# Determination of CPAP Titration Pressure by Mathematical Method in Obstructive Sleep Apnea Syndrome

## *Obstrüktif Uyku Apne Sendromu Tedavisinde CPAP Titrasyon Basıncının Matematiksel Yöntemle Belirlenmesi*

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## Summary

**Objective:** Development of continuous positive airway pressure (CPAP) therapy has become a cornerstone in the treatment of obstructive sleep apnea syndrome (OSAS). Currently, constant pressure CPAP therapy, determined by manual titration during attended second-night polysomnography (PSG), is the standard treatment for OSAS; however, it is expensive and time consuming. It is possible to predict the CPAP pressure by mathematical formula as alternative titration method. In our study, predicted titration pressure ($P_{pred}$) and automatic titration pressure ($P_{aut}$) was compared to reveal any benefit of predetermined CPAP pressure to CPAP therapy.
**Method:** Forty four OSAS patients underwent PSG and automatic CPAP titration. $P_{pred}$ was calculated with respect to equation which depended on anthropometric features and the apnea hipopnea index of cases as defined in the literature.
**Results:** There was no statistically significant differences between the mean values of $P_{pred}$ and $P_{aut}$ (P=0.363), correlation was determined between both pressure (r=0.407; p=0.002). In 48% of the cases the $P_{aut}$ value ranges were observed as $P_{pred}$ ± 1 cm $H_2O$, in 81% as $P_{pred}$ ± 2 cm $H_2O$, in 88% as $P_{pred}$ ± 3 cm $H_2O$.
**Conclusion:** It can be concluded that split-night, manual, or automatic CPAP titration with $P_{pred}$ as the reference value would be a practical method. $P_{pred}$ may be recalculated according to the changing anthropometric measurements of patients without a control PSG study for readjusting automatic CPAP. *(Archives of Lung 2007; 8: 74-7)*

**Key words:** Obstructive sleep apnea, CPAP therapy, CPAP titration

## Özet

**Amaç:** "Continuous positive airway pressure (CPAP)" tedavisinin geliştirilmesi "Obstructive sleep apnea syndrome (OSAS)" tedavisinde bir dönüm noktası olmuştur. Günümüzde, standart OSAS tedavisinde CPAP titrasyon basıncı laboratuvarda klinisyen gözetiminde ikinci bir polisomonografi (PSG) ile manuel olarak belirlenmektedir. Bu işlem, zaman alıcı ve pahalı bir yöntemdir. CPAP titrasyon basıncının önceden matematiksel formüllerle belirlenmesi mümkündür. Çalışmamızda, CPAP tedavisinde CPAP basıncını önceden belirlemenin yararlarını değerlendirmek için tahmini (hesaplanan) titrasyon basıncı ($P_{pred}$) ve otomatik titrasyon basıncı ($P_{aut}$) karşılaştırılmıştır.
**Yöntem:** OSAS'lı 44 hastaya PSG ve otomatik CPAP titrasyonu yapıldı. $P_{pred}$, literatürde tanımlanan ve hastaların antropometrik özellikleri ve apne hipopne indeksine dayanan formüle göre hesaplandı.
**Bulgular:** $P_{pred}$ ve $P_{aut}$ ortalama değerleri arasında istatistiksel olarak anlamlı fark yoktu (p=0.363), iki basınç arasında anlamlı korelasyon saptandı (r=0.407; p=0.002). $P_{aut}$ değerlerinin olguların %48'inde $P_{pred}$ ± 1 cm$H_2O$, %81'inde $P_{pred}$ ± 2 cm $H_2O$ ve %88'inde $P_{pred}$ ± 3 cm $H_2O$ sınırlarında olduğu görüldü.
**Sonuç:** Sonuç olarak split night, manuel ve otomatik CPAP titrasyonunda $P_{pred}$ değerinin referans alınması pratik bir yöntem olabilir. $P_{pred}$ değeri antropometrik ölçümlerdeki değişikliklere göre yeniden hesaplanarak kontrol amaçlı PSG çalışmasına gerek kalmadan otomatik CPAP tedavisi yeniden düzenlenebilir. (*Akciğer Arşivi 2007; 8: 74-7)*

