Oral Appliance Therapy Reduces Blood Pressure in Obstructive Sleep Apnea: a Randomized, Controlled Trial

Helen Gotsopoulos, BDS, MPH (Hons)[1]; John J. Kelly, MD, PhD[2]; Peter A. Cistulli, MD, PhD[1]

[1]Department of Respiratory & Sleep Medicine; [2]Department of Nephrology, St George Hospital and The University of New South Wales, Sydney Australia

Study Objective: To investigate the short-term effect (4 weeks) of oral appliance therapy for obstructive sleep apnea on blood pressure.
Design: Randomized, controlled, crossover trial.
Setting: Multidisciplinary sleep disorders clinic in a university teaching hospital.
Patients: Sixty-one patients diagnosed with obstructive sleep apnea on polysomnography (apnea hypopnea index ≥ 10 per hour and at least 2 of the following symptoms—daytime sleepiness, snoring, witnessed apneas, fragmented sleep; age > 20 years; and minimum mandibular protrusion of 3 mm).
Intervention: A mandibular advancement splint (MAS) and control oral appliance for 4 weeks each.
Measurements and Results: Polysomnography and 24-hour ambulatory blood pressure monitoring were carried out at baseline and following each 4-week intervention period. Patients showed a 50% reduction in mean apnea hypopnea index with MAS compared with the control and a significant improvement in both minimum oxygen saturation and arousal index. There was a significant reduction with the MAS in mean (± SEM) 24-hour diastolic blood pressure (1.8 ± 0.5 mmHg) compared with the control (P = .001) but not in 24-hour systolic blood pressure. Awake blood-pressure variables were reduced with the MAS by an estimated mean (± SEM) of 3.3±1.1 mmHg for systolic blood pressure (P = .003) and 3.4 ± 0.9 mmHg for diastolic blood pressure (P < .0001). There was no significant difference in blood pressure measured asleep.
Conclusion: Oral appliance therapy for obstructive sleep apnea over 4 weeks results in a reduction in blood pressure, similar to that reported with continuous positive airway pressure therapy.
Key Words: obstructive sleep apnea; orthodontic appliances; blood pressure
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INTRODUCTION

OBSTRUCTIVE SLEEP APNEA (OSA) IS A COMMON DISORDER CHARACTERIZED BY REPETITIVE EPISODES OF PARTIAL OR COMPLETE OBSTRUCTION OF THE UPPER AIRWAY DURING SLEEP, OFTEN RESULTING IN ARTERIAL OXYGEN DESATURATION AND AROUSALS.[1,2] The recurrent apneic events of OSA and the consequent transient elevations in nocturnal blood pressure (BP) have been implicated in the development of sustained hypertension.[3-6] A number of recent randomized controlled trials evaluating the effect of the most widely prescribed treatment for OSA, nasal continuous positive airway pressure (CPAP), on diurnal BP have demonstrated a significant improvement.[7-9]

Oral appliances are a treatment alternative for a significant proportion of patients with OSA.[10-12] They are typically designed to protrude the mandible during sleep, thereby preventing pharyngeal collapse. While such devices are overall less effective in controlling sleep-disordered breathing than CPAP, they are preferred by patients primarily due to their unobtrusive nature and ease of use.[13] In view of the demonstrated benefit of CPAP on BP in OSA, it is important to determine whether oral appliance therapy is associated with a similar benefit. Hence, the aim of our study was to assess the effect of oral appliance therapy on BP in patients with OSA.

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Address correspondence to: Peter Cistulli, Department of Respiratory Medicine, St George Hospital, Kogarah, NSW, 2217, Australia; Tel: 612 9350 2696; Fax: 612 9350 2570; E-mail: p.cistulli@unsw.edu.au

METHODS

Study Population

The present trial formed part of a larger study investigating the effect of oral appliance therapy on key health outcomes in patients with OSA, including symptoms, neurocognitive function, and cardiovascular outcomes. Symptomatic outcomes from the study have been previously published.[12] Patients were recruited from a multidisciplinary sleep disorders clinic in a university teaching hospital. Inclusion criteria were OSA on polysomnography (apnea-hypopnea index [AHI] ≥ 10 per hour), at least 2 of the following symptoms—daytime sleepiness, snoring, witnessed apneas, fragmented sleep; age > 20 years; and minimum mandibular protrusion of 3 mm. Exclusion criteria were predominant central sleep apnea, insufficient teeth for splint retention, or evidence of active periodontal disease or dental caries. Approval was obtained from the institutional Ethics Committee, and subjects gave their written informed consent.

Intervention

The mandibular advancement splint (MAS) was custom made, consisting of upper and lower removable oral appliances with design features as previously described.[12] The control consisted of the upper appliance alone and did not advance the mandible.[12] Patients were informed that the aim of the study was to evaluate the efficacy of oral appliance therapy for OSA by comparing 2 appliances. With ethics approval, patient blinding was achieved by concealing the likely inactive or subtherapeutic nature of the control.

