Determinants of Objective Compliance During Oral Appliance Therapy in Patients With Sleep-Disordered Breathing
A Prospective Clinical Trial

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IMPORTANCE The main reported reasons for discontinuation of oral appliance therapy for sleep-disordered breathing (SDB) are the presence of self-perceived adverse effects and self-appreciated lack of efficacy. However, these conclusions rely only on subjective compliance data.

OBJECTIVE To determine which parameters are correlated with objectively measured data on compliance with oral appliance therapy.

DESIGN, SETTING, AND PARTICIPANTS For 51 outpatients with SDB, a prospective clinical trial using oral appliance therapy was conducted at Antwerp University Hospital from February 7, 2011, to October 8, 2013 (38 [75%] males; mean [SD] age, 49.3 [9.0] years; mean [SD] apnea-hypopnea index, 14.9 [9.3] events per hour of sleep; mean [SD] body mass index [calculated as weight in kilograms divided by height in meters squared], 26.3 [2.8]). Analysis was performed November 5, 2014.

INTERVENTION Oral appliance therapy with a custom-made, titratable mandibular advancement device (OAm).

MAIN OUTCOMES AND MEASURES Possible correlations were assessed between objective compliance and patients’ anthropometric characteristics, polysomnographic parameters, and answers to 3 subjective questionnaires (the visual analog scale for snoring, the Epworth Sleepiness Scale, and an adverse effects questionnaire).

RESULTS Median oral appliance use was 6.4 hours per night (range, 4.7-7.2 hours per night) at the 3-month follow-up. None of the anthropometric and polysomnographic parameters were correlated with compliance. No correlation was found between objective compliance and reports of excessive daytime sleepiness. However, a significant inverse correlation was found between objective compliance and posttreatment visual analog scale values for snoring ($P = .006; \rho = -0.40$). In addition, objective compliance was correlated significantly with a more pronounced decrease in socially disturbing snoring ($P = .005; \rho = 0.39$). The presence of dry mouth was the only adverse effect that was negatively correlated with objective compliance at the 3-month follow-up ($P < .05; \rho = -0.31$).

CONCLUSIONS AND RELEVANCE Neither the anthropometric and polysomnographic parameters nor reports of excessive daytime sleepiness correlated with compliance during oral appliance therapy. The 2 parameters that were correlated with higher objective compliance during oral appliance therapy were a more pronounced decrease in snoring and the presence of dry mouth during treatment.

TRIAL REGISTRATION clinicaltrials.gov Identifiers: NCT01284881 and NCT01532050

Published online September 24, 2015.
Sleep-disordered breathing (SDB) comprises a pathophysiologic spectrum of sleep-related breathing abnormalities, ranging from snoring to the more severe obstructive sleep apnea-hypopnea syndrome.\(^1\)\(^2\) Obstructive sleep apnea (OSA) among adults is a prevalent public health issue, affecting approximately 26.6% to 33.9% of adult men and 8.7% to 27.8% of adult women.\(^3\) It is characterized by repetitive episodes of partial or complete upper airway obstruction during sleep.\(^4\)\(^6\) Obstructive sleep apnea is often associated with excessive daytime sleepiness, impaired cognitive performance, reduced quality of life\(^7\) and is a strong and independent risk factor for cerebrovascular and cardiovascular diseases.\(^8\)\(^12\) The severity of sleep apnea is expressed by the apnea-hypopnea index (AHI), which is defined as the number of apneas and hypopneas per hour of sleep.\(^4\)\(^13\) A diagnosis of sleep apnea is confirmed when the AHI is 5 events or more per hour of sleep. Mild sleep apnea is defined as an AHI of 5 to less than 15 events per hour, moderate sleep apnea as an AHI of 15 to less than 30 events per hour, and severe sleep apnea as an AHI of 30 events or more per hour.\(^4\)\(^13\)

Therapy with continuous positive airway pressure (CPAP) provides a pneumatic splint of the upper airway by applying constant positive pressure throughout the respiratory cycle.\(^14\) Therapy with CPAP has proved to be efficacious in reducing apnea severity and is currently the recommended therapy for patients with moderate to severe OSA.\(^15\) Oral appliance (OA) therapy is increasingly prescribed as a noninvasive treatment option for patients with mild to moderate OSA who prefer OA therapy to CPAP therapy, who do not respond to CPAP therapy, who are not appropriate candidates for CPAP therapy, or who fail treatment attempts with CPAP therapy.\(^13\)\(^15\) As a consequence, OA therapy is increasingly prescribed in patients with severe OSA who do not comply with or who refuse CPAP therapy.\(^16\)\(^17\)

