Health Outcomes of Continuous Positive Airway Pressure versus Oral Appliance Treatment for Obstructive Sleep Apnea
A Randomized Controlled Trial

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Rationale: Continuous positive airway pressure (CPAP) and mandibular advancement device (MAD) therapy are commonly used to treat obstructive sleep apnea (OSA). Differences in efficacy and compliance of these treatments are likely to influence improvements in health outcomes.

Objectives: To compare health effects after 1 month of optimal CPAP and MAD therapy in OSA.

Methods: In this randomized crossover trial, we compared the effects of 1 month each of CPAP and MAD treatment on cardiovascular and neurobehavioral outcomes.

Measurements and Main Results: Cardiovascular (24-h blood pressure, arterial stiffness), neurobehavioral (subjective sleepiness, driving simulator performance), and quality of life (Functional Outcomes of Sleep Questionnaire, Short Form-36) were compared between treatments. Our primary outcome was 24-hour mean arterial pressure. A total of 126 patients with moderate-severe OSA (apnea hypopnea index [AHI], 25.6 [SD 12.3]) were randomly assigned to a treatment order. CPAP was more efficacious than MAD in reducing AHI (CPAP AHI, 4.5 ± 6.6/h; MAD AHI, 11.1 ± 12.1/h; P < 0.01) but reported compliance was higher on MAD (MAD, 65.0 ± 1.3 h per night vs. CPAP, 5.20 ± 2 h per night; P < 0.00001). The 24-hour mean arterial pressure was not inferior on treatment with MAD compared with CPAP (CPAP-MAD difference, 0.2 mm Hg [95% confidence interval, 0.7 to 1.1]); however, overall, neither treatment improved blood pressure. In contrast, sleepiness, driving simulator performance, and disease-specific quality of life improved on both treatments by similar amounts, although MAD was superior to CPAP for improving four general quality-of-life domains.

Conclusions: Important health outcomes were similar after treatment with CPAP and MAD. This was likely explained by the greater efficacy of CPAP being offset by inferior compliance relative to MAD. These findings strongly challenge current practice parameters recommending MAD treatment be considered only in patients with mild to moderate OSA. Long-term comparative effectiveness studies between CPAP and MAD that include objectively measured treatment compliance are needed to better define treatment strategies for patients with OSA.

Keywords: obstructive sleep apnea; continuous positive airway pressure; mandibular advancement device; health outcomes; efficacy and compliance

Obstructive sleep apnea (OSA) affects up to 17% of adults in the United States. The prevalence is similar in other western and eastern populations (1). OSA is characterized by disordered breathing during sleep, resulting in sleep fragmentation and intermittent hypoxemia. Patients often suffer excessive daytime...
sleepiness and many are at increased risk for motor vehicle crashes (2). Neurocognitive decline (3) and a lower self-reported quality of life (QOL) are also common. In addition, hypertension is highly prevalent and there is an increased incidence of cardiovascular mortality, stroke, and heart attack (4–6). Hence, OSA is a major public health problem, imposing a financial burden on health systems (7, 8).

The usual treatment of choice for OSA is nasal continuous positive airway pressure (CPAP) (9). Randomized controlled trials have demonstrated improvements in many health outcomes including subjective sleepiness (10), QOL (11), and blood pressure (BP) (12). Evidence also suggests that this treatment may reduce motor vehicle and driving simulator crashes (13). Long-term treatment may also reduce the incidence of cardiovascular events, at least in patients with severe OSA (14). However, despite these health-related improvements, many patients either reject treatment outright or only partially tolerate it, resulting in significant residual OSA (15). This limits the clinical effectiveness of this treatment modality.

More recently, oral appliances have proved to be an effective treatment for OSA, particularly the mandibular advancement device (MAD), which repositions the tongue and/or lower jaw to increase the dimensions of the airway lumen. Although the overall effect of these devices on sleep-disordered breathing is inferior to CPAP, their uptake and acceptance as an alternative therapy is generally higher (11). Similar to CPAP, several randomized controlled trials have reported improvements in BP (16, 17), sleepiness (18), and QOL (16).

