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The effect of oral appliance therapy on blood pressure in patients with obstructive sleep apnea

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Abstract The objective of the study was to investigate the effects of oral appliance (OA) therapy on ambulatory blood pressure in patients with obstructive sleep apnea (OSA). Eleven OSA patients who received OA therapy were prospectively investigated. Ambulatory blood pressure was measured for 20 h from 4:00 P.M. to 12:00 noon the next day using an ambulatory blood pressure monitor. The Respiratory Disturbance Index (RDI) was measured in the pretreatment and posttitration periods. The OA was titrated to reach a therapeutic jaw position over 2 to 8 months, and

posttitration measurements were repeated. At posttitration, the RDI was significantly decreased from a mean (SD) of 24.7 (20.1) to 6.1 (4.5). Significant reductions in diastolic blood pressure (DBP) and mean arterial pressure (MAP) were found for the 20-h periods, and systolic blood pressure (SBP), DBP, and MAP while asleep. The mean values were 79.5 (5.5) to 74.6 (6.0) for DBP and 95.9 (5.4) to 91.2 (5.9) for MAP, for over a 20-h period, and 118.4 (10.0) to 113.7 (9.1) for SBP, 71.6 (8.0) to 67.2 (7.9) for DBP, and 88.4 (8.0) to 83.9 (7.5) for MAP, while asleep. This study suggests that successful OSA treatment with an OA may also be beneficial to lower blood pressure in OSA patients, as previously suggested for nasal continuous positive airway pressure therapy.

Keywords Blood pressure monitoring · Ambulatory · Sleep apnea · Obstructive · Mandibular advancement

Introduction

Obstructive sleep apnea (OSA) affects approximately 4% of individuals between the ages of 30 and 60 years in America [1]. This syndrome may be associated with arterial oxygen desaturation, sleep disruption, severe snoring, and excessive daytime sleepiness. Other primary health consequences that may result from this chronic sleep disruption or recurrent hypoxemia include neuropsychiatric and cardiovascular

sequelae. Cardiovascular sequelae may include pulmonary and systemic hypertension, congestive heart failure, arrhythmia, myocardial infarction, and stroke. Although controversy remains as to how much impact OSA has on blood pressure (BP), independent of other confounding factors such as obesity and age, evidence exists that the presence of OSA worsens BP status. A recent extensive study on a large cohort of middle-aged and older persons, as well as a large longitudinal study including a 4-year follow-up study,

Table 1 Demographic data and obstructive sleep apnea status of 11 patients

No.	BP Med	Sex	Age	BMI	Pre-RDI	Post-RDI
1	No	F	54	23.6	18.8	1.1
2	No	M	46	30.3	87.1	8.9
3	No	F	58	35.8	19.5	0.0
4	No	M	54	31.7	13.3	13.3
5	No	M	70	22.9	21.8	7.0 ^a
6	No	M	46	26.7	23.4	6.2 ^a
7	No	M	45	32.6	17.0	14.8 ^a
8	No	M	43	28.1	11.1	5.4 ^a
9	On	M	53	25.8	17.9	4.4 ^a
10	On	M	53	22.9	17.0 ^b	1.7 ^b
11	No	F	54	29.0	26.2 ^b	3.8 ^b
Mean			52.2	28.6	24.7	6.1
SD			7.2	4.0	20.1	4.5

BP Med a patient on antihypertensive medication(s), *BP* blood pressure, *BMI* Body Mass Index, *RDI* Respiratory Disturbance Index, *Pre-* pretreatment, *Post-* posttitration, *SD* standard deviation