**Anahtar kelimeler:** Obstrüktif uyku apne sendromu, CPAP tedavisi, CPAP titrasyonu

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## Introduction

Obstructive sleep apnea syndrome is the most common type of sleep disorder observed in both sexes, all races, and ethnic and socioeconomic groups (1, 2). Significant mortality and morbidity are associated with this disease. Development of continuous positive airway pressure (CPAP) therapy has become a cornerstone in the treatment of obstructive sleep apnea syndrome (OSAS). Currently, constant pressure CPAP therapy, determined by manual titration during attended second-night polysomnography, is the standard treatment for OSAS; however, it is expensive and time consuming.

To decrease the cost of CPAP therapy and to make it more practical, alternative methods such as split-night CPAP titration (3, 4), auto-CPAP titration by full night polysomnography (5,6), and unattended auto-CPAP titration at home(7-9) have been employed. Another alternative method is predicted formula titration. An equation determining the effective CPAP mathematically (depending on the anthropometric characteristics of the patients such as neck circumference, body mass index, and the frequency of respiratory events during sleep) has been developed by Hoffstein and coworkers (10,11). This method could be used to simplify standard and split-night CPAP titrations (12). Several studies have demonstrated that predicted formula titration has similar clinical effectiveness and patient adherence when compared with standard titration, and it could be used as a reference pressure for home auto-adjusted CPAP therapy (8, 9, 13, 14).

In our study, predicted formula titration pressure and automatic titration pressure, measured by the Autoset™ (ResMed; Sydney, Australia), were compared to determine the benefits of predetermined CPAP to CPAP therapy.

## Materials and Methods

**Patient selection:** Fifty four patients diagnosed with OSAS during a full-night sleep study in the polysomnography (PSG) laboratory of the Gazi University Faculty of Medicine Pulmonology Department in Ankara, Turkey, were included in the study. Inclusion criteria were no previous diagnosis of OSAS and no prior therapy for OSAS. Patients with chronic airway diseases such as chronic obstructive pulmonary disease and asthma, and with sleep disturbances other than OSAS diagnosed following PSG, such as obesity-hypoventilation syndrome and upper airway resistance syndrome, were excluded from the study.

**Anthropometric measurements:** Neck circumference was measured in centimeters at the level of the cricothyroid membrane, and body mass index (BMI) was calculated as $kg/m^2$ using the formula, $weight/length^2$.

**Polysomnography:** A questionnaire related to the diagnosis of OSAS was given to all patients, and each patient was evaluated by physical examination, complete blood count, serum chemistries, electrocardiography, arterial blood gases, chest radiograph, and pulmonary function tests prior to PSG. On the day of PSG, none of the patients ingested alcohol or sedatives or slept during the afternoon.

Overnight PSG was performed in all patients by a computerized system (Rembrandt; Medcare, Holland) and included the following variables: electro-oculogram (2 channels), electroencephalogram (4 channels), electromyelogram of submental muscles (2 channels), electromyelogram of the anterior tibialis muscle of both legs (2 channels), electrocardiogram, and airflow (with an oro-nasal thermistor). Chest and abdominal efforts (2 channels) were recorded using inductive plethysmography, arterial oxyhemoglobin saturation ($SaO_2$: 1 channel) by pulse oximetry with a finger probe. The recordings were conducted at a paper speed of 10 mm/s, and sleep stages were scored according to the standard criteria of Rechtschaffen and Kales (15). Arousals were scored according to accepted definitions (16). Apneas were defined as complete cessation of airflow ≥10 s. Hypopneas were defined as a reduction of > 50% in 1 of 3 respiratory signals, airflow signal, or either respiratory or abdominal signals of respiratory inductance plethysmography, with an associated fall of ≥ 3% in oxygen saturation or in arousal. The apnea-hypopnea index (AHI) was defined as the number of apneas and hypopneas per hour of sleep. Patients with an AHI ≥ 5 were considered OSAS. Indications of CPAP therapy were an AHI ≥ 15 cm $H_2O$, and an AHI between 5 and 15 cm $H_2O$, together with daytime hypersomnolence.

