RESEARCH ARTICLE / *Araştırma Makalesi*

Factors Affecting Optimal Continuous Positive Airway Pressure Level in Patients with Obstructive Sleep Apnea Syndrome

Obstrüktif Uyku Apne Sendromlu Hastalarda Optimal Sürekli Pozitif Havayolu Basınç Düzeyini Etkileyen Faktörler

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Geliş Tarihi / Received : **21.01.2020** Kabul Tarihi / Accepted : **06.03.2020**

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(Sakarya Med J / *Sakarya Tıp Dergisi* 2020, 10(1):99-106) Doi: 1031832678074

Abstract

Objective	This study aimed to examine factors (BMI, neck circumference, AHI etc.) affecting optimal CPAP levels in patients with obstructive sleep apnea syndrome (OSAS).
Materials and Methods	A total of 120 patients with OSAS who underwent successful auto-titration for CPAP treatment were included in this study. Correlations between the optimal CPAP level and baseline data were analyzed.
Results	The mean optimal pressure level in the 120 OSAS patients was 9.11 ± 2.81 cm H2O. The mean optimal pressure levels in the mild, moderate, and severe OSAS groups were 8.01 ± 2.60, 8.32 ± 2.22, and 9.71 ± 3.01 cm H2O, respectively. Apnea/hypopnea index (AHI) (r=0.297, p<0.001) and minimal SaO2 (r=-0.264, p<0.004) were significantly correlated with optimal pressure level. 22 patients in the titration failure group had severe AHI overall; 6 patients had REM-related and 2 had position-related OSAS. Patients in the titration failure group who did not have a specific diagnosis (rapid eye movement (REM) or positional OSAS) had very severe AHI levels (mean AHI of 67.90).
Conclusions	According to the correlation tests, AHI and the lowest saturation were the two most important predictors of optimal CPAP level.
Keywords	Obstructive sleep apnea syndrome; Continuous positive airway pressure; Polysomnography; Apnea

Öz

Amaç	*Bu çalışmada obstrüktif uyku apne sendromu (OUAS) olan hastalarda optimal CPAP düzeylerini etkileyen faktörlerin (VKİ, boyun çevresi, AHİ vb.) araştırılılması amaçlandı.*
Gereç ve Yöntemler	*Bu çalışmaya CPAP tedavisi için başarılı oto titrasyon uygulanan 120 OUAS hastası dahil edildi. Optimal CPAP seviyesi ile başlangıç verileri arasındaki korelasyonlar analiz edildi.*
Bulgular	*120 OUAS hastasında ortalama optimal basınç seviyesi 9.11 ± 2.81 cm H2O idi. Hafif, orta ve şiddetli OUAS gruplarında ortalama optimal basınç seviyeleri sırasıyla 8.01 ± 2.60, 8.32 ± 2.22 ve 9.71 ± 3.01 cm H2O idi. Apne / hipopne indeksi (AHI) (r = 0.297, p <0.001) ve minimal SaO2 (r = -0.264, p <0.004) optimal basınç seviyesi ile anlamlı korelasyon gösterdi. Titrasyon yetmezliği grubundaki 22 hastada genel olarak ağır AHI vardı; 6 hastada REM ilişkili, 2 hastada pozisyona bağlı OUAS mevcuttu. Titrasyon yetmezliği grubunda, belirli bir tanısı (hızlı göz hareketi (REM) veya pozisyon OUAS) bulunmayan hastalarda çok ciddi AHI düzeyleri vardı (ortalama AHI 67.90 idi).*
Sonuç	*Korelasyon testlerine göre optimal CPAP seviyesinin en önemli iki belirleyicisi AHI ve en düşük saturasyon olarak bulundu.*
Anahtar Kelimeler	*Obstrüktif uyku apne sendromu; Sürekli pozitif havayolu basıncı; Apne; Polisomnografi*

Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by collapse of the upper airway during sleep, recurring apnea, intermittent hypoxemia, and daytime sleepiness, and associated with decreased daytime performance and impaired quality of life.[1]

OSAS is a common sleep-breathing disorder that is estimated at least between 9% and 25% in the general population, and most patients are not aware of their illness.[2] Even asymptomatic OSAS is known to be associated with increased morbidity and mortality.[3] Patients undergoing surgery also have a high prevalence in OSAS and it is known that there is an increase in postoperative complications compared to general population.[4,5] It is possible to suspect from OSAS with preoperative osas screening surveys conducted in the anesthesia outpatient clinic. These patients would benefit from sleep medicine referral, expedited polysomnography (PSG), and continuous positive airway pressure (CPAP) treatment.[6]