The most common type of OA therapy for the treatment of OSA is an oral mandibular advancement device (OAm) worn intraorally during sleep.\(^18\) The OAm’s mechanism of action in patients who respond to treatment causes enlargement of the cross-sectional upper airway dimensions by anterior displacement of the mandible and the attached tongue, resulting in improved upper airway patency.\(^18\)\(^21\)

Neither CPAP nor OA therapy eliminates the underlying causes of upper airway collapse, so both are lifelong treatments that prevent upper airway obstruction. Given the fact that even the most efficacious medical device is only effective when used appropriately, follow-up to assess compliance during CPAP and OA therapy is of primary importance.\(^22\)

As part of the clinical routine, CPAP therapy incorporates an objective measurement of use.\(^23\)\(^25\) This objective compliance measurement reveals that the clinical effectiveness of CPAP therapy is often limited by low patient acceptance, poor tolerance, and suboptimal compliance.\(^23\)\(^26\) Some studies evaluated the correlations between objective compliance data and anthropometric and polysomnographic variables such as age, body mass index (BMI), sex, mean nocturnal saturation, and severity of SDB.\(^23\)\(^24\) When comparing compliant and noncompliant patients, both groups showed similar anthropometric and polysomnographic data before the start of treatment. In addition, an identical percentage of patients reported improvement in snoring and daytime sleepiness in the compliant and noncompliant subgroups, and there was no difference in reported adverse effects.\(^24\) However, satisfaction with CPAP therapy and a better daytime energy level with CPAP therapy correlated with objective frequency of CPAP use.\(^23\)

Previous studies of OAm therapy compliance were limited to self-reported use and lacked an objective compliance measurement. Only recently has an objective compliance monitor become available to the market.\(^27\) This monitor indirectly allows for the calculation of the therapeutic effectiveness of OAm therapy, which seems to be characterized by suboptimal efficacy combined with rather high compliance.\(^27\)\(^28\) Although studies showed high compliance during OAm therapy, the main reported reasons for discontinuation of OAm therapy include the presence of self-perceived adverse effects such as excessive salivation, xerostomia, tooth and gingival discomfort, temporomandibular joint discomfort,\(^29\)\(^30\) and self-appreciated lack of efficacy. These reasons for discontinuation emphasize the patient’s perception of the treatment.\(^29\)\(^31\) However, these conclusions rely only on subjective compliance data. The aim of our study was, therefore, to determine the relevant treatment parameters that correlate with objectively measured compliance with OAm therapy.

### Methods

#### Patient Population and Design

In Belgium, CPAP therapy is the standard treatment for patients with moderate to severe OSA (AHI of >20 events per hour), and patients undergoing this therapy are fully reimbursed. Therefore, our policy is to propose a trial of CPAP therapy to any patient with an AHI of at least 20 events per hour. In our multidisciplinary setting, patients with mild SDB (AHI of <20 events per hour) and patients with intolerance to CPAP therapy are referred to the multidisciplinary dental sleep clinic involved in the decision making for the implementation of OAm therapy in patients with OSA.

All patients who presented to our outpatient clinic from February 7, 2011, to October 8, 2013, with SDB based on results of a recent overnight polysomnography and who were candidates for OAm therapy were invited to participate in a prospective clinical study. The full study protocol can be found in the trial protocol in the Supplement. Seventy adult patients with SDB (male, 56 [80%]; mean [SD] age, 47.8 [9.4] years; mean [SD] AHI, 17.0 [11.5] events per hour; mean [SD] BMI [calculated as weight in kilograms divided by height in meters squared], 26.7 [2.9]) were included after written informed consent was obtained. Ethical approval for this study was obtained from the Antwerp University Hospital and University of Antwerp Institutional Review Board. All patients started treatment with a custom-made oral appliance (RespiDent Butterfly, Dormco).\(^32\) The OAm therapy included strict multidisciplinary follow-up, with visits at 1 and 3 months after the start of therapy. After 3 months of OAm therapy, all patients were invited to undergo polysomnography overnight with the OAm in situ. Analysis was performed November 5, 2014.
Objective Compliance
Objective compliance during OAm therapy was obtained at the 1- and 3-month follow-up visits using a temperature-sensitive microsensor (TheraMon, Handels- und Entwicklungsgesellschaft, Handelsagentur Gschlacht) embedded in the upper right side of the OAm. Temperature was recorded by the microsensor at a sampling rate of 1 measurement every 15 minutes, allowing data acquisition for 100 consecutive days. Objective compliance measurement was based on the assumption that the OAm was worn when a temperature greater than 35°C was recorded. Participants were informed that a microsensor was embedded in the OAm to serve fundamental research of intraoral mucosal temperature shifts during the night and as such were blinded to the aim of the study, resulting in covert monitoring of compliance.

