ORIGINAL ARTICLE

A Prospective Randomized Study Comparing Two Different Degrees of Mandibular Advancement with a Dental Appliance in Treatment of Severe Obstructive Sleep Apnea

Marie-Louise Walker-Engström, Ph.D.,[1] Ivar Ringqvist, M.D., Ph.D.,[1] Olle Vestling, D.D.S.,[2] Bo Wilhelmsson, M.D., Ph.D.,[3] and Åke Tegelberg, D.D.S., Ph.D.[1,2]

ABSTRACT

The objective of this study was to compare the effect of two different degrees of mandibular advancement (MA), 75% versus 50%, on somnographic variables after 6 months of dental appliance treatment in patients with severe obstructive sleep apnea (OSA). A further purpose was to compare the number of adverse events on the stomatognathic system and the effects of dental appliance treatment on the presence of daytime sleepiness.

Eighty-six males with severe OSA (apnea index $\geq$ 20) were randomly allocated to either 75% or 50% MA. Forty patients in the 75% MA group and 37 patients in the 50% MA group completed the 6-month follow-up.

The effectiveness of treatment in terms of normalization (apnea index < 5 and apnea/hypopnea index < 10) with 75% MA was 52%, which was significantly higher ($p = 0.04$) than the 31% achieved with 50% MA. The dental appliance had few adverse events on the stomatognathic system regardless of group, and the number of adverse events did not differ between the two groups. Finally, the mean value of Epworth Sleepiness Scale scores decreased significantly from 11.6 at baseline to 8.0 at follow-up ($p < 0.001$). No significant difference was observed between the two groups. The results indicate that a dental appliance could be an alternative treatment for some patients with severe OSA.

KEYWORDS: Randomized study, severe obstructive sleep apnea, somnography, dental appliance

Sleep and Breathing, volume 7, number 3, 2003. Address for correspondence and reprint requests: Marie-Louise Walker-Engström, Centre for Clinical Research, Central Hospital, 721 89 Västerås, Sweden. E-mail: marie-louise.engstrom@ltvastmanland.se. [1]Centre for Clinical Research, Central Hospital, Västerås, Uppsala University, and Departments of [2]Stomatognathic Physiology and [3]Otorhinolaryngology, Central Hospital, Västerås, Sweden. 1520-9512,p;2003,07,03,119,130,ftx,en;sbr00237x.

Obstructive sleep apnea (OSA) is a syndrome characterized by repeated collapse of the upper airway during sleep resulting in recurrent episodes of apnea. Patients with severe OSA have frequent apnea episodes per night, which are often associated with arousals leading to fragmented sleep, pronounced daytime sleepiness, and negative effects on cognitive performance.[1,2]

Continuous positive airway pressure (CPAP) therapy is the recommended initial treatment for patients with severe OSA.[3] The method is therapeutically effective[4–6] but the equipment is relatively bulky, noisy, and demands electricity. Some patients (15% to 50%) complain of disturbing side effects, including feelings of inconvenience and discomfort, poor mask fit, claustrophobia, and nasal problems.[4,7,8] Moreover, 20% of the patients with severe OSA refuse to accept, a priori, CPAP treatment.[9] With follow-ups of 1 to 2 years of CPAP treatment, failure occurred in 25% to 32% of the patients.[10–12]

Treatment with a mandibular advancement (MA) appliance is useful for patients with mild to moderate OSA.[13–15] Two crossover studies comparing the efficacy of CPAP and dental appliance in the treatment of patients with mild to moderate OSA showed substantial success in the apnea-hypopnea index (AHI) in most of the cases treated with the dental appliances. The results also showed that the dental appliance therapy was less effective than CPAP.[16,17] On the other hand, the dental appliance treatment was associated with fewer side effects and greater patient satisfaction than CPAP therapy.

The American Sleep Disorders Association recommends dental appliance treatment only for patients with severe OSA who are intolerant of, or refuse treatment with, CPAP.[3] Nevertheless, it has been shown in several studies that patients with severe OSA can also benefit from initial dental appliance therapy.[18–21] These studies included 10 to 35 (median, 17) patients with severe OSA. The results of these studies showed that 24% to 65% of the patients were normalized, that is, they had an AHI < 10 at follow-up (ranging from 2 weeks to 1 year). Because of few published studies and insufficient numbers of patients, the effect of dental appliance treatment on somnographic variables in severe OSA is not yet established.

Different fixed degrees of MA (50% or 75% of the patient's maximum protrusive capacity) have been used in previous studies.[14,20] Some studies have used adjustable appliances to ascertain patient comfort.[21–23] The difference in treatment effects that results from using more or less MA has not been established in clinical trials. However, in one study the effect of different degrees of advancement was assessed in patients with moderate OSA.[24] The advancement of the mandible produced a dose-dependent closing pressure reduction of the pharynx and a concomitant reduction of nocturnal desaturations. Patients with severe OSA have been shown to have more extended obstruction from the soft palate to the base of the tongue than mild to moderate OSA patients[25] and might therefore benefit from a more pronounced advancement.