Positive airway pressure (PAP) is a standard treatment for patients with OSAS. Three titration methods are used to determine the mean optimal pressure level: full-night, split-night, and auto-titrating positive airway pressure (APAP). Of these, full-night, attended titration with PSG is the gold standard for the determination of an optimal CPAP level.[7] Although the preferred method in a sleep laboratory is full-night manual titration, APAP titration may be performed to identify optimal CPAP levels for patients with moderate to severe OSAS who do not have additional diseases (e.g., chronic obstructive pulmonary disease, or hypoventilation syndrome).[8]

Accredited centers' protocols and procedures described for PAP titration vary widely among accredited centers' protocols.[9,10] Several factors have been identified as potentially affecting optimal pressure, such as amount of rapid eye movement (REM) sleep, length of the soft palate, and degree of respiratory effort.[11,12] Additionally, one might reason that the level of optimal PAP is correlated with OSAS severity and/or obesity; i.e. higher levels of PAP would be needed to control respiratory events in patients with severe OSA and/or those who are morbidly obese.

Although some studies have shown a good correlation between optimal CPAP levels and the apnea/hypopnea index (AHI) or obesity, this opinion has not been consistently supported in the literature.[13,14] A significant correlation for optimal CPAP and AHI has been observed only in patients whose sleep apnea is dependent on body position.[15] If the patient is uncomfortable or intolerant of high pressures on CPAP, or if there are continued obstructive respiratory events at 15 cm H2O of CPAP during the titration study, CPAP may be switched to Bilevel Positive Airway Pressure (BPAP).[16]

Various predictive formulas for optimal CPAP levels have been developed in several countries and for populations of different geographical origin.[17,18,19] The optimal CPAP level as determined using a predictive equation may improve the success rate of manual titration and increase the simplicity of treatments such as self-titration of CPAP or APAP.[20,21]. With this in mind, the objectives of the present study were: 1) to determine the mean optimal CPAP level according to the severity of OSAS; and 2) to examine the factors that influence the optimal CPAP level in patients with OSAS.

Materials and Methods

Subjects

All patients who were referred to the chest service and anesthesia outpatient clinic for preoperative preparation diagnosed with OSAS using the AHI with a standard polysomnographic test (≥15 on the Epworth Sleepiness Scale) who reported snoring, apnea, or daytime sleepiness, and who underwent successful manual titration for CPAP treatment between June 2017 and June 2018, were included in the cross-sectional descriptive study after Yuzuncu Yil University's Faculty of Medicine Review Board

(17.01.2020 – 2020 / 01-03) approved the study. Records of consecutive 120 patients were extracted from hospital registry.

Patients were selected consecutively. Demographic and health behavior–related data, including age, sex, body mass index (BMI), Epworth Sleepiness Scale scores, and medical histories regarding sleep habits and cardiovascular disease were collected from patient records. Mild, moderate, and severe OSAS for adults was defined as 5≤AHI<15, 15≤AHI<30, and AHI≥30, respectively.[22] Neck circumference (cm) was measured at the level just below the most prominent portion of the thyroid cartilage (Adam's apple).

Polysomnography and CPAP titration

Overnight polysomnography was performed with 16-channel Embla (Medcare Inc, Reykjavik, Iceland) continuous sleep technician monitoring. The system consists of 4 channels of EEG (with electrode placements at C4-A1, C3-A2, O2-A1, and O1-A2), 2 channels of EOG, submental EMG, oronasal air flow, thoracic and abdominal movements, pulse-oximetry oxygen saturation, tibial EMG, body position detector, an electrocardiogram, and tracheal sound. Apnea was defined as the complete cessation of airflow lasting more than 10 seconds. Hypopnea was defined as a >30% reduction in airflow lasting more than 10 seconds accompanied by >4% desaturation and/or arousal. The average number of episodes of apnea and hypopnea per hour of sleep were measured as AHI. The diagnosis of OSAS was made on the basis of AHI >5.

Sleep stages were scored following standard criteria with 30-second epochs and reviewed and verified by a certified sleep physician. The optimal pressure level was defined as the lowest effective pressure that brought most respiratory disturbances under control (including apnea, hypopnea, and snoring) for all body positions (especially in the supine position during REM sleep) and in all stages. Auto-titration was performed with the same PSG recording montage to determine the optimal pressure level for CPAP treatment.