**CPAP titration:** Automatic CPAP titration with the Autoset device (ResCareMed; Sydney, Australia), was performed on patients 15 days following determination of the need for CPAP therapy. The Autoset device was automatic and provided pressure in a constant, automatic CPAP mode set at pressure limits determined by the clinician. The Autoset device detected changes in air flow wave patterns and snoring during the titration period, measuring pressure changes from breath to breath. During this procedure, oxygen saturation was measured by pulse oximetry from the finger tip.

Automatic CPAP titration records were evaluated by the clinician, and the median pressure value was accepted as effective CPAP ($P_{aut}$). Periods of awakening or air leaking around the face mask were not considered. If the CPAP titration was unacceptable in time and quantity, the procedure was repeated on another night.

**Predicted formula titration:** CPAP titration ($P_{pred}$), neck circumference, BMI, and AHI, were calculated with a multiple regression analysis method using the equation: $P_{pred}$ = (0.16 _ BMI) + (0.13 x neck circumference) + (0.04 x AHI) - 5.12, as described in the literature (10).

**Statistical analysis:** Data were analyzed using SPSS software (Statistical Package for the Social Sciences, version 10.0, SSPS Inc, Chicago, Ill, USA). Tables were created illustrating anthropometric, polysomnographic, and $P_{aut}$ parameters. Mean values of $P_{aut}$ and $P_{pred}$ were compared using the Student t test to show the correlation between effective and calculated CPAP values. The differences between $P_{aut}$ and $P_{pred}$ ($P_{aut}$ - $P_{pred}$) are shown on the histogram. P values less than .05 were considered statistically significant.

## Results

The mean age of 54 patients (10 women, 44 men), included in the study was 48 ± 12 years. Demographic data and anthropometric measurements are given in Table 1. Based on AHI values, 3 patients were diagnosed with mild OSAS, 14

patients with moderate OSAS, and 37 patients with severe OSAS (Table 2). Indicators of CPAP therapy were AHI ≥ 15 cm $H_2O$ in 51 patients, or AHI between 5 cm $H_2O$ - 15 cm $H_2O$ plus the presence of hypersomnolence in 3 patients.
When anthropometric measurements, PSG parameters, and $P_{aut}$ were reviewed, a significant correlation was found only between AHI and $P_{aut}$ (Table 3). No significant differences between the mean values of $P_{aut}$ and $P_{pred}$ ($p = 0.363$) were noted; however, there was a significant correlation between the 2 variables ($r = 0.407$; $p = 0.002$). A histogram showing the distribution of the difference between $P_{aut}$ and $P_{pred}$ ($P_{aut}$ _ $P_{pred}$) showed $P_{aut} = P_{pred} \pm 1$ cm $H_2O$ in 48% of patients, $P_{aut} = P_{pred} \pm 2$ cm $H_2O$ in 81% of patients, $P_{aut} = P_{pred} \pm 3$ cm $H_2O$ in 88% of patients (Figure 1).

