

**Titrated mandibular advancement versus positive airway pressure for sleep apnea**

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## **ABSTRACT**

*Objectives:* To compare mandibular advancement device (MAd) and positive airway pressure (CPAP) for obstructive sleep apnea hypopnea syndrome (OSAHS) after one-night polysomnographic (PSG) titration of both treatments.

*Methods:* 59 OSAHS patients (apnea-hypopnea index [AHI]:34±13, Epworth scale: 10.6±4.5) were included in a crossover trial of 8 weeks of MAd and 8 weeks of CPAP after effective titration. Outcome measurements included home sleep study, sleepiness, health related quality of life (HRQL), cognitive tests, side effects, compliance, and preference.

*Results:* AHI was 2 [1-8] (median [interquartile range]) with CPAP and 6 [3-14] with MAd ( $p<0.001$ ). Positive and negative predictive values of MAd titration PSG for treatment success were respectively 85 and 45% respectively. Both treatments significantly improved subjective and objective sleepiness, cognitive tests and HRQL. Reported compliance was higher for MAd ( $p<0.001$ ) with > 70% of patients preferring this treatment.

*Conclusions:* These results support titrated MAd as an effective therapy in moderately sleepy and overweight OSAHS patients. Although less effective than CPAP, successfully titrated MAd was very effective to reduce AHI and was associated with a higher reported compliance. Both treatments improved functional outcomes to a similar degree. One-night titration of MAd had a low negative predictive value for treatment success.

**Abstract word count: 198**

**Key Words:** continuous positive airway pressure, mandibular advancement, obstructive sleep apnea, titration, treatment.

## INTRODUCTION

Obstructive sleep apnea hypopnea syndrome (OSAHS) is a highly prevalent disease<sup>1</sup> characterized by recurrent episodes of partial or complete obstruction of the upper airways during sleep. Nasal continuous positive airway pressure (CPAP) is the primary treatment of OSAHS, but many patients are unable or unwilling to comply with this treatment. Five to fifty per cent of OSAHS patients in whom CPAP is recommended reject this treatment and 12-25% of the remaining patients can be expected to discontinue CPAP especially if they have mild OSAHS and/or if they are not "subjectively sleepy"<sup>2,3</sup>. Mandibular advancement device (MAd) therapy has emerged over the last decade as an alternative therapy for OSAHS<sup>4</sup>. Randomized control trials have demonstrated a reduction of apnea-hypopnea index (AHI) and an improvement of daytime sleepiness on MAd therapy<sup>5,6</sup>. In most randomized studies evaluating MAd therapy in OSAHS, the degree of mandibular advancement (MA) was arbitrarily set without any titration procedure, for example at 80% of the maximal comfortable MA<sup>5,7</sup>. A dose-dependent effect of MA on AHI, nocturnal oxygen desaturations and pharyngeal collapsibility has been previously demonstrated<sup>8-10</sup> suggesting the potential benefit of an individual MA titration in patients with OSAHS. Comparative studies of MAd and CPAP should therefore include a titration procedure for both treatments. In a pilot study<sup>11</sup>, it was demonstrated that it is possible to mobilize the mandible during PSG without waking the patient during the advancement manoeuvres. The simple propulsion system that was used in this study allowed one-night titration of the effective MA away from the patient's bedside and prediction of the capacity of MAd to reduce AHI. To the best of our knowledge, no published randomized study has evaluated MAd therapy in OSAHS after PSG titration of the effective MA.

The aim of this multisite randomized crossover study was to compare 8 weeks of MAd therapy and 8 weeks of CPAP in a mixed-severity group of patients with OSAHS in terms of

efficacy, reported side effects, compliance and preference, after one-night PSG titration of both effective MA and CPAP pressure.