Statistical analysis

Statistical analyses were performed using SPSS software version 20 (IBM; Armonk, New York, USA). Continuous data are expressed as means ± standard deviation (SD). Statistical comparisons were performed using a one-way analysis of variance (ANOVA) and chi-square test. Pearson's correlation coefficients were calculated to separately determine the relationships between these variables in each group, Overall AHI in patient whose symptoms were controlled or not controlled by their titration regimens (referred to as the failure and success groups, respectively) was assessed and used in the separating cut-off value for receiver operating characteristic (ROC) analysis. A p value <0.050 was considered statistically significant.

Results

The anthropometric and polysomnographic variables according to the severity of OSAS are shown in Table 1. The mean optimal pressure level in the 120 OSAS patients was 9.11±2.81 cm H2O. The mean optimal pressure levels in the mild, moderate, and severe OSAS groups were 8.01 ± 2.60, 8.32 ± 2.22, and 9.71 ± 3.01 cm H2O, respectively. The titration failure group consisted of patients who were uncomfortable because of the high pressure and in whom respiratory obstruction continued to cause events at 15 cm H2O of CPAP; this group was switched to BPAP. Anthropometric and polysomnographic variables in the failure and success groups are shown in Table 2. Anthropometric and polysomnographic variables in the failure group are shown in detail in Table 3. The roc curve for AHI in the failure group is shown in Figure 1.

Table 4 presents the correlations among the 120 patients between the baseline variables (including demographic and polysomnographic data) and the optimal pressure level for CPAP treatment. AHI (r=0.297, p<0.001) and minimal SaO2 (r=-0.264, p<0.004) were significantly correlated with optimal pressure level.

Table 1 Anthropometric and polysomonographic variables according to the severity of OSAS

		Mild (n=18)	Moderate (n=31)	Severe (n=71)	Total (n=120)
Anthropometric variables	Age: years ± SD	49.30±9.10	50.31±11.61	49.11±11.61	49.50±11.20
	Sex (n) (male:female)	12:6	22:9	58:13	92:28
	Neck circumference (cm± SD)	37.92±3.41	37.51±2.81	39.60±3.32	38.80±3.31
	Body mass index (kg/m2± SD)	33.11±6.72	32.00±5.32	33.11±5.51	32.80±5.61
Polysomnographic variables	Mean optimal CPAP (range± SD)	8.01±2.61	8.31±2.21	9.70±3.01	9.10±2.80
	AHI overall (events/hour of TST± SD))	10.51±3.01	21.76±4.55	60.80±26.37	43.11±29.71
	Minimal SaO2 (%± SD)(at first PSG)	77.53±12.47	74.18±11.41	69.30±10.91	71.80±11.61
	Desaturation time (sec± SD) under %90 SaO2	50.36±74.93	86.29±92.94	110.01±121.32	95.01±110.11
	Minimal SaO2 (%± SD))(at titration)	82.06±10.51	82.1±10.11	83.04±7.82	82.67±8.82
	Desaturation time (sec± SD)(at titration) under %90 SaO2	30.84±49.22	43.06±65.09	39.02±61.35	38.80±60.31

Values are given as the mean ± SD
Abbreviations: CPAP, continuous positive airway pressure; OSAS, obstructive sleep apnea syndrome; TST: total sleep time; AHI: apnea-hypopnea index.

Table 2- Antropometric and polysomnographic variables in successful and failure titration group

	Successful (n=98)	Failure(n=22)	P value
Age: years ± SD	49.90±10.80	47.33±12.54	0.320
Body mass index (kg/m^2± SD)	32.56±5.90	34.21±4.25	0.220
Neck circumference(cm± SD)	38.83±3.34	38.90±3.61	0.880
AHI overall (events/hour of TST± SD))	39.76±28.01	58.43±32.82	0.007
Mean pressure	8.09±1.86	13.81±1.41	0.001
Minimal SaO2 (%± SD)(at first PSG)	73.30±11,00	65.10±12.32	0.003
AHI(events/hour of TST± SD) attitration	5.43±9.76	8.84±12.22	0.160
Minimal SaO_2 (%± SD) (at titration)	83.03±8.62	81.05±9.71	0.344

Values are given as the mean ± SD
Abbreviations: TST, total sleep time; AHI, apnea-hypopnea index; PSG, Polysomnography

22 patients in the titration failure group had severe AHI overall; 6 patients had REM-related and 2 had position-related OSAS. Patients in the failure group who did not have a specific diagnosis (rapid eye movement (REM) or positional OSAS) had very severe AHI levels (mean AHI of 67.90).

