Optimal Time for a Control Titration in Patients with Obstructive Sleep Apnea Treated with Non-Invasive Mechanical Ventilation

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ABSTRACT

Objective: The pressure requirements for patients with obstructive sleep apnea syndrome (OSAS) who use a positive airway pressure (PAP) device may change over time for various reasons. We determined the optimal time for a controlled titration study and its associated factors in patients with OSAS using a PAP device.

Methods: We retrospectively identified 82 patients diagnosed with OSAS who used a PAP device and underwent a second PAP titration study for control purposes at our sleep center. The demographic characteristics and anthropometric measurements of the patients during first and second PAP titration studies were recorded. We compared pressures and BMI values after both titration tests.

Results: The patients were divided into three groups according to the pressure changes following the second titration study: those with elevated, unchanged, and decreased PAP pressure. The BMI calculated following both studies increased significantly in the group with elevated pressure ($p < 0.001$), decreased significantly in the group with decreased pressure ($p < 0.001$), and no significant difference was observed in the group with unchanged pressure ($p = 0.235$). A positive correlation was found between the change in BMI and the change in Cpap, Ipap, and Epap values following both titration tests ($p < 0.001$, $r = 0.898$; $p < 0.001$, $r = 0.884$; $p < 0.001$, $r = 0.896$, respectively).

Conclusion: The results show that weight changes in patients with OSAS receiving PAP therapy during follow-up can be accompanied by pressure changes in the device, suggesting the need for a second controlled titration test.

Key words: Noninvasive mechanical ventilation, sleep apnea, PAP titration

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INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent complete or partial episodes of upper airway obstruction that result in episodic hypoxia and arousal during sleep (1). It affects approximately 4% of males, and 2% of females (2). OSAS is an important risk factor for neural, metabolic and cardiovascular diseases (CVD) such as ischaemic heart disease, arrhythmia, and hypertension (3-6). The precise aetiologies of cardiovascular events in OSAS patients are not fully understood but are likely to be multifactorial, including elevated sympathetic activity developing secondary to recurrent hypoxia and sleep arousal, endothelial dysfunction, and increased oxidative stress secondary to recurring oxygen desaturation and resaturation (7,8).

Several factors such as male sex, alcohol consumption, smoking, obesity, aging, and an anatomically narrow upper airway contribute to the development of OSAS. However, obesity appears to be among the most important risk factors for developing OSAS (9).

Nasal continuous positive airway pressure (CPAP) has been used as standard therapy for treating OSAS (10,11). Therapeutic pressure is frequently determined by manual titration performed by a technician with polysomnography (PSG) in a sleep laboratory (12). During follow-up of patients using a positive airway pressure (PAP) device, therapeutic pressure may be altered due to changes in weight and other factors that influence disease severity. Thus, a controlled titration study is required in patients using a PAP device. We were unable to find a single study that examined when and in which patients a control titration test should be performed when using a PAP device. Thus, we determined the optimal time for a control PAP titration study and its associated factors in patients with OSAS using noninvasive mechanical ventilation.

METHODS

Subjects

We retrospectively identified 105 patients who used CPAP or bilevel positive airway pressure (BIBAP) with a diagnosis of OSAS and who underwent a second PAP titration study for control purposes between January 2007 and April 2014. Of these patients, seven who used the device irregularly (<5 h per night on average), five who underwent surgical intervention for soft palate and/or uvula, and 11 who used a PAP device for a concomitant indication (central sleep apnea syndrome, chronic obstructive pulmonary disease, restrictive respiratory insufficiency, or obesity-hypoventilation syndrome) were excluded. The remaining 82 patients with OSAS were included. A questionnaire was administered to the participants to examine snoring, witnessed apnea, and daytime sleepiness using the Epworth Sleepiness Scale. The demographic and anthropometric [height, weight and body mass index (BMI)] features of the patients at the time of diagnosis and the controlled PAP titration study were recorded. The period between the two titration studies was calculated. This study was approved by our Ethics Committee, and written consent was obtained from each participant.

Sleep study

Each patient underwent full PSG monitoring in the sleep center using two different computer systems (55-channel Respironics, Murrysville, PA, USA and 58-channel Compimedics, Sydney, Australia). PSG monitoring included electroencephalogram, electrooculogram, submental and bilateral leg electromyogram, and electrocardiogram. Airflow and snoring were measured using an oral thermistor and nasal transducer; thoracic and abdominal wall movements, and body position was assessed using inductive plethysmography. Blood oxygen saturation was measured by pulse oximetry. The PAP titration was performed manually by a technician using two devices (Respironics and Weinmann) under full PSG monitoring. PAP titration was started with pressure set at 4

cmH_2O under full-night PSG, and was increased in incremental steps until apnea-hypopnea events disappeared. The lowest pressure that eliminated apnea and hypopnea was considered the optimal pressure. A titration study was performed to last at least 5 h. PSG scoring was performed in accordance with the "AASM Manual for Scoring Sleep" published by the American Academy of Sleep Medicine in 2007 (13). After the recording, sleep staging, changes in heart rate and rhythm, changes in breathing patterns (apnea, hypopnea, and arousal), and periodic leg movements were scored manually. Subjects with Apnea-Hypopnea Index (AHI) score < 5 were considered to have simple snoring. OSAS was defined as either AHI ≥ 5, with associated symptoms such as sleep attacks or excessive daytime sleepiness, unsatisfying sleep, insomnia or fatigue, witnessed heavy snoring and/or breathing pauses referred by the partner or AHI ≥ 15 regardless of associated symptoms.

