Beneficial Effects of Long-Term CPAP Treatment on Sleep Quality and Blood Pressure in Adherent Subjects With Obstructive Sleep Apnea

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BACKGROUND: Obstructive sleep apnea (OSA) is associated with increased risk of cardiovascular diseases. Although CPAP is the first treatment choice for moderate-to-severe OSA, acceptance of and adherence to CPAP remain problematic. High CPAP adherence is generally defined as ≥4 h of use/night for ≥70% of the nights monitored. We investigated the long-term beneficial effects of CPAP on sleep quality and blood pressure in subjects with moderate-to-severe OSA according to high or low CPAP adherence. METHODS: We retrospectively analyzed 121 subjects with moderate-to-severe OSA from August 2008 to July 2012. These subjects were divided into 3 groups: (1) no CPAP treatment ($n = 29$), (2) low CPAP adherence ($n = 28$), and (3) high CPAP adherence ($n = 64$). All subjects were followed up for at least 1 y. The 3 groups were compared regarding anthropometric and polysomnographic variables, presence of cardiovascular comorbidities, and blood pressure at baseline and at the last follow-up. RESULTS: The no-treatment group showed significant increases in oxygen desaturation index and blood pressure. The high-adherence group showed significant improvement in daytime sleepiness, apnea-hypopnea index (AHI), oxygen desaturation index, and blood pressure. Although the AHI was also significantly decreased after CPAP treatment in the low-adherence group, blood pressure remained unchanged. CONCLUSIONS: CPAP treatment had beneficial effects on both sleep quality and blood pressure only in subjects with OSA and high CPAP adherence who used CPAP for ≥4 h/night for ≥70% of nights monitored. Subjects with low CPAP adherence received beneficial effects on AHI, but not blood pressure. Key words: obstructive sleep apnea; CPAP; sleep quality, blood pressure.

Introduction

The incidence of obstructive sleep apnea (OSA) increases with age.1 It is known that OSA is a considerable risk factor for both cardiovascular and cerebrovascular diseases.2 CPAP treatment is the standard for managing OSA and has been proven to reduce the apnea-hypopnea index (AHI), improve sleep quality in subjects with OSA,3 and decrease the risk for cardiovascular comorbidities.4 An increase in blood pressure has a high correlation with OSA, and CPAP lowers the mortality rate in subjects with severe OSA.5 However, the limitations of CPAP treatment lie mainly in acceptance and adherence. CPAP adherence is reported in up to 50% of subjects with OSA.4 Failure to adhere to CPAP therapy may occur in up to 25–50% of patients, with patients typically abandoning therapy within the first 4 weeks of treatment.6

The differences in CPAP adherence are noted in many studies with various outcomes, but the long-term effects of CPAP have not been studied according to different CPAP adherence in detail. Thus, the purpose of this study was to compare the long-term effects of CPAP on sleep quality and blood pressure among CPAP-resistant, CPAP-adherent, and CPAP-nonadherent subjects.
Methods

Study Subjects

This study was approved by the institutional review board at Taipei Tzu Chi Hospital of the Buddhist Tzu Chi Medical Foundation (registration code 00-IRB-011-X). We retrospectively reviewed the medical charts of subjects with moderate-to-severe OSA between August 2008 and July 2012. All subjects' information was anonymized and de-identified before analysis.

Figure 1 demonstrates the flow chart for subject selection. Initially, there were 638 patients referred for overnight polysomnography (PSG) to rule out OSA. None of the patients were diagnosed as having OSA previously. Thirty-five patients who underwent split-night PSG were excluded. Therefore, 603 patients entered the full-night PSG study. Subsequently, 132 patients with PSG results showing non-apnea (AHI < 5 episodes/h) and 147 patients with an AHI of 5–15 episodes/h were also excluded. Thus, there were 324 patients with an AHI of ≥15 episodes/h.

Among these 324 patients with moderate-to-severe OSA, there were 103 patients who refused CPAP treatment and 221 patients who accepted CPAP treatment. One-hundred twenty-three patients who accepted CPAP were excluded because they used CPAP for <6 months. Thus, there were 98 subjects who accepted and used CPAP for >6 months. Patients who had no second PSG examination at follow-up were also excluded including 6 of 98 CPAP acceptors and 74 of 103 CPAP resisters. Finally, 121 subjects with moderate-to-severe OSA were included in the final analysis. Twenty-nine subjects who refused CPAP composed the no-treatment group, and 28 and 64 subjects who accepted CPAP composed the low- and high-adherence group, respectively.