Although several randomized trials have also directly compared CPAP with MAD (16, 19–26), outcomes are often limited to OSA alleviation and this has often been without gold standard polysomnography (20, 21). Few studies have assessed more clinically relevant health outcomes and used polysomnography to also assess treatment efficacy. Furthermore, many studies are small (19–23) or exclude patients with severe OSA (16, 20, 22), limiting the generalizability of the findings. Many studies have also not considered variation in treatment acclimatization and optimization periods (16, 19, 21, 22). Finally, because of the rapid changes in device development there are no studies that have used state-of-the-art MAD devices that are optimally titrated and applicable to current clinical practice.

In the present study, we aimed to compare the effect of CPAP and MAD treatments on health outcomes across multiple clinically relevant domains including cardiovascular function, sleepiness, driving simulator performance, and QOL. We hypothesized that the suboptimal efficacy with MAD would be counterbalanced by superior compliance relative to CPAP, resulting in similar overall alleviation of OSA. This would in turn result in similar effectiveness of both treatments for health outcomes related to OSA. The results from this study have previously been reported in the form of abstracts (27, 28).

METHODS

A randomized crossover open label study design was used to compare the health effects of 1 month of optimal treatment of OSA with CPAP versus MAD therapy. Optimal treatment was defined as attaining the highest compliance and best efficacy with each treatment under standard clinical practices.

Sample

The study was conducted at three sleep centers in Sydney, Australia (see online supplement). Eligibility criteria included patients with newly diagnosed OSA (apnea hypopnea index [AHI] >10 events per h); aged 20 years or older; greater than or equal to two symptoms of OSA (snoring, fragmented sleep, witnessed apneas, or daytime sleepiness); and a willingness to use both treatments. Recruitment was enriched for moderate-severe OSA. Patients were excluded for any of the following reasons: previous OSA treatment or a need for immediate treatment based on clinical judgment; central sleep apnea; a coexisting sleep disorder; regular use of sedatives or narcotics; preexisting lung or psychiatric disease; and any contraindication for oral appliance therapy (e.g., periodontal disease or insufficient dentition). Dental eligibility was assessed by an orthodontist at the Sydney Dental Hospital. All study procedures were approved by the site-specific Institutional Human Research Ethics Committees. Before consenting, patients were told they would be compensated for participating in the study by receiving the treatment device recommended by their sleep physician at no cost.

Procedures

All sleep studies were performed using full polysomnography according to standard procedures (see online supplement) (29). Treatment efficacy was established by polysomnography at the end of each treatment period under intention-to-treat conditions, with device use during the night before patient consent. Patients who met all eligibility criteria were randomized to both the treatment acclimatization and treatment arm orders. This was to minimize any bias related to treatment preference based on the order of treatment exposure and resulted in four randomized sequences (Figure 1).

The CPAP device used in the trial was the ResMed Autoset S8 (ResMed, Bella Vista, Australia). The MAD was the Somnodent (Somnomed Ltd., Sydney, Australia), a custom fitted and titratable two-piece device with proved clinical effectiveness in treating OSA (17, 30, 31). The procedures for fitting, titration, and acclimatization to each device are described in detail in the online supplement. Briefly, a fixed CPAP pressure was determined using a previously validated autotitrating method based on the 95th percentile pressure that controlled most of the OSA events (32). In contrast, MAD was self-titrated by gradually advancing the device until the maximum comfortable limit of mandibular advancement was achieved. During each of the 4–6 weeks of acclimatization with each device, all patients were asked to use their device for as long as they could tolerate it on a nightly basis. After usage patterns had stabilized, treatment was considered to be optimized.