Statistical Analysis

The statistical analysis was performed using the SPSS ver. 13.0 software (SPSS Inc., Chicago, IL, USA). Categorical variables are expressed as frequencies and percentages. Continuous variables were measured using means and standard deviations, medians, and ranges. Analysis of the distribution of constant variance for normality was performed using the Shapiro–Wilk test. The independent (unpaired) *t*-test was used to compare the groups in terms of normally distributed variables. Differences in continuous variables among the three groups were evaluated with the Kruskal–Wallis test. The Wilcoxon test was used to analyze variables not normally distributed within the groups. Spearman's test was used for correlation calculations. A *P*-value < 0.05 was considered to indicate significance for all tests.

RESULTS

The study included 82 patients diagnosed with OSAS who used a PAP device and who underwent a second titration study for control purposes. The participant characteristics are shown in Table 1. Approximately 30% of patients (n = 25) were on BIPAP and 70% (n = 57) were on CPAP. The mean period between the first and second titration studies was 21.4 ± 17 (range, 3–74) months. The changes in BMI and pressure during first and second titration studies are shown in Table 2. No significant difference was found in BMI between the two studies (p = 0.400). The patients were divided into three groups depending on the pressure changes after the second titration study: those with an elevated, unchanged and decreased PAP pressure on the second titration night. We compared the BMI values of patients between the first PAP titration study and the second PAP titration study. We found that the BMI increased significantly in the group with elevated pressure (33.1 ± 5.6 kg/m^2, 38.6 ± 5.9 kg/m^2, p < 0001), decreased significantly in the group with decreased pressure (36.5 ± 6.2 kg/m^2, 33.8 ± 6 kg/m^2, p < 0001), and no significant difference was observed in the group with unchanged pressure (33.8 ± 6.7 kg/m^2, 33.9 ± 6.6 kg/m^2, p = 0.235) during second titration (Tables 3 and 4).

A positive correlation was found between the change in BMI and changes in Cpap, Ipap, and Epap values following both studies (p < 0.001 r = 0.898; p < 0.001, r = 0.884; and p < 0.001, r = 0.896, respectively) (Table 5).

DISCUSSION

Obesity is one of the most important factors in the etiology of OSAS. We showed that weight changes in patients with OSAS undergoing PAP therapy over time were accompanied by

pressure changes in the device. As BMI decreased, the need for pressure decreased, whereas higher pressures were required as patients gained weight.

We were unable to find any study that examined in which patients and when a control titration should be performed while using a PAP device. Reduced activity in the device can be observed depending on several factors that emerge during PAP use by patients, which, in turn, may result in clinical symptoms or increase complaints. In contrast, complications, including disturbed patient compliance and central apnea, may occur due to excess pressure. All of these complications suggest the need for a second titration study in patients using a PAP device.

PAP is widely examined the gold standard, based on the experience that the AHI can be diminished or normalized in most patients using this technique (14). PAP therapy has been used since invention of the CPAP device in 1981 (15). PAP devices help keep the upper respiratory airway open with a motor that ensures continuous positive pressure and deliver room air to the patient at a desired pressure through a mask and tubing. This keeps the upper respiratory airway patent and regulates respiration and quality of sleep (16). As a PAP device has no impact on the muscles of the upper respiratory airway and it shows a therapeutic effect only when patients use the device, PAP therapy is not curative (16, 17). Effective pressure is determined manually by a technician during attended PSG or alternatively by automated titration (12).

Various factors and different mechanisms are involved in the etiology of OSAS but obesity is among the most important factors. Obesity increases the risk of developing OSAS, particularly in the young-middle-aged population (18). A 10% increase in body weight may result in a 30% increase in the AHI whereas a 10–15% reduction in body weight may reduce the AHI by 50% (19])

Studies have shown that reducing weight is associated with reducing the AHI in patients with OSAS (19,20). In a study by Nerfeldt, a weight reduction program reduced the AHI along with weight loss in patients with OSAS (20). A meta-analysis showed that dietary weight loss is associated with a reduction in apnea severity (21). Lankford demonstrated a reduced need for PAP in an automated CPAP titration study at the end of postoperative month 3 in 15 obese patients who used a CPAP device and underwent bariatric surgery (22). In the present study, a significant reduction in BMI was observed in the decreased PAP pressure group. Similarly, a significant correlation was observed between decreased PAP pressure and a reduction in BMI. We found no significant difference in BMI in the unchanged PAP pressure group after the second PAP titration study.

