Mandibular Advancement Titration for Obstructive Sleep Apnea*

Optimization of the Procedure by Combining Clinical and Oximetric Parameters

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Background: **Oral appliances (OAs) have been used for the treatment of obstructive sleep apnea syndrome (OSAS), with different degrees of effectiveness having been shown in previous studies. But, in the absence of a consensual recommendation, the method of the determination of effective mandibular advancement varies from one study to another.**

Study objective: **We prospectively evaluated an OA titration protocol based on a combined analysis of symptomatic benefit and oximetric recording to guide the progressive mandibular advancement.**

Setting: **University hospital sleep disorders center.**

Patients: **Forty patients with OSAS (mean [±SD] apnea-hypopnea index [AHI], 46 ± 21 events per hour) found on baseline polysomnography, who were intolerant of nasal continuous positive airway pressure, completed all aspects of the study.**

Methods: **Two acrylic appliances connected by Herbst attachments were constructed. The mandible was advanced 1 mm every week until there was a resolution of the symptoms and a reduction in the oxygen desaturation index (*ie*, the number of desaturations yielding a > 3% fall in pulse oximetric saturation per hour of recording) [ODI] of <10 events per hour of recording or a maximum comfortable limit of advancement was obtained. The final response to OA was evaluated by full polysomnography recording.**

Results: **A complete response (*ie*, mean AHI, 5 ± 3 events per hour; mean snoring reduction [SR], 91 ± 13%; mean Epworth sleepiness scale [ESS] score, 5 ± 3) was obtained in 63.6% of patients, and a limited response (*ie*, mean AHI, 21 ± 11 events per hour; mean SR, 88 ± 15%; mean ESS, 6 ± 3) was obtained in 18.2% of patients. Twenty-five percent of mandibular advancements were motivated by an abnormal ODI (*ie*, 21 ± 10 events per hour) despite resolution of the symptoms, while 20% were motivated by persistent symptoms with a normal ODI (*ie*, 6 ± 2 events per hour). After a mean duration of 17 ± 4 months, 34 patients declared that they had used the OA 5 ± 2 days a week for 89 ± 19% of their sleep time.**

Conclusions: **A combination of the patient's subjective evaluation and oximetric score improves the effectiveness of the OA titration procedure.** ***(CHEST 2004; 125:1761–1767)***

Key words: obstructive sleep apnea; oral appliance; treatment

Abbreviations: AHI = apnea-hypopnea index; ESS = Epworth sleepiness scale; MAI = microarousal index; MMA = maximum mandibular advancement; nCPAP = nasal continuous positive airway pressure; OA = oral appliance; ODI = oxygen desaturation index; OSAS = obstructive sleep apnea syndrome; REM = rapid eye movement; Spo_2 = pulse oximetric saturation; TST = total sleep time; VAS = visual analog scale

Obstructive sleep apnea syndrome (OSAS) is characterized by the recurrent obstruction of the upper airway during sleep. Forward displacement of the mandible widens retropalatal airway patency as well as that at the base of the tongue in the passive pharynx,[1] and improves upper airway collapsibility during sleep in OSAS patients.[2] The anatomic changes induced by mandibular advance-

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ment during oral appliance (OA) therapy appear to be complex, presumably due to intricate interactions among upper airway structures. A growing body of evidence supports the use of an OA as a treatment for OSAS, but with varying degrees of effectiveness shown in various studies.[1–13] Ideally, assessment of the effectiveness of an OA should be conducted during a single night of polysomnography, in the same way as the titration of effective continuous positive airway pressure,[3,4] but this procedure is still only experimental.