All outcomes were assessed on three occasions, at baseline before treatment acclimatization and then at the end of each of the 1-month treatment arms. The primary outcome was the difference in 24-hour mean arterial pressure (24MAP) between CPAP and MAD determined from 24-hour ambulatory BP monitoring. Secondary cardiovascular outcomes included other 24-hour ambulatory BP and central BP and arterial stiffness (Sphy- moCor, AtCor Medical, Ryde, Australia) (33). We also assessed neurobehavioral function and QOL using the Functional Outcomes of Sleep Questionnaire (FOSQ) (34), the Short Form-36 (SF-36) (35), the Epworth Sleepiness Score (ESS) (36), and the AusEd driving simulator (Australasian Sleep Trials Network, Australia) (37). Daily diaries were also used to monitor treatment side effects and compile subjective compliance data. After completing the trial but before knowledge of their results, patients reported their treatment preference (CPAP, MAD, either, or neither). Details of all outcome assessments are available in the online supplement.

Statistical Analysis

To ensure an adequate sample size to assess multiple unrelated outcomes, we powered the study on a BP outcome. The analysis was designed to establish noninferiority of MAD compared with CPAP for the primary outcome (24MAP). A previous study that also did not select patients on the basis of their hypertensive status showed that OSA treatment with therapeutic CPAP lowered 24MAP by 3.3 mm Hg relative to sham CPAP (38). Therefore, we assumed that we could establish noninferiority of MAD to CPAP for control of 24MAP with a noninferiority margin of 1.6 mm Hg. Based on our own data (17) we estimated a within-subject mean square error of 3.9 for 24MAP. Hence, to detect noninferiority of this outcome with 90% power, using a noninferiority margin of 1.6 mm Hg, a sample size of 108 completers was deemed to be required.

We limited our analyses to the 108 subjects who completed the trial, regardless of compliance with their assigned treatment. In an initial analysis, no acclimatization or treatment arm order effects were found (see online supplement). The primary hypothesis was tested by comparing the upper limit of the 95% confidence interval for the MAD-CPAP difference in 24MAP with the a priori noninferiority margin using the paired t test. All other outcomes were compared using repeated measures analysis of variance (see online supplement).
RESULTS

Patient Flow

The patient flow through the study is detailed in Figure 1. Among the 51 screening failures, 36 patients did not fulfill dental criteria and an additional 6 declined to have the required dental work that would make them eligible for MAD treatment. Only 18 patients (14%) withdraw after randomization leaving 108 (86%) who completed the study. However, only two patients withdrew because of treatment intolerance (one CPAP and one both CPAP and MAD). None of the investigator-initiated withdrawals that were caused by adverse or serious adverse events were trial related.

Patient Characteristics

Of the 126 randomized patients, 81% were male and a majority (82%) had moderate or severe OSA with AHI greater than or

Figure 1. Study flowchart. A total of 108 patients completed the trial. Based on the separate randomization to the acclimatization phase and to the treatment phase for each of mandibular advancement device (MAD, M) and continuous positive airway pressure (CPAP, C), there were four randomization sequences with patient numbers as follows: M/C/M/C = 26; M/C/C/M = 29; C/M/C/M = 27; and C/M/M/C = 26. AHI = apnea hypopnea index; SAE = serious adverse event.
TABLE 1. BASELINE CHARACTERISTICS OF ALL RANDOMIZED PATIENTS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number randomized</td>
<td>126</td>
<td>—</td>
</tr>
<tr>
<td>Mild/moderate/severe OSA</td>
<td>23/69/34</td>
<td>—</td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M/F</td>
<td>102/24</td>
<td>—</td>
</tr>
<tr>
<td>Age, yr</td>
<td>49.5 (11.2)</td>
<td>22–78</td>
</tr>
<tr>
<td>Anthropometry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29.5 (5.5)</td>
<td>18.7–55.5</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>101.2 (15.8)</td>
<td>37.5–139</td>
</tr>
<tr>
<td>Neck circumference, cm</td>
<td>40.5 (3.8)</td>
<td>32–56</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI, h⁻¹</td>
<td>25.6 (12.3)</td>
<td>10.2–68.8</td>
</tr>
<tr>
<td>ODI, 3%</td>
<td>20.8 (12.5)</td>
<td>1.7–67.6</td>
</tr>
<tr>
<td>SaO₂, T &lt;90%</td>
<td>5.4 (8.8)</td>
<td>0–59.5</td>
</tr>
<tr>
<td>Minimum SpO₂</td>
<td>82.7 (7.6)</td>
<td>62–93</td>
</tr>
<tr>
<td>Arousal index, h⁻¹</td>
<td>34.3 (15.3)</td>
<td>8.1–79.6</td>
</tr>
<tr>
<td>Epworth Sleepiness Score</td>
<td>9.1 (4.2)</td>
<td>1–18</td>
</tr>
<tr>
<td>Office blood pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>123.7 (14.1)</td>
<td>98–163</td>
</tr>
<tr>
<td>Diastolic</td>
<td>80.6 (9.1)</td>
<td>67–106</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>48</td>
<td>—</td>
</tr>
<tr>
<td>Antidiabetic</td>
<td>7</td>
<td>—</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>24</td>
<td>—</td>
</tr>
<tr>
<td>Reflux</td>
<td>15</td>
<td>—</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>16</td>
<td>—</td>
</tr>
<tr>
<td>Antithrombotic</td>
<td>11</td>
<td>—</td>
</tr>
</tbody>
</table>