## **METHODS**

### **Patients and study protocol**

Patients aged from 18 to 70 years with OSAHS newly diagnosed by PSG were recruited from the departments of Pulmonary Medicine of Angers University Hospital, and Saint-Antoine Hospital, Paris, France. Inclusion criteria were an AHI between 10 and 60 and two or more symptoms of OSAHS including snoring, witnessed apnoea or complaint of daytime sleepiness. Exclusion criteria were previous treatment for OSAHS, body mass index (BMI)  $\geq 35$  kg/m<sup>2</sup>, coexisting sleep disorder other than OSAHS, inadequate dental structure or temporomandibular joint disease contraindicating MAd treatment as assessed by a dentist, unstable medical illness and severe sleepiness which may constitute risk to self or others. At baseline, patients underwent anthropometric measurements and individual custom-fitting of MAd. Each patient then underwent 2 consecutive in-laboratory PSG separated by 1 week in a randomized order for CPAP and MA titration. Titration PSG was considered to be ineffective in the case of intolerance of CPAP or MAd and/or inability to achieve a  $\geq 20\%$  reduction in AHI. This relatively low threshold for AHI reduction during MA titration was based on our pilot study<sup>11</sup> demonstrating a further reduction in AHI between the titration PSG and the treatment PSG. Patients with effective titration for both CPAP and MAd were randomized for treatment order and were asked to use each treatment for 2 months. The 2 treatment periods were separated by a 1-week washout period. Outcomes were to be measured during the last week of each treatment period. Outcome measurements included home limited sleep study, sleepiness, health related quality of life (HRQL), cognitive tests, reported side effects, treatment compliance, satisfaction and preference.

The study was approved by the University of Angers ethics committee and patients gave their informed consent.

### **CPAP and MAd treatments**

CPAP titration was conducted during PSG according to our standard procedure<sup>12</sup>, and patients were then treated at the manually titrated pressure with a CPAP device (Sullivan S6 Elite™, Resmed, Australia) equipped with a microprocessor and pressure monitor providing a precise index of daily use by measuring the time spent with the mask on.

For MAd therapy, we used a previously described adjustable bi-bloc acrylic oral appliance (AMC™, Artech Médical, Pantin, France) (Figure 1)<sup>10</sup> with attachments of various sizes allowing MA adjustment. The maximum MA while awake was determined for each patient on three consecutive voluntary manoeuvres. MA titration was performed during PSG after one week of acclimatization to MAd at 50% of the maximum MA. In the pilot study<sup>11</sup>, the arches of the MAd were connected by two lateral hydraulic systems. In order to decrease the dimensions of the appliance in the mouth and to improve comfort during titration, the hydraulic system was replaced by two thin plastic-coated metal cables connected to the upper and lower dental arches. A modified infusion pump (Artech Medical, Pantin, France) was used to perform remote progressive MA via a computer interface program (Cidelec, Angers, France). Using this propulsion system, MA was increased by 1 mm increments every 15 minutes until a significant reduction of the incidence of the sleep-disordered breathing was obtained or until reaching the maximum advancement position (i.e. 150% of maximum MA) or the position causing discomfort or pain, waking the patient and preventing any further progression. The length of the MAd attachments was then adjusted to obtain the optimal advancement reached during the titration night.

## **Sleep recordings**

In-laboratory PSG (CID 102™, Cidelec, Angers, France) was performed as previously described<sup>12</sup> and scored according to standard criteria<sup>13</sup> using nasal pressure cannulae and tracheal sounds (suprasternal microphone) for airflow measurement. Home limited sleep studies (CID 102 L™, Cidelec, Angers, France) under CPAP and MAd included nasal pressure cannulae, tracheal sounds and oxygen saturation (SaO<sub>2</sub>) (finger pulse oxymetry). Respiratory events were scored manually. Apnea was defined as cessation of airflow for at least 10 s. Hypopnea was defined as a > 50% reduction of airflow or a < 50% reduction of airflow accompanied by a 3% decrease in SaO<sub>2</sub>.

## **Measures of sleepiness, cognitive function and HRQL**

Subjective sleepiness was assessed by the Epworth Sleepiness Score (ESS)<sup>14</sup>. Objective sleepiness was measured using the OSLER test with calculation of the sleep latency and the number of errors<sup>15</sup>. Attention and concentration were also investigated using the Trail Making A (TMT A) and B (TMT B) cognitive tests<sup>16</sup>. HRQL was evaluated using the Nottingham Health Profile (NHP)<sup>12</sup>. Each subject completed a single 09:00 A.M. OSLER test after a quiet period of filling in questionnaires with the investigator. Measures of sleepiness, HRQL and cognition were performed at baseline, on MAd and on CPAP.