^aRemmers sleep recorder

^bOxygen Desaturation Index

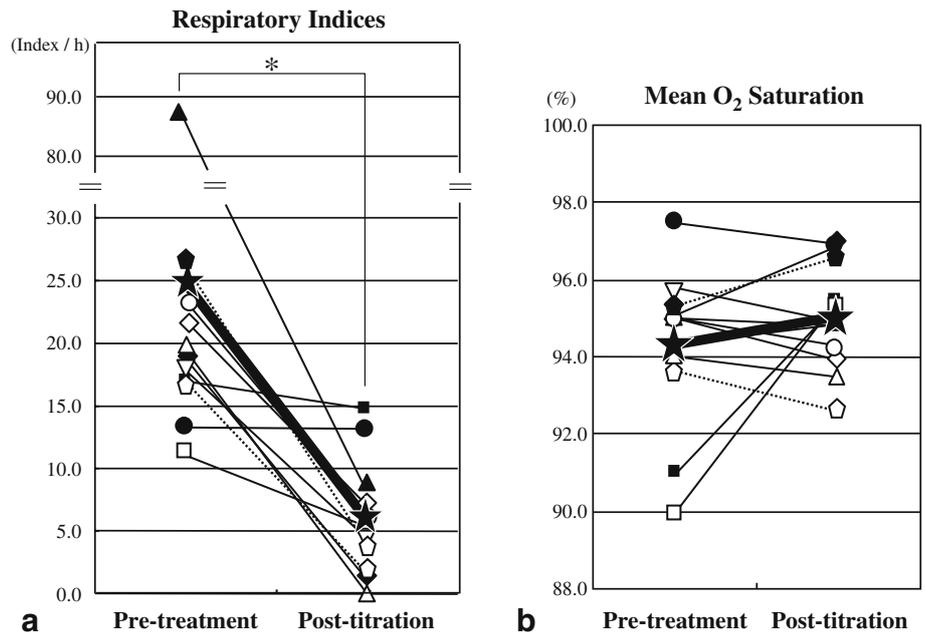
supported the relationship between hypertension and OSA [2, 3].

In terms of treatment for OSA, the effects of nasal continuous positive airway pressure (nCPAP) have been extensively studied, and this therapy significantly decreases the Respiratory Disturbance Index (RDI) [4]. However, despite its high effectiveness, nCPAP is not universally accepted by patients because of its cumbersome nature. Treatment with oral appliances (OAs) has been suggested as one alternative [5, 6]. It has been well documented that anterior displacement of the mandible reduces the severity of OSA [7–9]. Thus, OA therapy can be an important treatment option, especially in milder cases of sleep apnea and in patients with moderate to severe OSA who cannot tolerate or refuse nCPAP use [10].

Recently, Gotsopoulos et al. [11] reported the short-term effect of OA therapy on BP. They found a significant

reduction in BP with an OA when compared to controls. The association between OSA and hypertension has also been investigated through an evaluation of the effect of nCPAP on BP. Previous reports have measured BP using an invasive or a noninvasive method and in a continuous or an intermittent manner. Subjects included in these studies consisted of normotensive and/or hypertensive individuals. Results varied [12–15], most likely because of differences in methodology and study design. However, recent studies have shown that nCPAP may reduce BP in patients with OSA. An ambulatory BP monitor (ABPM) can provide noninvasive and intermittent but repeated BP measurements. Using an ABPM, Dimsdale et al. [16] have shown that therapeutic nCPAP decreased nighttime BP greater than placebo nCPAP, and Faccenda et al. [17] have shown that nCPAP decreased the 24-h average diastolic BP, particularly in patients with nocturnal oxygen desaturation.

Fig. 1 **a** Individual and mean changes in respiratory indices in pretreatment and posttitration. Each *solid line* indicates a change in the RDI, and each *dotted line* indicates a change in the ODI. The *thick line with stars* indicates the mean change, and each *thin line with symbols* indicates each individual change. **b** Individual and mean changes in mean O₂ saturation. The *thick line with stars* indicates the mean change, and each *thin line with symbols* indicates each individual change. **p*<0.05



Since OAs also improve OSA symptoms and decrease the RDI, it is reasonable to postulate that they may have a similar effect on BP. The aim of this study was to test the hypothesis that successful OA treatment reduces BP in patients with OSA.