Study Design

We conducted a randomized, controlled, crossover trial (AB/BA). At baseline, patients underwent overnight polysomnography, standard sphygmomanometry (clinic BP), and 24-hour ambulatory BP monitoring (ABPM). This was followed by acclimatization to the MAS during which the mandible was incrementally advanced to the maximum comfortable limit. The aim of acclimatization was to permit MAS adaptation to ensure an adequate therapeutic trial during the subsequent crossover phases. Patients then underwent a washout period of 1 week, after which they were randomly assigned to a group via a presealed and numbered opaque white envelope that included the assignment to receive 4 weeks of treatment with MAS and control in alternating order, with an intervening 1-week washout. At the end of each 4-week period, patients underwent polysomnography with the respective appliance, followed by ABPM. Randomization was by means of a balanced design in blocks of 4. Sequence allocation was determined by a random number generator. The research assistant who assigned patients to their treatment group was not involved in outcome assessment.

Outcome Measures

Blood Pressure

BP was recorded in the sitting position using mercury sphygmomanometry and an appropriate cuff size. This was followed by ABPM (Spacelabs 90207, Spacelabs Medical Products, Sydney, Australia). BP was recorded half hourly throughout the 24-hour period. Patients recorded their time *asleep* and *awake* in a diary. Criteria for acceptable BP monitoring were > 80% successful readings encompassing at least 18 awake and 9 asleep readings. The primary study endpoints were average systolic (SBP) and diastolic (DBP) BP for the 24-hour, awake, and asleep intervals. Mean arterial pressure (MBP) and heart rate (HR) were secondary outcomes. For those patients on BP treatment, the type and dose of antihypertensive medication was recorded. The use of medication in each treatment phase was quantified using a medication score, defined by the number of medications used and the defined daily dose of antihypertensive therapy. BP monitoring was carried out blind to intervention type.

Polysomnography

Nocturnal polysomnography was performed in a standard fashion.[14] Respiration measurement techniques and the definition of arousal have been reported previously.[12,15] In brief, apnea was defined as cessation of airflow for at least 10 seconds with oxygen desaturation of more than 3% and/or associated with arousal. Hypopnea was defined as a reduction in amplitude of airflow, measured as pressure change at the nares, or thoracoabdominal wall movement of greater than 50% of the baseline measurement for more than 10 seconds with an accompanying oxygen desaturation of at least 3% (no time limit), and/or associated with arousal. These events were considered obstructive if they occurred in association with continued diaphragm electromyogram activity and thoracoabdominal wall movement. Sleep recordings were scored without knowledge of patient clinical status.

Treatment Outcome

A priori definitions of treatment outcome were used. A complete response to treatment was defined as a reduction in AHI to < 5 per hour, and a partial response as a reduction of ≥ 50% in AHI compared to baseline, but with the AHI remaining ≥ 5 per hour. Treatment failure was defined as < 50% reduction in AHI compared to baseline.[11,12]

Statistical Analysis

Data were stored and analyzed on SPSS (Version 10.0; SPSS, Inc, Chicago, Ill., USA). Data analysis was carried out according to a preestablished analysis plan. BP treatment effects were predefined and were first assessed using paired *t* tests, on an intention-to-treat basis with no change being assumed when follow-up BP data were unavailable. On subsequent analysis of patients with complete BP outcome data, neither the direction nor statistical significance of the results was affected. Thus, we proceeded with our analysis in those participants with complete BP outcome data. Treatment response, period effects, and interactions between treatment and period were determined using 2-way analysis of variance, with treatment order as a between-subject factor and treatment as a within-subject factor.[16] A 2-sided significance level of 0.1 was considered significant for carryover.[17] Relationships between continuous variables were examined using Pearson correlation coefficient. The association between BP treatment response and potential prognostic variables was assessed using repeated measures analysis of variance, after adjustment for potential regression to the mean. Categorical data were analyzed by the χ^2 test or Fisher exact test. Descriptive statistics are presented as mean ± SD and estimated means as mean ± SEM. A significance level of .01 was considered significant at a 2-sided .05 level for BP treatment effects and correlations using the Bonferroni correction. A significance level of .05 was used for all other analyses. A sample size of 62 was chosen a priori to detect a difference in both SBP and DBP between treatments of 5 mmHg with a power of 90% at the .01 significance level.[18]

RESULTS

Study Population

The trial profile is shown in Figure 1. A total of 74 patients were recruited for study participation between February 1999 and October 2001. Sixty-seven patients were randomly assigned to treatment groups, and 61 completed the protocol with complete outcome data. Overall, the study sample included predominantly men, who were middle aged and overweight (Table 1). A predominance of moderate to severe OSA was revealed with 36 patients (54%) and 19 patients (28%) in each subgroup, respectively. Twenty-six patients (39%) were on antihypertensive medication. Baseline characteristics were comparable for patients in each of the 2 sequence groups (Table 1). Sex groups did not differ in age, body mass index (BMI), AHI or BP.