A prospective randomized study was designed to test the hypothesis that treatment with a more pronounced advancement with a dental appliance would be more effective than a shorter advancement in patients with severe OSA. The primary aim was to compare the effect of two different degrees of MA (75% versus 50% of the maximum mandibular protrusive capacity) on somnographic variables after 6 months of dental appliance treatment in patients with severe OSA. Secondary aims were to compare the number of adverse events on the stomatognathic system and the effects of dental appliance treatment on the presence of daytime sleepiness.

MATERIALS AND METHODS

Definitions

Apnea was defined as cessation of respiratory airflow for 10 seconds or longer as measured by a thermistor. Hypopnea occurred when there was a 50% reduction of the airflow signal recorded by a thermistor combined with a decrease in hemoglobin oxygen saturation of at least 4%. The apnea index

(AI) was defined as the average number of apneas per hour of sleep and the AHI was defined as the average number of apneas and hypopneas per hour of sleep. The oxygen desaturation index (ODI) was defined as an average number of episodes of oxygen desaturation of at least 4% per hour of sleep. Snoring was recorded with a sound level meter, which was placed on a table close to the patient's head. The snoring index (SI) was defined as the registered duration of snoring per hour of sleep.

The diagnosis of OSA was defined as an AI ≥ 5 or an AHI ≥ 10 in accordance with the guidelines established by the Swedish Medical Research Council in 1994.[26] The success rate was defined as the percentage of patients with a decrease in the AI or the AHI of at least 50%. Normalization was defined as an AI < 5 and an AHI < 10.

Selection of Patients

All patients in the catchment area of 260,000 people (the county of Västmanland) with suspected OSA who were referred to the sleep laboratory between 1998 and 2000 for a somnographic registration at the Central Hospital, Västerås, and fulfilled the inclusion criteria were eligible. Inclusion criteria were: confirmed severe OSA (AI ≥ 20); age 20 to 65 years; no mental illness; no drug abuse; no significant nasal obstruction; sufficient number of teeth to anchor an appliance; no pronounced dental malocclusion; and no severe cardiovascular, neurological, or respiratory disease.

Eighty-six male patients consenting to treatment and who met the inclusion criteria were randomly assigned to treatment with an MA of either 75% or 50%. Four patients outside the catchment area were included in the study population.

Trial Design

Before and after 6 months of treatment, all patients underwent somnographic registration and an ear-nose-throat physician performed a clinical examination of the nasal and pharyngeal structures. In addition, before treatment and at the 6-month follow-up, a dentist examined the stomatognathic system, including measurement of mandibular mobility, palpation of the temporomandibular joints (TMJs) and masticatory muscles, and pain on mobility. To measure the general level of daytime sleepiness, patients were given the Epworth Sleepiness Scale (ESS) questionnaire[27] before and at the 6-month follow-up. At follow-up, patients were asked to evaluate the effect of the treatment and what symptoms they experienced from the stomatognathic system.

One patient in each group reversed his decision to participate and withdrew after randomization but before treatment. Consequently, 42 patients in the 75% MA group and 42 patients in the 50% MA group were eligible for treatment. Two patients withdrew before the 6-month follow-up in the 75% MA group; one patient could not tolerate the dental appliance, and one patient could not achieve an acceptable sleep registration despite several attempts. In the 50% MA group, five patients withdrew before the 6-month follow-up; two patients could not tolerate the dental appliance; one patient moved from the catchment area; one patient chose treatment of uvulopalatopharyngoplasty (UPPP) instead; one patient acquired heart problems and underwent a percutaneous transluminal coronary angioplasty. Consequently, the 6-month follow-up was completed by 40 patients in the 75% MA group and by 37 patients in the 50% MA group.

The results are presented according to the intention to treat (ITT) principle, that is, the patients were analyzed in the groups they were randomized into, regardless of whether they complied with the treatment they were given.

Extended Follow-Up after the Randomized Study
All 24 patients in the 50% MA group who were not normalized at the 6-month follow-up were offered a reconstruction of the dental appliance to an MA of 75%. Nineteen of the 24 patients accepted this reconstruction and were followed-up with somnography after a further 6-month treatment period.

The study protocol and informed consent form were approved by the ethics committee of Uppsala University, Uppsala, Sweden.

Dental Appliance Treatment

One dentist performed the clinical examination of the stomatognathic system on all patients at baseline. The patients fulfilling the inclusion criteria were referred to a second dentist who made the dental impressions for the appliances and conducted the randomization of the patients. Randomization (in blocks of four patients) was performed using a closed-envelope system where the envelopes were drawn in sequential order. The first dentist who performed all the baseline examinations also performed all clinical examinations and asked questions about compliance in using the dental appliance at the 6-month follow-up. This dentist was blinded to the degree of MA used.