## Discussion

Development of CPAP therapy has become a cornerstone in the treatment of OSAS. Sullivan and colleagues have reported that they successfully treated OSAS with CPAP in 1981 (17). After this first study, CPAP was shown to be an effective and safe method for treating OSAS in many other studies.
Constant pressure CPAP therapy is considered to be the reference therapy for OSAS today. Effective CPAP titration is done manually in PSG studies by adjusting the pressure until apnea, hypopnea, snoring, respiratory arousal, and sleep fragmentation in all sleep episodes and body positions disappear. However, a standard method of CPAP titration was not developed until recently. CPAP titration begins with 3-5 cm $H_2O$ pressure in many PSG laboratories and optimal pressure to achieve desired AHI changes of between 5 and 15 cm $H_2O$, with the patient observed for 10-60 minutes to evaluate all stages of sleep and body positions at each pressure adjustment. Usually, pressure changes of 3-10 cm $H_2O$ are required to achieve the effective CPAP titration, so in many cases, a 1-night PSG study is not sufficient for successful titration.
Protocols that minimize the number of pressure adjustments during CPAP titration are required. Hoffstein and investigators have shown that the CPAP determined by predicted formula titration ($P_{pred}$) correlated with the effective CPAP ($P_{eff}$) determined by manual titration. The distribution of the difference between $P_{pred}$ and $P_{eff}$ was shown to be $P_{eff} = P_{pred} \pm 1$ cm $H_2O$ in 63% of patients, $P_{eff} = P_{pred} \pm 2$ cm $H_2O$ in 83% of patients, and $P_{eff} = P_{pred} \pm 3$ cm $H_2O$ in 95% of patients (11). It was concluded that achieving effective CPAP with fewer pressure adjustments was possible by calculating the reference CPAP during manual titration.
In our study, no significant difference between $P_{aut}$ and $P_{pred}$ was found ($p = 0.363$), whereas $P_{aut}$ and $P_{pred}$ correlated significantly ($r = 0.407$, $p = 0.002$). Further, we found that $P_{aut}$ was between $P_{pred} \pm 1$ cm $H_2O$ in 48% of patients, $P_{pred} \pm 2$ cm $H_2O$ in 81% of patients, and $P_{pred} \pm 3$ cm $H_2O$ in 88% of patients. According to this data, if $P_{pred}$ was accepted as the initial pressure during manual CPAP titration, $P_{aut}$ can be achieved with a maximum of 3 pressure adjustments in 48 of 54 cases. More than 3 pressure adjustments were required in only 6 pa-

**Table 1. Demographic and anthropometric data of the patients**

| | Mean±SD | Range |
|---|---|---|
| Age (year) | 48±12 | 24-79 |
| Sex (F/M) | 10/44 | |
| BMI (kg/m$^2$) | 32.9±5.5 | 25.1-49.6 |
| Neck circumference (cm) | 43.2±4.2 | 35-56 |

SD- standard deviation, BMI- body mass index

**Table 2. Results of the polysomnographic evaluation of the patients**

| | Mean±SD | Range |
|---|---|---|
| Total sleep time (min.) | 372±74 | 114-477 |
| Total sleep time (NREM) (%) | 75±10 | 49-92 |
| Total sleep time (REM) (%.) | 7±7 | 0-34 |
| Sleep efficiency (%) | 81±10 | 53-98 |
| AHI (mean ± SD) | 57.6±26.5 | 8.6-121 |
| Awakening mean $SaO_2$ | 92.7±4.4 | 71-96 |
| Mean $SaO_2$ during sleep | 86.8±7.5 | 60-95 |
| Minimum $SaO_2$ during sleep | 71.6±11.9 | 41-88 |

SD- standard deviation, REM- rapid eye movement, NREM- non rapid eye movement, AHI: apnea hypopnea index

**Table 3. The correlation between $P_{aut}$ and the other parameters**

| | Paut | |
|---|---|---|
| | r | p |
| Age | -0.003 | 0.982 |
| BMI | 0.131 | 0.354 |
| Neck circumference | 0.082 | 0.555 |
| AHI | 0.406 | 0.002 |
| Epworth Sleepiness Score | -0.172 | 0.237 |
| Awakening mean $SaO_2$ | 0.257 | 0.071 |
| Mean $SaO_2$ during sleep | 0.031 | 0.829 |
| Minimum $SaO_2$ during sleep | -0.057 | 0.696 |