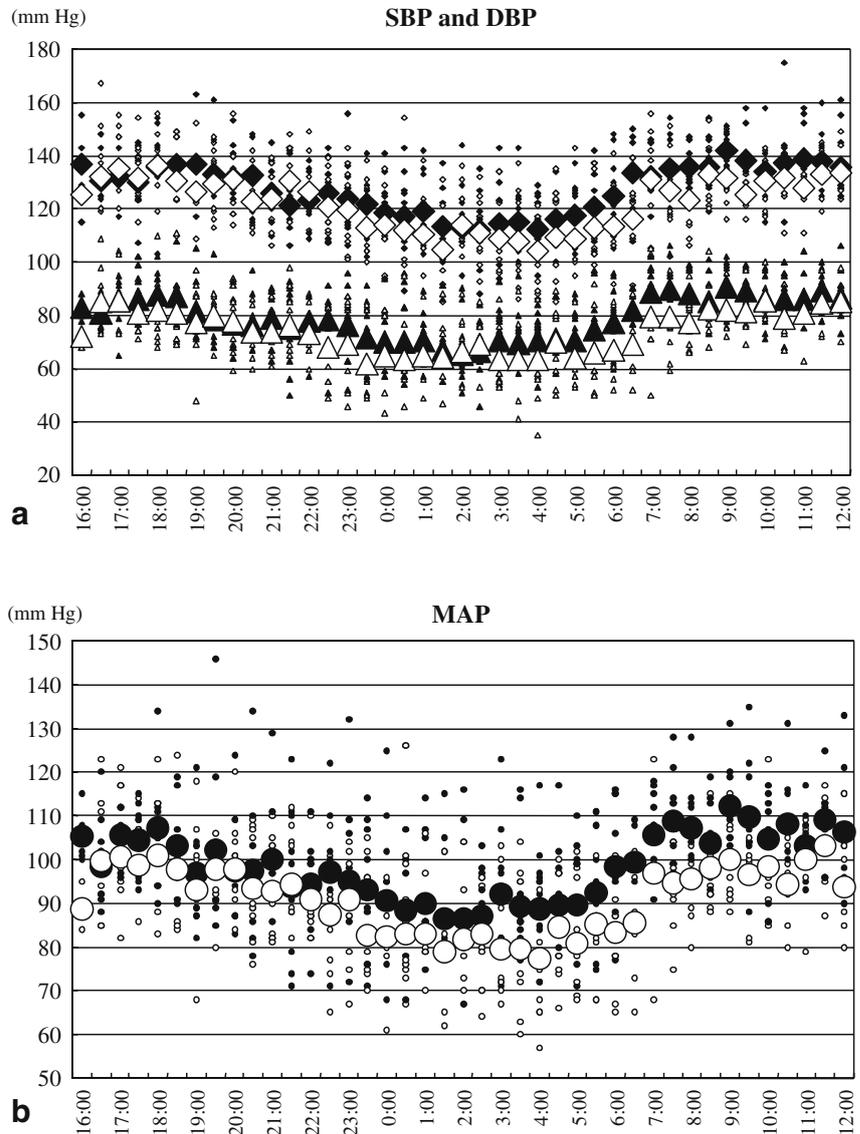
Methods

Patients

Twenty-two consecutive OSA patients referred to the Dental Sleep Apnea Clinic at The University of British Columbia or the orthodontic practice of Dr. Alan A. Lowe to be treated

with a Klearway oral appliance [8] were invited to the study. Out of 22 patients, 14 patients met the following inclusion and exclusion criteria and agreed to participate in the study. The inclusion criteria were as follows: (1) patients who were diagnosed as having OSA made by a sleep specialist; (2) patients who had systolic BP (SBP) of at least 120 mmHg and/or diastolic BP (DBP) of at least 80 mmHg, who were not categorized as having normal BP [18] at screening; screening BP measurements were done with the ABPM (Spacelabs, model number 90207, Redmond, WA) but inflations were started manually [19] (If a patient had been on medication, he/she and his/her physician were advised to maintain the antihypertensive medication(s) at the current dosage for the duration of the study.); and (3) patients who

Fig. 2 **a** Time course changes of systolic and diastolic blood pressure in pretreatment (*black*) and posttreatment (*white*). *Diamond and triangle symbols* indicate SBP and DBP, respectively. *Small and large symbols* indicate individual and mean data, respectively. *Black and white symbols* indicate pretreatment and posttreatment data, respectively. **b** Time course changes of MAP in pretreatment (*black*) and posttreatment (*white*). *Small and large symbols* indicate individual and mean data, respectively. *Black and white symbols* indicate pretreatment and posttreatment data, respectively