Definition of abbreviations: AHI = apnea hypopnea index; ODI = oxygen desaturation index; OSA = obstructive sleep apnea; SaO₂, T <90% = percentage of total sleep time spent with arterial oxygen saturation less than 90%; Mild OSA: AHI between 5 and 15 events per hour; Moderate OSA: AHI between 15 and 30 events per hour; Severe OSA: AHI more than 30 events per hour.

In the entire group, 24-hour ambulatory BP profiles (see Figure E3) showed a clear sleep–wake pattern during each treatment with no apparent between-treatment differences resulting in MAD being noninferior to CPAP for control of 24hMAP (mean CPAP-MAD difference [95% confidence interval], 0.2 [−0.7 to 1.1] mm Hg). However, ultimately neither treatment lowered any BP from baseline in the entire group. In contrast, in the subgroup of patients who were initially hypertensive, there were consistent treatment-related 24-hour BP improvements of between 2 and 4 mm Hg in all indexes with neither treatment having a superior effect (Figure 3; see Table E1). Central BP measured during pulse wave analysis also remained unchanged in the entire group (see Table E2) but there were reductions from baseline in arterial stiffness (aortic augmentation index) of between 1% and 2% with no between-treatment differences.

**Neurobehavioral Outcomes**

In contrast to BP, most neurobehavioral outcomes improved after both treatments (Table 3). In particular, there was no between-treatment difference in the improvement in subjective sleepiness (ESS) or in total and subscale measures of disease-specific QOL (FOSQ). However, MAD performed better than CPAP for improving four of eight SF-36 general QOL domains and the overall mental component score. Finally, speed deviation and reaction times to divided attention tasks during driving simulation improved to the same extent with both treatments. Figure 4 shows the ESS scores measured after acclimatization and treatment washout and after treatment (MAD or CPAP). Washout values were similar to baseline indicating a return to pretreatment sleepiness levels.

**DISCUSSION**

This is the largest randomized trial comparing the two leading forms of treatment for OSA on a range of unrelated health outcomes. The study has addressed many deficits from previous trials that have examined these treatments in head-to-head comparisons. Although CPAP demonstrated superior efficacy in terms of AHI reduction, self-reported compliance with MAD treatment was higher. The resulting effects on clinically important OSA-related health outcomes were either equivalent between treatments or better with MAD. Notably, these outcomes were achieved in the context of moderate to severe OSA. Overall, the comparable impact of both treatments on health outcomes has potential implications for clinical practice and future research.

**Efficacy and Compliance**

In all previous randomized trials that have directly compared CPAP with MAD, both treatments are shown to alleviate OSA but CPAP is consistently superior to MAD, particularly in patients with severe OSA (16, 19–26). In contrast, no studies have yet shown that nightly usage of CPAP is superior to MAD. In fact, results either favor MAD (16, 22) or do not favor either treatment (20, 21, 26). On this basis, we hypothesized that comparable outcomes between treatments would be achieved because the well-known superior efficacy of CPAP in alleviating OSA would be offset by inferior compliance relative to MAD. Indeed, our efficacy and compliance data and the resultant outcomes support this hypothesis. Finally, we have also confirmed the finding from most studies showing a clear patient preference for MAD therapy (20, 21, 23, 24, 27). These results are likely to have an important bearing on treatment effectiveness.
BP and Arterial Stiffness

