

Comparison of a Custom-made and a Thermoplastic Oral Appliance for the Treatment of Mild Sleep Apnea

Olivier M. Vanderveken^{1,2}, Annick Devolder², Marie Marklund³, An N. Boudewyns¹, Marc J. Braem⁴, Walter Okkerse⁴, Johan A. Verbraecken², Karl A. Franklin⁵, Wilfried A. De Backer², and Paul H. Van de Heyning²

¹Department of Otorhinolaryngology, Head and Neck Surgery, and ²Department of Pulmonary Medicine, University Hospital Antwerp, Edegem, Belgium; ³Department of Orthodontics, Umeå University, Umeå, Sweden; ⁴Department of Dentistry, University Hospital Antwerp, Edegem, Belgium; and ⁵Department of Pulmonary Medicine, Umeå University, Umeå, Sweden

Rationale: The efficacy of immediate adaptation of mandibular advancement devices made of thermoplastic material as a treatment option for sleep-disordered breathing (SDB) has been demonstrated in clinical studies. To date, there have been no studies comparing the efficacy of such prefabricated devices with custom-made devices.

Objectives: Our purpose was to compare the efficacy of both types of devices in patients with SDB.

Methods: A randomized controlled cross-over trial, comprising 4 months of treatment with a thermoplastic and a custom-made device, with a 1-month washout interval.

Measurements and Main Results: A total of 35 patients (29 males; age, 49 ± 9 yr; apnea-hypopnea index [AHI], 13 ± 11 events/h; body mass index, 28 ± 4 kg/m²) completed the protocol. AHI was only reduced with the custom-made device ($P = 0.005$). In addition, this device reduced snoring to a greater extent than the thermoplastic device. The success rate was higher with the custom-made device (60 vs. 31%; $P = 0.02$). One-third of the patients demonstrated compliance failure with the thermoplastic device, mainly because of insufficient overnight retention. Total failure rate with the thermoplastic device was 69%, whereas the majority (63%) of these were successfully treated with the custom-made device. At the end of the study, 82% of the patients preferred the custom-made device, and 9% had no preference ($P < 0.0001$).

Conclusions: In this study, a custom-made device turned out to be more effective than a thermoplastic device in the treatment of SDB. Our results suggest that the thermoplastic device cannot be recommended as a therapeutic option nor can it be used as a screening tool to find good candidates for mandibular advancement therapy.

Keywords: excessive somnolence; oral appliances; polysomnography; sleep apnea; snoring

Sleep-disordered breathing (SDB) spans a continuum from snoring over upper airway resistance syndrome to obstructive sleep apnea-hypopnea syndrome (OSAHS). OSAHS, characterized by repetitive pharyngeal collapse during sleep, can be diagnosed in 4% of middle-aged men and 2% of women (1).

The standard treatment for moderate to severe OSAHS is nasal continuous positive airway pressure (CPAP) (2, 3). There is no consensus concerning the indications for surgical interventions to treat mild obstructive SDB (4). Mandibular advancement devices (MADs), which are worn intraorally at night to advance the lower jaw, have emerged as a conservative, noninvasive treatment for snoring and sleep apnea (5–7). There is evidence that MADs can reduce the collapsibility of the upper airway during sleep in a significant way (8–10). The

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Mandibular advancement devices (MADs) have emerged as a conservative, noninvasive treatment for sleep-disordered breathing. To date, there is only limited information available comparing the efficacy of thermoplastic with custom-made MADs.

What This Study Adds to the Field

This randomized controlled cross-over study shows that a custom-made MAD is more effective in the treatment of sleep-disordered breathing than is a thermoplastic MAD.

widening of the pharyngeal cross-sectional area as induced by MADs can occur at the level of velo-, oro-, and/or hypopharynx (10–13).

MAD therapy may be a first-line treatment in snorers with or without excessive daytime sleepiness (EDS) and in patients with mild to moderate OSAHS (14–18). Treatment with MADs may also be considered in subjects with OSAHS who do not tolerate or comply with CPAP or as a temporary alternative (7, 18, 19). Finally, MAD treatment should be considered as a rescue treatment after upper airway surgery failure (20, 21).

Traditionally, MADs have been individually fabricated by a dental technician from plaster casts of patients' teeth and construction bites obtained by the dentist. Potential disadvantages of this custom-made method are the costs and time required to construct the device. Therefore, prefabricated MADs made out of thermoplastic material, which can be adapted immediately at the outpatient clinic, have been studied as a treatment option (16, 22). It has been hypothesized that these thermoplastic devices could provide a reasonable alternative to custom-made devices to reduce the costs as well as to predict the success with the custom-made devices (22, 23).