For each patient, the average OAm use in hours per night and in percentage of days per week was calculated and was referred to as the objective mean wearing time. Similar to definitions used in the literature for CPAP therapy, patients with an average individual use of at least 4 hours per night were considered compliant, while patients who used the OAm at least 4 hours per night on at least 70% of all nights were considered regular users.

Treatment Outcome
Responders were defined as patients with an AHI reduction of at least 50% compared with baseline. Treatment success was defined as an AHI of fewer than 5 events per hour on the follow-up polysomnography while using the OAm.

Subjective Questionnaires
At both the 1- and 3-month follow-up visits, patients were asked to complete a questionnaire regarding the subjective symptoms of excessive daytime sleepiness and snoring. Patients also completed a separate questionnaire indicating how frequently (never, rarely, occasionally, often, or always) they experienced some of the most commonly reported adverse effects (excessive salivation, xerostomia, tooth discomfort or pain, and temporomandibular joint discomfort or pain).

Epworth Sleepiness Scale
Daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS), a self-administered questionnaire. The ESS measures the probability of falling asleep in 8 different sedentary situations. The total ESS score can range from 0 to 24, with a score of 11 or more being indicative of excessive daytime sleepiness.

Visual Analog Scale for Snoring
The subjective report of snoring by the bed partner was assessed using a 10-point visual analog scale (VAS) ranging from 0 to 10. A score of 0 indicates no snoring, and a score of 10 indicates snoring that causes the bed partner to leave the room or go to sleep separately. A decrease of at least 3 points on the VAS during treatment with OAm compared with baseline recordings represents a decrease of 1 level of snoring severity and is considered to be satisfactory. To be considered an important reduction, snoring had to be reduced to a level that was no longer evaluated as bothersome, meaning a score of 3 points or fewer on the VAS.

Statistical Analysis
Results are presented as mean (SD) if normally distributed and as median (Q1-Q3) if not. Possible correlations between objective compliance and patients’ anthropometric characteristics (sex, age, height, weight, and BMI), polysomnographic parameters (AHI, total sleep time, oxygen desaturation index, minimal and mean oxygen saturation, and OAm efficacy), and answers to the subjective questionnaires (VAS for snoring, ESS for excessive daytime sleepiness, and the adverse effects questionnaire) were evaluated using Spearman rank correlation. A linear regression model was used to study the effect of a combination of the parameters above on compliance. A stepwise model building procedure was applied, and normality of the residuals was checked.

Results
Patient Population
Seventy adult patients with SDB were included in this study. Two patients did not return for the 1-month follow-up visit; thus, compliance data could not be obtained for those patients. At the 3-month follow-up, the microsensor data exceeded the 100-day storage period for 6 patients. In addition, 11 patients did not return and were thus considered lost to follow-up (Figure 1).

For the complete 3-month follow-up period, objective compliance data were thus available for 51 patients (male, 38 [75%]; mean [SD] age, 49.3 [9.0] years; mean [SD] AHI, 14.9 [9.3] events per hour of sleep; and mean [SD] BMI, 26.3 [2.8]).

Objective Compliance
For 51 patients, objective compliance was determined 1 and 3 months after the start of OAm therapy. At the 1-month follow-up, median compliance was 6.2 hours per night (range, 5.1-7.4 hours per night), with a median use of 93.1% (range, 77.5%-100%) of the nights. Forty-two patients (82%) were considered compliant, and 37 (73%) were classified as regular users (Table 1).

Three months after the start of OAm therapy, the OAm was used for 6.4 hours per night (range, 4.7-7.2 hours per night) on
a median of 92.2% (range, 73.6%-98.4%) of the nights. At the 3-month follow-up, 42 patients (82%) could be considered compliant, and 36 (71%) were classified as regular users (Table 1).