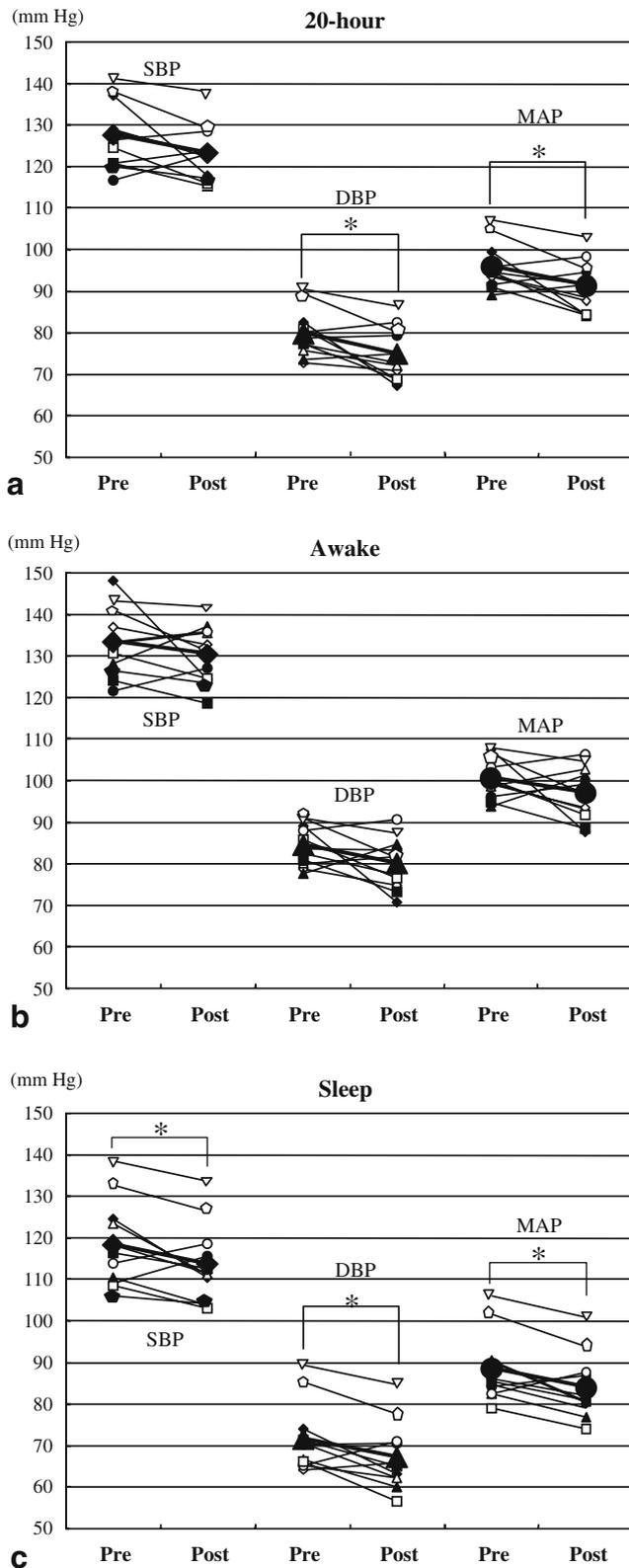


Fig. 3 **a** Systolic blood pressure, diastolic blood pressure, and MAP changes for 20-h measurement. **b** Systolic blood pressure, diastolic blood pressure, and MAP changes while awake. **c** Systolic blood pressure, diastolic blood pressure, and MAP changes during sleep. The *thick line with diamond, triangle, and circle symbols* indicate the mean change in systolic blood pressure, diastolic blood pressure, and MAP, respectively. Each *thin line* indicates individual changes. * $p < 0.05$

met our clinical criteria for treatment with the OA who had enough teeth to retain the device, no current or history of severe temporomandibular dysfunction [10]. Patients were excluded from the study when they (1) were unable to give informed consent; (2) had SBP below 120 mmHg and DBP below 80 mmHg at screening and no history of hypertension; (3) had SBP and/or DBP at least 160 and 100 mmHg, which is considered stage 2 hypertension, regardless if they were taking antihypertensive medications; (4) had a high alcohol intake (>80 g/day); (5) had a major illnesses other than OSA and hypertension; and (6) were taking medication(s) other than antihypertensive medication. Patients who changed antihypertensive medication status and/or had any symptoms which prevent regular OA use were excluded from the statistical analysis. This study was approved by the Clinical Research Ethics Board at The University of British Columbia. All subjects gave written informed consent prior to the study.

