quality of life in OSAS. When left untreated, OSAS may lead to life-threatening conditions including cardiovascular and cerebrovascular complications.

The treatment of OSAS can be broadly divided into two categories: surgical interventions and non-surgical treatments (3). Surgical interventions include nasal surgery, palate surgery, hypopharyngeal surgery and orthognathic surgery and non-surgical treatments mainly consist of positive airway pressure (PAP) treatment, positional therapy and intraoral appliances. While newer therapeutic options have been introduced for the management of OSAS over the years, PAP therapy remains the most effective treatment modality (4). Before initiation of PAP treatment, a titration procedure is performed to determine the optimal positive airway pressure required to control respiratory events for the patient and then, PAP treatment is given at the selected pressure value. The pressure determined at the titration study is subject to inter-individual variability. The pathologies causing obstruction of the upper airway such as nasal septum deviation and concha hypertrophy are known to be associated with greater pressure requirement during titration. However, it is still unknown why patients without obstructed airways require different pressure levels. This may be related to many factors including individual differences in upper airway characteristics among patients and the severity of the disease. Thus, the current study aimed to investigate the factors associated with the required PAP levels in OSAS patients.

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Corresponding Author: Suleyman Emre Karakurt, Clinic of Otorhinolaryngology, Ankara Numune Training and Research Hospital, Ankara, Turkey **E-mail:** suleymanemrekarakurt@gmail.com

MATERIALS and METHODS

Ethical approval for the study was obtained from the institutional review board (Number: E-19-086, December 12, 2019). Each patient was informed about the study and signed informed consent. A retrospective review was conducted on data from patients diagnosed with OSAS who underwent polysomnography and titration of continuous positive airway pressure (CPAP) at our clinic between January 2017 and March 2019. Age, sex, body mass index (BMI), panendoscopic otolaryngological examination findings, Muller maneuver findings and polysomnographic data that form the basis of OSAS diagnosis were recorded for all patients.

Muller maneuver was performed using a flexible nasal endoscope. The endoscope was passed through the nasal space into the nasopharynx and then the soft palate. At this point, the patient was asked to close his mouth and his nostrils were plugged. Subsequently, he was asked to inhale with a maximum effort. During maximal inspiration, the degrees of antero-posterior and lateral obstruction at the soft palate level were recorded as percentage. Then, the endoscope was advanced to the hypopharynx. The same maneuver was repeated at this level and the degrees of antero-posterior and lateral obstruction were recorded as percentage. A 50% or greater obstruction at the palatal level detected by Muller maneuver in at least one of the antero-posterior and lateral palatal planes was noted as palatal level obstruction. Similarly, a 50% or greater obstruction detected in at least one of the antero-posterior and lateral hypopharyngeal planes was noted as hypopharyngeal level obstruction. Then, patients with obstruction in the soft palate or hypopharynx were considered as having one level of obstruction and patients with both palatal and hypopharyngeal obstruction were noted as having two levels of obstruction.

The study included patients of both sexes, aged 18 years or older. Another study inclusion criterion was related to the findings of Muller maneuver. As such, patients with 50% or greater narrowing in at least one of the antero-posterior and lateral palatal or antero-posterior and lateral hypopharyngeal planes were included in the study. Patients with nasal, nasopharyngeal, oropharyngeal or hypopharyngeal pathology that led to narrowing of the upper airways, patients with concomitant lung disease, patients whose respiratory events could not be controlled with CPAP titration and patients with a sleep efficiency of less than 60% as detected by CPAP titration were excluded. Patients were divided into two groups as low-pressure group (≤9 cmH2O) and high-pressure group (≥10 cm H2O) based on the pressure level detected by CPAP titration that prevented 95% of the nocturnal respiratory events. The study groups were compared with respect to age, percentage distribution of sex, BMI, percentage distribution of the number of obstruction levels (one or two), apnea-hypopnea index (AHI), rapid eye movement (REM)-AHI and supine-AHI.

Polysomnography was conducted overnight under the supervision of a sleep technician using the Alice 5 PSG device (Philips Respironics, Best, The Netherlands) for all patients. Data on electroencephalogram, electromyogram (submental and tibialis anterior), electrooculogram, nasal air flow, respiratory effort (chest and abdomen), blood oxygen saturation (by pulse oximetry) and body position were recorded. Scoring was performed manually by an otorhinolaryngologist with a polysomnography certificate and expert knowledge on sleep disorders and using the criteria established by the American Academy of Sleep Medicine. The AHI of 5–15 indicated mild OSAS, the AHI of 15–30 indicated moderate OSAS and the AHI of >30 indicated severe OSAS.