Anthropometric Measurements and Demographic Data

We collected the baseline clinical characteristics, including age, sex, neck circumference, body mass index (BMI, kg/m²), smoking status, alcohol consumption, and cardiovascular comorbidities (including hypertension, coronary artery disease, and cerebrovascular accident). Morning and evening systolic (SBP) and diastolic (DBP) blood pressure were also checked and recorded before and after each PSG examination.

Blood Pressure Measurement

Blood pressure was measured while subjects were supine by technicians using an automated sphygmomanom-
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Assessment of Excessive Daytime Sleepiness

Before the overnight PSG study, excessive daytime sleepiness was evaluated at the sleep center using the Epworth Sleepiness Scale (ESS). It was defined as an ESS score of >11.

Sleep Parameters

A standard overnight PSG was performed by trained sleep technicians who had received appropriate training from the Taiwan Society of Sleep Medicine and had at least 1 year of experience. The PSG was recorded for at least 6 h with standard monitoring, including electroencephalography, electrooculography, chin and bilateral anterior tibial surface electromyography, electrocardiography, air flow through the nose and mouth by thermistor, thoraco-abdominal movements by respiratory inductive plethysmography, position sensor on the respiratory inductive plethysmography, snore sensor, and SpO2 simultaneous.

PSG data were analyzed by manual scoring of every 30 s epoch. Sleep stage was scored by trained sleep technicians according to the standard criteria of Rechtschaffen and Kales. Apnea events were categorized into obstructive apnea, central apnea, mixed apnea, or hypopnea events. An apnea event was defined as the 80–100% reduction of air flow for at least 10 s. Obstructive apnea was defined as the requisite reduction of 80–100% of air flow for at least 10 s with continued respiratory effort recorded in the chest and abdomen movement channels. Central apnea was defined as a cessation of both air flow and respiratory effort for at least 10 s. Mixed apnea was defined by a period of both air flow and respiratory effort cessation, followed by a period of continued air-flow cessation despite gradually increasing respiratory effort. A hypopnea event was defined as at least 50% reduction of air flow for at least 10 s or at least 30% reduction of air flow for at least 10 s compared with baseline and associated with at least 3% oxygen desaturation or with an electroencephalogram arousal. The AHI was calculated as the total number of ≥3% desaturations/h. Sleep efficiency was defined as the fraction of total sleep time to total recording time.

CPAP Acceptance and Adherence

All subjects were offered CPAP treatment. CPAP acceptance refers to the subjects who meet the selection criteria for CPAP treatment and were willing to try CPAP for use at home. CPAP adherence refers to the subjects who used CPAP and delivered a pre-set level over a given time period. Subjects were routinely followed up every 3 months at the out-patient clinic. According to the policy of our sleep center, we routinely downloaded objective CPAP use data (recorded by the device software) at each visit. The CPAP use data included percentage of days used, percentage of nights during which CPAP was used for ≥4 h, and the overall mean hours of use/night. High CPAP adherence was defined as ≥4 h of CPAP use/night for ≥70% of the nights monitored. Subjects who did not meet these levels of CPAP use were defined as having low CPAP adherence.

Statistical Analysis

SAS 9.2 (SAS Institute, Cary, North Carolina) was used for the statistical analysis. The continuous variables (ie, demographics, ESS scores, overnight PSG data, blood pressure data, and CPAP adherence hours) were presented as mean ± SD. The categorical variables (ie, sex, disease history, excessive daytime sleepiness, and smoking and alcohol habits) were expressed by count and percentage. For comparisons of the 3 treatment groups, one-way analysis of variance was performed to examine the continuous variables at baseline. A chi-square test was used to examine the categorical variables. When a significant difference between groups was apparent, multiple comparisons were performed using the Bonferroni procedure with type-1 error adjustment. To determine the difference between baseline and follow-up within the treatment groups, a paired t test was performed for continuous variables, and the McNemar test was performed for categorical variables. All statistical assessments were evaluated at a 2-sided α level of .05.

Results

Demographics of Study Population

The study analyzed 121 subjects with moderate-to-severe OSA; there were 103 males (85.1%) and 18 females (14.9%) (Table 1). There was no difference in neck circumference, BMI, smoking status, alcohol consumption, cardiovascular disease (including hypertension, cerebrovascular accident, and coronary artery disease), excessive...
daytime sleepiness, and PSG variables. The low-adherence group was significantly younger than the high-adherence group (49.7 ± 12.5 vs 57.2 ± 12.7 y, \( P = .037 \)). The no-treatment group showed a significant lower morning SBP than the high-adherence group (125.1 ± 12.8 vs 133.3 ± 14.9 mm Hg, \( P = .02 \)).