Study Outcomes

Blood Pressure

Findings for treatment effects on ABPM are detailed in Tables 2 (intention to treat) and 3 (subset efficacy). The 24-hour profile of BP and HR with MAS and control are shown in Figures 2 and 3, respectively. The MAS resulted in a reduced 24-hour DBP compared with the control, primarily due to its effect on awake DBP. ABPM variables measured awake were reduced by an estimated mean (± SEM) of 3.3 ± 1.1 mmHg for SBP ($P = .003$), 3.4 ± 0.9 mmHg for DBP ($P < .0001$), and 3.6 ± 0.9 mmHg for MBP ($P < .0001$). Similarly, HR was reduced with the MAS during the 24-hour period, mainly due to a mean awake reduction of 4 ± 1 beats per minute compared with the control, ($P < .0001$). There

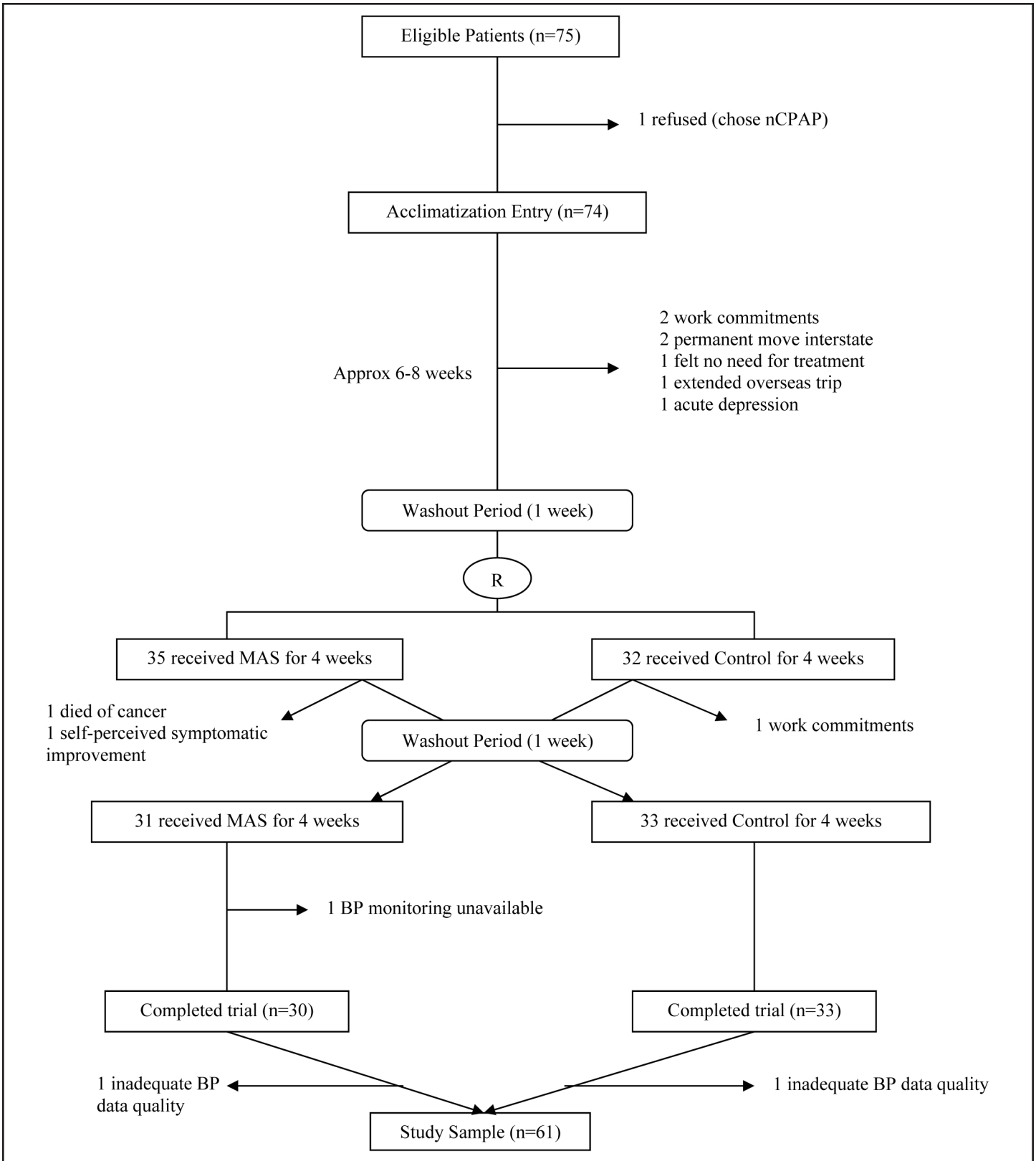

Figure 1—Trial Profile. nCPAP refers to nasal continuous positive airway pressure; MAS, mandibular advancement splint; BP, blood pressure.

was no significant difference in any BP outcome variables during sleep, or in any other ABPM variables between treatments. The control had no statistically significant effect on BP in comparison to baseline.