BMI- body mass index, AHI- apnea hypopnea index

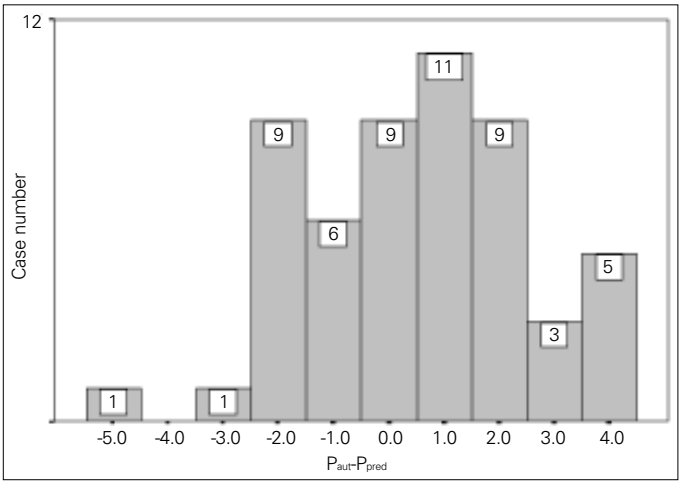


**Figure 1. The distribution of the cases according to the difference of ($P_{aut}$ - $P_{pred}$)**

tients. In our opinion, achieving $P_{aut}$ with approximately 3 pressure adjustments is a practical method for manual CPAP titration. We believe that a minimum duration of 3 hours is required for CPAP titration in split-night PSG studies, and that $P_{aut}$ can be achieved with 3 pressure adjustments if $P_{pred}$ is accepted as the initial pressure. Patients may be observed for 60 minutes for each pressure adjustment and in this way, will be evaluated more effectively over a shorter period of time.

In a study conducted by Series, home CPAP therapy was initiated by calculating CPAP with a similar equation without a prior PSG titration study. In that study, upper and lower threshold values were $P_{pred}$ + 3 cm $H_2O$ and $P_{pred}$ - 4 cm $H_2O$, respectively. Optimal pressure was determined on examination of CPAP records of 1-2 weeks' duration. In the majority of cases (38 of 40), compliance with and effectiveness of therapy at the end of the third and 12th month was excellent (8). In another study, sleep fragmentation, hypersomnolence, and AHI similarly improved in patients receiving constant pressure CPAP therapy, reference pressure automatic CPAP therapy with manual titration, and calculated reference pressure ($P_{pred}$) automatic CPAP therapy in PSG studies at the end of the third week (13). In a recent multicenter PSG study using the same equation, no difference was found between standard manual CPAP titration, automatic CPAP titration at home, and predicted formula titration of CPAP, with regard to compliance with therapy and effectiveness and safety of therapy at the end of the 12th week (9). Based on these findings, it is speculated that CPAP therapy at home could be started by calculating the reference pressure without a prior PSG study for titration.

In the period following, effective CPAP required during sleep decreases with weight loss, ventilatory control, and nasal obstruction (18). In these patients, especially those where $P_{aut}$ and $P_{pred}$ values have been correlated, $P_{pred}$ may be determined periodically according to changing anthropometric measurements. In this way, CPAP therapy may be continued without the need for a new PSG study. Further, the cost of treating patients with OSAS will be reduced, as will the amount of time and energy expended by the patient and clinician.

Although the distribution of $P_{aut}$-$P_{pred}$ for our patients was similar to that of other studies, an equation modified according to the anthropometric measurements of the Turkish population would be more appropriate (see histogram). In Taiwan, Lin and colleagues noted in a regression analysis that CPAP correlated with the severity of the disease (AHI), while BMI and neck circumference were found not to affect the pressure. CPAP was calculated with a different equation dependent upon AHI and BMI (19). A study similar to the Taiwanese investigation has not been done in Turkey. In our other study (data not published), however, specificity of neck circumference accepted as significant for OSAS (≥ 43 cm for men, ≥ 38 cm for women) was found to below (59.4%). In the present study, when the correlation between $P_{aut}$, anthropometric data and PSG measurements was examined, only AHI showed a significant correlation (Table 3). Additional studies examining factors affecting optimal CPAP in the Turkish population are required. An equation developed on the basis of these factors may increase the probability of determining effective CPAP.

In conclusion, although the number of studies that support initiating automatic CPAP titration at home by predicted formula titration is increasing, new studies examining larger populations are required. Split-night, manual, or automatic CPAP titration with $P_{pred}$ as the reference value would be a practical method for use in such studies. $P_{pred}$ may be recalculated according to the changing anthropometric measurements of patients without a control PSG study for readjusting automatic CPAP. For optimal results, regression analyses should be adapted to the anthropometric measurements by considering ethnic differences.

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