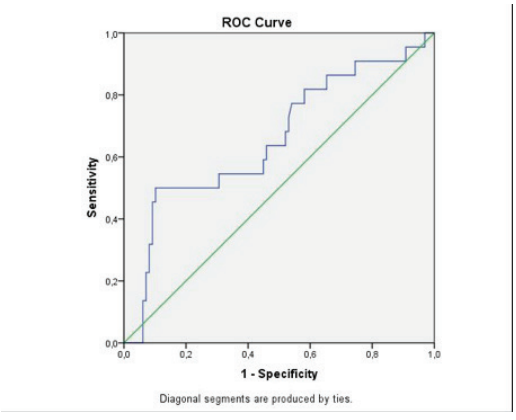

Figure 1: The roc curve for AHI in the failure group

Table 3- Anthropometric and polysomnographic variables in the failure group are shown in detail.

	Age: years ± SD	Body mass index (kg/m2± SD)	gender	Diagnosis (m,m,s)	Special diagnosis	Effective pressure	AHI overall (events/hour of TST)	AHI(events/hour of TST) at titration	Minimal SaO2 (%) (at first PSG)	Desaturation time(sec) under %90 SaO_2	Minimal SaO2 (%) (at titration)	Desaturation time(sec) (at titration)under %90 SaO_2
1	36	37,10	F	Sev re	rem related	12,61	99.00	15,62	50	44,40	65	74
2	52	35,20	M	Severe	rem related	14,61	37,63	5,62	61	107	79	75
3	68	42,21	F	Severe	rem related	13,72	36,55	8.00	65	51	81	179
4	59	41.00	F	Severe	rem related	12.00	71,31	17.00	71	129	85	7
5	40	32,32	M	Severe		12,74	80,20	8.00	61	44	80	1
6	42	30,71	M	Mild	Position related	12,36	33,45	0,55	84	20	90	0
7	45	33,11	M	Severe		15,28	81.09	5,67	66	16	84	2,55
8	32	31,26	M	Severe		15.00	98.04	6,23	61	32,33	84	1
9	32	28,45	M	Severe	Position related	14,73	46.00	0,67	82	6,73	90	0
10	63	43.00	F	Severe		17,57	95.00	0,74	55	341	80	21
11	62	31,31	F	Moder-ate	rem related	12,20	50,53	0,74	53	231	74	199
12	53	32,70	M	Severe		14.00	70,53	0.00	69	55	90	0
13	41	37,24	M	Severe		14.00	88,93	43,77	68	365	83	0
14	49	36,28	F	Moder-ate	rem related	15,35	32,89	0.00	78	23	89	0
15	53	30,15	M	Severe		13,12	78,74	0.00	75	33	90	0
16	72	34,43	F	Moder-ate		12,92	47.98	6,67	50	278	63	156
17	28	36,39	M	Severe		13,73	99,25	23,37	51	246	52	59
18	33	26,31	M	Mild	Position related	15.00	53,51	37,62	90	0	87	0
19	32	32,76	M	Severe		12,91	80,51	0,95	50	243	83	12,52
20	45	35,78	M	Severe		16.00	88,66	13,71	80	16,93	86	0
21	53	31,12	M	Severe		13,32	91,87	0,63	62	144	83	13
22	52	34,42	M	Severe		11,85	30,79	0.00	51	4	85	0

Values are given as the mean ± SD
Abbreviations: TST, total sleep time; AHI, apnea-hypopnea index; PSG, Polysomnography; F, female; M, male

Table 4- Relationship between optimal CPAP level and baseline variables in 120 patients with OSAS

		OSAS (n=120)	Correlation coefficient (r)	P value
Anthropometric variables	Age: years ± SD	49.52±11.26	-0.022	0.811
	Body mass index (kg/m^2± SD)	32.84±5.12	0.037	0.689
	Neck circumference(cm± SD)	38.87±3.31	0.130	0.159
Polysomnographic variables	AHI overall (events/hour of TST± SD	43.11±29.71	0.297	0.001
	Minimal SaO_2 (%± SD) (at first PSG)	71.80±11.61	-0.264	0.004
	Minimal SaO_2 (%± SD) (at titration)	82.62±8.81	0.156	0.920

Relationship between optimal CPAP level and baseline variables in 120 patients with OSAS
Values are given as the mean ± SD
Abbreviations: CPAP, continuous positive airway pressure; OSAS, obstructive sleep apnea syndrome; TST, total sleep time; AHI, apnea-hypopnea index; PSG, Polysomnography

The relationships between optimal CPAP level and baseline variables were as follows. Minimal SaO2 (%) was negatively correlated and desaturation time under 90% was positively correlated with AHI for all 3 levels of OSAS severity. In the REM-related OSA group, optimal CPAP level was positively correlated with AHI overall and negatively correlated with minimal SaO2.