### Treatment Outcome

Baseline polysomnography and polysomnography with the OAm in situ were performed for all 51 patients (Table 2). The mean (SD) AHI decreased significantly from 14.9 (9.3) hours per night at baseline to 8.3 (7.8) hours per night ($P < .001$) with the OAm in situ after 3 months of treatment. Twenty-six patients (51%) were defined as responders, with an AHI reduction of 50% or more, and 21 patients (41%) met the criteria for treatment success (AHI of <5 events per hour of sleep during polysomnography with OAm).

### Subjective Questionnaires

The total mean (SD) ESS score for all patients decreased significantly with OAm therapy from 10.1 (4.9) at baseline to 6.8 (4.4) with OAm ($P < .001$). Twenty-two patients (43%) reported excessive daytime sleepiness with an ESS score (out of 24) of 11 or greater at baseline. Of these patients, excessive daytime sleepiness was completely eliminated with OAm therapy (ie, ESS score of <11) in 12 patients (55%). All but 1 of these 12 patients were considered compliant and regular users at the 3-month follow-up.

### A satisfactory decrease in snoring was seen with OAm therapy: 19 patients (37%) had a decrease of 3 or more points on the VAS. All these patients were compliant users and 16 (84%) were regular users.

### Adverse effects were subjectively scored. Unpleasant sensations in the teeth (14 of 20 patients [70%]), pain in the teeth (27 of 45 [60%]), hypersalivation (24 of 45 [53%]), and pain in the temporomandibular joint (24 of 45 [53%]) were the most reported adverse effects (Figure 2).

### Correlations

At the 1- and 3-month-follow-up visits, none of the anthropometric and polysomnographic parameters correlated with objective compliance with mean wearing time (Table 3). No correlation was found between objective compliance and ESS score or OAm efficacy in terms of AHI reduction. However, a significant inverse correlation was found between objective compliance at 3 months' follow-up and posttreatment VAS values for snoring ($P = .006$; $\rho = -0.40$) (Figure 3). Objective compliance correlated significantly with a more pronounced decrease in socially disturbing snoring as reported by the partner compared with baseline VAS scores for snoring without the OAm ($P = .005$; $\rho = 0.39$) (Figure 3).

In patients who never or rarely experienced adverse effects, median objective compliance at the 1-month follow-up was 7.10 hours per night (range, 5.85-7.61 hours per night) compared with 5.81 hours per night (range, 4.66-7.34 hours per night) in patients who occasionally, often, or always experienced one of the adverse effects mentioned. However, this difference was not statistically significant. At 3 months' follow-up, median objective compliance was 6.73 hours per night (range, 5.85-7.27 hours per night) in patients who did not experience adverse effects and 6.42 hours per night (range, 4.42-7.20 hours per night) in patients who experienced some adverse effects. The presence of dry mouth was the only adverse effect that correlated with objective compliance at 3 months' follow-up, with the infrequent occurrence of xerostomia leading to higher compliance ($P < .05$; $\rho = -0.31$).

According to a multiple linear model for the objective mean wearing time at the 3-month follow-up, including baseline VAS score for snoring, ESS score, AHI, age, BMI, sex, decrease in
VAS score for snoring, decrease in ESS score, decrease in AHI, and the presence of adverse effects, a decrease in VAS score for snoring and a lower baseline AHI were predictors of higher objective mean wearing time ($P = .003$ for decrease in VAS score for snoring and $P = .03$ for baseline AHI; $R^2 = 0.24$).

**Discussion**

This study evaluated possible correlations between objective compliance and patients’ anthropometric characteristics, polysomnographic parameters, and subjective reports of snoring, daytime sleepiness, and adverse effects. Neither the anthropometric and polysomnographic parameters nor excessive daytime sleepiness correlated with compliance in a group of patients with, on average, mild sleep apnea. The only 2 parameters that correlated with higher objective compliance during OAm therapy were a more pronounced decrease in reports of snoring and the presence of dry mouth.

Objective compliance was analyzed in 51 patients with a median compliance of 6.2 hours per night (range, 5.1-7.4 hours per night) at 1 month and 6.4 hours per night (range, 4.7-7.2 hours per night) at 3 months. In addition, the patients used their appliance almost every night: 93.1% (range, 77.5%-100%) of the nights at 1 month and 92.2% (range, 73.6%-98.4%) of the nights at 3 months. The compliance rate was 82% at both 1 and 3 months, with a regular user rate of 73% and 71%, respectively. This compliance rate is lower than that reported in the literature, although still relatively high.