## **Treatment related side effects, compliance, satisfaction and preference**

At the end of each treatment period, patients were asked to give a score from 0 to 3 (0: absent, 1: mild, 2: moderate, 3: severe) regarding 6 common side effects of CPAP (nose congested, drippy, irritated, skin lesion, eyes irritated, and dry mouth) and MAd (jaw pain, tooth pain, muscle stiffness, dry mouth, hypersalivation, and occlusal change). A mean side effects score from 0 to 18 was then calculated for each treatment. Compliance with CPAP and MAd was

assessed by self-reporting. Objective data regarding CPAP compliance were downloaded from the internal memory of the device. Global treatment satisfaction was assessed using a 0-10 visual analogic scale (VAS). At the end of the study, patients were asked to indicate their preferred treatment.

### **Statistical analysis**

Continuous variables were described as mean±SD for variables with a normal distribution and median (interquartile range) for variables with a non-normal distribution. Normality of distribution was assessed using Kolmogorov-Smirnov test. A sample size of n=60 patients was calculated to detect a 1 SD difference in AHI between the two treatments with a power of 99% and a significance level of 5% (two-sided). Between-treatment differences were assessed by paired t test and unpaired t test for variables with a normal distribution, and by a Wilcoxon signed-rank test and Mann-Whitney test, for variables with a non-normal distribution. Treatment-by period interaction (carryover effect) was tested by analysis of variance for repeated measures. The correlation between continuous variables was assessed by Spearman's rank correlation coefficient. All reported p values are two-sided and Bonferroni correction was used for pair wise comparisons. A p value of 0.05 or less was considered to indicate statistical significance. All analyses were performed using SPSS (V15.0) statistical software.

### **RESULTS**

A flow diagram summarizing the distribution of the subjects is shown in Figure 2. Sixty nine patients underwent PSG titration of both MAd and CPAP. Comparison of sleep data during CPAP and MAd titration showed no significant difference in sleep efficiency (83.7±8.2 vs 82.7±12%), stage 1-2 sleep (58.3±12.1vs 56.8±13.7% of total sleep time), stage 3-4 sleep (21.5±9.1 vs 21±9.1% of total sleep time), REM sleep 20,2±6.7 vs 22.2±7.8% of total sleep

time) and micro arousal index ( $15.9 \pm 10.5$  vs  $15.5 \pm 10$  n/h of sleep). MA titration was ineffective in 8 patients. Five patients were intolerant to progressive MA with jaw pain, discomfort and/or repeated awakenings preventing further progression. In 3 patients, it was impossible to achieve a  $\geq 20\%$  reduction in AHI at the position of maximum MA. Two patients did not tolerate CPAP during the titration PSG. A total of 59 patients with successful titration of both CPAP (mean effective pressure:  $9.1 \pm 1.7$  mmH<sub>2</sub>O) and MAd (mean effective MA:  $9.8 \pm 2.1$  mm corresponding to  $103 \pm 20\%$  of the maximum voluntary advancement) were randomized for treatment sequence. Patients' characteristics at the time of enrolment are shown in Table 1. Twenty five patients had mild to moderate OSAHS with AHI between 11 and 29 and 34 patients had severe OSAHS with AHI between 30 and 60. Thirty patients were randomized to MAd for 2 months followed by a 1-week washout, then CPAP for 2 months. One of these patients withdrew during the MAd period and was lost to follow-up and another withdrew during the CPAP period and refused to undergo any further evaluation. The remaining 28 patients completed the protocol. Twenty nine patients were randomized to the reversed treatment sequence with CPAP for two months followed by a 1-week washout, then MAd for 2 months. One of these patients withdrew during the CPAP period and was lost to follow-up. Twenty eight patients completed the protocol. A total of 56 patients completed the study. No significant difference in body weight was observed between values at baseline ( $77.8 \pm 11.5$  kg), on CPAP ( $79.3 \pm 11.4$  kg) and on MAd ( $78.9 \pm 11.5$  kg).

### **Home limited sleep studies under CPAP and MAd**

Home sleep studies data under CPAP and MAd in the patients who completed the trial are compared in Table 2. No treatment-by-period interaction was observed for any home sleep study variable. CPAP was significantly more effective on snoring index, AHI and nocturnal oxygenation. Treatment AHI was less than 10 for 39 (70%) patients on MAd and 46 (82%)



patients on CPAP. A complete response ( $\geq 50\%$  reduction in AHI to  $< 5/h$ ) was obtained in 73.2% of patients with CPAP and 42.8% with MAd. A partial response ( $\geq 50\%$  reduction in AHI but AHI remaining  $\geq 5/h$ ) was observed in 23.2% of patients with CPAP and 51.7% with MAd. Treatment failure ( $< 50\%$  reduction in AHI) occurred in 3.5% of patients with CPAP and 5.3% with MAd. Figure 3 illustrates the percentages of complete response, partial response and treatment failure on MAd according to baseline OSAHS severity. A complete response on MAd was achieved in 58.3% of patients with mild to moderate OSAHS versus 31.2% of patients with severe OSAHS. After including the patients who were not randomized due to ineffective titration and those who dropped out of the study, treatment failure occurred in 18.4% of patients for MAd and 6.6% for CPAP.