Protocol

When patients came to our clinic to have records taken for their OA construction, they were instructed by one of the investigators (RO) on how to wear the BP cuff and how to use the ABPM. The instruction included the position and tightness of the cuff, how to turn the device on and off, and telling the patient to relax and rest as much as possible while the cuff inflates. Each patient was asked to wear the ABPM by him/herself from 4:00 P.M. 1 day to 12:00 noon the next day for a total of 20 h, and readings were taken every 30 min. Patients were also asked to indicate the time they went to bed and the time they got out of bed. Between 1 day and 2 weeks after the pretreatment BP measurement, an OA was inserted. Based on our regular clinical protocol of the OA, we used an acclimatization period of 1 to 3 weeks at the original two-thirds of maximum mandibular advancement position. The OA was then titrated using an advancement screw in the appliance to reach the therapeutic mandibular position over 2 to 8 months. When a patient and/or bed partner noticed subjective symptomatic improvements, we stopped the titration, and a posttitration ABPM recording was performed while the patient slept wearing the OA. The posttitration ABPM recording was scheduled on a similar activity day (e.g., weekday and weekday, weekend and weekend) to the baseline study. Posttitration sleep monitoring was also performed within 2

Table 2 Summary of mean BP values and statistical analysis

	Systolic BP					Diastolic BP					MAP				
	Pre		Post		<i>p</i> value	Pre		Post		<i>p</i> value	Pre		Post		<i>p</i> value
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		Mean	SD	Mean	SD	
20-h	127.6	7.8	123.1	6.5	0.067	79.5	5.5	74.6	6.0	0.017*	95.9	5.4	91.2	5.9	0.022*
Awake	133.3	7.9	130.2	6.8	NS	84.4	4.7	80.2	6.0	0.076	100.7	4.8	96.9	6.2	NS
Afternoon	131.1	7.7	130.9	8.2	NS	82.1	4.7	79.2	7.6	NS	98.4	4.9	96.4	7.7	NS
Morning	136.5	8.2	130.1	6.2	0.086	87.5	6.8	82.6	5.7	NS	103.6	6.2	98.2	5.9	0.074
Sleep	118.4	10.0	113.7	9.1	0.033*	71.6	8.0	67.2	7.9	0.017*	88.4	8.0	83.9	7.5	0.009*

20-h 20-h measurement, MAP mean arterial pressure, NS not significant

A *p* value above 0.10

*Significant at 5% level

weeks by either hospital PSG or a home sleep monitoring system (Remmers sleep recorder, Sagatec, Calgary, Canada) for patients who had pretreatment PSG records, or by overnight oximetry in two patients who had pretreatment oximetry records only.

Analysis

The ABPM device stores raw data on SBP, DBP, mean arterial pressure (MAP), and heart rate (HR) for each time period. These data were downloaded to a personal computer and transferred to a software program (Excel 2001, Microsoft) to calculate 20-h, sleep, awake in the morning and in the afternoon, and awake (total awake) time mean values for each of SBP, DBP, MAP, and HR based on the patient's diary record. For statistical analysis purposes, the Oxygen Desaturation Index (ODI) was taken as an alternative of RDI in patients with oximetry records. Pretreatment and posttitration data regarding each BP variable and RDI were compared for each recording time period using a two-tailed paired *t* test. A *p* value below 0.05 was taken as statistically significant. Statistical analysis was done using a statistical software package (StatView 5.0; SAS Institute Inc., North Carolina, USA).