Polysomnography

The effect of each intervention on polysomnography is shown in Table 4. The MAS resulted in a 50% reduction in mean AHI compared with the control and an improvement in minimum oxygen saturation ($MinSaO_2$). The arousal index with the MAS was reduced compared with the control. There was no difference between treatments in any other measured polysomnographic variables. Twenty-one patients (34%) achieved a complete response with the MAS and 18 patients (30%) had a partial response to active treatment. Twenty-two patients (36%) were treatment failures. Mean (± SEM) AHI with the control (24 ± 2 per hour) was marginally lower than at baseline (28 ± 2 per hour), (P = .018). Polysomnographic variables did not differ between control and baseline. There was no significant treatment-by-period interaction or period effect for polysomnographic or ABPM variables.

Table 1—Characteristics of Study Participants at Baseline*

Variable	Group I (AB) (n = 35)	Group II (BA) (n = 32)	Total (N = 67)
Sex, men	29	24	53
Age, y	48 ± 11	48 ± 12	48 ± 11
Anthropomorphic			
BMI, kg/m^2	28.4 ± 5.2	30.0 ± 4.2	29.2 ± 4.8
Neck circumference, cm	40.0 ± 3.3	40.9 ± 3.3	40.4 ± 3.3
Waist-hip ratio	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1
Respiratory			
AHI, events/h	28 ± 17	26 ± 13	27 ± 15
Min SaO_2, %	85 ± 6	85 ± 6	85 ± 6
Sleep architecture			
TST, min	353 ± 68	339 ± 64	346 ± 66
TST in REM, min	66 ± 29	63 ± 30	65 ± 30
TST in NREM, min	287 ± 54	276 ± 46	282 ± 50
TST in REM, %	18 ± 7	18 ± 7	18 ± 7
TST in NREM, %	82 ± 7	82 ± 7	82 ± 7
Sleep efficiency, %	81 ± 12	80 ± 13	80 ± 12
Arousal index, events/h	34.7 ± 14.7	35.9 ± 11.3	35.2 ± 13.1
Blood pressure, mmHg			
Systolic			
24-h	126.9 ± 11.7	127.7 ± 9.8	127.3 ± 10.8
Awake	130.7 ± 12.4	131.6 ± 11.6	131.1 ± 11.9
Asleep	115.6 ± 12.7	116.0 ± 10.1	115.8 ± 11.5
Diastolic			
24-h	76.8 ± 7.6	78.6 ± 7.1	77.7 ± 7.4
Awake	79.9 ± 7.9	81.4 ± 8.9	80.6 ± 8.4
Asleep	68.0 ± 9.2	69.5 ± 7.6	68.7 ± 8.4
Mean			
24-h	93.4 ± 8.0	95.1 ± 7.4	94.2 ± 7.7
Awake	96.6 ± 8.2	98.2 ± 9.3	97.3 ± 8.7
Asleep	83.9 ± 9.8	85.0 ± 8.1	84.4 ± 9.0
Heart rate, bpm			
24-h	74 ± 8	75 ± 8	75 ± 8
Awake	77 ± 7	78 ± 9	77 ± 8
Asleep	67 ± 11	65 ± 8	66 ± 10

BMI refers to body mass index; AHI, apnea hypopnea index; Min SaO_2, minimum oxygen saturation; TST, total sleep time; REM, rapid eye movement sleep; NREM, non-rapid eye movement sleep; bpm, beats per minute.
*Groups compared using Student 2-sample t test. No significant differences noted. Data are presented as mean ± SD.

Oral Appliance Treatment

The mean advancement of the mandible with the MAS was 7 ± 2 mm. Patient diaries revealed MAS and control use for a mean (± SEM) duration of 6.8 ± 0.1 hours and 6.9 ± 0.1 hours per night, respectively. Both interventions were used on average 97% ± 1% of nights during the 4 weeks.

Prognostic Variables

The BMI, neck circumference, and self-reported time slept at night during each treatment phase did not differ between treatments (data not shown). Similarly, there was no significant change in medication score (1 ± 0 for both treatments) or type of antihypertensive agents used between treatments. However, the mean percentage of total sleep time spent supine during polysomnography with the MAS was higher compared with that when using the control (50% ± 4% versus 41% ± 4%, P = .014).