A significant correlation ( $r=0.52$ ,  $p<0.001$ ) was observed between the AHI determined during MA titration (median [IQR] = 12 [6-14]) and that obtained during home sleep study with MAd (median [IQR] = 6 [3-14]) in the 56 patients who completed the study (Figure 4). Among the 27 patients with  $AHI \leq 10$  during MA titration, 23 had an  $AHI < 10$  with MAd on limited sleep study (positive predictive value = 85%) and 4 had an  $AHI \geq 10$ . Among the 29 patients with  $AHI > 10$  during MA titration, 16 (55%) had an  $AHI < 10$  on MAd on limited sleep study and 13 had an  $AHI \geq 10$  (negative predictive value = 45%).

### **Measures of sleepiness, cognitive function and HRQL**

In the patients who completed the study CPAP and MAd both significantly improved subjective and objective daytime sleepiness compared to baseline (Table 3). No significant difference was observed between MAd and CPAP for ESS and OSLER test data. CPAP and MAd both significantly improved the TMT A cognitive test with no significant difference between CPAP and MAd values. In contrast, a significant improvement of TMT B was only observed with CPAP. No treatment-by-period interaction was observed for any parameters of

sleepiness and cognitive function. HRQL data assessed by the NHP questionnaire at baseline on MAd and on CPAP are presented in Figure 5. For CPAP, a significant improvement was observed for 2/6 domains of HRQL including emotional reaction and energy. For MAd, HRQL was significantly improved for 4/6 domains including physical mobility, pain, emotional reaction and sleep. A significant treatment-by-period interaction was observed for emotional reaction and sleep with a significantly better emotional reaction and subjective sleep quality with MAd for the second treatment period but no difference between treatments for the first treatment period.

### **Treatment related side effects, compliance, satisfaction and preference**

The mean side effects score was similar for MAd and CPAP in the patients who completed the study (Table 4). In contrast, reported daily compliance was significantly higher with MAd for both the number of hours of daily use and the percentage of nights on which treatment was use. No treatment-by-period interaction was observed for reported compliance. For CPAP, comparison of reported compliance with objective data downloaded from the internal memory of the device [respectively 6.0(4.0-7.0) versus 4.0(0.9-5.4) hours for daily use and 90(40-99) versus 79(42-93) for % of nights on treatment respectively] showed that patients overestimated actual CPAP use. A treatment-by-period interaction was observed for treatment satisfaction with a higher level of satisfaction for MAd during the second treatment period but no difference between the two treatments during the first treatment period. At the end of the study 42/55 patients (71.2%) preferred MAd, 5 (8.5%) preferred CPAP and 8 had no treatment preference.

## DISCUSSION

The efficacy and acceptance of CPAP and MAd were compared after one-night titration of the two treatments in a mixed-severity group of subjects with newly diagnosed OSAHS. CPAP was more effective than MAd to reduce AHI. Both treatments were associated with a similar improvement in subjective and objective sleepiness, cognitive function tests and HRQL. Side effects were similar in frequency and intensity but self-reported compliance was higher with MAd with > 70% of patients preferring this treatment.

To the best of our knowledge, this is the first randomized study comparing CPAP and MAd after one-night PSG titration of both treatments. Titration of MA was designed to optimize MAd efficacy. Recent reviews on oral appliances for OSAHS treatment concluded that treatment success (AHI<10) was achieved in an average of 52-54% of treated patients<sup>6,17</sup>. By pooling 7 randomized control trial comparing CPAP and MAd in 232 OSAHS patients, Hoffstein<sup>17</sup> found a mean AHI of 24 at baseline, 6 on CPAP and 14 on MAd. None of these randomized trials included any MA titration procedure excepted for one study using a partly adjustable appliance with progressive titration over the four months treatment period<sup>18</sup>. Although CPAP remained superior to MAd in terms of AHI reduction in the present study, a higher response rate (AHI<10 in 70% of patients) and a lower AHI (median [IQR] = 6 [3-14]) were observed with MAd than in previous randomized studies<sup>17</sup>.