The effective pressures for our patients were compared with those yielded by the prediction formulas developed by Hoffstein for Caucasian populations and by Lin for Asian populations.[17,23] The mean predicted pressure (Ppred) calculated from the group in whom the Hoffstein formula was used was 7.21 ± 1.75 cm H2O, and with use of the Lin formula was 8.24 ± 1.63 cm H2O. These formulas were also positively correlated with the effective pressure level. 28% of 120 patients were patients referred from the Anesthesia outpatient clinic, and CPAP was performed for 2 weeks and their operations were delayed.

Discussion

The objective of this study was to observe the causes of titration failure for optimal CPAP level during diagnostic evaluation in OSAS patients.

Nasal CPAP has been the gold standard of treatment for OSAS. Traditionally, the implementation of CPAP has required an in-laboratory CPAP titration procedure that can be costly and time-consuming while limiting access to therapy.

Several previously mentioned factors have been identified as potentially affecting optimal pressure, including amount of REM sleep, length of the soft palate and the degree of respiratory effort, OSA severity, and/or obesity and body position. In the present study, 8 prediction variables (age, gender, NC, BMI, AHI, lowest SpO2, desaturation time under 90% SaO2, and REM-related or position-related sleep apnea) were used in the Pearson's correlation analysis. AHI (r=0.297, p<0.010) and minimal SaO2 (r=-0.264, p<0.010) were significantly correlated with optimal pressure level.

Various solutions have been posed as alternatives to conventional titration in individuals with OSA, including pressure prediction using mathematical formulas.[24,25,26] These prediction formulas cannot replace CPAP titration, but rather predict optimal titration levels. Several formulas exist in which an equation to predict the optimal pressure is different depending on ethnic group.[14,17,23] Akahoshi et al. produced a predictive equation derived from anthropometric, polysomnographic, and cephalometric data in 170 Japanese patients with OSAS.19 The inclusion of mean saturation differentiated this formula from others. Basoglu

and Tasbakan produced a predictive equation derived only from the circumference of the neck and the oxygen desaturation index.[27] According to their new formula, no significant difference existed between Ppred and Hoffstein's or Lin's formulas. These researchers comment in particular that race/ethnicity may not be an important factor in predicting CPAP levels. Habesoglu and Kokturk concluded that Ppred calculated by patients based on anthropometric properties and formula based on apnea hypopnea index and automated titration pressures were correlated with each other.[28]

We also compared the effective pressures with the prediction formulas developed by Hoffstein[18] for Caucasian populations and by Lin for Asian populations.[17,23] Our effective pressure levels closely agreed with these equations; a positive correlation existed between mean effective pressure and results from Hoffstein's and Lin's equations. However, this correlation did not exist in the failure group. The 18% failure detected is considerable when we compare automatic titration pressure (Paut) and estimated (calculated) titration pressure (Ppred) to evaluate the benefits of predicting CPAP pressure in CPAP treatment. Our clinical experience is that titration should be performed with different devices for the second and even third time in these cases. Patients with morbid obesity, deep desaturation on deep REM period during all night sleep and very high AHI values, , the AHI was 67.9 in our failed group, should be monitored more closely. We believe that the titration priority should be BPAP.

According to the correlation tests, AHI and the lowest saturation were the two most important predictors of optimal CPAP level; neither Lin's nor Hoffstein's equations included lowest saturation level. In the evaluation of OSA related to REM and position, the failure percentages were 26.90% for REM-related OSA and 13.70% for position-related OSA; in the failure group, both of these OSA groupings had severe overall AHI levels. The mean AHI was 67.90 in the failure group that did not have REM-related or position-related OSA. This number is very high in OSA patients in general, and also brings about the lowest saturation levels. The possibility exists that the terminology related to mild, moderate, severe, and very severe OSAS will change over time. BPAP auto titration could be performed in patients with additional diseases such as congestive heart failure, chronic obstructive pulmonary disease, or hypoventilation syndrome as well as in those with very severe OSA.

In conclusion, a predictive equation for optimal CPAP level could be developed using AHI and minimal SaO2 (%) in a larger patient series, which can be easily measured during diagnostic polysomnography. Predictive equations for optimal CPAP level should be helpful for designing optimal titration protocols in patients who have simple OSAS without additional diseases, severe REM-related or position-related OSAS, or very severe OSA. Predictive equations for simple OSA would be preferable to manual titration, which is costly and time-consuming and would require waiting for treatment, limiting access.

Acknowledgments

Funding-No funding was received for this research.

All authours have no conflict of interest to disclouse

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

The study was approved by the Yuzuncu Yil University's Faculty of Medicine Review Board (17.01.2020-2020/01-03)

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