Awake and 24-hour DBP at baseline were both positively correlated with baseline AHI, (r = 0.39, P = .002) and (r = 0.38, P = .003) respectively. In addition, a trend was shown toward a positive correlation between both of the above BP variables and baseline arousal index, (r = 0.30, P = .017) and (r = 0.32, P = .011) respectively. There was no correlation between any DBP variables and $MinSaO_2$ on entry or between baseline SBP and the above sleep variables.

The within-subject change in BP between treatments was unrelated to age, sex, or BMI at baseline. While the magnitude of the positive correlation of the within-subject change in mean 24-hour DBP between interventions and concurrent changes in arousal index (r = 0.34, P = .008) and AHI (r = 0.31, P = .016) was similar, this was only significant for the former. There was no correlation between within-subject changes in other measured ABPM variables and concurrent changes in the above sleep variables. No correlations were found between changes in any ABPM variables and change in $MinSaO_2$ or between self-reported mean hours slept with the control and any measured ABPM variables.

Age, sex, BMI, BP, and AHI at baseline, measures of protrusion, and change in $MinSaO_2$ between treatments were not independent predictors of BP treatment effects. A positive association was shown between change in arousal index between treatments and 24-hour DBP treatment response (P = .009), after allowing for the effect of baseline DBP. There were no significant interactions between treatment outcome and any other ABPM variables.

DISCUSSION

This study shows that 4 weeks of MAS therapy for OSA resulted in a significant fall in 24-hour DBP attributed mainly to a reduction of approximately 3 mmHg in the early morning period. A similar reduction was also achieved in SBP during the early morning.

Overall, the MAS resulted in a 50% reduction in mean AHI compared with the control and a significant improvement in $MinSaO_2$ and arousal index, as previously reported.[12] A complete

response was achieved in 34% of patients, across all grades of OSA severity, similar to the results from a previous efficacy study by Mehta et al.[11] Despite the fact that treatment success was not achieved in all patients, a significant overall treatment effect on BP was still observed. The magnitude of the BP reduction during MAS treatment, while small (~ 3 mmHg reduction in awake DBP), is clinically significant. This result may indeed be an underestimation of the benefit of active treatment in view of a significantly higher mean percentage of total sleep time spent supine during polysomnography with the MAS. Based on published data, one might expect a 20% reduction in the risk of stroke if this degree of BP reduction were maintained for 2 to 3 years.[19,20] Furthermore, the BP reduction observed with MAS treatment was apparent in the early morning, which is the time of peak risk of acute myocardial infarction[21] and stroke.[22] BP reduction at this time of the day may provide further protection against these adverse cardiovascular events. Thus, both the magnitude and timing of BP reduction observed with MAS treatment is likely to be beneficial in terms of reducing the excess cardiovascular morbidity and mortality reported in OSA.

Randomized controlled trials have shown conflicting evidence on the impact of CPAP on BP in patients with OSA, with some studies reporting limited or no effect[23-25] while others have found benefit.[7-9] Our study, the first to evaluate the effect of oral appliance therapy on BP in patients with OSA, showed treatment effects that were similar in terms of magnitude and timing to

Table 2—Analysis by intention-to-treat of 24-hour ambulatory blood pressure monitoring*

Variable	Baseline	Control	MAS	Difference (99% CI)	*P* value†
Blood pressure, mmHg					
Systolic					
24-h	127.3 ± 1.3	126.7 ± 1.3	125.2 ± 1.3	-1.5 ± 0.7 (-3.4 to 0.5)	.05
Awake	131.1 ± 1.5	129.7 ± 1.5	126.7 ± 1.7	-3.0 ± 1.0 (-5.7 to -0.4)	.003
Asleep	115.8 ± 1.4	116.3 ± 1.5	116.2 ± 1.5	0.1 ± 1.3 (-3.3 to 3.5)	.96
Diastolic					
24-h	77.7 ± 0.9	78.0 ± 0.8	76.4 ± 0.9	-1.6 ± 0.5 (-2.9 to -0.3)	.001
Awake	80.6 ± 1.0	80.5 ± 1.0	77.3 ± 1.2	-3.1 ± 0.8 (-5.2 to-1.1)	< .0001
Asleep	68.7 ± 1.0	69.7 ± 1.0	69.3 ± 1.1	-0.4 ± 0.9 (-2.8 to 2.0)	.66
Mean					
24-h	94.2 ± 0.9	94.3 ± 0.8	92.8 ± 0.9	-1.5 ± 0.5 (-3.0 to -0.1)	.006
Awake	97.3 ± 1.1	97.0 ± 1.0	93.7 ± 1.3	-3.2 ± 0.8 (-5.5 to -1.0)	< .0001
Asleep	84.4 ± 1.1	85.5 ± 1.1	85.2 ± 1.2	-0.3 ± 1.0 (-3.0 to 2.5)	.78
Heart rate, bpm					
24-h	75 ± 1	76 ± 1	74 ± 1	-2 ± 1 (-4 to 0)	.009
Awake	77 ± 1	79 ± 1	76 ± 1	-3 ± 1 (-5 to -1)	< .0001
Asleep	66 ± 1	67 ± 1	67 ± 1	0 ± 1 (-2 to 3)	.70

MAS refers to mandibular advancement splint; CI, confidence interval.
*Data are for 67 patients and are presented as mean ± SEM.
†Comparisons between MAS and controls, made using paired *t* test.