In this trial we could only demonstrate clear improvements in BP in patients who were hypertensive at baseline. However, no improvements were evident with either treatment in the whole group. In this context, hypertensive status together with sleepiness, OSA severity, and treatment compliance have all been proposed to influence BP responses to treatment (39). Apart from hypertension, however, we do not believe that any of these other factors explain the lack of change in BP after treatment because we could not find any correlation between changes in any BP outcome with any of these factors (data not shown). The literature indicates that treatment-related improvements in BP are at best relatively small (2–3 mm Hg), even in patients with hypertension (32). It follows that demonstrating any BP improvement is difficult, particularly if the prevalence of untreated hypertension turns out to be lower than expected, as occurred in our study. However, we have demonstrated that both treatments were associated with small reductions in arterial stiffness and neither treatment proved superior. Arterial stiffness has increasingly been shown to improve cardiovascular risk stratification (40, 41) and both uncontrolled (33, 42) and randomized controlled studies (43, 44) have shown improvements after CPAP. Overall, our results point to the need for further comparative effectiveness studies that specifically target patients with hypertension.

Neurobehavioral Function and QOL

Overall, this study has found that improvements with MAD in sleepiness, QOL, and driving simulator performance were as good as or better than CPAP. Previous studies that have compared subjective sleepiness and QOL after treatment with oral appliance and CPAP therapies have either favored CPAP (21, 24) or have shown similar effects between treatments (16, 23, 25, 26). However, in the studies that favored CPAP, nonadjustable oral appliances were used and these may have been inferior to fully adjustable models, as used in our study. We found in the whole group that neither treatment had a superior effect in reducing subjective sleepiness determined from the ESS score. Additional analyses in patients who were sleepy (ESS >10) or who had severe OSA (AHI >30)
also indicated a comparable improvement between treatments (data not shown). Furthermore, neither treatment was superior for improving disease-specific QOL determined from the overall and subscale scores in the FOSQ. This is consistent with two other studies (16, 25). In contrast, our study is the first to show that MAD treatment was superior to CPAP for improving four of eight SF-36 domains. Finally, we have shown in over 100 patients that driving simulator performance improves equally between oral appliance and CPAP therapies. One small study examined driving simulator performance between 9 patients treated with oral appliances and 10 patients treated with CPAP and found a similar result (45). Hence, the data that suggest that CPAP treatment reduces the risk of motor vehicle crashes may also apply for MAD treatment (46). Overall, our data support more widespread use of MAD treatment for OSA.

**Study Strengths**

The variations in health outcomes found in previous trials comparing CPAP with MAD are likely caused by multiple factors. These include the exclusion in some studies of patients with severe OSA (16, 20, 22); small sample sizes (<50 patients) (19–23); high dropout rates (>20%) (16, 20); nonadjustable oral appliances (21); and suboptimal compliance with CPAP therapy (<4 h) (16). In addition, the acclimatization and optimization periods with each device may have varied from one patient to another but were often included as part of the treatment period (16, 19, 21, 22). Our trial was designed to address many of these deficiencies. In addition, we believe that our choice to power the study using a noninferiority design with mean BP as the outcome has given us some degree of confidence that we would have the statistical power to examine multiple clinically important health outcomes. We also deliberately enriched our study population with patients with moderate to severe OSA including those with associated comorbid hypertension and sleepiness. Our findings in this context suggest that the clinical role of MAD treatment should be extended beyond the currently accepted mild to moderate OSA range (American Academy of Sleep Medicine practice parameters [47]). Importantly, our protocol design ensured that all patients were fully acclimatized and optimally titrated with both devices over the same timeframe before commencing the interventions. Hence, every patient had equal opportunity for exposure to both treatments. Furthermore, we randomized the order of acclimatization and intervention to equal opportunity for exposure to both treatments. Furthermore, we randomized the order of acclimatization and intervention to reduce the risk of compliance being altered by treatment order exposure. In the end we achieved an objective CPAP compliance (4.6 h) that was comparable or better than previous trials and despite the demanding protocol, our dropout rate was only 15%.