One dental technician was responsible for the manufacturing of all the appliances. The one-piece, individually designed dental appliance was made of heat-cured acrylic polymer and advanced the mandible by 75% or 50% of the patient's maximum protrusive capacity as measured from a position of intercuspidation (Fig. 1). The construction of the appliance meant that the vertical distance between the upper and lower teeth was 2 mm. Labial and lingual to the mandibular front teeth, bars linked the acrylic parts of the construction on each side in the premolar-molar regions. Adams clasps, mostly retained on the first molars in each jaw, were used as an extra attachment to ensure individual retention. Eichner's index was used as an indicator of occlusal stability between the maxilla and the mandible.[28] Based on this index, 90% of the patients had maximal dental support in all four possible support zones. Three patients had dental support in three zones and five patients had support in two zones.

No change in the degree of MA was introduced during the treatment period in either group, except for four patients in the 75% MA group who did not tolerate this advancement degree and hence were given the shorter advancement of 50%.

Somnography

The sleep studies, performed in the patient's home with a portable unit, were performed before and after 6 months of treatment. The following five variables were recorded simultaneously: hemoglo-

Figure 1 The dental appliance used in this study.

bin oxygen saturation using a pulse oximetry device with a finger probe; flow through the nose and mouth using a thermistor; respiratory movements, by impedance measurements between one electrode placed on each side of the chest; body position with a sensor on the chest; and snoring sounds using a sound level meter. These data were stored in a digital recording unit (SAMBA, Electronico AB, Västerås, Sweden) and transferred to a personal computer for subsequent data analysis. One technician, blinded regarding treatment group, performed all the sleep analyses. Sleep recordings lasting less than 4 hours were not accepted: in such cases, a second recording was made.

Questionnaire

EPWORTH SLEEPINESS SCALE

The ESS is a questionnaire used to assess the general level of daytime sleepiness in patients with OSA.[27] The questionnaire has been validated[27] and has high reliability and internal consistency.[29] Each question was rated on a four-point scale ("never doze" to "high chance of dozing") about the chances patients might doze off in eight specific situations: sitting and reading; watching TV; sitting inactive in a public place (e.g., a theater or a meeting); as a passenger in a car for 1 hour without a break; lying down to rest in the afternoon when circumstances permit; sitting and talking to someone; sitting quietly after lunch without alcohol; and in a car while stopped for a few minutes in traffic. The total ESS score ranges from 0 to 24, with lower scores indicating mild daytime sleepiness and higher scores excessive daytime sleepiness.

SUBJECTIVE EVALUATION OF THE TREATMENT EFFECT

At the 6-month follow-up, the patients answered two questions about changes in daytime sleepiness and problems associated with apnea and snoring after treatment. Each question was rated on a seven-point scale with 1 equal to a large decrease in the degree of symptom severity and 7 equal to a large increase in the degree of symptom severity.

Sample Size and Statistical Analysis

Sample size was calculated according to the hypothesis that patients with severe OSA could yield a 25% higher normalization rate with a 75% MA compared with a 50% MA. To detect a significant difference ($\alpha = 0.05$, $\beta = 0.20$), 40 patients in each group were required.

Numerical results are expressed as means and 95% confidence intervals (CI). Differences in somnographic variables and body mass index (BMI) between the two groups at baseline and over time were tested using Student's *t*-test. Because of a skewed distribution, the Mann-Whitney U test, the nonparametric counterpart to the *t*-test, was performed to test differences between the two groups in age and the somnographic variables at the 6-month follow-up.

A nonparametric chi-square test of significance was conducted to compare differences in smoking, success rates, and normalization rates between the two groups.

Pearson's correlation coefficient was used for the analysis between ESS scores at baseline and the AHI at baseline, as well as for the changes in ESS scores and changes in the AHI.

RESULTS

The mean value (95% CI) for the advancement of the mandible was 7.2 mm (6.7 to 7.6) in the 75% MA group and 5.0 mm (4.8 to 5.3) in the 50% MA group.

The patients used their appliance, on average, 6.4 nights/week (median, 7.0; range, 3 to 7). No difference between the two groups was noted.

During the study, the acrylic parts of two dental appliances were repaired while there was no damage to the linking bars. All together, 15 Adams

clasps, the weakest component of the construction, were broken in eight dental appliances.

Before Intervention

The mean age (95% CI) for the 75% MA group was 50.4 years (47.7 to 53.1) and 54.3 years (52.2 to 56.4) for the 50% MA group. BMI did not differ between the groups at baseline nor was there a significant change during the course of the study in either group (Table 1). Obesity, that is, a BMI $\geq$ 30, was observed in 53% of the patients. The proportion of regular smokers was 23% (9/40) in the 75% MA group and 8% (3/37) in the 50% MA group. The difference between the two groups was not statistically significant.