A study by Charuzi et al. showed a significant reduction in the apnea index along with weight loss during the first postoperative year follow-up in patients who underwent bariatric surgery and an increase in the apnea index in patients who regained weight during the follow-up at postoperative year 7 (23). In the present study, a significant increase in BMI was observed in the increased PAP pressure group. Similarly, a significant correlation was detected between the increase in PAP pressure and BMI.

A second titration study is usually scheduled at sleep centers for patients using a PAP device who present with complaints about non-compliance to a device or inefficient or excess pressure. In the present study, the mean period between the first and second titration studies was 21.4 months. No time interval has been recommended in the literature for a second titration study.

This study had several limitations. As it was a retrospective study, patients visited the center for controls within a broad range of intervals. Another limitation was that we focused only on BMI, although many factors influence the severity of OSAS and upper respiratory airway passage.

In summary, we demonstrated the necessity of performing a second titration study in patients diagnosed with OSAS who use PAP. The second study should be performed within a short period of time, particularly in patients with significant changes in BMI. We think that a second titration study can be delayed slightly in those patients who have no significant change in BMI. The readjusted PAP pressure will improve effectiveness of the device, patient comfort, and compliance. However, we believe that further studies will help to determine the optimal time for a second titration study, as complex mechanisms and several factors are involved in the etiology of OSAS.

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Conflict of Interest: None of the authors has any conflicts of interest with regard to this study.

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Table 1: Baseline clinical and polysomnographic characteristics of the patients with OSAS.

Characteristic	Mean ± SD
Age, years	54.6 ± 10.5
Sex	54/28
BMI, kg/m^2	34.6 ± 6.3
Smoker/nonsmoker	22/60
AHI, h	44 ± 22
Minimum SpO_2	70.8 ± 14.1
ODI, h	42.1 ± 28.7
Arousal, h	27.3 ± 18.8
Device (CPAP/BİPAP)	57/25
*Duration between two titrations, months	21.4 ± 17

OSAS, Obstructive sleep apnea syndrome; BMI body mass index; AHI, apnea-hypopnea index; SpO_2, arterial oxygen saturation; ODI, oxygen desaturation index; CPAP, continuous positive airway pressure; BIPAP, bilevel positive airway pressure; SD, standard deviation.

*Time from CPAP titration at the time of first to titration at the time of the second study.

Table 2: Changes in BMI and pressure during diagnostic and controlled titration studies in patients with OSAS.

	First titration study (n = 82)	Second titration study (n = 82)	**P**
BMI, kg/m^2	34.6 ± 6,3	35.2 ± 6.5	0.400
CPAP, cmH_2O	7.5 ± 1.8	7.8 ± 1.9	0.282
IPAP, cmH_2O	14.7 ± 2.3	13.2 ± 2.2	0.002
EPAP, cmH_2O	10.9 ± 2.3	9.3 ± 2.2	0.003

OSAS, obstructive sleep apnea syndrome; BMI body mass index; CPAP, continuous positive airway pressure; IPAP, inspiratory positive airway pressure; EPAP, expiratory positive airway pressure.

Table 3: Patients with elevated PAP pressure based on the current pressures on the night of the second titration study.

	First titration study (n = 23)	Second titration study (n = 23)	p
BMI, kg/m^2	33.1 ± 5.6	38.6 ± 5.9	<0.001
CPAP, cmH_2O	7 ± 1.5	9.5 ± 1.6	<0.001
*IPAP, cmH_2O	14.3 ± 4.7	16 ± 3.6	**N/A
*EPAP, cmH_2O	10.3 ± 4.7	12 ± 3.6	**N/A

PAP, positive airway pressure; BMI, body mass index; CPAP, continuous positive airway pressure; IPAP, inspiratory positive airway pressure; EPAP, expiratory positive airway pressure.
* n = 3.
** Not applicable.

Table 4: Patients with decreased PAP pressure based on the current pressures on the night of the second titration study.

	First titration study (n=31)	Second titration study (n=31)	p
BMI, kg/m^2	36.5 ± 6.2	33.8 ± 6	<0.001
CPAP, cmH_2O	8.5 ± 1.9	6.6 ± 1.4	<0.001
IPAP, cmH_2O	15.3 ± 2.2	12.1 ± 1.8	<0.001
EPAP, cmH_2O	11.6 ± 2.1	8.3 ± 1.7	<0.001

PAP, positive airway pressure; BMI body mass index; CPAP, continuous positive airway pressure; IPAP, inspiratory positive airway pressure; EPAP, expiratory positive airway pressure

Table 5: Correlation between changes in BMI and pressure**.**

Percent change in	CPAP	IPAP	EPAP
BMI	r = 0.898 p < 0.001	r = 0.884 p < 0.001	r = 0.896 p < 0.001

BMI, body mass index; CPAP, continuous positive airway pressure; IPAP, inspiratory positive airway pressure; EPAP, expiratory positive airway pressure.