Our one-night MA titration procedure had a high positive predictive value, with 85% of effective MAd therapy (AHI<10) in patients with AHI≤10 during MA titration PSG. In contrast, it had a low (45%) negative predictive value for treatment success compared to that recently obtained by Dort et al<sup>19</sup> (78%). One possible explanation for this low negative predictive value is a progressive accommodation to MAd resulting in an increased efficacy over time. Even in patients with MA titration AHI>10, a partial response was observed during

PSG titration with a 35% decrease in AHI compared to baseline. Sleep disruption caused by the MAd titration procedure may also have falsely elevated AHI due to a higher percentage of light non REM sleep or more arousals than during CPAP titration. However, no difference in sleep architecture was observed between CPAP and MAd titration PSG. The denominator for AHI calculation was total sleep time during MA titration and time in bed during home sleep study. This may have erroneously contributed to the decrease in AHI between titration and home sleep study. Finally, it may reflect a technical failure of our propulsion system to predict the long term therapeutic efficacy of MAd in some patients. The need of a supervised PSG in the sleep laboratory with the presence of a trained technician throughout the night and the low negative predictive value of our titration procedure may potentially reduce its clinical utility in routine clinical practice.

In agreement with previous randomized studies<sup>20-22</sup>, no significant difference in terms of ESS improvement was observed between CPAP and MAd. In contrast, two recent trials concluded to a lower improvement in ESS under MAd<sup>7,23</sup>. The conflict between the current and recent studies<sup>7,23</sup> may be explained by differences in patients characteristics and/or efficacy of MAd to control sleep disordered breathing. The patients included in the present study were less sleepy (mean ESS: 10.6) than those included by Engleman et al.<sup>7</sup> and Lam et al.<sup>23</sup> (mean ESS: 14 and 12 respectively) and MAd was more effective than in the studies by Engleman and Lam studies as assessed by mean AHI on MAd (respectively 7.8 vs 15 and 10.6) although baseline AHI was equivalent or even higher (34.2 vs 31 and 21 respectively). Two studies evaluated objective sleepiness using the maintenance of wakefulness test (MWT) on CPAP and MAd<sup>7,22</sup>. In both studies<sup>7,22</sup>, MWT values were not significantly different between the two treatments. Using the OSLEP test, we demonstrated a similar improvement in objective daytime alertness with CPAP and MAd. A significant improvement was observed for 4 of the

6 domains of HRQL with MAd and 2 of the 6 domains with CPAP with no significant difference between the two treatments. A significant treatment-by-period interaction was observed for two domains of HRQL, i.e. emotional reaction and sleep with a better emotional reaction and subjective sleep quality with MAd only for the second treatment period. As these variables are assessed subjectively by the patient, it can be hypothesized that the global impression expressed by the patients in the second treatment period was probably modified by comparison with the treatment received during the first treatment period. Finally, the study confirmed previous reports<sup>18,20,21,24</sup> of higher patient preference for MAd. Although reported side effects were similar in frequency and intensity, MAd was preferred by more than 70% of patients and was associated with a significantly higher reported compliance.

This study presents a number of potential limitations. The higher rate of ineffective titration with MAd compared to CPAP may have biased the results of the comparative study toward a more favorable outcome for MAd than would have otherwise been the case. However, it appeared unacceptable to submit to 2 months of MAd treatment the patients for whom we failed to determine an at least partially effective MA during titration PSG. The selective nature of the study population may also have contributed to the discordant results between the present study and previous randomized trials<sup>7,23</sup>. The overall treatment failure rate with MAd including the patients who were not randomized due to ineffective titration or who dropped out of the study was 18%, similar to the failure rate reported in a previous study using the same device with progressive MA titration based on sequential sleep recordings over several weeks<sup>10</sup>. Our study was a superiority trial and therefore we cannot claim formal equivalence between the two treatments in terms of improvement of functional outcomes. The patients in the present study were moderately sleepy. However, the mean ESS was not different from that reported in a previous study from our group including 263 consecutive OSAHS patients<sup>12</sup>.