Results

Of the 14 patients who started the protocol, 3 patients did not complete the follow-up recording due to a change in antihypertensive medication, unwillingness to wear the ABPM device in the posttitration period, or being uncontactable during the titration period. All results subsequently shown are data from the 11 patients who completed the protocol. Demographic and sleep study data in pretreatment and posttitration are shown in Table 1. The mean (SD) age was 52.2 (7.2) years. The Body Mass Index (BMI) of the patients was 28.6 (4.0). No patient demonstrated a signif-

icant change in BMI during the study period, which could have represented a confound for explaining treatment outcomes.

Figure 1a shows individual changes in RDI. Figure 1b shows individual changes in mean O₂ saturation. The average length of time between the pretreatment and posttitration ABPM was 5.2 months. The RDI decreased from 24.7 (20.1) to 6.1 (4.5), which was statistically significant and represents a large effect size of $d=-1.51$. The mean O₂ saturation increased from 94.1 (2.1) to 95.0 (1.4), although this was not significant (effect size $d=-0.5$). In pretreatment, the SBP and DBP were 133.3 (7.9) mmHg and 84.4 (4.7) mmHg while awake and 118.4 (10.0) mmHg and 71.6 (8.0) mmHg while asleep, respectively. While not hypertensive as a whole, 8 out of 11 of our patients would be classified as hypertensive according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [18], in which normal BP values taken by an ABPM are SBP and DBP <135 and 85 mmHg while awake and <120 and 75 mmHg while asleep.

Figure 2a shows the time courses of raw SBP and DBP readings of each patient and the means plotted from 4:00 P.M. to 12:00 noon the next day in pretreatment and posttitration. A small symbol indicates each individual reading. Large symbols indicate mean values, which were calculated from available readings for each recording time. Upper lines (diamonds) indicate SBP and lower lines (triangles) indicate DBP. Values in black are pretreatment and values in white are posttitration. Both the SBP and DBP seem to have decreased especially during the night after 10:00 P.M. Figure 2b shows time courses of raw MAP readings of each patient and the averages plotted from 4:00 P.M. to 12:00 noon the next day in pretreatment and posttitration. MAP showed a clear decrease during the whole 20-h recording.

Figure 3a–c shows individual and mean changes in SBP, DBP, and MAP between pretreatment and posttitration. In these figures, each patient is represented by a thin line and a

unique symbol. Thick lines with large diamonds, triangles, and circles indicate the mean values of SBP, DBP, and MAP, respectively. All BP results show a reduction, although not all reached significance. Figure 3a shows data collected over 20 h. DBP and MAP for 20-h recording were significantly reduced from 79.5 to 74.6 mmHg and 95.9 to 91.2 mmHg, respectively (with effects sizes of $d=-0.84$ and $d=-0.84$). While awake, there were no significant changes in SBP, DBP, or MAP (Fig. 3b). Figure 3c shows significant reductions in SBP, DBP, and MAP during sleep with changes of 118.4 to 113.7 mmHg, 71.6 to 67.2 mmHg, and 88.4 to 83.9 mmHg ($d=-0.47$, $d=-0.55$, and $d=-0.58$), respectively (Table 2).

Discussion

We found a possible effect of a reduction in BP after OA use in patients with OSA similar to the documented effects of nCPAP. Although previous results regarding possible effects of nCPAP in lowering BP varied among studies [12–17], a recently published prospective, randomized study using a portable instrument with two finger cuffs showed that SBP and DBP as well as MAP decreased significantly using therapeutic nCPAP, both during the day and night, compared to subtherapeutic nCPAP. The decrease in MAP for the total recording period in the study was 9.9 mmHg [20]. Compared to the instrument used in that study, an ABPM may awaken the patient through intermittent inflations of the cuff. Although this characteristic of the ABPM would be expected to work against the hypothesis that “nCPAP can reduce BP while asleep,” several controlled studies using an ABPM have successfully demonstrated a reduction in BP with nCPAP therapy. Among them, one recent study compared the effects of nCPAP on BP in hypertensive patients with an RDI above 5 and those with an RDI below 5 [21]. The study demonstrated that mean nocturnal SBP and DBP changes after nCPAP treatment in the group with RDI above 5 were significantly different from those in the group with RDI below 5 by -7.8 vs $+0.3$ mmHg and -5.3 vs -0.7 mmHg. Another prospective, randomized trial demonstrated that therapeutic nCPAP reduced mean ambulatory BP by 2.5 mmHg, whereas subtherapeutic nCPAP increased BP by 0.8 mmHg [22]. Thus, we consider the ABPM to be a useful method in detecting the effects of an OA on BP in patients with OSA.