Shapiro-Wilk test was used to analyze the distribution of the data. Continuous variables were presented with mean and standard deviation and number and percentage was used to express categorical variables. Categorical variables were assessed using the chi-square test. The t-test or Mann-Whitney U test was used to test the differences between means from independent groups. A p value less than 0.05 was considered statistically significant. The SPSS statistical software (SPSS for Windows version 21.0; SPSS Inc., Chicago, IL) was used for statistical analyses.

RESULTS

A total of 87 patients including 22 (25.2%) females and 65 (74.8 %) males met the study inclusion criteria. The mean age of the study group was 49.19 ± 10.22. Among the patients, 61 (70.1%) had severe OSAS (AHI≥30/h), 20 (22.9 %) had moderate OSAS (AHI=15-29) and 6 (7%) had mild OSAS (Table 1).

Table 1. Characteristics of the study group

Age (years)	49.19±10.22
Sex	
Female	22 (25.2 %)
Male	65 (74.8 %)
Disease Severity	
Severe OSAS	61 (70.1 %)
Moderate OSAS	20 (22.9 %)
MildOSAS	6 (7%)

Values are presented as mean with standard deviation or number with percentage

There were 54 patients in the low-pressure group and 33 patients in high-pressure group. The mean age was 50.22±10.50 and 47.51±9.66 years in low- and high-pressure groups, respectively and no significant difference was observed between the groups (p=0.233) (Table 2). The low-pressure group consisted of 15 (27.8%) females and 39 (72.2%) males and the high-pressure group comprised 7 (21.2%) females and 26 (78.8%) males. The percentage distribution of sex between the groups was not significantly different (p=0.494) (Table 2). The mean BMI was 31.04±5.26 kg/m^2 in patients in the low-pressure group and 33.27±8.17 kg/m^2 in patients in the high-pressure group, with a non-significant difference between groups (p=0.154) (Table 2). In the low-pressure group, 30 (55.6%) patients had one level obstruction and 24 (44.4%) had two level obstruction, whereas in the high-pressure group, 8 (24.2%) patients had one level obstruction and 25 (75.8%) patients had two level obstruction (Table 2). The number and percentage of patients with two level obstruction were significantly greater in the high- pressure group versus the low-pressure group (p=0.004) (Table 2).

Table 2. Basic clinical characteristics and obstruction levels of the groups

	Low-Pressure Group (n=54)	High-Pressure Group (n=33)	P Value
Age (years)	50.22±10.50	47.51±9.66	0.233
Sex			
Female	15 (27.8 %)	7 (21.2 %)	0.494
Male	39 (72.2 %)	26 (78.8 %)	
BMI (kg/m^2)	31.04±5.26	33.27±8.17	0.154
Obstruction Level n (%)			
One Level	30 (55.6%)	8 (24.2%)	0.004
Two Level	24 (44.4%)	25 (75.8%)	

Values are presented mean with standard deviation or number with percentage. BMI, body mass index

Comparing the polysomnography findings between low- and high-pressure groups showed a non-significant difference in mean AHI (42.88±26.63 versus 54.16±31.29, respectively; p=0.082) and supine-AHI (66.04±32.98 versus 64.03±31.15, respectively (p= 0.694) (Table 3). The mean REM-AHI values were 37.38±30.72 and 58.21±26.09 in the low- and high-pressure groups, respectively (Table 3). Patients in the high-pressure group had a significantly higher mean REM-AHI value in comparison to patients in the low-pressure group (p=0.002) (Table 3).

Table 3. Polysomnography findings of the groups

	Low-Pressure Group	High-Pressure Group	P Value
AHI	42.88±26.63	54.16±31.29	0.082
REM-AHI	37.38±30.72	58.21±26.09	0.002
Supine-AHI	66.04±32.98	64.03±31.15	0.694

Values are presented as mean with standard deviation. AHI, apnea-hypopnea index

DISCUSSION

In the present study, two level obstruction detected by Muller maneuver was greater in patients requiring a high level of pressure based on CPAP titration than in patients in the low-pressure group. Comparison of polysomnography findings between the groups showed higher REM-AHI values in patients in the high-pressure group than in low-pressure group.