Treatment Effects at the 6-Month Follow-Up

In their evaluation of using the appliance during the night, 90% of the patients who completed the 6-month follow-up reported that they were "satisfied" or "very satisfied"; 9% reported that they were neither "satisfied" nor "dissatisfied"; and one patient reported that he was "dissatisfied" with the appliance. There was no difference between the two groups regarding their satisfaction using the device.

SOMNOGRAPHY

The somnographic variables (AI, AHI, ODI, and SI) decreased significantly between baseline and the 6-month follow-up in both groups (Table 1). No significant difference between the two groups was observed for any of the somnographic variables.

The individual AHI values in the two groups before intervention and at the 6-month follow-up are shown in Figures 2 and 3.

Normalization According to the criteria for normalization (AI < 5 and AHI < 10) the effectiveness of treatment (i.e., including all randomized treated patients and counting all withdrawals as failures) was 52% (22/42) with 75% advancement, which was significantly higher (p = 0.04) than the 31% (13/42) achieved with 50% advancement. The efficacy

Table 1 Comparison between Baseline Values and Values After 6 Months of Treatment in the 50% and 75% Mandibular Advancement Groups

	50% MA Group Mean value (± 95% CI)		Difference between Baseline and 6 Months p-value	75% MA Group Mean Value (± 95% CI)		Difference between Baseline and 6 Months p-value	Difference between the Two Groups at 6 Months p-value
	Before n = 42	6 Months n = 37		Before n = 42	6 Months n = 40		
BMI	30.5 (± 1.4)	30.0 (± 1.5)	ns	30.2 (± 1.2)	29.9 (± 0.7)	ns	ns
AI	35.0 (±3.5)	11.3 (±4.8)	< 0.001	37.5 (± 4.4)	9.4 (± 5.0)	< 0.001	ns
AHI	47.0 (± 5.1)	17.4 (± 5.7)	< 0.001	50.4 (± 4.7)	15.6 (± 6.2)	< 0.001	ns
ODI	44.6 (± 5.9)	18.0 (± 6.0)	< 0.001	49.7 (± 5.6)	19.1 (± 7.0)	< 0.001	ns
SI	0.83 (± 0.1)	0.66 (± 0.1)	< 0.01	0.86 (± 0.1)	0.57 (± 0.1)	< 0.001	ns
ESS	11.7 (± 3.1)	8.6 (± 2.8)	< 0.001	11.5 (± 3.1)	7.5 (± 2.6)	< 0.001	ns
Mouth opening capacity	52.0 (± 2.2)	53.1 (± 2.2)	ns	49.9 (± 1.9)	50.3 (± 2.0)	ns	ns
Protrusion capacity	9.8 (± 0.6)	9.7 (± 0.6)	ns	9.6 (± 0.6)	10.0 (± 0.6)	ns	ns

MA, mandibular advancement; CI, confidence interval; BMI, body mass index; AI, apnea index; AHI, apnea/hypopnea index; ODI, oxygen saturation index; SI, snoring index; ESS, Epworth sleepiness scale; ns, not significant.

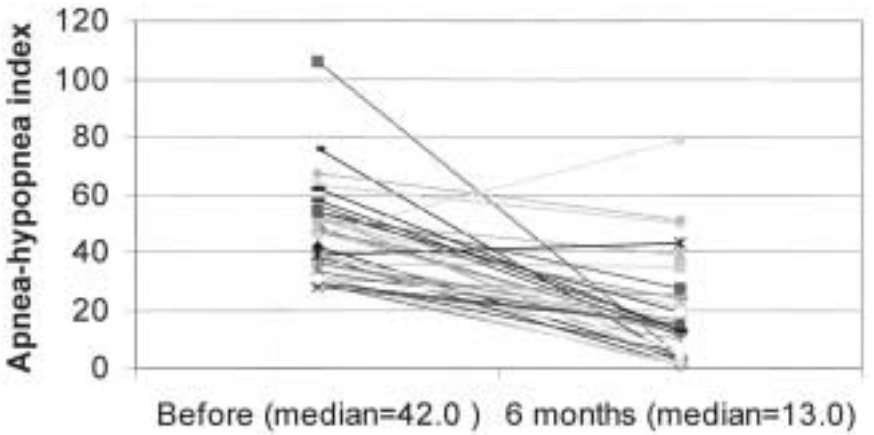

Figure 2 Individual AHI values (n = 37) in the 50% MA group before intervention and at the 6-month follow-up.

of treatment (i.e., including only the patients who attained the 6-month follow-up) was 55% (22/40) with 75% advancement and 35% (13/37) with 50% advancement. The difference did not reach statistical significance (p = 0.07).