To date, only one published report documents that OAs also have a beneficial effect on ambulatory BP [11]. Gotsopoulos et al. showed significant 3-mmHg reductions in 24-h DBP. They also found similar reduction in 24-h SBP during the early morning. Compared to their study, several limitations in study design need to be taken into account when interpreting our data. The patient sample was heter-

ogeneous regarding OSA severity and BP status. The portable sleep monitoring system used in some follow-up measurements has been shown to be valid for calculating the RDI using its special algorithm [23]; however, we included two patients diagnosed by overnight oximetry. In addition, the design was a simple intervention study without control subjects, and for that reason, acclimatization to wearing the ABPM might have contributed to reductions in BP. We discovered significant reductions in MAP during sleep but not while awake, which lessens the likelihood that the changes were due to acclimatization. In addition, the findings were consistent across all time epochs and BP indices, and a clinical trial reported that untreated patients undergoing 24-h ABPM showed no discernible BP changes for more than 3 months [24]. We excluded one patient from the analysis who did change antihypertensive medication, and consequently, patients on antihypertensive medications included did not change the dose or type of medications during the study. Our results show significant reductions in DBP and MAP during the 20-h recording period and SBP, DBP, and MAP during sleep. Mean changes in our study in MAP for the whole 20 h and during sleep between pretreatment and posttreatment were 4.7 and 4.5 mmHg, which are comparable to previous nCPAP studies and Gotsopoulos et al.’s study. The differences between an OA and nCPAP treatment need to be taken into account. Provided the patient can tolerate nCPAP, it should be more effective and have a higher success rate than an OA. On the other hand, the effectiveness of treatment is compromised with noncompliance which is higher for nCPAP [5, 6, 9]. Compliance and duration of nCPAP use during the night may affect the reductions in BP. Every patient in our study reported regular (7/7) and whole night (entire time in bed) use of the OA. In their study with the OA, Gotsopoulos et al. found significant reductions during 24 h and awake, and pointed out that the BP reduction observed with OA was apparent in the early morning period. Since our titratable appliance usually took more than 2 months to achieve therapeutic jaw position and treatment success (Post-RDI<10) was high in our current study (9/11), it is possible that these differences may lead to different results. We found significant differences in 20-h and sleep periods; however, apparent reductions were found in early morning period, which were shown in Figs. 1 and 2. Gotsopoulos et al.’s study had strengths in the design, we believe we also looked at the same changes with OA, and it also supports the hypothesis that successful OA treatment reduces BP in patients with OSA.

Conclusion

Comparing pretreatment and posttreatment ambulatory BP in OSA patients, MAP during a 20-h time period and

during sleep decreased significantly in the posttitration period. This result suggests that successful OSA treatment with OA could be beneficial in lowering BP. Although the requirement for further controlled trials with larger sample sizes is obvious, this study supports the hypothesis that successful OA treatment for OSA may reduce BP.