Table 3—Subset efficacy analysis of 24-hour ambulatory blood pressure monitoring*

Variable	Baseline	Control	MAS	Difference (99% CI)	*P* value
Blood pressure, mmHg					
Systolic					
24-h	127.6 ± 1.3	126.9 ± 1.3	125.3 ± 1.3	-1.6 ± 0.8 (-3.7 to 0.6)	0.052
Awake	131.6 ± 1.5	130.1 ± 1.5	126.7 ± 1.7	-3.3 ± 1.1 (-6.2 to -0.5)	0.003
Asleep	116.2 ± 1.4	116.6 ± 1.5	116.7 ± 1.5	0.1 ± 1.4 (-3.6 to 3.8)	0.95
Diastolic					
24-h	77.7 ± 0.9	78.0 ± 0.8	76.2 ± 0.9	-1.8 ± 0.5 (-3.2 to -0.4)	0.001
Awake	80.9 ± 1.0	80.7 ± 1.0	77.2 ± 1.2	-3.4 ± 0.9 (-5.7 to-1.2)	<0.0001
Asleep	68.7 ± 1.1	69.8 ± 1.0	69.3 ± 1.1	-0.4 ± 1.0 (-3.0 to 2.2)	0.67
Mean					
24-h	94.3 ± 0.9	94.4 ± 0.8	92.7 ± 0.9	-1.7 ± 0.6 (-3.3 to -0.1)	0.006
Awake	97.7 ±1.0	97.3 ± 0.9	93.7 ± 1.3	-3.6 ± 0.9 (-6.0 to -1.1)	<0.0001
Asleep	84.6 ±1.1	85.7 ± 1.1	85.4 ± 1.2	-0.3 ± 1.1 (-3.3 to 2.8)	0.80
Heart rate, bpm					
24-h	74 ± 1	76 ± 1	74 ± 1	-2 ± 1 (-4 to 0)	0.009
Awake	77 ± 1	79 ± 1	75 ± 1	-4 ± 1 (-6 to -1)	<0.0001
Asleep	65 ± 1	66 ± 1	67 ± 1	1 ± 1 (-3 to 4)	0.67

MAS refers to mandibular advancement splint; CI, confidence interval.
*Data are for 61 patients and are presented as mean ± SEM. Comparisons between MAS and controls, made using paired *t* test.

those of trials by Faccenda et al[7] and Pepperell et al.[8] This is a remarkable finding given that the active treatment with MAS was successful in only a subgroup of patients. A potential explanation is that compliance with oral appliance therapy is higher than with CPAP treatment. Granted its limitations, self-reported compliance was 6.8 hours per night on average with MAS, exceeding the mean objective CPAP compliance in the studies by Faccenda et al[7] (3.3 hours per night) and Pepperell et al[8] (4.9 hours per night). Hence, a partial benefit of MAS on sleep-disordered breathing sustained over a longer period of the night appears to produce a BP lowering effect similar to that seen with CPAP, which is generally more effective at eliminating OSA but appears to be used for less of the night. Furthermore, patients in 1 study[7] were normotensive on entry, which may account for a possible floor effect.

The mechanism by which OSA leads to an increase in BP remains poorly understood, although increased sympathetic nervous system activity appears to play a key role.[26,27] While our study did not investigate mechanisms by which reductions in BP occurred, the reduction in pulse rate observed during treatment is

