Effects of Continuous Positive Airway Pressure Titration on Nocturnal Blood Pressure Fluctuation in Severe Sleep Apnea Patients with Hypertension

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Abstract
This case report presents two hypertensive patients with severe sleep apnea (SA) who were effectively treated with optimized SA therapy using manual continuous positive airway pressure (CPAP) titration.

Case 1: A 52-year old woman was receiving treatment for severe obstructive SA and hypertension. She noticed residual drowsiness after the initiation of auto-adjusting CPAP. After manual CPAP titration, her sleepiness improved, and home blood pressure (BP) values were almost completely controlled, despite the reduced use of antihypertensives.

Case 2: A 68-year old man with chronic heart failure was receiving treatment for severe SA by means of auto-adjusting CPAP. A favorable decrease in morning BP was observed after manual CPAP titration.

Remarkable antihypertensive effects were observed in hypertensive patients with severe SA after administering individualized and optimized CPAP therapy. SA treatment that is optimized with CPAP titration should be considered as an approach for strict antihypertensive management in hypertensive SA patients.

Key words
Sleep disordered breathing, positive airway pressure, optimal therapy, nighttime blood pressure, morning hypertension

Introduction
Continuous positive airway pressure (CPAP) therapy is an established form of treatment for patients with sleep apnea (SA). The antihypertensive effect of CPAP therapy on hypertensive SA patients has been found to be limited and differs from person to person. Auto-adjusting CPAP is prescribed to many patients when CPAP therapy is initiated; later, some patients undergo laboratory CPAP manual titration to determine an adequate treatment pressure and suitable mask to obtain sufficient antihypertensive effects. CPAP titration should be an effective approach to strict antihypertensive management in SA patients with poorly controlled hypertension. Here, we report on the antihypertensive effects of CPAP titration in two hypertensive patients with severe SA based on data collected using a BP monitoring device at home which automatically measures blood pressures (BPs) and nighttime oxygen saturation (SpO₂)².

Methods
Home BP measurement
The BP monitoring device (HEM-780 system [Omron Healthcare Co, Ltd, Kyoto, Japan]) measured BP at home as follows: 1) a fixed-interval function measured BPs at a fixed interval, e.g., at 2:00, 3:00, and 4:00 a.m.; 2) the patients measured their BP three times at one opportune moment on their own; and 3) SpO₂ trends were recorded during nighttime. All BPs

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and SpO₂ data were recorded and displayed on a time series. The device was used to record BPs and SpO₂ trends as follows: for Case 1, 1) on 2 nights 20 days after the initiation of CPAP therapy and 2) on 2 nights 2 months after the CPAP titration, and for Case 2, 1) on 7 nights 24 months after the initiation of CPAP therapy and 2) on 7 nights 12 months after the CPAP titration. The average values of the obtained BP records were analyzed.

**Office BP and morning BP**

Office BP was measured during outpatient consultation times between 13:00 and 17:00; morning BP was measured at home after awakening in accordance with the Japanese guidelines for home BP monitoring on the measurement days. The BP monitoring device measured BP three times after a few minutes of rest as the patient was seated with their back supported and without crossing the legs: BP was measured with both arms positioned at the heart level. The average value of three BP measurements was analyzed.

**SpO₂**

This device measured the lowest SpO₂, and the number of 3% oxygen desaturation episodes per hour (3% ODI) during BP recording and cumulative percentages of time at saturation below 90% (CT90%) were calculated.

**Ethics**

The present study was performed in accordance with the ethical principles set forth in the Declaration of Helsinki. The study protocol was reviewed and approved by the Institutional Review Board of the St. Marianna University School of Medicine, and it was subsequently implemented in compliance with the Personal Information Protection Law (Ethical Committee Approval No. 2828).

**Case 1**

The patient was a 53-year-old woman. She had received treatment for hypertension for several years. She was obese (body mass index [BMI], 29.5 kg/m²; weight, 69.0 kg; height, 1.53 m) and had been diagnosed with severe obstructive SA (apnea hypopnea index [AHI], 51.6/h; Table 1). CPAP therapy was prescribed for excessive daytime sleepiness rated as 12 points based on the Epworth Sleepiness Scale (ESS). The nighttime BPs recorded by the BP monitoring device under CPAP therapy are shown in Table 2. A therapeutic pressure between 4.0 and 10.0 cm H₂O was firstly prescribed in the auto-adjusting mode. The percentage of CPAP use on given days of therapy was 53%, the average hours of CPAP use was 5.1 hours/night, the mean AHI was 6.7/h, the 95th percentile pressure was 9.8 cm H₂O, and the maximum pressure was 9.9 cm H₂O. The patient gradually noticed residual drowsiness (ESS, 10 points) several months after the initiation of CPAP therapy. A CPAP prescription pressure increase was attempted at a rate of 1.0 cm H₂O/month in the outpatient treatment; however, she complained of respiratory distress, and eventually, the prescription pressure could not be increased. A manual CPAP titration during one night was subsequently implemented 8 months after CPAP initiation. According to the results of the CPAP titration, the therapeutic pressure was changed to 4.0–15.0 cm H₂O in the auto-adjusting mode. The type of mask was also changed from a nasal mask to a nasal pillow mask. After the CPAP titration, the percentage of days of CPAP use on given days of therapy was 60%, the average hours of CPAP use were 6.1 hours/night, the mean AHI was 6.8/h, the 95th percentile pressure was 11.9 cm H₂O, and the maximum pressure was 13.3 cm H₂O. As a result, her residual drowsiness completely disappeared (ESS, 3 points). Even though antihypertensive agent doses were reduced (Table 2), nocturnal mean BP dropped to al-