**Sleep Quality and Blood Pressure at Baseline and Follow-Up**

Table 2 summarizes the changes in BMI, daytime sleepiness, PSG variables, and blood pressure in the 3 groups at baseline and follow-up. The BMI was not significantly different in the 3 groups at follow-up. The ESS (11.1 ± 5.6 vs 9.5 ± 4.9, \( P = .006 \)) and excessive daytime sleepiness (57.8% vs 37.5%, \( P = .004 \)) of the high-adherence group decreased significantly. The sleep efficiency of the high-adherence group significantly decreased by 3.6% from baseline (79.7 ± 12% vs 76.1 ± 15.9%, \( P = .046 \)). Stage 1 sleep in the high-adherence group significantly decreased by 5.9% from baseline (37.7 ± 18.9% vs 31.8 ± 14.6%, \( P = .01 \)). The rapid eye movement sleep of the no-treatment group significantly increased by 3.2% from baseline.
Table 2. Sleep Quality and Blood Pressures at Baseline and Follow-Up in the 3 Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Treatment (n = 29)</th>
<th>Low Adherence (n = 28)</th>
<th>High Adherence (n = 64)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-Up</td>
<td>P</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>30.3 ± 4.4</td>
<td>29.9 ± 4.6</td>
<td>.26</td>
</tr>
<tr>
<td>Daytime sleepiness</td>
<td>11.0 ± 4.1</td>
<td>11.7 ± 5.3</td>
<td>.34</td>
</tr>
<tr>
<td>ESS score</td>
<td>17 (58.6)</td>
<td>19 (65.5)</td>
<td>.73</td>
</tr>
<tr>
<td>Overnight PSG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>79.3 ± 13.7</td>
<td>77.2 ± 14.3</td>
<td>.48</td>
</tr>
<tr>
<td>Stage 1, %</td>
<td>30.6 ± 15.7</td>
<td>30.1 ± 14.3</td>
<td>.84</td>
</tr>
<tr>
<td>Stage 2, %</td>
<td>56.3 ± 14.7</td>
<td>55.9 ± 12.8</td>
<td>.88</td>
</tr>
<tr>
<td>Stage 34, %</td>
<td>4.2 ± 12.1</td>
<td>1.8 ± 4.5</td>
<td>.35</td>
</tr>
<tr>
<td>REM, %</td>
<td>9.0 ± 6.0</td>
<td>12.2 ± 6.7</td>
<td>.046*</td>
</tr>
<tr>
<td>AHI, episodes/h</td>
<td>47.8 ± 19.6</td>
<td>50.2 ± 21.5</td>
<td>.45</td>
</tr>
<tr>
<td>ODI, episodes/h</td>
<td>35.5 ± 21.4</td>
<td>42.7 ± 24.1</td>
<td>.02*</td>
</tr>
<tr>
<td>Evening blood pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>123.8 ± 13.1</td>
<td>130.1 ± 13.9</td>
<td>.01*</td>
</tr>
<tr>
<td>DBP</td>
<td>78.5 ± 10.2</td>
<td>79.0 ± 9.7</td>
<td>.78</td>
</tr>
<tr>
<td>Mean arterial blood pressure</td>
<td>93.6 ± 10.4</td>
<td>96.1 ± 10.7</td>
<td>.20</td>
</tr>
<tr>
<td>Morning blood pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>125.1 ± 12.8</td>
<td>134.6 ± 12.1</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>DBP</td>
<td>80.2 ± 10.1</td>
<td>84.4 ± 8.1</td>
<td>.006*</td>
</tr>
<tr>
<td>Mean arterial blood pressure</td>
<td>95.2 ± 10.4</td>
<td>101.2 ± 8.9</td>
<td>&lt;.001*</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD or n (%). * P < .05 indicates a significant difference before and after treatment within treatment groups.
BMI = body mass index
ESS = Epworth Sleepiness Scale
PSG = poly somnography
REM = rapid eye movement
AHI = apnea-hypopnea index
ODI = oxygen desaturation index
SBP = systolic blood pressure
DBP = diastolic blood pressure