Although this study was based on a mixed-severity group of subjects with mild-to-severe OSAHS, mean BMI was lower than in previous studies<sup>12</sup>. A higher BMI has been associated with lower efficacy of MAd in several studies<sup>6</sup>. Furthermore, a higher body weight was independently associated with CPAP preference in a previous randomized study<sup>7</sup>. The relatively low BMI of the present population may therefore have contributed to MAd efficacy and preference. The absence of a control period constitutes another potential limitation of this study as previous randomized controlled trial comprising 3 months of placebo treatment demonstrated a significant improvement after placebo on many of the neurobehavioral tests<sup>22</sup>. A placebo effect may therefore have contributed to improvement of some parameters in our study. As there is no way to record objective daily use of MAd at the present time, CPAP and MAd were compared on the basis of reported daily compliance. As previously described<sup>25</sup>, reported use of CPAP significantly overestimated actual running-time of the device. Patients in this study may therefore also have overestimated actual daily use of MAd. Various dental-skeletal effects have been documented after long term use of MAd including changes in the degree of vertical and horizontal overlap of the teeth<sup>17</sup>. No objective assessment of orthodontic change was performed in this study. However, reported side effects including subjective occlusal changes were reported to be mild and did not constitute an obstacle to long-term regular use of MAd.

In conclusion, despite these potential limitations, the results of our study support titrated MAd as an effective therapy in moderately sleepy and overweight OSAHS patients. Although less effective than CPAP, successfully titrated MAd was very effective to reduce AHI and was associated with a higher reported compliance than that observed on CPAP. Both treatments improved functional outcomes in a similar way. PSG titration of MA required the presence of

a trained technician throughout the night and had a low negative predictive value for treatment success which may potentially reduce its role in routine clinical practice.

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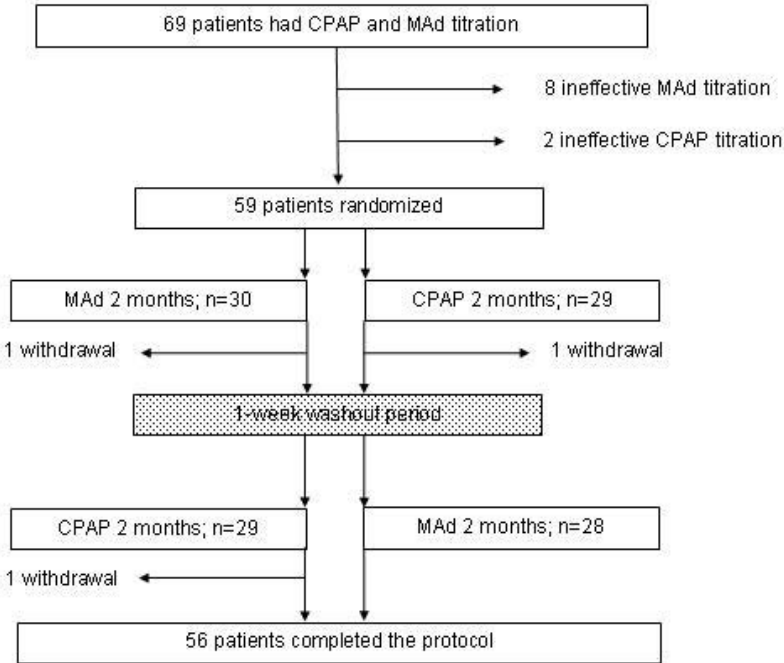
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**Figure 1:** photograph of the mandibular advancement device (AMC™, Artech Medical, Pantin, France) used in the study. Full-coverage acrylic appliances designed to fit to the upper and lower dental (left) arches are connected by acrylic plates of increasing length (right)



**Figure 2: Flow diagram of subjects during the study**



**Table 1: Baseline characteristics of randomized patients (n=59; 13 females)**

<b>Parameter</b>	<b>Mean±SD</b>	<b>[range]</b>
<b>Age, years</b>	<b>50.3±9.1</b>	<b>[26-69]</b>
<b>Body mass index, kg/m<sup>2</sup></b>	<b>26.7±3.5</b>	<b>[20.3-34.6]</b>
<b>Apnea/hypopnea-index</b>	<b>34.2± 13.0</b>	<b>[11-60]</b>
<b>Epworth Sleepiness Scale</b>	<b>10.6±4.5</b>	<b>[0-21]</b>
<b>Maximum mandibular advancement, mm</b>	<b>9.5±1.5</b>	<b>[6-13]</b>