The patients who were normalized had a significantly lower (p = 0.02) mean value for BMI (28.9 ± 1.2) than those patients who were not normalized (31.4 ± 1.4). However 49% (17/35) of the patients who were normalized had a BMI ≥ 30.

Success Rate The success rates for the AI was 88% and 78%, and for the AHI it was 83% and 76%, for the 75% and 50% MA groups, respectively. The differences between the groups were not significant.

Per Protocol Principle Thirty-seven of the patients in the 50% MA group and 36 in the 75% MA group continued with the original treatment. The analyses performed according to the per protocol (PP) principle yielded results comparable to the ITT principle analyses.

Extended Follow-Up after the Randomized Study Of the 24 patients who were not normalized in the 50% MA group, 19 patients accepted a reconstruction of the dental appliance with a more pronounced

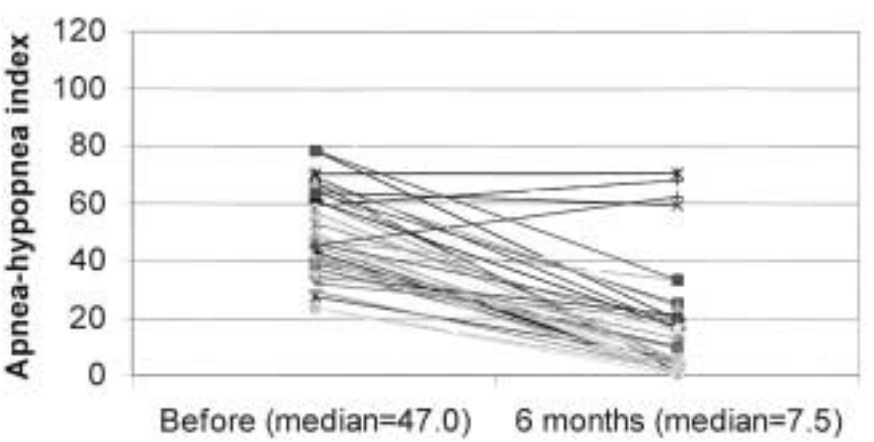

Figure 3 Individual AHI values (n = 40) in the 75% MA group before intervention and at the 6-month follow-up.

MA of 75%. These patients were followed-up for an additional 6-month period. After the extended period, 8 of these patients were normalized and 4 showed improvement on both the AI and the AHI.

EFFECTS AND ADVERSE EVENTS ON THE STOMATOGNATHIC SYSTEM

Mandibular mobility, such as mouth-opening capacity and protrusion, did not differ between the two groups at the 6-month follow-up (Table 1). Further, no changes in mandibular mobility were noted throughout the study.

Thirty-four patients in each group had not observed any changes in tooth contacts at intercuspidation after treatment; two patients in the 50% MA group and six patients in the 75% MA group did, however, note minor changes. One patient in the 50% MA group was not able to occlude his teeth in the same way as before treatment.

Few patients reported symptoms from the stomatognathic system at the 6-month follow-up; however, some patients reported even these symptoms before treatment (Table 2). During the study, there were five patients in the 75% MA group who reported complaints of pain from the TMJ after an average time of 3 months (range, 1 to 5 months). For one of these five patients the problem disappeared, while in the other four the dental appliance was reconstructed with a reduced MA to 50%. Suffering from headache at least once a week was the most commonly reported symptom before intervention. This symptom was significantly reduced ($p < 0.05$) after 6 months in the 75% MA group but not in the 50% MA group. There was no difference in the frequency of headache between the two groups at baseline or at the 6-month follow-up.

DAYTIME SLEEPINESS

ESS scores decreased significantly in both groups between baseline and the 6-month follow-up. No significant difference was observed between the two groups at baseline or at the 6-month follow-up (Table 1). No difference in ESS mean scores was noted between normalized and nonnormalized patients. No correlation was found between ESS scores at baseline and the AHI at baseline. There was, however, a weak correlation ($r = 0.25$; $p < 0.05$) between the changes in ESS scores and changes in the AHI. Only 6% percent of the changes in ESS could be explained by the changes in the AHI.

SUBJECTIVE EVALUATION OF THE TREATMENT EFFECT

In the 75% MA group, a large decrease in daytime sleepiness was reported by 54% of the patients, less influence was reported by 33% of the patients, and 13% reported no difference.

Table 2 The Number of Patients with Symptoms from the Stomatographic System

	50% MA Group n = 37		75% MA Group n = 40	
	Before Treatment	After 6 Months of Treatment	Before Treatment	After 6 Months of Treatment
Tiredness/ stiffness on jaw function	0	3	2	3
TMJ pain	2	2	1	1
TMJ sound	6	4	6	4
TMJ locking	1	2	0	1
Headache, once a week or more often	16	10	19	9

For the patients in the 50% MA group, a large decrease in daytime sleepiness was reported by 43% of the patients, less influence was reported by 43% of the patients, and 14% reported no difference.