(9.0 ± 6.0% vs 12.2 ± 6.7%, P = .046). The AHI significantly decreased in both the low-adherence group (52.0 ± 23.3 vs 42.0 ± 27.0 episodes/h, P = .03) and high-adherence group (54.8 ± 21.2 vs 39.7 ± 21.4 episodes/h, P < .001). The ODI significantly decreased in the high-adherence group (46.8 ± 24.8 vs 33.9 ± 20.5 episodes/h, P < .001), but increased in the no-treatment group (35.0 ± 21.4 vs 42.7 ± 24.1 episodes/h, P = .02). The evening SBP (123.8 ± 13.1 vs 130.1 ± 13.9 mm Hg, P = .01) and the morning SBP (125.1 ± 12.8 vs 134.6 ± 12.1 mm Hg, P < .001), DBP (80.2 ± 10.1 vs 84.4 ± 8.1 mm Hg, P = .006), and mean arterial blood pressure (95.2 ± 10.4 vs 101.2 ± 8.9 mm Hg, P < .001) significantly increased at follow-up in the no-treatment group. The evening DBP (79.3 ± 11.0 vs 76.3 ± 10.4 mm Hg, P = .01) and the morning SBP (133.3 ± 14.9 vs 127.2 ± 12.5 mm Hg, P = .001), DBP (84.6 ± 14.6 vs 81.1 ± 11.3 mm Hg, P = .02), and mean arterial blood pressure (100.8 ± 13.6 vs 96.6 ± 10.8 mm Hg, P = .004) significantly decreased at follow-up in the high-adherence group. Although there was no statistical significance, we still observed a trend of increasing blood pressure in the low-adherence group at follow-up (Table 2 and Fig. 2).

**CPAP Adherence**

Subjects in the high-adherence group had higher CPAP adherence than those in the low-adherence group (91.5 ± 7.8% vs 53.4 ± 16.5%, P < .001) (Table 3). The mean hours of CPAP use were longer in the high-adherence group than in the low-adherence group (6.5 ± 1.1 vs 3.9 ± 1.1 h, P < .001). There were no significant differences in the total follow-up duration among the 3 groups. The CPAP adherence was significantly different between the high- and low-adherence groups.

**Discussion**

In this study, we observed significant beneficial effects of long-term CPAP on sleep quality and blood pressure only in subjects with moderate-to-severe OSA and high CPAP adherence. If subjects with moderate-to-severe OSA did not receive CPAP treatment, their sleep quality and blood pressure would likely be affected.
blood pressure became worse over time. Although subjects with moderate-to-severe OSA and poor CPAP adherence had some beneficial effects on AHI, their blood pressure still had the potential to increase with time, leading to increasing risk of cardiovascular comorbidities. Better adherence to CPAP resulted in more beneficial effects in subjects with moderate-to-severe OSA.

**CPAP Acceptance in Subjects of Different Ages**

In this study, we noted that older subjects with OSA either completely refused CPAP treatment (no-treatment group, 55.9 ± 13.4 y old) or used CPAP very well (high-adherence group, 57.2 ± 12.7 y old), in contrast to the younger subjects with OSA (low-adherence group, 49.7 ± 12.5 y old). This was also documented in our previous study. This interesting result showing that subjects in the low-adherence group were younger reveals that savvy and health concern seem more common in older subjects. We claim that this is also possibly related to socioeconomic status. In Taiwan, OSA patients must purchase CPAP equipment at their own expense because it is not covered by national or commercial insurance, and the cost of CPAP...
Elderly patients with a higher economic status are able to pay for their health maintenance. However, some older patients with lower economic status choose not to treat OSA because they are struggling with costs of other aging-related medical problems.

**BMI**

The BMI has been noted as being highly correlated with OSA severity and blood pressure. As indicated in Table 2, the BMI at baseline and follow-up showed no significant changes among the 3 groups, indicating that the changes in AHI, ODI, or blood pressure in our study were not related to the BMI changes.

**Daytime Sleepiness and CPAP**

CPAP treatment can improve excessive daytime sleepiness in patients with OSA both short- and long-term. Zhao et al reported significant improvement in excessive daytime sleepiness after 1 month of CPAP treatment in subjects with moderate-to-severe OSA and coronary heart diseases. In other previous studies, a dose-response effect on ESS scores was documented after 3 months of CPAP treatment. In another earlier study, Pietrzyk et al found a beneficial effect of 1 y of CPAP treatment on excessive daytime sleepiness in subjects with OSA. Our findings were compatible with previous studies and also supported the dose-dependent response of excessive daytime sleepiness to long-term CPAP treatment. Subjects with poor CPAP adherence could not benefit from CPAP in relation to excessive daytime sleepiness.