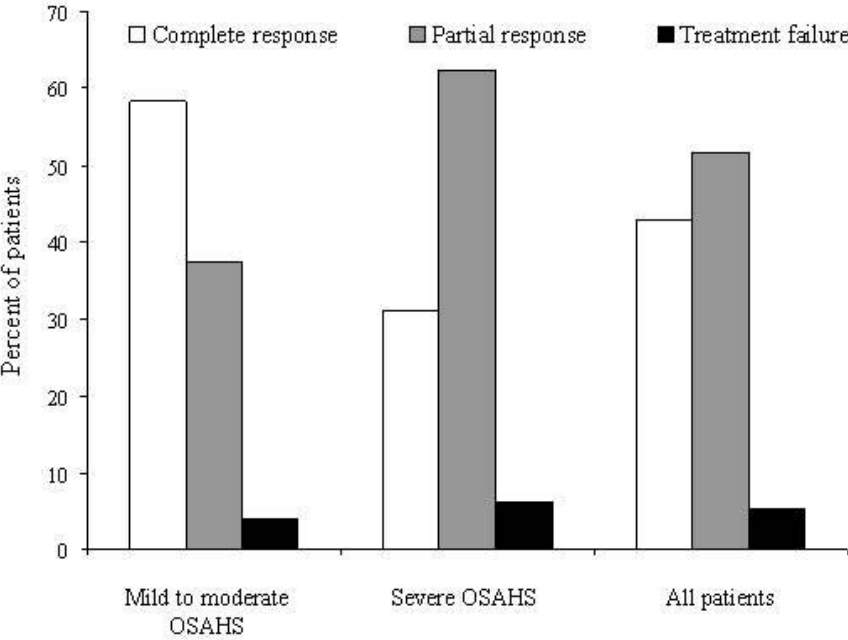
**Table 2: Comparison of home sleep study data with CPAP and mandibular advancement device (MAd)**

	CPAP	MAd	p
Total recording time, min	456(384-477)	449(416-476)	0.4
Snoring index	16(2-52)	55(10-149)	<0.001
Apnea-hypopnea index (AHI)	2(1-8)	6(3-14)	0.001
3% oxygen desaturation index	1.7(0.7-5.1)	6.3(3.0-9.7)	<0.001
Mean SaO <sub>2</sub> , %	96(95-96)	94(93-95)	<0.001

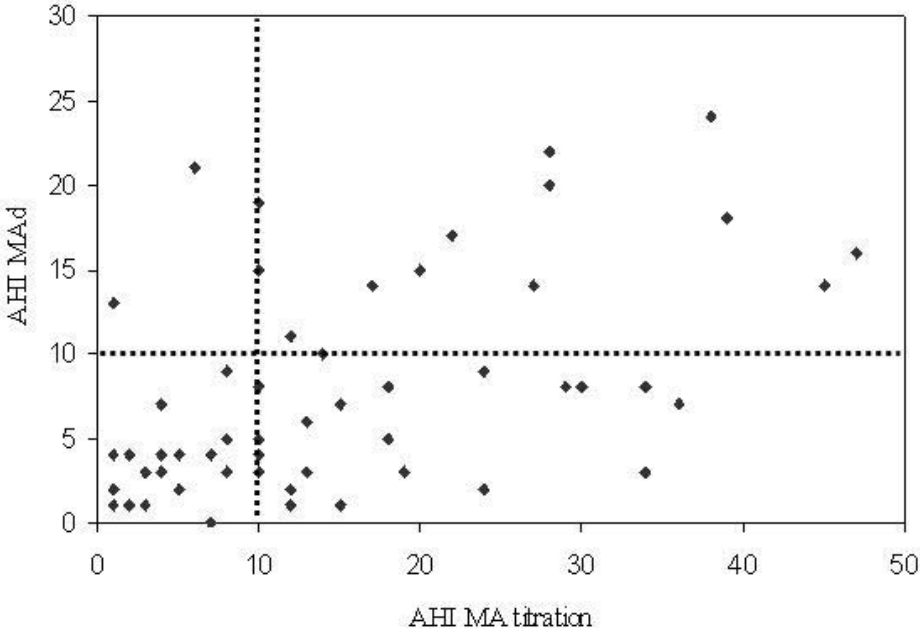
Values are expressed as median(interquartile range)