Problems with episodes of apnea and snoring were found to decrease substantially in 77% of the patients in the 75% MA group, had decreased a little in 18% of the patients, and no difference was reported by 5%. In the 50% MA group, these problems of episodes of apnea and snoring decreased substantially in 62% of the patients and decreased a little in 29% of the patients. No difference was reported in 9%.

There was no difference between the groups in decreased sleepiness or in problems associated with episodes of apnea and snoring.

DISCUSSION

Although the American Sleep Disorders Association[3] has asserted that dental appliances can be considered when patients fail with CPAP treatment in severe OSA, there is only scanty evidence available indicating that dental appliances are effective. One reason for this lack of evidence is that there are few patients with severe OSA in studies reporting treatment with a dental appliance. In four studies that included between 10 and 35 patients, a normalization rate between 24% and 65% was achieved.[18–21] However, all these studies were nonrandomized, uncontrolled clinical trials. In our randomized study we found that dental appliance could be an alternative for patients with severe OSA. A mean normalization rate of 45% and a compliance of 92% was observed after 6 months of treatment. Moreover, treatment with a more pronounced advancement yielded a significantly higher normalization rate (52%) than a shorter advancement (31%).

A dental appliance designed as a monoblock with fixed advancement degree is one of the available appliances on the market. Most dentists use this appliance because it is cheaper and easier to manufacture compared with adjustable appliances. Although some authors are of the opinion that adjustability and titration are essential for optimal patient management,[30] no clinical randomized, controlled study has confirmed the long-term superiority of adjustable dental appliances over nonadjustable appliances. Moreover, a difference in treatment effects of using more (~75%) or less (~50%) MA is not established. We hypothesized that patients with severe OSA might produce a 25% higher normalization rate with a 75% MA compared with 50% MA, a difference that would be statistically significant with 80 patients, which therefore became the target sample size of this study. The 75% MA yielded only a 21% ($p = 0.044$) higher normalization rate measured as effectiveness and 20% ($p = 0.076$) measured as efficacy compared with the 50% advancement. In our extended follow-up a further MA to 75% was undertaken in 19 of the patients in the 50% MA group who were not normalized at the 6-month follow-up. That 8 of these patients were normalized after an additional 6 months, and that 4 patients showed improvement in the AI and the AHI, are indications that a 75% advancement might have a better efficacy than a 50% advancement. In one of our earlier studies,[14] patients with mild to moderate OSA who were treated with a 50% MA had a significantly higher normalization rate, 78% compared with 35% in patients with severe OSA with the same MA in this study. The dental appliance construction was the same in both studies. These results support the contention that patients with severe OSA might improve with more pronounced advancement of the mandible.

There is some evidence indicating that moderate to severe OSA is closely associated with obesity.[31] Millman reported that nonresponders after dental appliance treatment (AHI $\geq$ 10) had a higher BMI than responders, a finding consistent with our results.[23] However, even obese patients with a BMI $\geq$ 30 in our study had a significant reduction of apnea episodes.

Laboratory-based polysomnography is the recommended method to diagnose OSA, but the method requires a great deal of time and effort and is very expensive. Today several good and useful por-

table systems exist, though such systems have to be validated against polysomnography. Our portable recording device is comparable (using the same type of signals and transducers) to Edentrace 2700, which was validated with simultaneously recorded polysomnography in 67 patients.[32] Using a respiratory disturbance index (RDI) of > 5 to define abnormality, the sensitivity and specificity for OSA diagnosis were 95% and 96%, respectively. In another study using an Edentrace 4700 with a RDI of > 10 in defining abnormality, the sensitivity was 95% and specificity 100%.[33]

At the 6-month follow-up in our study, the patients were highly satisfied with the effects of the dental appliance treatment with regard to daytime sleepiness, episodes of apnea, and snoring. Daytime sleepiness, as measured with the ESS questionnaire, showed a significant decrease in the ESS score between baseline and the 6-month follow-up in both groups. The mean ESS score of 8.0 after treatment in our study is comparable with the ESS score of 7.6 in a study including 104 normal controls.[29] Moreover, the mean ESS score in all patients at the 6-month follow-up was similar to the reported level in two recent reports after CPAP treatment.[34,35] These results suggest that the dental appliance had a clinically favorable effect on daytime sleepiness in patients with severe OSA.

In earlier dental appliance studies there has been a wide variation in the degree of MA used.[13,14,20] To our knowledge, however, there is only one study examining the effects of different degrees of MA in each patient.[24] Each 2 mm MA (20%, 40%, 60% of the maximum protrusive capacity) gave a 20% improvement in the number of nocturnal desaturations. One drawback with dental appliance treatment with a 75% MA is the relatively high frequency of symptoms from the stomatognathic system.[36,37] In the present study, however, we found only few adverse events from the stomatognathic system after 6 months and there was no difference in reported symptoms between the 75% and 50% MAs. The discrepancy in the frequency of symptoms between our study and others could be related to differences in the construction of the dental appliances. In a randomized crossover trial using two different oral appliances, Block and associates showed that one of these appliances was favored by the patients because it caused fewer side effects.[38]

Another drawback concerns dental and skeletal changes. In a study with 75% MA with a 2-year follow-up of 30 patients, Bondemark and Lindman found small, but statistically significant changes in mandibular position (0.4 mm), in overbite (0.1 mm), and in overjet (0.4 mm).[39] There is only one published study on dental and skeletal side effects when using a 75% MA for more than 2 years.[40] In that study significant skeletal and dental changes were found after 30 months and the most prominent change was found in overbite (1.8 mm). In one study with less advancement of the mandible (i.e., 50%), the changes were clinically insignificant even after 4 years of treatment.[41] Because treatment with the dental appliance is a lifetime process, long-term follow-ups are notably important to determine the treatment effects not only by somnography but also in evaluating symptoms from the stomatognathic system and dental and skeletal side effects.

In conclusion, our findings show that the effectiveness of treatment in terms of normalization rate was significantly higher with a more pronounced advancement (75%) compared with a lesser advancement (50%). A mean normalization rate of 45%, a success rate in the AHI of 79%, few side effects, good patient satisfaction, and a compliance of 92% after 6 months of treatment are results indicating that dental appliance treatment could be an alternative to CPAP for some patients with severe OSA.

ACKNOWLEDGMENTS

This trial was supported by a grant from the county of Västmanland. The authors wish to thank Jan Ulfberg, M.D., Ph.D., Tore Bremer, M.D., Kristina Sundgren, assistants Yvonne Pettersson, Gunilla Andersson, Carina Eriksson, and Laila Olsson for valuable help with the patients in this study.

REFERENCES

1. Cheshire K, Engleman H, Deary I, Shapiro C, Douglas N. Factors impairing daytime performance in patients with sleep apnea/hypopnea syndrome. Arch Intern Med 1992; 152:538–541
2. Yamadera W. Improvement in excessive daytime sleepiness after surgical treatment for obstructive sleep apnea syndrome. Psychiatry Clin Neurosurg 1995;49:213–221
3. American Sleep Disorders Association. Practice parameters for the treatment of snoring and obstructive sleep apnea with oral appliances. An American Sleep Disorders Association report. Sleep 1995,18:511–513
4. Waldhorn R, Herrick T, Nguyen M, et al. Long-term compliance with nasal continuous positive airway pressure therapy of obstructive sleep apnea. Chest 1990;97:33–38
5. Wright J, Johns R, Watt I, Melville A, Sheldon T. Health effects of obstructive sleep apnea and the effectiveness of continuous positive airways pressure: a systematic review of the research evidence. BMJ 1997;314:851–860
6. Engleman H, Asgari-Jirhandeh N, McLeod A, et al. Self-reported use of CPAP and benefits of CPAP therapy. Chest 1996;109:1470–1476
7. Hoffstein V, Viner S, Mateika S, Conway J. Treatment of obstructive sleep apnea with nasal continuous positive airway pressure. Am Rev Respir Dis 1992;145:841–845
8. Rauscher H, Formanek D, Popp W, Zwick H. Self-reported vs measured compliance with nasal CPAP for obstructive sleep apnea. Chest 1993;103:1675–1680
9. Rauscher H, Popp W, Wanke T, Zwick H. Acceptance of CPAP therapy for sleep apnea. Chest 1991;100:1019–1023
10. Grunstein R. Nasal continuous positive airway pressure treatment for obstructive sleep apnea. Thorax 1995;50:1106–1113
11. Meurice J-C, Dore P, Paquereau J, et al. Predictive factors of long-term compliance with nasal continuous positive airway pressure treatment in sleep apnea syndrome. Chest 1994;105:429–433
12. Lojander J, Brander PE, Ammala K. Nasopharyngeal symptoms and nasal continuous positive air pressure therapy in obstructive sleep apnea syndrome. Acta Otolaryngol 1999;119:497–502
13. Marklund M, Franklin K, Sahlin C, Lundgren R. The effect of a mandibular advancement device on apneas and sleep in patients with obstructive sleep apnea. Chest 1998; 113:707–713
14. Wilhelmsson B, Tegelberg Å, Walker-Engström M, et al. A prospective randomized study of a dental appliance compared with uvulopalatopharyngoplasty in the treatment of obstructive sleep apnea. Acta Otolaryngol 1999;119:503–509
15. Lindman R, Bondemark L. A review of oral devices in the treatment of habitual snoring and obstructive sleep apnea. Swed Dent J 2001;25:39–51
16. Fergusson K, Ono T, Lowe A, Keenan S, Fleetham J. A randomized crossover study of an oral appliance vs nasal-continuous positive airway pressure in the treatment of mild-moderate obstructive sleep apnea. Chest 1996;109: 1269–1275
17. Clark G, Blumenfeld I, Yoffe N, Peled E, Lavie P. A crossover study comparing the efficacy of continuous positive airway pressure with anterior mandibular positioning devices on patients with obstructive sleep apnea. Chest 1996; 109:1477–1483
18. Cohen R. Obstructive sleep apnea: oral appliance therapy and severity of condition. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;85:388–392
19. George P. Is adjustability advantageous in mandibular advancement appliances in the treatment of sleep-disordered breathing? Sleep Breath 2001;5:139–147
20. O'Sullivan R, Hillman D, Mateljan R, Pantin C, Finucane K. Mandibular advancement splint: an appliance to treat snoring and obstructive sleep apnea. Am J Respir Crit Care Med 1995;151:194–198
21. Pancer J, Al-Faifi S, Al-Faifi M, Hoffstein V. Evaluation of variable mandibular advancement appliances for treatment of snoring and sleep apnea. Chest 1999;116:1511–1518
22. Fergusson K, Ono T, Lowe A, Al-Majed S, Love L, Fleetham J. A short-term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnea. Thorax 1997;52:362–368
23. Millman R, Rosenberg C, Carlisle C, et al. The efficacy of oral appliances in the treatment of persistent sleep apnea after uvulopalatopharyngoplasty. Chest 1998;113:992–996
24. Kato J, Isono S, Tanaka A, et al. Dose-dependent effects of mandibular advancement on pharyngeal mechanics and nocturnal oxygenation in patients with sleep-disordered breathing. Chest 2000;117:1065–1072
25. Hillarp B, Nylander G, Rosén I, et al. Videoradiography of patients with habitual snoring and/or sleep apnea. Acta Radiol 1996;37:307–314
26. Swedish Medical Research Council. Diagnosis and management of obstructive sleep apnea syndrome. Paper presented at: A State of the Art Conference; 1994; Stockholm, Sweden
27. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 1991;14:540–545
28. Eichner K. Über eine Gruppeneinteilung des Lückengebisses für die Prothetik. Dtsch Zahnaerztl Z 1955;18: 1831–1834
29. Johns M. Reliability and factor analysis of the Epworth Sleepiness Scale. Sleep 1992;15:376–381
30. Schmidt-Nowara W. Recent developments in oral appliance therapy of sleep-disordered breathing. Sleep Breath 1999;3:103–106
31. Wittels E, Thompson S. Obstructive sleep apnea and obesity. Otolaryngol Clin North Am 1990;23:751–760
32. Emsellem H, Corson W, Rappaport B, Hackett S, Smith L, Hausfeld J. Verification of sleep apnea using a portable sleep apnea screening device. South Med J 1990;83:748–752
33. Redline S, Tosteson T, Boucher MA, Millman R. Measurement of sleep-related breathing disturbances in epidemio-

logical studies. Assessment of the validity and reproducibility of a portable monitoring device. Chest 1991;100:1281–1286
34. Kiely J, McNicholas W. Bed partners' assessment of nasal continuous positive airway pressure therapy in obstructive sleep apnea. Chest 1997;111:1261–1265
35. Engleman H, Kingshott R, Wraith P, Mackay T, Deary J, Douglas N. Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med 1999;159:461–467
36. Clark G, Sohn J, Hong C. Treating obstructive sleep apnea and snoring: assessment of an anterior mandibular positioning device. JAMA 2000;131:765–771
37. Pantin C, Hillman D, Tennant M. Dental side effects of an oral device to treat snoring and obstructive sleep apnea. Sleep 1999;22:237–240
38. Block K, Iseli A, Zhang J, et al. A randomized, controlled crossover trial of two oral appliances for sleep apnea treatment. Am J Respir Crit Care Med 2000;162:246–251
39. Bondemark L, Lindman R. Craniomandibular status and function in patients with habitual snoring and obstructive sleep apnea after nocturnal treatment with a mandibular advancement splint: a 2-year follow-up. Eur J Orthod 2000;22:53–60
40. Robertson CJ. Dental and skeletal changes associated with long-term mandibular advancement. Sleep 2001;24:531–537
41. Ringqvist M, Walker-Engström M, Tegelberg Å, Ringqvist I. Dental and skeletal changes after 4-years of obstructive sleep apnea treatment with a mandibular advancement device: a prospective randomized study. Am J Orthod Dentofacial Orthop 2003;124:53–60