At the present time, in the absence of a consensual recommendation, the method of the determination of effective mandibular advancement varies from one study to another. In some studies,[5–10] the degree of mandibular advancement was arbitrarily set between 50% and 75% of the patient's maximum protrusive range of movement, as measured from the position of maximum intercuspation. However, this procedure does not appear to be satisfactory as dose-dependent enlargement of the upper airways has been clearly demonstrated during progressive mandibular advancement.[1,11,12] In some other studies,[13–16] progressive mandibular advancement was performed until the improvement or resolution of the symptoms, meaning a significant reduction or disappearance of subjective symptoms of OSAS such as witnessed apneas, snoring, and excessive daytime sleepiness. This approach has the great advantage of introducing the concept of titration of mandibular advancement, but it presents the disadvantage of being exclusively based on subjective elements (*ie*, daytime sleepiness and/or snoring), which may be improved before polysomnographic improvement and may encourage the premature interruption of advancement.[12] Although clinical features are useful, they are insufficient to guide titration, and successive sleep recordings are necessary. Repeated polysomnographic recordings are a perfect solution but would be difficult to apply in routine practice because this examination is too complex and too expensive.[12] Ambulatory oximetry could constitute an easily repeatable objective tool to assess the course of sleep-disordered breathing in response to treatment, as desaturations reflect the persistence of apneas and/or hypopneas.[11]

The aim of this study was to evaluate an OA titration protocol based on the combined analysis of symptomatic benefit and oximetric recording to guide progressive mandibular advancement.

Materials and Methods

Patients

The study population consisted of 44 snorers (36 men) with OSAS that had been confirmed during an all-night diagnostic sleep study. Patients with inadequate dental structures for the anchoring of the OA, temporomandibular joint dysfunction, and/or previous uvulopalatopharyngoplasty were excluded.

All patients were initially treated by nasal continuous positive airway pressure (nCPAP) for a mean (± SD) duration of 1,185 ± 876 days. Despite attentive management and correction of the usual side effects of nCPAP therapy (*eg*, 52% of patients used a heated humidifier),[17,18] the patients decided to abandon this treatment modality. After being informed of the various treatment options and the procedure of titration, the patients gave their informed consent to be enrolled into this study.

Dental Appliance

After taking impressions of the upper and lower teeth, and recording the central occlusion position, separate upper (maxillary) and lower (mandibular) full-coverage acrylic appliances were constructed that could be clipped onto the two dental arches. The two dental arches were connected by Herbst attachments (*ie*, rod and tube devices) allowing the opening, the protrusion, and some side-to-side movement of the mandible, but no retrusion (Fig 1).

Outcome Measures

Questionnaire: The global patient evaluation of the effectiveness of the treatment was rated on the basis of the resolution of the symptoms or no resolution of the symptoms. In addition to this global evaluation, daytime sleepiness was tested using the Epworth sleepiness scale (ESS),[19] and snoring reduction (by bed partner's evaluation) and the potential side effects (*ie*, jaw pain, tooth pain, muscle stiffness, mucosal dryness, hypersalivation, and occlusal change) were assessed by visual analog scale (VAS) [scale, 0 to 10 mm]. Treatment compliance was monitored by diary completion.

Oximetry: Home nocturnal oximetry was performed using a pulse oximeter (model 8500 M; Nonin Medical; Plymouth, MN). An oxygen desaturation index (*ie*, the number of desaturations yielding a $> 3\%$ fall in pulse oximetric saturation [Sp_{O_2}] per hour of recording) [ODI] was calculated.

Polysomnography: Measurements included sleep stage (by EEG, electrooculogram, and submental electromyogram), nasal airflow (by nasal cannulae), oral airflow (by thermistance), rib cage and abdominal wall motion (by respiratory inductance plethysmography), and Sp_{O_2}. All polysomnographic data were analyzed visually. Sleep analysis was performed according to

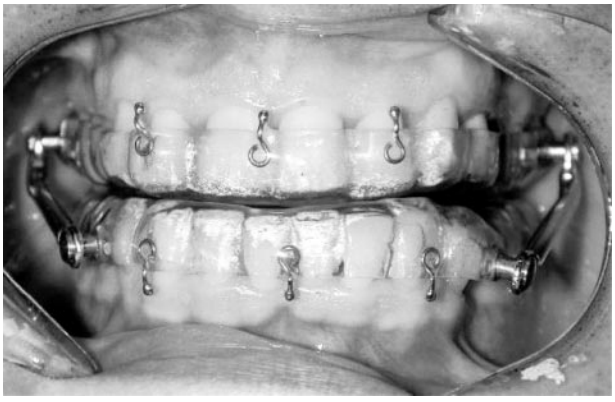

Figure 1. The dental OA. Two dental arches are connected by Herbst attachments.

standard criteria.[20] Apnea was defined as a cessation of airflow for > 10 s. Hypopnea was defined as a reduction of airflow, regardless of its amplitude, with > 3% fall in Spo_2 or arousal. The number of apneas and hypopneas per hour of sleep (*ie*, apnea-hypopnea index [AHI]) was calculated.