**Figure 3: Graph showing treatment response with mandibular advancement device in all patients who completed the study and according to OSAHS severity defined as mild to moderate (AHI<30) and severe (AHI≥30). Complete response was defined by a ≥ 50% reduction in AHI to < 5/h, partial response by a ≥ 50% reduction in AHI but AHI remaining ≥ 5/h and treatment failure by < 50% reduction in AHI**



**Figure 4: Comparison of apnea-hypopnea index during mandibular advancement titration polysomnography (AHI MA titration, events/hour of sleep) and during home limited sleep study with mandibular advancement device (AHI MAd, events/hour of recording)**



**Table 3: Measures of sleepiness, and cognitive function at baseline, on CPAP and on mandibular advancement device (MAd)**

<b>Parameter (direction of improvement)</b>	<b>Baseline</b>	<b>CPAP</b>	<b>MAd</b>
<b>Epworth Sleepiness Scale (↓)</b>	<b>10.6±4.5</b>	<b>8.2±3.9*</b>	<b>7.7±4.0*</b>
<b>Osler test</b>			
<b>Sleep latency, s (↑)</b>	<b>2094±674</b>	<b>2300±391†</b>	<b>2312±322†</b>
<b>Errors, n (↓)</b>	<b>12.5±17.9</b>	<b>8.7±19.8†</b>	<b>4.3±7.5‡</b>
<b>Trail Making Test A (↓)</b>	<b>36.4±10.9</b>	<b>30.1±8.9*</b>	<b>32.5±9.6†</b>
<b>Trail Making Test B (↓)</b>	<b>79.3±26.2</b>	<b>68.5±22.2*</b>	<b>73.4±33.0</b>

Values are expressed as mean±SD

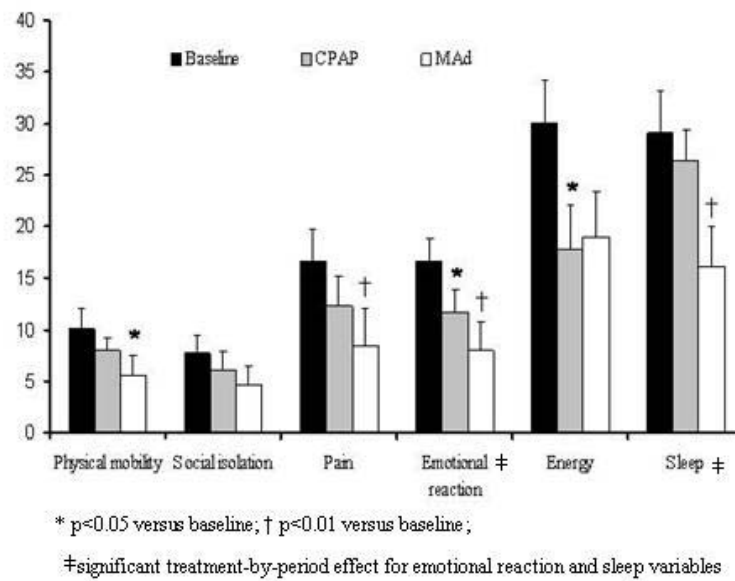
\* p<0.001 for the comparison of treatment versus baseline

† p<0.05 for the comparison of treatment versus baseline

‡ p<0.01 for the comparison of treatment versus baseline

For each variable, p values are adjusted for multiple comparisons by using Bonferroni correction, i.e. p values are multiplied by 3.

**Figure 5: Nottingham Health Profile domains of quality of life at baseline, on CPAP and on mandibular advancement device (MAd) [(data expressed as mean(SEM)]. For each variable, p values are adjusted for multiple comparisons by using Bonferroni correction, i.e. p values are multiplied by 3. Lower scores indicate better functioning**



**Table 4: Comparison of treatment related side effects and compliance on CPAP and mandibular advancement device (MAd)**

<b>Parameter</b>	<b>CPAP</b>	<b>MAd</b>	<b>p</b>
<b>Mean side effects score</b>	<b>3.2±3.4</b>	<b>3.2±3.1</b>	<b>0.8</b>
<b>Reported compliance</b>			
<b>Hours per night, h</b>	<b>6.0(4.0-7.0)</b>	<b>7.0(6.0-8.0)</b>	<b>&lt;0.001</b>
<b>Nights on treatment, %</b>	<b>90(40-99)</b>	<b>98(90-100)</b>	<b>&lt;0.001</b>

**Values are expressed as mean±SD or median(interquartile range) when not normally distributed.**