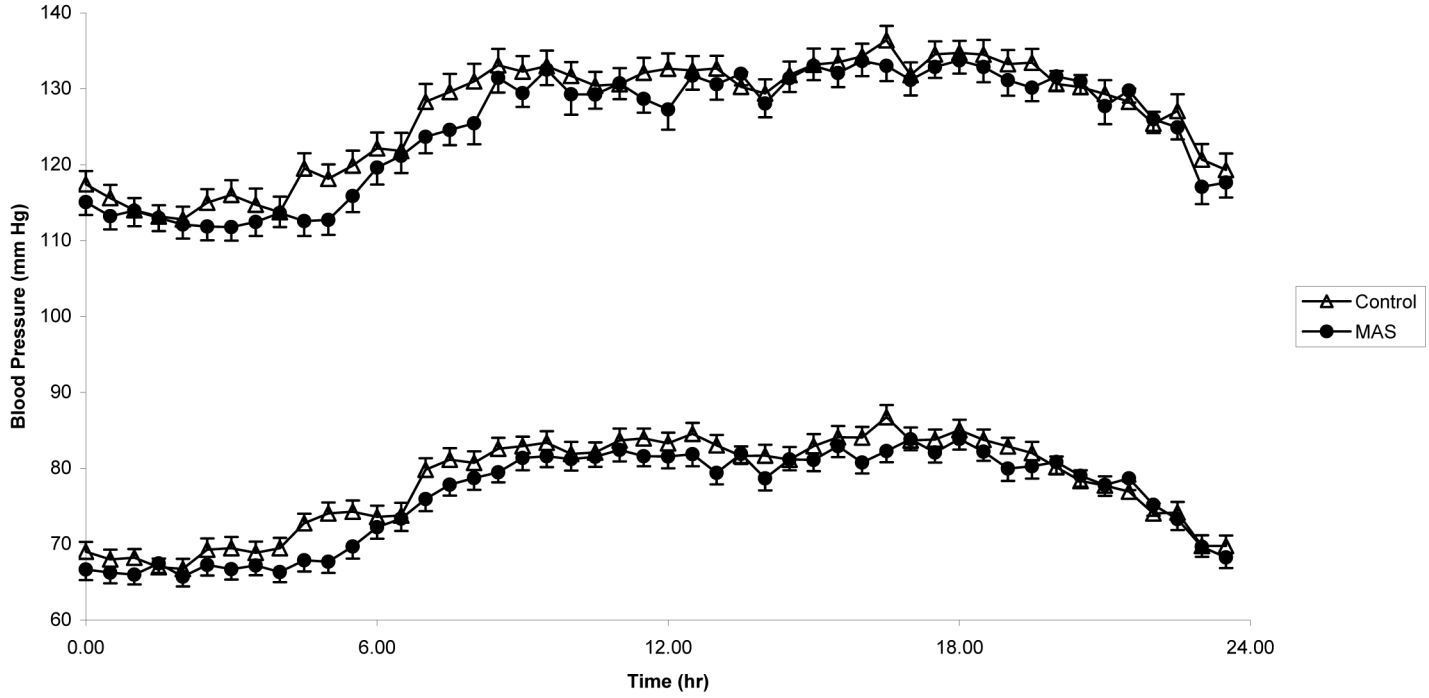

Figure 2—Graph comparing 24-hour systolic and diastolic blood pressure (BP) profiles between mandibular advancement splint and control. Error bars represent SEM for every 30-minute BP reading, with all recordings synchronized from midnight (00:00 hours) to midnight (24:00 hours), (N = 61). Note that the greatest differences in systolic and diastolic BP are evident during the morning period.