CPAP therapy is still recognized as the gold standard treatment of OSAS (5). However, compliance with therapy is a major issue which makes it difficult or even impossible for patients to continue CPAP therapy over the long-term. In a study exploring the factors predicting CPAP adherence in OSAS, greater pressure requirement was associated with better adherence (6). Consistently, the pressure level was cited as one of the factors that could help predict CPAP compliance in a separate study (7). Therefore, it is possible that the factors associated with the required level of PAP may also affect adherence to PAP therapy.

Aging is associated with an increased risk for the development of OSAS (8,9). Although the exact mechanism involved in this process has not been elucidated, age-related changes in pharyngeal collapsibility and increased size of parapharyngeal fat tissue were implicated as possible causes (10). Thus, aging may lead to changes in the upper airway mechanics. The required PAP level may vary according to the upper airway mechanics in OSAS patients. Considering the impact of aging on pharyngeal mechanics, it is likely that age can affect the required PAP level. In our study, no age difference was found between patients in low-pressure and high-pressure groups. This finding suggests that age does not result in substantial changes in pharyngeal mechanics enough to affect the required level of PAP.

Gender and BMI might be factors that could potentially affect upper airway characteristics in OSAS. Women and men have a different pattern of body fat distribution. While men have more fat deposits in the upper body, women have relatively more adipose tissue in thighs and hips (11-13). Different body fat distribution may account for differences in the amount of fat pads in the upper pharyngeal region and therefore, differences in upper airway characteristics between males and females. In this context, the effects of gender and BMI on the required PAP level were also examined in the present study and no gender- or BMI-based difference was found between low- and high-pressure groups. This result suggests that upper pharyngeal fat volume and distribution related to obesity and gender do not have a significant impact on the required PAP level.

The Muller maneuver is an established technique to demonstrate the site of obstruction in patients with OSAS (14). There are mixed views on the value of this maneuver with some studies advocating its benefits and the opposite findings reported by others (15-17). Muller maneuver has received criticism for being subjective because of potential variations between individuals in its interpretation. Different observers are likely to interpret the percentage of obstruction at a given level differently. In order to overcome this subjectivity, 50% or greater narrowing at any level was considered significant.

It was suggested that since the Muller maneuver is performed on an awake patient, it may not fully reveal the obstructed site during sleep (16). When the degree of pharyngeal obstruction in the retroglossal region during the

Muller maneuver was compared versus nasal endoscopy under induced sleep, more retroglossal obstruction was detected with sleep endoscopy than the Muller maneuver (18). Although sleep endoscopy has a potential to demonstrate the level of obstruction during sleep more accurately, concerns have been raised about its success in mimicking natural sleep. In addition, this procedure is more difficult to perform than the Muller maneuver. The Muller maneuver has been a part of routine practice due to its success in detecting the level of obstruction and the severity of disease with no additional cost.

Obstruction of the upper airways may result in the occurrence of respiratory events in OSAS. The negative pressure generated in the upper airways during inspiration causes obstruction in OSAS patients but not in normal individuals. Thus, upper airway characteristics differ between normal individuals and OSAS patients. The factors affecting the collapsing tendency of the upper airways in OSAS may include the activity of upper airway dilator muscles and muscle tone (19). The aim of applying positive pressure during PAP therapy is to prevent the collapse of the upper airways and potential respiratory events. However, the level of positive airway pressure required to prevent respiratory events varies from patient to patient. Thus, it can be considered that each OSAS patient may have distinct upper airway characteristics. The negative pressure generated in the upper airways during Muller maneuver may potentially demonstrate the level at which the muscle groups tend to collapse. In our study, there were more patients with two level obstructions (palatal + hypopharyngeal) in the high-pressure group than in the low-pressure group. Therefore, greater amount of pressure would be needed to prevent two level obstructions. At the same time, these findings suggest that the number of obstruction levels detected by the Muller maneuver is correlated with the required PAP level.

Respiratory events occur during both the non-REM and REM phases of sleep. The non-REM phase takes up the largest portion of sleep cycle. The REM sleep represents about 20% of the total sleep time and is more concentrated in the second half of sleep time (20). Inhibition of the hypoglossal nerve mediated by the cholinergic system during REM sleep causes decreased tone of the genioglossus muscle and increased collapsibility of the upper airways (21,22). We found greater REM-AHI values in the group requiring higher levels of pressure but AHI and supine-AHI values were not different between the groups. Thus, patients in the high-pressure group were more likely to experience respiratory events specifically during the REM phase. Considering the increased collapsibility of the upper airways during REM sleep, this finding suggest that greater collapsing tendency is associated with a greater pressure requirement.