**Study Limitations**

There are several limitations that should be considered in relation to our study. First, we acknowledge that the interpretation of our results is limited to patients that are eligible and willing to trial both treatments. In this context we found that 20% of

**Table 2. Intention-to-Treat Polysonomography and Self-Reported Compliance**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD) CPAP</th>
<th>Mean (SD) MAD</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Polysomnography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI, h⁻¹</td>
<td>4.5 (6.6)</td>
<td>11.1 (12.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ODI 3%, h⁻¹</td>
<td>6.0 (9.7)</td>
<td>9.0 (11.6)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Min SpO₂, %</td>
<td>90.6 (5.0)</td>
<td>87.2 (5.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SpO₂ T90, % total sleep time</td>
<td>2.8 (16.9)</td>
<td>6.6 (15.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>Arousal index, h⁻¹</td>
<td>16.6 (10.6)</td>
<td>19.2 (11.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Sleep latency, min</td>
<td>11.5 (15.7)</td>
<td>15.3 (21.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>82 (12)</td>
<td>82 (12)</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Diary data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subj compliance, h/night</td>
<td>5.2 (2.0)</td>
<td>6.5 (1.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Subj sleep, h/night</td>
<td>6.9 (0.9)</td>
<td>7.1 (0.7)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Definition of abbreviations: AHI = apnea hypopnea index; compliance (h/night) = total hours of use divided by the number of nights with access to treatment; CPAP = continuous positive airway pressure; Min SpO₂ = minimum arterial oxygen saturation; ODI = oxygen desaturation index; SpO₂ T90 = % total sleep time below 90% arterial oxygen saturation; Subj = subjective (self-reported).*
assessed patients were not eligible for trialing MAD, whereas all patients were able to trial CPAP. We also recognize that we had no objective measure of MAD compliance, because this was not available at the time the study was conducted. We have therefore assumed that the small discrepancy between objective and subjective CPAP compliance would be similar with MAD, making it likely that the small discrepancy between objective and subjective compliance. This was despite all patients being strongly committed to improve BP from baseline, which likely relates to the normotensive status of most participants. This then limits the ability to claim true noninferiority for BP control. Regardless, we believe our decision to pursue a noninferiority analysis for BP was well founded. Noninferiority designs rely on the premise that the active treatment (in this case CPAP) has superior efficacy to placebo as established in previous trials (52). Based on meta-analyses of randomized trials (12, 53), we believed this has been adequately demonstrated, even in trials in which elevated BP was not a specific inclusion criterion (17, 38), which was the case in this study. It could also be argued that our treatment periods were relatively short, limiting the impact on BP. However, studies using similar treatment periods have reported significant treatment effects. Ultimately our crossover design made the study challenging and time-consuming.

In this study we found that overall neither treatment seemed to improve BP from baseline, which likely relates to the normotensive status of most participants. This then limits the ability to claim true noninferiority for BP control. Regardless, we believe our decision to pursue a noninferiority analysis for BP was well founded. Noninferiority designs rely on the premise that the active treatment (in this case CPAP) has superior efficacy to placebo as established in previous trials (52). Based on meta-analyses of randomized trials (12, 53), we believed this has been adequately demonstrated, even in trials in which elevated BP was not a specific inclusion criterion (17, 38), which was the case in this study. It could also be argued that our treatment periods were relatively short, limiting the impact on BP. However, studies using similar treatment periods have reported significant treatment effects. Ultimately our crossover design made the study challenging and time-consuming.