| table | Sleep Data before and after Continuous Positive Airway Pressure Titration. |
|-------|-------------------------------------------------------------------------|
| **Case 1** | **Case 2** |
| **Body weight (kg)** | 51.6 | 87.9 |
| **Mean BP (100)** | 4.0 | 12.5 |
| **AHI (1/hour)** | 51.6 | 21.7 |
| **AT (1/hour)** | 4.0 | 3.5 |
| **CA (1/hour)** | 21.4 | 1.0 |
| **OA (1/hour)** | 0.3 | 1.7 |
| **CTS% (%)** | 10.6 | 15.9 |
| **Lowest oxygen saturation (%)** | 50.0 | 74.0 |
| **SWS (%)** | 4.9 | 12.0 |
| **Arousal index (1/hour)** | 35.5 | 12.5 |
| **Case 2** | **Case 1** |
| **Body weight (kg)** | 80.0 | 80.0 |
| **Mean BP (100)** | 74.8 | 21.9 |
| **AHI (1/hour)** | 54.5 | 42.9 |
| **AT (1/hour)** | 78.0 | 78.0 |
| **OA (1/hour)** | 43.0 | 43.0 |
| **OA (1/hour)** | 50.0 | 50.0 |
| **CTS% (%)** | 50.0 | 50.0 |
| **Lowest oxygen saturation (%)** | 50.0 | 50.0 |
| **SWS (%)** | 50.0 | 50.0 |
| **Arousal index (1/hour)** | 50.0 | 50.0 |

PSG, polysomnography; CPAP, continuous positive airway pressure; AHI, apnea–hypopnea index; AI, apnea index; OA, obstructive apnea; CA, central apnea; CT 90%, cumulative percentages of time at saturation below 90%; and SWS, slow wave sleep.
Table 2. Blood Pressure and Saturation Data before and after Continuous Positive Airway Pressure Titration.

|                          | Case 1                                                                 | Case 2                                                                 |
|--------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|
| Antihypertensive drugs   | Amlodipine 7.5 mg and candesartan cilexetil 4 mg in the morning       | Valsartan 80 mg, furosemide 40 mg and bisoprolol fumarate 2.5 mg       |
| Blood pressure (mmHg)    | Before CPAP titration (2 nights mean) After CPAP titration (2 nights mean) | Before CPAP titration (7 nights mean) After CPAP titration (7 nights mean) |
| Office BP                | SBP: 127 After CPAP titration 128                                      | SBP: 177                                                                |
|                          | DBP: 89 After CPAP titration 84                                        | DBP: 67                                                                |
| Morning BP               | SBP: 107 After CPAP titration 124                                      | SBP: 171                                                                |
|                          | DBP: 72 After CPAP titration 81                                        | DBP: 102                                                                |
| Fixed-interval function  | Mean BP at 2 AM and 4 AM                                               | Mean BP at 2 AM and 4 AM                                               |
|                          | SBP: 96 After CPAP titration 111                                       | SBP: 138                                                               |
|                          | DBP: 66 After CPAP titration 75                                        | DBP: 76                                                                |
| Saturation               | 3%ODI (hour)                                                          | 3%ODI (hour)                                                          |
|                          | SBP: 3.0 After CPAP titration 4.0                                       | SBP: 6.4                                                              |
|                          | DBP: 0.1 After CPAP titration 0.1                                       | DBP: 1.7                                                              |
| Lowest oxygen saturation | (%) 86 After CPAP titration 89                                         | (%) 81                                                                |

CPAP, continuous positive airway pressure; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; ODI, oxygen desaturation index; and CT 90%, cumulative percentages of time at saturation below 90%.

most below 120/70 mmHg2) (mean nighttime BP recorded by fixed-interval function, 111/75 mmHg) after the CPAP titration, and morning BP was below 135/85 mmHg (mean morning BP, 124/81 mmHg) (Table 2).