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References

1. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr A (1993) The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 328:1230–1235
2. Nieto FJ, Young TB, Lind BK, Shahar E, Samet JM, Redline S, D'Agostino RB, Newman AB, Lebowitz MD, Pickering TG (2000) Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *JAMA* 283:1829–1836
3. Peppard PE, Young T, Palta M, Skatrud J (2000) Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med* 342(19):1378–1384
4. Sullivan CE, Issa FG, Berthon-Jones M, Eves L (1981) Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet* 1(8225):862–865
5. Randerath WJ, Heise M, Hinze R, Ruehle KH (2002) An individually adjustable oral appliance vs continuous positive airway pressure in mild-to-moderate obstructive sleep apnea syndrome. *Chest* 122:569–575
6. Ferguson KA, Ono T, Lowe AA, Keenan SP, Fleetham JA (1996) A randomized crossover study of an oral appliance vs nasal-continuous positive airway pressure in the treatment of mild-moderate obstructive sleep apnea. *Chest* 109:1269–1275
7. Ferguson KA, Ono T, Lowe AA, Al-Majed S, Love LL, Fleetham JA (1997) A short term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnoea. *Thorax* 52:362–368
8. Lowe AA, Sjöholm TT, Ryan CF, Fleetham JA, Ferguson KA, Remmers JE (2000) Treatment, airway and compliance effects of a titratable oral appliance. *Sleep* 23:S172–S178
9. Randerath WJ, Heise M, Hinze R, Ruehle KH (2002) An individually adjustable oral appliance vs continuous positive airway pressure in mild-to-moderate obstructive sleep apnea syndrome. *Chest* 122:569–575
10. Lowe AA (2000) Oral appliances for sleep breathing disorders. In: Kryger M, Roth T, Dement W (eds) *Principles and practice of sleep medicine*, 3rd edn. Saunders, Philadelphia, PA, pp 929–939
11. Gotsopoulos H, Kelly JJ, Cistulli PA (2004) Oral appliance therapy reduces blood pressure in obstructive sleep apnea: a randomized, controlled trial. *Sleep* 27:934–941
12. Jennum P, Wildshiodt G, Christensen NJ, Schwartz T (1989) Blood pressure, catecholamines, and pancreatic polypeptide in obstructive sleep apnea with and without nasal continuous positive airway pressure (nCPAP) treatment. *Am J Hypertens* 2:847–852
13. Wilcox I, Grunstein RR, Collins FL, Doyle JM, Kelly DT, Sullivan CE (1992) Circadian rhythm of blood pressure in patients with obstructive sleep apnea. *Blood Pressure* 1:219–222
14. Suzuki M, Otsuka K, Guilleminault C (1993) Long-term nasal continuous positive airway pressure administration can normalize hypertension in obstructive sleep apnea patients. *Sleep* 16:545–549
15. Engleman HM, Gough K, Martin SE, Kingshott RN, Padfield PL, Douglas NJ (1996) Ambulatory blood pressure on and off continuous positive airway pressure therapy for the sleep apnea/hypopnea syndrome: effects in “non-dippers”. *Sleep* 19:378–381
16. Dimsdale JE, Lored JS, Profant J (2000) Effect of continuous positive airway pressure on blood pressure. *Hypertension* 35:144–147
17. Faccenda JF, Mackay TW, Boon NA, Douglas NJ (2001) Randomized placebo-controlled trial of continuous positive airway pressure on blood pressure in the sleep apnea-hypopnea syndrome. *Am J Respir Crit Care Med* 163:344–348
18. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ, Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, National Heart, Lung, and Blood Institute. National High Blood Pressure Education Program Coordinating Committee (2003) Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension* 42:1206–1252

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19. Amoore JN, Dewar D, Gough K, Padfield PL (2005) Do SpaceLabs ambulatory non-invasive blood pressure recorders measure blood pressure consistently over several years use? *Blood Press Monit* 10(1):51–56
 20. Becker HF, Jerrentrup A, Ploch T, Grote L, Penzel T, Sullivan CE, Peter JH (2003) Effect of nasal continuous positive airway pressure treatment on blood pressure in patients with obstructive sleep apnea. *Circulation* 107:68–73
 21. Hla KM, Skatrud JB, Finn L, Finn L, Palta M, Young T (2002) The effect of correction of sleep disordered breathing on BP in untreated hypertension. *Chest* 122:1125–1132
 22. Pepperell JCT, Ramdassingh-Dow S, Crosthwaite N, Mullins R, Jenkinson C, Stradling JR, Davies RJO (2002) Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomized parallel trial. *Lancet* 359:204–210
 23. Vazquez JC, Tsai WH, Flemons WW, Masuda A, Brant R, Hajduk E, Whitelaw WA, Remmers JE (2000) Automated analysis of digital oximetry in the diagnosis of obstructive sleep apnoea. *Thorax* 55:302–307
 24. Linden W, Lenz JW, Con AH (2001) Individualized stress management for primary hypertension: randomized trial. *Arch Intern Med* 161:1072–1080