Study Design

Each patient's maximum protrusive range of movement was measured from the position of maximum intercuspation, and the type of dental malocclusion[21] was determined. The greatest advancement measured on three consecutive maneuvers (*ie*, maximum mandibular advancement [MMA]), was adopted. The Herbst attachments of the OA were adjusted on a semi-adjustable articulator to obtain an initial advancement of 80% of the MMA.

After a 2-week acclimatization period, the mandible was incrementally advanced, by a step of 1 mm every week, until either resolution of the symptoms and a reduction of ODI of < 10 events per hour, or the attainment of the maximum comfortable limit of advancement was achieved. At this point, the patient underwent all-night polysomnography recording.

Treatment Outcome

A complete response was defined as a resolution of the symptoms plus a reduction in the AHI to < 10 events per hour. Partial response was defined as a resolution of the symptoms plus a ≥ 50% reduction in AHI, but with AHI remaining at ≥ 10 events per hour. Treatment failure was defined as ongoing clinical symptoms and/or a < 50% reduction of AHI.

Statistical Analysis

The results were analyzed on an intention-to-treat basis. All results are expressed as the mean ± SD. Continuous variables at baseline and outcome were compared within each group by a paired *t* test or one-way analysis of variance. Cross-classified variables were compared using the Fisher exact test.

Results

Study Population

Of the 44 eligible subjects enrolled in the project, 40 completed all aspects of the study. Three patients dropped out of the study as they were unable to adapt to OA because of temporomandibular joint pain, and one patient was lost to follow-up because he failed to attend the scheduled appointments.

The mean age of the 40 patients was 57 ± 9 years, and their mean body mass index was 28 ± 4 kg/m^2. Their mean ESS score was 12 ± 4. Polysomnography recordings confirmed an elevated mean AHI of 46 ± 21 events per hour and a mean minimum Spo_2 of 81 ± 11%. Dental occlusion was classified as type I (*ie*, normal mesiodistal relation of the dental arches) in 29 patients, type II (*ie*, the lower dental arch was distal to the upper arch on one or both lateral halves) in 8 patients, and type III (*ie*, the lower dental arch was mesial to the upper arch on one or both lateral halves with protruding lower incisors) in 3 patients.

Objective Outcomes

After a mean of 3.7 ± 2.1 advancements, the mean mandibular advancement with an OA was 11.6 ± 2.9 mm (128.9 ± 23.8% of the MMA) in the 40 subjects who completed the project. On average, a mean reduction of 90 ± 14% of the intensity of snoring was reported by the patients. Comparison of the results of diagnostic polysomnography and those obtained during treatment with an OA showed a significant reduction of AHI by an average of 75% (*ie*, 11.9 ± 14.2 vs 45.9 ± 20.8 events per hour, respectively; $p < 0.001$), ESS score (5.1 ± 2.7 vs 11.8 ± 3.8, respectively; $p < 0.001$), and microarousal index (MAI) [18.8 ± 8.8 vs 44.8 ± 18 events per hour, respectively; $p < 0.001$]. An improvement of sleep architecture characterized by increased effectiveness (81.3 ± 7.4% vs 71.5 ± 16.2%, respectively; $p < 0.01$) and an increased duration of rapid eye movement (REM) sleep (19.5 ± 6.9% vs 9.6 ± 7.7% of total sleep time (TST), respectively; $p < 0.001$) also were observed.

Treatment Outcome

As represented in Tables 1 and 2, a complete response was obtained in 28 patients (63.6%; group 1), a partial response was obtained in 8 patients (18.2%; group 2), and the treatment was considered to be ineffective for 8 patients (18.2%; group 3). For all of the patients in groups 2 and 3, mandibular advancement had to be stopped due to temporomandibular discomfort.

Predictive Factors of OA Effectiveness

No between-group differences were noted for MMA (group 1, 9 ± 2 mm; group 2, 7 ± 2 mm; group 3, 11 ± 4 mm), final mandibular advancement (group 1, 12 ± 3 mm; group 2, 11 ± 4 mm; group 3, 14 ± 3 mm), age, anthropometric parameters, and initial AHI.

Titration Parameters

At the first assessment, which was performed at 80% of MMA, only four patients (9%) presented sufficient clinical and oximetric improvement (ODI, 4 ± 2 events per hour) to allow polysomnography. These four patients were in the success group.

For the remaining 36 patients, advancement was continued beyond the initial advancement. Twenty-five percent of advancements were motivated by abnormal ODI (mean ODI, 21.2 ± 9.9 events per hour), despite resolution of the symptoms. Among these patients, 2.1 ± 1.4 additional mandibular advancements were necessary to obtain satisfactory

Table 1—*Effect of OA on Subjective and Polysomnographic Data According to Response Groups

Variables	Complete Response (n = 28)			Partial Response (n = 8)			Failure (n = 8)		
	Baseline	OA	p Value	Baseline	OA	p Value	Baseline	OA	p Value
Snoring reduction, %		91 ± 13			88 ± 15			88 ± 25	
ESS	12 ± 4	5 ± 3	< 0.001	10 ± 3	6 ± 3	< 0.05	13 ± 5	5 ± 3	< 0.05
AHI, events/h	42 ± 18	5 ± 3	< 0.001	57 ± 25	21 ± 11	< 0.001	56 ± 25	43 ± 20	NS
MAI, events/h	44 ± 20	15 ± 6	< 0.001	48 ± 14	25 ± 7	< 0.001	47 ± 16	33 ± 10	NS
Stage 1/2, % TST	65 ± 13	54 ± 13	< 0.01	79 ± 18	64 ± 10	NS	62 ± 27	60 ± 16	NS
REM sleep, % TST	10 ± 7	21 ± 7	< 0.001	9 ± 9	19 ± 4	< 0.05	7 ± 10	10 ± 8	NS
Sleep efficiency, %	73 ± 16	83 ± 7	< 0.01	66 ± 21	78 ± 8	NS	74 ± 4	81 ± 7	NS
Min Spo_2, %	83 ± 8	87 ± 4	< 0.05	75 ± 15	80 ± 6	NS	77 ± 10	79 ± 5	NS
ODI, events/h	30 ± 13	4 ± 2	< 0.001	39 ± 23	16 ± 7	0.02	41 ± 20	33 ± 16	NS

*Values given as mean ± SD unless otherwise indicated. NS = not significant.

oximetric recordings. On the other hand, 20% of advancements were motivated by an insufficient symptomatic benefit, according to the subjective evaluation of the patient, despite an improved ODI (on average, 6.6 ± 1.9 events per hour). Among these patients, 1.7 ± 1.3 additional mandibular advancements were necessary to obtain sufficient symptomatic benefit.

Patient Outcome

Thirty-four patients were treated by OA on a long-term basis. All 28 patients in the success group were treated by OA. After a mean duration of 17 ± 4 months of treatment, these patients declared using the OA 6.7 days a week for an average of 95 ± 2% of their TST. Six of the eight patients in the partial-response group, after refusing to resume nCPAP therapy, were treated by OA. After a mean duration of 18 ± 2 months of follow-up, these six patients declared using OA 5.6 ± 2.1 days a week for an average of 89.5 ± 19.4% of their TST. Two patients abandoned OA treatment and agreed to resume nCPAP therapy. The intensity of the disturbance created by the adverse effects reported by the 34 patients after the prolonged use of an OA (*ie*, 17 ± 4 months) are summarized in Table 3.

Table 2—*Dental Occlusion and Mandibular Advancement Characteristics According to Response Groups

Variables	Complete Response (n = 28)	Partial Response (n = 8)	Failure (n = 8)	p Value
MMA, mm	9 ± 2	8 ± 3	12 ± 4	NS
FMA, mm	12 ± 3	11 ± 4	14 ± 3	NS
Advancement, No.	3 ± 2	5 ± 3	5 ± 2	NS
Dental occlusion				
Type I (n = 28)	19 (68)	5 (18)	4 (14)	
Type II (n = 9)	8 (89)	1 (11)	0	
Type III (n = 3)	1 (33)	2 (67)	0	

*Values given as mean ± SD or No. (%), unless otherwise indicated. FMA = final mandibular advancement. See Table 1 for other abbreviation not used in the text.

Discussion

This study confirms that a titratable OA can be a satisfactory treatment in a large proportion of patients with moderate-to-severe OSAS refusing long-term nCPAP therapy, as this modality achieved a complete response in 64% of these patients. This response consisted of a reduction in AHI of < 10 events per hour combined, with clinical improvement together with improvement in the quality of sleep. This result was obtained by progressively advancing the mandible according to a titration protocol based on a combined analysis of subjective effect on clinical symptoms and oximetric data recorded at each new mandibular position. Our results showed that clinical or oximetric score alone was insufficient to predict the effects of OA.

A growing body of evidence supports the use of an OA as a treatment for OSAS, but with varying degrees of effectiveness in the various studies. In a review of the literature, Pancer et al[13] reported an average success rate of 53% with the OA based on an

Table 3—*The Intensity of Disturbance by the Side Effects After Long-term Use of OA Evaluated by a VAS

Variables	VAS, mm (mean ± SD)
Jaw pain	1.7 ± 2.0
Tooth pain	1.4 ± 1.7
Muscle stiffness	0.5 ± 1.0
Mucosal dryness	2.1 ± 2.6
Hypersalivation	2.2 ± 2.8
Occlusal change	0.8 ± 1.6

*VAS, 0 to 10 mm.

AHI of < 10 events per hour, and 51% of patients in his own study satisfied this definition. In our study, 64% of the patients can be considered to be complete responders to OA, according a robust definition of complete response associating the resolution of the symptoms and an AHI of < 10 events per hour. In this group, the AHI decreased from an average of 43 to 5 events per hour. They no longer experienced excessive daytime sleepiness (as the ESS score decreased from an average of 12 to 5), and they considered that their snoring was no longer a social problem (it was reduced by an average of 87% on the VAS). As previously reported,[6,7,13,22,23] an improvement of the sleep architecture also was observed in these responding patients, characterized by a reduction of the MAI (by 70%), a reduction of the proportion of light slow-wave sleep, and an increased proportion of REM sleep (by 50%). In addition to this, it should be stressed that our patients who responded partially (18%) obtained a very marked reduction in their AHI (initially, 17 vs 54 events per hour). In the partial responders, a polysomnographic improvement also was accompanied by improvement in the patient's comfort related to the normalization of the ESS (*ie*, 5 vs 12) and a reduction of snoring by 88%. In our study, a complete response was achieved in some patients with moderate and severe OSAS. This finding is similar to that reported by Mehta et al[15] but contrasts with other studies that have frequently reported that OA was more effective at the mild end of the severity spectrum.[11,12,16,23] This emphasizes the need for a progressive titration procedure that is performed under close monitoring.

The subjective clinical impact of treatment in completely or partially responding patients probably explains their good compliance with treatment, which they declared to use 6 nights per week for an average of 7 h. Obviously, it would have been preferable to obtain objective information on compliance with treatment, as was done for nCPAP therapy,[24] but no suitable methodology is available.[25] As for nCPAP therapy, the patient's own reported use of an OA is probably biased. Patients usually overestimate nCPAP use by about 1 h.[26] However, even if a similar overestimation is observed for OA use, compliance with treatment would remain high. The cardiovascular risk, particularly that of developing hypertension, is correlated with the AHI.[27] This risk is therefore markedly reduced by the use of the OA even in patients with a partial response compared to no treatment. This result is all the more encouraging in that all of these patients refused treatment with long-term nCPAP therapy.

This result was obtained by optimal OA titration. A dose-dependent effect of mandibular advancement on the reduction of upper airways obstruction has been clearly demonstrated both experimentally, in anesthetized and paralyzed subjects,[1] and clinically, in sleeping OSAS patients.[11] More recently, de Almeida et al[12] reported a reduction of AHI that was proportional to the degree of mandibular advancement in a series of seven patients in whom the titratable OA was gradually adapted on the basis of successive polysomnography recordings. Our data confirm the need for a titration procedure to obtain the optimal effectiveness of an OA as a treatment for OSAS. Only four of our patients (9%) were correctly treated by the initial advancement (*ie*, 80% of the MMA), and the final mandibular position was obtained after an average of four successive advancements. Ideally, the titration procedure could have been performed during an all-night polysomnography recording. We have shown that it is possible to mobilize the jaw of a sleeping OSAS patient without waking him and, therefore, to predict the degree of effectiveness of the OA.[4] However, this experimental procedure cannot be routinely applied to a large number of patients. Similarly, repeated polysomnography recording is not compatible with a study based on a large patient population.[12] To obtain objective information on breathing during sleep, we decided to repeat a simple recording (*ie*, oximetry), in which abnormal findings can only correspond to the persistence of sleep-disordered breathing,[28] justifying further mandibular advancement. Kato et al[11] demonstrated the value of this approach. In their study, each 2-mm mandibular advancement coincided with improvement in the number and severity of nocturnal desaturations during sleep in their OSAS patients. To guide the titration of the OA, we added the clinical item resolution of symptoms (*ie*, a significant subjective reduction or disappearance of symptoms of OSAS such as witnessed apneas, snoring, and excessive daytime sleepiness) to the ODI, because the patient's symptoms can persist despite a significant reduction in the AHI.[12] This global item has been used in a well-designed study by Mehta et al,[15] in which they demonstrated the superiority of an OA vs a sham appliance. However, using a AHI cutoff of < 10 events per hour, only 54% of their patients obtained a complete response. In the study by Mehta et al,[15] the mandible was advanced until resolution of the symptoms or attainment of the maximum comfortable limit of advancement, which could explain the lower response rate compared to that obtained in our study.

Our results clearly show that a patient's subjective evaluation, which is frequently used for OA titration[5,8,9] or oximetry score,[11] is insufficient to determine effectiveness of treatment. Oximetry remained abnormal despite clinical improvement in 25% of

our patients, and 20% of advancements were motivated by residual clinical symptoms despite a normalized ODI. However, we have demonstrated the value of successively using both parameters during the titration procedure. Advancement can be initiated and continued until the correction of symptoms, and oximetry can then be used as a guide to final adjustment in a majority of the cases. Compared to conventional OA titration, our procedure was more efficient but much more intensive and therefore more expensive, requiring an average of four medical consultations and three oximetric recordings. However, the final proposed titration protocol simplifies the procedure by limiting additional oximetric recordings prior to the performance of treatment evaluation polysomnography recordings to an average of two among the 25% of patients in whom ODI remains abnormal, despite clinical improvement.

Clearly, the uncontrolled design of our study is a methodological weakness. We did not compare our results to those obtained with a titration procedure based on clinical features or oximetric score alone. However, one can note that when a normalization of the clinical features and oximetric scores was achieved, the AHI on the control polysomnography recording was < 10 events per hour in 87% of cases and, at the opposite end, when the clinical and/or the oximetric scores were above the chosen limits, the AHI was > 10 events per hour in 67% of the cases.

The use of treatment with an OA carries a potential risk of dental or temporomandibular adverse effects.[21,29,30] Until now, they have been considered to be frequent, but minor, and never to require the discontinuation of treatment. Theoretically, these effects are likely to be more severe with the greater degree of mandibular advancement. In view of this hypothetical risk, mandibular advancement was limited to a fraction of the maximum active protrusion in a large number of previous studies. By definition, the titration protocol results in sometimes marked variations in the degree of mandibular advancement. In our study, the mean mandibular advancement, including nonresponding patients, was 11.6 mm, as the protocol was guided by the maximum tolerated advancement. These values are similar to those reported by de Almeida et al,[12] who demonstrated the absence of impact of this degree of advancement on the temporomandibular joint by comparative analysis of MRI images obtained before the insertion of the OA and after an average of 12 months of treatment. Close follow-up during long-term therapy by OA is obviously advisable in order to detect potentially relevant orthodontic changes as early as possible.

In conclusion, optimal mandibular advancement must be evaluated by a titration procedure, in the same way that it is performed for nCPAP therapy. This procedure must be multiparametric, successively including a clinical item, resolution of symptoms, and the course of a simple indicator of the quality of breathing during sleep (ODI in the present study).

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