Table 3: Sleepiness, quality of life, and driving simulator performance (N = 108)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline Mean (SE)</th>
<th>CPAP Mean (SE)</th>
<th>MAD Mean (SE)</th>
<th>Mean Baseline – CPAP Difference (95% CI)</th>
<th>Mean Baseline – MAD Difference (95% CI)</th>
<th>Mean CPAP – MAD Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleepiness and quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESS</td>
<td>9.1 (0.4)</td>
<td>7.5 (0.4)</td>
<td>7.2 (0.4)</td>
<td>-1.6 (1.0 to 2.2)*</td>
<td>-0.3 (0.4 to 0.6)*</td>
<td>0.5 (0.4 to 0.2)*</td>
</tr>
<tr>
<td>FOSQ</td>
<td>16.3 (0.2)</td>
<td>17.3 (0.2)</td>
<td>17.3 (0.2)</td>
<td>-1.0 (-1.4 to -0.6)*</td>
<td>-1.0 (-1.4 to -0.6)*</td>
<td>0.0 (-0.4 to 0.3)</td>
</tr>
<tr>
<td>Vigilance</td>
<td>3.08 (0.06)</td>
<td>3.12 (0.05)</td>
<td>3.3 (0.05)</td>
<td>-0.21 (-0.33 to -0.13)*</td>
<td>-0.23 (-0.33 to -0.13)*</td>
<td>0.02 (-0.01 to 0.06)</td>
</tr>
<tr>
<td>Intimacy</td>
<td>3.15 (0.08)</td>
<td>3.35 (0.08)</td>
<td>3.4 (0.08)</td>
<td>-0.20 (-0.35 to -0.05)*</td>
<td>-0.19 (-0.35 to -0.03)*</td>
<td>0.01 (-0.01 to 0.2)</td>
</tr>
<tr>
<td>Productivity</td>
<td>3.43 (0.04)</td>
<td>3.6 (0.04)</td>
<td>3.6 (0.04)</td>
<td>-0.17 (-0.26 to -0.09)*</td>
<td>-0.19 (-0.27 to -0.11)*</td>
<td>0.02 (-0.09 to 0.06)</td>
</tr>
<tr>
<td>Social</td>
<td>3.57 (0.05)</td>
<td>3.76 (0.05)</td>
<td>3.73 (0.05)</td>
<td>-0.18 (-0.28 to -0.08)*</td>
<td>-0.15 (-0.26 to -0.05)*</td>
<td>0.03 (-0.07 to 0.13)</td>
</tr>
</tbody>
</table>

Definition of abbreviations: CI = confidence interval; CPAP = continuous positive airway pressure; ESS = Epworth Sleepiness Score; FOSQ = Functional Outcomes of Sleep Questionnaire; MAD = mandibular advancement device; RT to DAT = reaction time to divided attention task; SF-36 = Short Form-36.

*P < 0.01.
†P < 0.05.

Figure 4: Epworth Sleepiness Score (ESS) at baseline, after continuous positive airway pressure (CPAP) or mandibular advancement device (MAD) treatment, and after acclimatization and treatment washout periods.
consuming for our patients and extending the treatment periods would have negatively impacted the feasibility of completing such a large study. The finding of a significant treatment effect among patients who were hypertensive at baseline is an indication that the treatment period was of sufficient duration. Furthermore, we observed very clear therapeutic effects from each treatment for important neurobehavioral and QOL outcomes that were either comparable or favored MAD. Sleepiness, which is arguably the main factor motivating patients to seek OSA treatment, showed clear clinical improvement and deterioration after initiation and withdrawal of either treatment. Finally, we cannot claim that the improvements in health outcomes would be sustained in the long term, or indeed whether BP may deteriorate because of partially effective treatment. Further long-term studies with objective assessment of compliance with both devices will clarify how true night-to-night residual OSA impacts on health outcomes.

**Conclusions**

This short-term study has demonstrated that the health outcomes in patients with moderate to severe OSA were similar after treatment with CPAP and MAD. The results are likely explained by the greater efficacy of CPAP being offset by inferior compliance relative to MAD resulting in a similar “treatment” AHI with each device. These findings strongly challenge current practice parameters that recommend that MAD treatment should only be considered in patients with mild to moderate OSA or in those who have failed or refuse CPAP treatment. Our findings provide a strong rationale for a long-term comparative effectiveness study of these two treatment modalities. It is hoped that such studies will allow a rigorous evidence-based approach to changing current treatment recommendations.

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**References**