CONCLUSION

The number of obstruction levels determined by Muller maneuver and REM-AHI appear to be the prominent factors affecting the positive airway pressure level required in OSAS patients. We hope that our study findings inspire future research on the physiopathological mechanisms that influence the determination of pressure requirements in OSAS patients.

Competing Interests: The authors declare that they have no competing interest.

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Ethical Approval: Ankara Numune Training and Research Hospital Clinical Research Ethics Committee (Number: E-19-086).

REFERENCES

1. Lakadamyali H, Kivanc T, Yilmaz Avci A. Correlation of changes in the red blood cell distribution width with the response to continuous positive airway pressure in patients with obstructive sleep apnea. Sleep Biol Rhythms 2019;17:141-8.
2. Maspero C, Giannini L, Galbiati G, et al. Obstructive sleep apnea syndrome: a literature review. Minerva Stomatol 2015;64:97-109.
3. Tingting X, Danming Y, Xin C. Non-surgical treatment of obstructive sleep apnea syndrome. Eur Arch Otorhinolaryngol 2018;275:335-46.
4. Karakurt SE, Karakus MF, Eravcı FC, et al. Evaluation of the relationship between the required pressure level in continuous positive airway pressure treatment and voice in patients with obstructive sleep apnea syndrome. J Voice 2019.
5. Inoue A, Chiba S, Matsuura K, et al. Nasal function and CPAP compliance. Auris Nasus Larynx 2019;46:548-58.
6. Riachy M, Najem S, Iskandar M, et al. Factors predicting CPAP adherence in obstructive sleep apnea syndrome. Sleep Breath 2017;21:295-302.
7. Nadal N, de Batlle J, Barbé F, et al. Predictors of CPAP compliance in different clinical settings: primary care versus sleep unit. Sleep Breath 2018;22:157-63.
8. Shahar E, Redline S, Young T, et al. Hormone replacement therapy and sleep-disordered breathing. Am J Respir Crit Care Med 2003;167:1186-92.
9. Dancey DR, Hanly PJ, Soong C, et al. Impact of menopause on the prevalence and severity of sleep apnea. Chest 2001;120:151-5.
10. Eikermann M, Jordan AS, Chamberlin NL, et al. The influence of aging on pharyngeal collapsibility during sleep. Chest 2007;131:1702-9.
11. Horner RL, Mohiaddin RH, Lowell DG, et al. Sites and sizes of fat deposits around the pharynx in obese patients with obstructive sleep apnea and weight matched controls. Eur Respir J 1989;2:613-22.
12. Bixler EO, Vgontzas AN, Lin HM, et al. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med 2001;163:608-13.
13. Hoffstein V, Mateika S. Differences in abdominal and neck circumferences in patients with and without obstructive sleep apnoea. Eur Respir J 1992;5:377-81.
14. Borowiecki BD, Sassin JF. Surgical treatment of sleep apnea. Arch Otolaryngol 1983;109:508-12.

15. Kim HY, Bok KH, Dhong HJ, et al. The correlation between pharyngeal narrowing and the severity of sleep-disordered breathing. Otolaryngol Head Neck Surg 2008;138:289-93.
16. Friedman M, Tanyeri H, La Rosa M, et al. Clinical predictors of obstructive sleep apnea. Laryngoscope 1999;109:1901-7.
17. Ozdas T, Ozcan KM, Ozdogan F, et al. Investigation of lateral pharyngeal walls in OSAS. Eur Arch Otorhinolaryngol 2013;270:767-71.
18. Gregorio MG, Jacomelli M, Figueiredo AC, et al. Evaluation of airway obstruction by nasopharyngoscopy: comparison of the Muller maneuver versus induced sleep. Rev Bras Otorrinolaringol 2007;73:618-22.
19. Lévy P, Kohler M, McNicholas WT, et al. Obstructive sleep apnoea syndrome. Nat Rev Dis Primers 2015;25;1:15015.
20. Koo DL, Kim HR, Nam H. Moderate to severe obstructive sleep apnea during REM sleep as a predictor of metabolic syndrome in a Korean population. Sleep Breath. 2020.
21. Grace KP, Hughes SW, Horner RL. Identification of the mechanism mediating genioglossus muscle suppression in REM sleep. Am J Respir Crit Care Med 2013;187:311-9.
22. McSharry DG, Saboisky JP, Deyoung P, et al. Physiological mechanisms of upper airway hypotonia during REM sleep. Sleep 2014;37:561-9.