Case 2

A 68-year-old man was diagnosed with chronic heart failure caused by atrial fibrillation and hypertension; he had a preserved ejection fraction (Simpson’s left ventricular ejection fraction was 67% and the brain natriuretic peptide level was 54.5 pg/mL). His height was 170 cm, his body weight was 80.0 kg, and his BMI was 25.8 kg/m². CPAP therapy was prescribed for frequent snoring and apnea (ESS, 9 points) and severe SA (AHI, 87.9/h; Table 1). A therapeutic pressure between 4.0 and 10.0 cm H₂O in the auto-adjusting mode was initially prescribed. The percentage of days of CPAP use on given days of therapy was 72%, the average hours of CPAP use was 6.7 hours/night, the mean AHI was 5.5/h, the 95th percentile pressure was 10.0 cm H₂O, and the maximum pressure was 10.0 cm H₂O. He exhibited no snoring or apnea during sleep after CPAP implementation. However, his morning BP became poorly controlled. His medications are shown in Table 2. Oral antihypertensive agents were prescribed to be taken before bedtime, but he did not take them because he could not stop drinking at night. The CPAP therapy pressure was subsequently changed to 6.0–12.4 cm H₂O after manual CPAP titration in one night. Afterwards, the percentage of days of CPAP use on given days of therapy was 70%, the average hours of CPAP use were 6.5 hours/night, the mean AHI was 4.4/h (central apnea index, 2.5/h), the 95th percentile pressure was 11.2 cm H₂O, and the maximum pressure was 12.2 cm H₂O. Morning BP decreased considerably after CPAP titration (morning BP, 171/102 to 148/72 mmHg; Figure 1-A, 1-B and Table 2). His ESS was 6 points after CPAP titration.

In both cases, risk factors for secondary hypertension, other than SA were ruled out based on ultrasound and blood test findings.

Discussion

In Case 1, the patient immediately experienced dizziness after CPAP titration, which appeared to be due to the significant BP reduction; therefore, the antihypertensive agent doses were reduced (Table 2). In Case 2, since the patient had apnea-dominant severe SA, heart failure with preserved ejection fraction, and considerable arousal reactions, both CPAP upper- and lower-limit pressures were optimized in the auto-adjusting mode. This adjustment led to the improvement of circadian BP fluctuation3).

CPAP titration in SA patients

In general, auto-adjusting CPAP is prescribed for SA patients. A meta-analysis conducted by Ip et al.4) demonstrated that the compliance with auto-ad-
justing CPAP use was higher than that for fixed-mode CPAP use, in which therapy pressure was determined by manual CPAP titration during a labor-intensive procedure. CPAP titration plays a crucial role in providing a good quality of sleep by eliminating apnea, hypopnea, snoring, flow limitation, and electroencephalographic arousal\(^5\). The optimization of SA therapy with manual CPAP titration in the laboratory along with mask adjustment, the use of a humidifier, and other measures definitely improves treatment compliance and the CPAP therapy effect. In Case 1, the patient complained of residual hypersomnia for several months after CPAP initiation. It has been reported that residual sleepiness is observed from immediately after CPAP therapy to 36 months despite SA treatment\(^6\) and that the frequency of residual hypersomnia patients is 13% among patients treated for SA\(^7\). In Case 2, CPAP titration was conducted to optimize the CPAP therapy because the patient was not fully aware of sleepiness during the SA treatment. Inadequate CPAP pressures may have been initially prescribed to our patients due to the reasons described in an earlier study\(^6\). The present cases clearly demonstrated the possibility that individualized and optimized CPAP therapies improved their sleep quality and symptoms.

**Effect of CPAP titration on SA patients with hypertension**

Our hypertensive SA patients revealed the antihypertensive effects of CPAP titration, although there were no remarkable changes in the sleep data recorded by the CPAP machines. One study demonstrated that the AHI calculated from polysomnographic data was almost equivalent to that calculated using data recorded by CPAP\(^8\). However, the CPAP machines are unable to record the arousal reactions and short-time respiratory efforts\(^9\). It is noteworthy in our cases that the auto-adjusting CPAP mode was not changed and that only the prescribed therapeutic pressures were changed. Some studies\(^10,11\) have reported that fixed-pressure CPAP was more effective at reducing BP than auto-adjusting CPAP. Meanwhile, one recent study\(^12\) reported that auto-adjusting CPAP and fixed-pressure CPAP are equivalent in terms of BP reduction. The question of which form of

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**Figure 1.** Time trend data of oxygen saturation and nighttime blood pressure (BP) under continuous positive airway pressure (CPAP) recorded by the nocturnal BP monitoring system in Case 2.  
A: The data obtained in the auto-adjusting mode CPAP before CPAP titration.  
B: The data obtained after manual CPAP titration.  
SBP, systolic blood pressure.
CPAP, i.e. auto-adjusting-CPAP or fixed-pressure CPAP, is more effective for BP reduction remains controversial.

The optimization of SA treatment will probably contribute to the improvement of positive intrathoracic pressure, decreased arousal, prolonged CPAP usage, and suppression of sympathetic hyperactivity. Individualized and optimized SA therapy with CPAP titration will be indispensable during strict antihypertensive management for SA patients with uncontrolled hypertension.

Conflicts of Interest and Source of Funding

The authors have no conflicts of interest or sources of funding in relation to this case report.

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