**Sleep Quality and CPAP**

Cooke et al found that in mild-to-moderate Alzheimer’s disease subjects with OSA, CPAP resulted in deeper sleep after just one night, with improvements maintained for 3 weeks. Loredo et al found that CPAP improved sleep quality in subjects with OSA by consolidating sleep, reducing stage 1 sleep, and improving rapid eye movement sleep, but had no significant effect on stage 2 sleep or slow-wave sleep. CPAP can improve the AHI and ODI. In our study, we also observed some improvements in sleep quality: reducing stage 1 sleep, AHI, and ODI in the high-adherence group and reducing AHI in the low-adherence group. However, the sleep efficiency of the high-adherence group became worse because withdrawal from usual CPAP use made it difficult for them to maintain normal sleep. If patients with OSA do not receive adequate CPAP treatment, the OSA will become more severe.

**Blood Pressure and CPAP**

CPAP treatment is known to reduce the risk of fatal and nonfatal cardiovascular events, which are significantly increased by severe OSA. In a previous report, we found increasing evidence of greater cardiovascular risk for untreated mild OSA, and improving CPAP acceptance by subjects with mild OSA may be clinically important. However, the important issue is just how much CPAP use is enough to reduce blood pressure? Most previous studies (focused on the blood pressure-lowering effect of CPAP) used different definitions of CPAP adherence and thus make it difficult to draw conclusions. One earlier study, published in 2005, concluded that low CPAP use is better than no use in reducing OSA-related mortality. Another study in 2007 found a dose-dependent effect of CPAP on improvement of quality of life. Other studies also showed that a daily average of 3 h of CPAP use is sufficient to decrease DBP in subjects with severe OSA and hypertension. However, one report showed that CPAP therapy has little effect on reducing blood pressure in subjects with OSA. Until recently, there were 3 meta-analyses that focused on duration of CPAP use, and they found that both diurnal SBP and DBP were significantly reduced only with CPAP use for ≥4 weeks and for ≥4 h/night. In our present study, we used the same duration to define CPAP adherence (≥4 h/night for ≥70% of nights) and obtained comparable results showing the long-term beneficial effects of CPAP on blood pressure in subjects with moderate-to-severe OSA who adhere to CPAP treatment.

**Adherence Effect on Outcome**

The American Academy of Sleep Medicine states that adherence to CPAP treatment is crucial and that routine assessment is necessary. Although it is known that CPAP is an effective therapy for OSA and long-term adherence has a considerable influence on its effectiveness, only about half of patients with OSA have high long-term adherence. Our present study revealed that subjects with moderate-to-severe OSA and high CPAP adherence obtained beneficial effects in reducing cardiovascular comorbidities with lower blood pressure. How to improve CPAP acceptance and adherence is always problematic and should be addressed in the future.

**Possible Mechanism of CPAP on Blood Pressure**

CPAP improves endothelial function (not arterial stiffness) in minimally symptomatic OSA, which is a cardiovascular risk factor. Endothelial dysfunction is known to play a central role in the development of atherosclerosis and is associated with cardiovascular risk factors.
oll et al\textsuperscript{40} reported that CPAP therapy had a correlation with down-regulation of renal renin-angiotensin system activity. A randomized controlled study also showed that CPAP significantly reduced plasma aldosterone concentration in subjects with OSA and hypertension.\textsuperscript{41} In addition, research has emphasized that thrombotic tendency and blood viscosity are possible mechanisms of disease in subjects with OSA and cardiovascular comorbidity.\textsuperscript{2}

**Limitations of This Study**

First, our study had the inherent weakness of a retrospective design and a relatively small sample size. Larger, prospectively controlled studies are warranted to further study the effects of CPAP treatment on sleep quality, blood pressure, and long-term cardiovascular comorbidities in different patterns of CPAP use. Second, in our sleep center, we used a thermistor, not a nasal pressure transducer, to detect air flow, and we did not use an esophageal pressure sensor to detect respiratory effort-related arousal. This might result in an underestimation of the severity of OSA and consequently a misclassification of some subjects with moderate-to-severe OSA as mild. Third, we did not evaluate the impact of antihypertensive medicine, possible sleeping pill use, or other medical conditions that would affect blood pressure control (such as diabetes mellitus and hyperlipidemia). In addition, arbitrarily defining CPAP adherence using a 4-h cutoff value may not be optimal because subjects normally have varied sleep durations.

**Conclusions**

This study demonstrated that subjects with moderate-to-severe OSA and high CPAP adherence obtained long-term beneficial effects in sleep quality and reduced cardiovascular comorbidities with lower blood pressure. Subjects with low CPAP adherence demonstrated beneficial effects on only AHI, but not blood pressure. Future studies are needed to identify the key obstacles and solutions to CPAP adherence. Strategies for improving CPAP adherence are still an issue.

**REFERENCES**