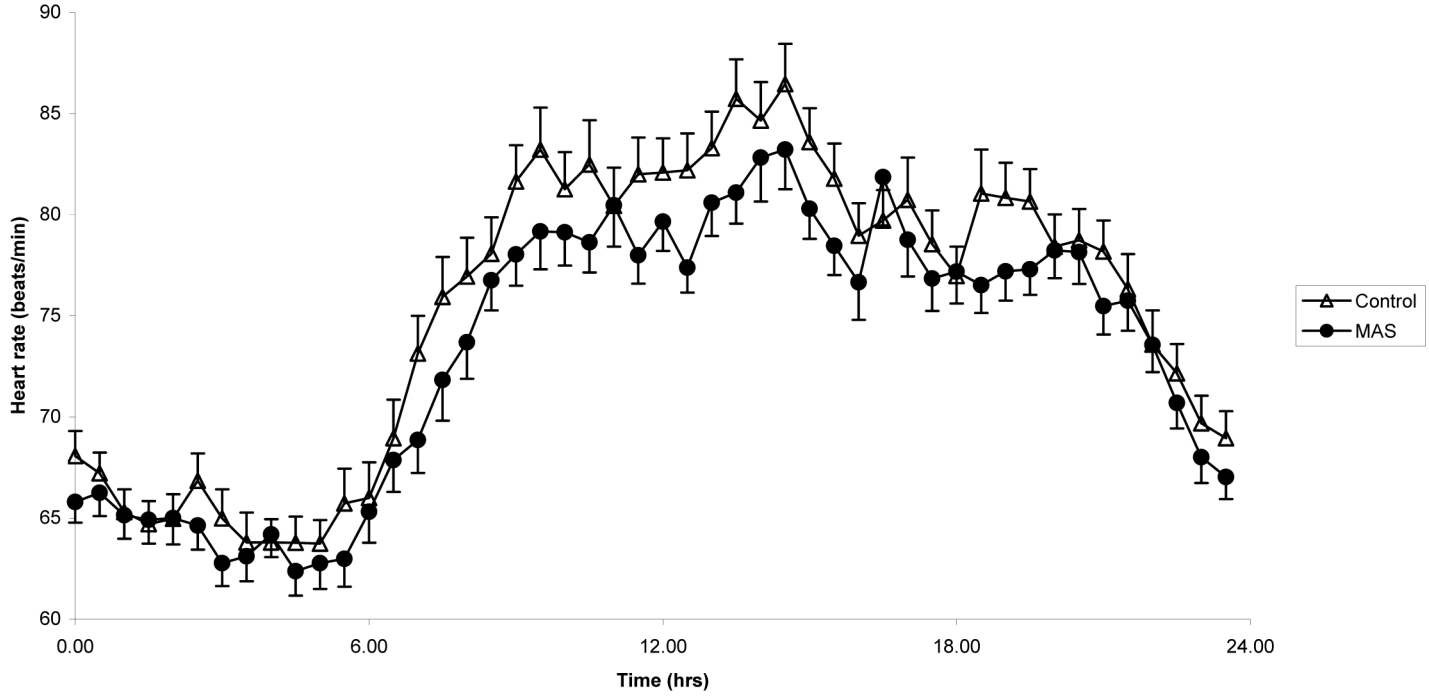

Figure 3—Graph comparing 24-hour heart-rate recordings between patients treated with mandibular advancement splint and control, (N = 61).

consistent with a reduction in sympathetic activity. The concurrent improvement in arousal index between treatments and 24-hour DBP treatment response is consistent with the suggestion that cortical arousals can mediate increased sympathetic activity.[28,29] However, unlike researchers in 2 trials of CPAP,[7,8] we did not find a correlation between the magnitude of oxygen desaturation during sleep and BP, which is somewhat surprising in light of the concept that hypoxia is another mediator of sympathetic activation in OSA.[30]

Our study has a number of strengths. Firstly, it used a randomized, controlled, crossover design. Our control was physically similar to the device being evaluated but without producing any improvement in OSA or BP. While use of a matched "placebo" control would be ideal to eliminate the "placebo effect" and to ensure double blinding, this is not achievable with a physical therapy such as a MAS. This approach has been adopted in CPAP studies, in which subtherapeutic pressures (sham CPAP) acted as the control.[8,25] The comparable usage rates of our 2 appliances suggest that patients were equally interested in the 2 treatments. Secondly, 24-hour ABPM was used to measure BP, as this correlates more closely than conventional measurement with target organ damage associated with hypertension[31] and is a more sensitive predictor of cardiovascular outcome.[32] Finally, our study did not exclude patients who were taking antihypertensive medication. Hence, we believe that the results of this trial can be generalized to the broad OSA population. Patients were representative of a typical OSA clinic population, with a wide range of OSA severity and the presence of comorbid hypertension.

In conclusion, we have demonstrated that treatment of OSA with a MAS for 4 weeks results in a reduction in BP, similar to that achievable with CPAP therapy. With growing evidence in favor of the acceptable efficacy of oral appliances,[11,12] their positive impact on OSA symptoms,[12] and their greater acceptance than that of CPAP,[13] we suggest that oral appliance therapy is a viable alternative to CPAP treatment in a significant number of patients. However, further studies are required to determine whether the magnitude of BP reduction observed in this study is maintained during more extended periods of treatment and to determine the mechanism by which MAS treatment reduces BP.

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Table 4—Comparison of polysomnographic variables between controls and mandibular advancement splint

Variable	Control	MAS	Difference (99% CI)	*P* value
Respiratory				
AHI, events/h	24 ± 2	12 ± 2	-12 ± 1 (-16 to -8)	< .0001
Min SaO_2, %	86 ± 1	89 ± 1	2 ± 1 (1 to 4)	.001
Sleep architecture				
TST, min	362 ± 8	365 ± 7	3 ± 8 (-19 to 25)	0.73
TST in REM, min	64 ± 4	66 ± 4	1 ± 4 (-8 to 11)	0.71
TST in NREM, min	297 ± 7	295 ± 7	-2 ± 9 (-27 to 22)	0.81
TST in REM, %	18 ± 1	18 ± 1	0 ± 1 (-2 to 2)	.85
TST in NREM, %	82 ± 1	81 ± 1	-1 ± 2 (-5 to 3)	.49
Sleep efficiency, %	81 ± 2	83 ± 1	1 ± 2 (-3 to 6)	.43
Arousal index, events/h	33 ± 2	26 ± 2	-7 ± 1 (-11 to -3)	< .0001

* Mandibular advancement splint (MAS) treatment and control data from 61 patients compared using 2-way analysis of variance. Data are presented as mean ± SEM.
AHI refers to apnea hypopnea index; Min SaO_2, minimum oxygen saturation; TST, total sleep time; REM, rapid eye movement sleep; NREM, non-rapid eye movement sleep.

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