**Table 3. Correlation Between Study Variables and Objective Mean Wearing Time**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Spearman $\rho$</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
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<td></td>
</tr>
<tr>
<td>AHI</td>
<td>$-0.18$</td>
<td>.21</td>
</tr>
<tr>
<td>ESS score</td>
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<td>.80</td>
</tr>
<tr>
<td>VAS score</td>
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<td>.73</td>
</tr>
<tr>
<td>With OAm</td>
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<td></td>
</tr>
<tr>
<td>AHI</td>
<td>$-0.02$</td>
<td>.88</td>
</tr>
<tr>
<td>ESS score</td>
<td>$-0.06$</td>
<td>.71</td>
</tr>
<tr>
<td>VAS score</td>
<td>$-0.40$</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Change at 3-month follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHI</td>
<td>$-0.01$</td>
<td>.96</td>
</tr>
<tr>
<td>ESS score</td>
<td>$0.16$</td>
<td>.28</td>
</tr>
<tr>
<td>VAS score</td>
<td>$0.39$</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Abbreviations: AHI, apnea-hypopnea index; ESS, Epworth Sleepiness Scale; OAm, oral mandibular advancement device; VAS, visual analog scale.

There have been previous studies on subjective compliance and tolerability of OAm therapy; disease severity, age, sex, and excessive daytime sleepiness did not correlate with poor compliance during OAm therapy. Our results based on objective compliance data also confirmed that baseline polysomnographic and anthropometric data and reports of excessive daytime sleepiness did not correlate with lower compliance in a group of patients with, on average, mild sleep apnea.

In the literature, patients who are satisfied with the effect of the OAm on their sleep apnea symptoms have a higher compliance rate than patients who are not satisfied with the effect of the OAm on their symptoms. Therefore, the most important finding of our study is that patients who subjectively experienced a greater improvement in their snoring as reported by their partner exhibited a higher objective mean wearing time. Indeed, snoring is often the patients’ major symptom and, therefore, most often the principal reason to seek medical help. A reduction in snoring is perceived by patients as therapeutic efficacy and therefore favors the use of the OAm, thereby improving compliance.

Another common reason for OAm discontinuation described in the literature is the presence of self-perceived adverse effects. However, in our study, no OAm discontinuation was reported, at least for the patients who returned for the 3-month follow-up visit. The results of this study therefore could not confirm the previous results that the discontinuation rate is correlated with self-perceived adverse effects. A possible explanation for the low discontinuation rate in our study could be the recent advances in the technology and comfort of OAm devices. Another reason for the low discontinuation rate could be the intense patient management at our multidisciplinary clinic. It is known that most adverse effects caused by OAm therapy are mild and transient, occurring during the initial phase of OAm therapy, and tend to resolve with time. If physicians are aware of the importance of early management of adverse effects, the patients will be motivated and encouraged to become accu-
The correlation between the objective mean wearing time at the 3-month follow-up visit and scores on the visual analog scale for snoring with the oral mandibular advancement device (OAm) as well as the decrease in scores on the visual analog scale for snoring with the OAm compared with baseline. A, Visual analog scale scores for snoring with the OAm ($P = .006; \rho = –0.40$). B, Decrease in scores on the visual analog scale for snoring with the OAm compared with baseline ($P = .005; \rho = 0.39$). A positive value is regarded as a decrease in visual analog scale scores.

Compliance with therapy can be achieved with an intensive follow-up program, including thorough patient education, detailed explanation of the treatment itself, and management of adverse effects. Long-term persistence of adverse effects lead to discontinuation of treatment. In a study on compliance during CPAP therapy, nightly use increased by 1.7 hours on average with multidimensional intervention and follow-up. There is little reason to think that an identical approach in OAm therapy will not benefit patients receiving OAm therapy.

**Conclusions**

In this study, a more pronounced decrease in socially disturbing snoring during OAm therapy was significantly correlated with better compliance. In addition, the presence of dry mouth correlated with lower compliance. These results highlight the importance of the effect of the cardinal symptom of snoring on therapeutic compliance during OAm therapy.
Reference Text:


