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Prospective evaluation of an oral appliance in the treatment of obstructive sleep apnea syndrome

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Abstract The purpose of this study was to investigate the effects of an oral appliance (OA), with and without mandible advance, in the treatment of obstructive sleep apnea syndrome (OSA). Twenty-four patients diagnosed with OSA agreed to participate in this study. The patients were treated for 3 months (with a removable soft elastic silicone positioner customized with thermoplastic silicone and with a 5-mm opening). Patients were selected, using a randomized design, to receive an OA model either with (12 patients) or without advance (12 patients). Before treatment, a snoring questionnaire, the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), the Functional Outcomes of Sleep Questionnaire (FOSQ), the Epworth Sleepiness Scale (ESS), and polysomnography were completed. Fifteen subjects completed the protocol (13 men, two women). With respect to basal values, the mandible-advanced OA group presented a decrease in the mean apnea–hypopnea index (AHI) (33.8±4.7 versus 9.6±2.1; $p<0.01$), number of arousals per hour (33.8±13.9 versus 16.0±1.5; $p<0.05$), ESS score (14.7±5.1 versus 5.1±1.9; $p<0.05$), snoring score (15.4±1.9 versus 10.1±3.2; $p<0.05$), and total FOSQ score (78.1±22.6 versus 99.3±14.4; $p<0.05$). After treatment, the non-advanced group presented a decrease in the mean AHI (24.0±12.2 versus. 11.7±7.9; $p<0.05$). However, no significant differences were found in the number of arousals per hour, ESS score, snoring, and total FOSQ score in the non-advanced group. Neither study group showed significant difference in mean SF36 scores. Oral appliances, especially those that advance the mandible, offer an effective treatment for OSA.

Keywords Obstructive sleep apnea · Oral appliance · Quality of life

Introduction

Obstructive sleep apnea syndrome (OSA) is a common disorder affecting approximately 2% of middle-aged women, 4% of middle-aged men [1], and 6% of people between the ages of 50 and 70 [2]. This disorder is characterized by recurrent cessation of airflow caused by total or partial collapse of the upper airway [3]. The gold standard for treatment of OSA is continuous positive airway pressure (CPAP), but problems of noncompliance exist mainly among younger and less-severely affected patients [4, 5]. Oral appliances (OA) have emerged as an increasingly popular alternative, and the use of these appliances is gaining attention and acceptance [6–10]. The majority of OSA patients have symptoms related to poor-quality sleep, such as excessive daytime sleepiness and tiredness, lack of concentration, memory impairment, and deterioration in quality of life [11, 12]. Several studies analyzing the health-related quality of life (HRQoL) of patients with OSA syndrome have focused on the effect of CPAP treatment [13–17]; however, few studies have centered on the effect of OA treatment [18, 19]. Therefore, we conducted a clinical effectiveness study for the

purpose of determining the impact of OA therapy (with and without mandible advance) on the HRQoL of patients with OSA in our community.

Patients and methods

Study population

Twenty-four patients (20 men, four women) diagnosed with OSA were asked to participate. Suspicion of OSA was due to daytime sleepiness, loud snoring, nocturnal choking and awakenings, cease-breathing events, or all four of these, as reported by the patient or bedmate. Inclusion criteria were the presence of at least two OSA symptoms and an apnea–hypopnea index (AHI) ≥10/h, as determined by polysomnography. Exclusion criteria were over 75 years of age, body mass index (BMI) >40 kg/m^2, inadequate dental anchoring structures (too few teeth) for the OA, temporomandibular joint dysfunction (pain during mandibular advancement or limitation of mouth opening), high-risk professions, or cardiovascular, neurological, or psychiatric disorders. Excluded patients were provided alternative therapy.

Patients were selected, using a randomized design, to receive either an advanced mandible model OA (advanced group: 12 patients) or a nonadvanced mandible model OA (nonadvanced group: 12 patients). After undergoing the first tests, three patients preferred CPAP and one decided to join a weight-loss program. Thus, 20 patients (17 men, three women) agreed to continue in this study. The Review Board on Human Studies at Orense approved the protocol, and each patient gave informed consent.

Appliance design

A soft elastic silicone positioner for opening and advancing the mandible was used (Fig. 1). This bimaxilar appliance joins in a position, which is preset through the construction bite, the maxillary and the jaw. The appliance is fitted with superior and inferior tooth prints as well as openings at the front to facilitate oral breathing. For the manufacture and placement of the appliance, alginate impressions were taken of both dental arches, and a mold was taken using wax of the maximum intercuspation of the maxillary and mandibular teeth and of the construction bite where the appliance was to be placed. The wax mold of the construction bite was made with a variant of the George Gauge System. The alginate dental impressions were poured in plaster and attached to a semiadjustable articulator according to the construction bite. Dental models were waxed, silicone was applied and polished, and sheen was given. Two models of oral appliances with 5 mm were applied, one model with advance and one without. The advanced model included an advance equal to 75% of the maximum forced advance. After placing the appliance, tests were carried out to assure that it was not excessively bothersome. In case of rubbing in the mouth or on the tongue, the appliance was trimmed and polished. In patients experiencing nausea, the posterior and superior zone of the appliance was adapted.

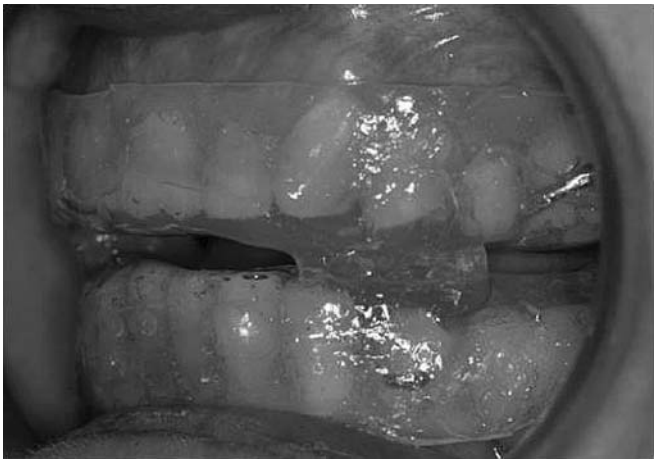

Fig. 1 View of the oral appliance. A soft elastic silicone positioner fitted with superior and inferior teeth prints as well as openings at the front to facilitate oral breathing.

Sleep study

Sleep study was carried out in the sleep laboratory and included two-channel electroencephalogram (C3-A2, C4-A1), electrooculogram, submental electromyograms, air flow (three-port thermistor), electrocardiogram, and measurement of chest wall movement. The polysomnographic register was analyzed in periods of 30 s and during phases I, II, III, IV, and REM, according to the system of Rechtschaffen and Kales [20]. Apnea was defined as the absence of airflow for more than 10 s and hypopnea as the reduction of respiratory flow for at least 10 s accompanied by a 4% or more decrease in the saturation of hemoglobin and/or an arousal. The average of AHI was calculated in hourly samples of sleep. AHI results were distinguished between supine and lateral AHI. An arousal was defined according to the American Sleep Disorders Association [21]. The arousal index was the average number of arousals per hour of sleep. SaO_2 recording was done with a Criticare 504 oximeter with a finger probe and sampled at a frequency of 0.2 Hz (one sample every 5 s). The percentage of time spent with SaO_2 below 90 (CT90) was also calculated.

Outcome measurements

Before treatment, subjects were applied a complete case history and a general sleep questionnaire. The questions dealing with snoring were answered by the bedmate on a five-point scale [22], and the followings questions were used: “Does

your husband/wife snore loudly"? "Does your husband/wife snore in all positions"? "How often were you kept awake by snoring"? "How often were you forced to sleep in another room"? Each question was scored 0 (never snores) to 5 (always snores).

Subjective sleepiness was evaluated by means of the Epworth sleepiness scale (ESS) at baseline and repeated after CPAP treatment using the cross-culturally valid Spanish version [23]. This scale consists of eight questions regarding the tendency to fall asleep in situations of different stimulation. Each question is scored 0 to 3: the total score can vary from 0 (no sleepiness) to 24 (extremely sleepy) with 10 being the upper limit of normal.

Perceived health status and quality of life were evaluated through a generic questionnaire—Medical Outcome Survey Short Form 36 (SF-36) [24]—as well as with an OSA questionnaire more closely adapted for OSA, the Functional Outcomes of Sleep Questionnaire (FOSQ) [25]. Scores of the eight SF-36 subscales range from 0 (minimum well-being) to 100 (maximum well-being). The SF-36 addresses the following eight domains: physical functioning, role physical, role emotional, social functioning, mental health, vitality, bodily pain, and general health perception. FOSQ contains 30 items divided into five scales: activity level, vigilance, intimacy and sexual relationships, general productivity, and social outcome. Scale scores were added to compute a global score ranging from 0 (maximal dysfunction) to 120.

Treatment outcome was classified into the following categories: Complete response was defined as a resolution of symptoms together with reduction in AHI to a level below 5/h, and partial response was defined as more than 50% reduction in AHI with AHI remaining above 5/h. Treatment failure was defined as ongoing clinical symptoms and/or less than 50% reduction in AHI. Compliance was assessed from the information provided by the patients and their partners. Sufficient compliance was assumed when subjects gave assurance that the device had been worn every night for at least 6 h throughout the study period. If a patient could not tolerate the appliance or failed to use it for at least three successive weeks, a lack of compliance was assumed and the subject was excluded from the study.

Study design

Treatment was tested by randomly placing either an advanced or nonadvanced mandible model OA in patients for 3 months. A gradual adjustment by the patient was recommended during the first 2 weeks, and thereafter, the appliance was worn every night (a little before going to bed for better adaptation). After 1 month of use, compliance and side effects were evaluated. If the patient informed mobility in the appliance, dental pain, or pain in the mastication muscles, a new clinical visit was advised. Regardless of findings or snoring, another polysomnography, a complete range of questionnaires, and recording of any side effects were performed 3 months after placement.

Statistical methods

Continuous variables were expressed as the mean ± standard deviation unless otherwise indicated. The *t* test, two tailed, for paired samples was applied to test differences pre- and posttreatment; non-normally-distributed variables were compared using Wilcoxon rank sum test. Next, we compared the change in total FOSQ scores and in SF-36 dimension between pretreatment and posttreatment for the two groups. In order to identify changes that were clinically significant—rather than only statistically significant—effect sizes were calculated in each variable by dividing the mean change in a variable by the standard deviation of the variable at baseline [26]. As an indicator of the magnitude of therapeutic benefit, we used the Cohen indicators [27]: 0.20 means *small*, 0.50 *moderate*, and 0.80 or higher *large*. The chi-square test was used to compare categorical and ordinal data. Statistical significance was accepted at $p<0.05$.

Results

Study population

Of the 20 patients receiving an OA, five withdrew from the study within the first month due to side effects. In the advanced group, one patient withdrew because of nausea and two because of appliance displacement. In the nonadvanced group, one withdrew because of nausea and one because of appliance displacement. Consequently, complete evaluation was performed in 15 patients (13 men, two women), eight with the advanced model and seven with the nonadvanced model. Patient characteristics at baseline did not differ between advanced and nonadvanced groups. The mean age was 55.6±11.8 years in the advanced group versus 53.0±12.7 years in the nonadvanced group. The mean BMI was 27.9±4.3 versus 28.4±4.2 kg/m^2. The five patients (four men, one woman) who withdrew from the study presented no significant difference in baseline values compared to the 15 patients who completed the study. The mean age was 54.6± 6.3 years in the group that withdrew versus 53.5±13.5 years the completing group. BMI was 26.8±2.8 versus 28.3±5.3 kg/m^2. Body weight presented no change during the study (86.3±2.3 kg at baseline versus 86.2±2.4 kg at follow-up).

Polysomnographic outcomes are summarized in Table 1. The mean AHI after treatment decreased significantly in both groups. It was only in the advanced group that we found significant changes in AHI in the supine position. After treatment, the advanced group also presented a significant decrease in the number of arousals per hour. However, no statistically significant differences were found

Table 1 Polysomnographic variables: a comparison of both study groups at baseline and posttreatment

	Advanced group (n=8)			Nonadvanced group (n=7)		
	Pretreat	Posttreat	p values	Pretreat	Posttreat	p values
AHI (h)	33.8 (14.7)	9.6 (12.1)	<0.01	24.0 (12.2)	11.7 (7.9)	0.05
Lateral AHI	10.2 (14.1)	7.0 (14.6)	N.S.	12.6 (24.4)	13.4 (21.4)	N.S.
Supine AHI	69.4 (24.4)	19.8 (26.7)	<0.01	23.6 (17.1)	33.9 (22.1)	N.S.
CT90	10.8 (14.7)	8.4 (12.1)	N.S.	8.5 (6.4)	7.7 (6.1)	N.S.
Sleep efficiency (%)	65.8 (15.2)	71.3 (12.0)	N.S.	63.6 (14.5)	56.7 (9.8)	N.S.
REM sleep (%)	16.8 (4.3)	15.5 (5.9)	N.S	10.7 (1.9)	10.1 (5.6)	N.S.
NREM sleep (%)	84.2 (5.9)	83.2 (4.3)	N.S.	89.2 (1.9)	88.4 (6.7)	N.S.
Arousal index (h)	33.8 (13.9)	16.0 (11.5)	<0.05	27.0 (15.4)	34.4 (23.8)	N.S.

Pretreat Before treatment, *Posttreat* after 3 months of treatment, *AH* apnea hypopnea index, *CT90* percentage of time spent with SaO_2 below of 90, *NREM* nonrapid eye movement sleep, *REM* rapid eye movement sleep

in the percentages of sleep efficiency, sleep stages, or CT90 in either group.

The snoring scale improved in the advanced group (15.4±1.9 versus 10.1±3.2; p<0.05) after treatment. No significant differences were found in the nonadvanced group (14.4±3.0 versus 14.6±1.7). The ESS improved in the advanced group (14.7±5.1 versus 5.1±1.9; p<0.05) after treatment. No significant differences were found in the nonadvanced group (16.3±2.5 versus 13.6±6.7). The FOSQ and SF36 parameters at baseline and posttreatment in each group with and without advance are summarized in Table 2. Total FOSQ score showed significant improvement in the advanced group with a large effect size (0.90). However, no significant differences with respect to basal values were found in the non-advanced group. At 3 months, neither study group showed significant difference in mean SF36 dimensions or in the effect sizes.

After treatment with OA, 15 patients (100%) presented partial or complete response. OA was effective in completely controlling OSA symptoms in six patients (40%). In the advanced group, four patients (57%) achieved complete response and three 43%) achieved partial response. In the nonadvanced group, two patients (25%) achieved complete response and six 75%) achieved partial response. No treatment failure occurred in either group. Compliance was 7.7±0.5 in the advanced group versus 6.5±1.4 h in the nonadvanced group. Of patients completing treatment, two in the advanced group presented excessive salivation without serious consequences.

Discussion

The results of our study demonstrate that symptoms and measured breathing disturbances in OSA patients were alleviated by oral appliance treatment (both with and without mandible advance). Although both appliances significantly reduce AHI, the group treated with the OA which advances the mandible presented a greater reduction, and more than half of the patients in this group achieved complete control of OSA symptoms as well as significant improvement in specific quality of life scores. The reduction in AHI observed in our study has also been reported in other studies[10, 28–32]. It is interesting to note that patients in the advanced group presented a decrease in the number of apneas in the supine position, suggesting that the device could be particularly effective in cases of position-dependent OSA [33]. Moreover, only this group presented a significant improvement in the snoring scale.

Some authors have reported better values for sleep architecture or for the arousal index with oral appliance treatment,

Table 2 Quality-of-life questionnaire results: a comparison of both study groups at baseline and posttreatment.

	Advanced group (n=8)				Nonadvanced group (n=7)			
	Pretreat	Posttreat	p values	Effect size	Pretreat	Posttreat	p values	Effect size
FOSQ (total score)	78.1 (22.6)	99.3 (14.4)	<0.05	0.90	83.7 (20.8)	82.3 (13.9)	NS	0.02
SF-36 dimension								
Physical functioning	70.7 (16.4)	74.1 (18.4)	NS	0.20	71.5 (20.7)	78.8 (19.1)	NS	0.30
Role physical	83.4 (30.2)	87.5 (30.6)	NS	0.13	81.2 (34.7)	87.5 (35.6)	NS	0.18
Role emotional	81.0 (37.7)	77.7 (46.6)	NS	0.09	80.0 (29.9)	87.5 (12.5)	NS	0.25
Social functioning	78.3 (13.6)	78.2 (12.4)	NS	0.00	81.3 (18.8)	79.4 (26.9)	NS	0.10
Mental health	60.1 (19.3)	59.4 (19.2)	NS	0.00	52.0 (15.7)	56.0 (18.0)	NS	0.25
Energy/vitality	49.3 (18.8)	50.7 (8.4)	NS	0.00	55.2 (12.2)	56.2 (19.2)	NS	0.08
Bodily pain	70.3 (38.7)	67.0 (21.3)	NS	0.08	65.3 (37.4)	65.5 (19.2)	NS	0.00
General health perception	60.7 (22.0)	61.0 (20.7)	NS	0.00	57.4 (6.8)	58.4 (10.5)	NS	0.14

Pretreat Before treatment, *Posttreat* after 3 most of treatment, *FOSQ* Functional Outcomes of Sleep Questionnaire, *SF-36* Medical Outcome Survey Short Form 36

suggesting a significant decrease in sleep fragmentation [28, 32, 34]. The advanced group in our study presented a decrease in the arousal index after treatment (though normal ranges are not attained), but no changes were found in sleep architecture. Furthermore, only this group presented a significant improvement in the Epworth somnolence scale after treatment, which may be associated to the decrease in the arousal index mentioned above.

The majority of our patients derived a significant subjective benefit from the OA. Complete response was observed in 40% of patients, which is within the range observed by other authors. Mehta et al. [35] reported complete response in 37.5% of patients. Also, Pitsis et al. [36] reported complete response ranging from 52% to 57% of patients. As reported in other studies [37], the most common side effects in our study from using an OA were nausea and device displacement. Although excessive salivation was reported by some patients (especially in the advanced group), this was not cause for abandonment [38]. The compliance rate was high in both groups, with no significant differences, and this was also in line with the findings of other authors [34]. Quality of life was assessed using two self-administered questionnaires. The first was the generic SF-36, and the second the more specific FOSQ specially developed for patients with sleep disorders leading to excessive sleepiness.

Despite the limitation of the small number of evaluated patients, the present study shows that OSA patients undergoing treatment with the advanced mandible OA improved under the FOSQ questionnaire but not in SF36 scores. This may be due to the fact that the FOSQ is OSA specific [25, 39]. Although other studies exist demonstrating the increased effectiveness of OAs with advance [19], we know of no other study that demonstrates the ameliorative effects of OA treatment on HRQoL.

In conclusion, OAs (both those that advance the mandible and those that do not) have proven to be an effective treatment for patients with OSA.

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