Only a few studies have reported on the clinical use of one-piece prefabricated MADs made of thermoplastic material, so-called boil-and-bite devices (16, 22, 23). In a prospective study (22), the effect of SnorBan (Snoring Relief Labs, Inc., Sacramento, CA) was investigated in 22 consecutive patients with mild to moderate OSAHS (apnea-hypopnea index [AHI], 33 ± 18 events/h). Eleven of 22 subjects (50%) were labeled as responders. In a pilot study (16), we evaluated the commercially available SomnoGuard (Tomed Dr. Toussaint GmbH, Bensheim, Germany) in 20 consecutive heavy snorers with mild SDB (AHI, 6 ± 5 events/h). A significant decrease in snoring, Epworth Sleepiness Scale (ESS), and AHI was noted. Recently, SomnoGuard was evaluated in 44 patients with more severe SDB (AHI, 32 ± 18 events/h). A significant decrease in both

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Correspondence and requests for reprints should be addressed to Olivier M. Vanderveken, M.D., Ph.D., University Department of Otorhinolaryngology, Head and Neck Surgery, Antwerp University Hospital, University of Antwerp, Wilrijkstraat 10, BE-2650 Edegem, Belgium. E-mail: Olivier.Vanderveken@telenet.be

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AHI and snoring was reported with SomnoGuard compared with baseline (23).

The aims of the present study were to determine the efficacy of a thermoplastic appliance compared with that of a classical, custom-made MAD and to test this thermoplastic MAD as a screening tool in search of good candidates for a definitive custom-made MAD.

Some of the results of this study have been previously reported in the form of an abstract (24).

METHODS

Participants and Setting

The study was performed at a multidisciplinary tertiary referral center (Antwerp University Hospital, Edegem, Belgium).

Patients were considered technically eligible for this trial when a recent one-night polysomnography revealed a diagnosis of snoring and/or mild to moderate OSAHS (AHI \leq 40 events/h). All patients were seen at our university-based, multidisciplinary sleep clinic in coordination with the departments of neurology, pulmonary medicine, and the ear, nose, and throat (ENT) department.

In Belgium, CPAP is the standard treatment for patients with moderate to severe OSAHS (AHI \geq 20 events/h) and is fully reimbursed in these patients. Therefore, our policy is to propose a trial of CPAP therapy to any patient with an AHI of at least 20 events/hour. In our multidisciplinary setting, patients with mild SDB (AHI < 20 events/h) and patients with CPAP intolerance are referred to the ENT department by the pulmonologist. On the basis of standard ENT clinical examination, the patient is then considered a candidate for upper airway surgery or MAD therapy (25, 26). In the latter case, the patient is referred to a qualified dentist at the department of dentistry for a clinical and radiologic dental, periodontal, and temporomandibular joint examination (6, 15). In our study, if one or more absolute contraindications to MAD therapy (Table 1) were present, patients were excluded from participation (27). Caries and periodontal disease were considered relative contraindications and were treated first when necessary.

The reported trial was conducted in accordance with the institutional guidelines and all patients gave written, informed consent.

Thirty-eight successive patients who were eligible for the study (32 males; age, 50 ± 9 yr; body mass index [BMI], 28 ± 4 kg/m²) were enrolled between January 2003 and July 2004. The majority of included subjects had no previous treatment for SDB (n = 24). All study patients diagnosed at baseline with moderate OSAHS (20 events/h \leq AHI \leq 40 events/h) were proposed a trial of nasal CPAP first but were intolerant or refused CPAP treatment (n = 6). Eight patients had a history of an unsuccessful uvulopalatopharyngoplasty (UPPP).

Three male patients of the original series of 38 patients discontinued participation during the study: one patient discontinued because of an important decrease in subjective complaints after a significant weight loss and reduced alcohol consumption; another patient experienced a complaint of increasing headache; a third patient withdrew consent because of socioeconomic reasons. Complete data are therefore available for 35 patients who completed the protocol.

The patients' characteristics at the time of study enrollment are outlined in Table 2.

MADs

Both MADs evaluated in this study are one-piece appliances, termed "mono-bloc splints".

TABLE 1. ABSOLUTE CONTRAINDICATIONS TO MANDIBULAR ADVANCEMENT DEVICE TREATMENT

Insufficient teeth to support the device
Periodontal problems including tooth mobility
Active temporomandibular joint dysfunction
Limited maximum protrusive capacity (<6 mm)

TABLE 2. BASELINE PATIENT CHARACTERISTICS

Parameter	Mean \pm SD (range)
Age, yr	49 \pm 9 (26–74)
Body mass index, kg/m ²	28 \pm 4 (22–40)
Apnea-hypopnea index, events/h	13 \pm 11 (0–40)
Snoring index (VAS 0–10)	8 \pm 3 (3–10)
Epworth Sleepiness Scale	8 \pm 5 (0–17)

Definition of abbreviation: VAS = visual analog scale.

Total n = 35; 83% male.

The custom-made MAD (MAD_{cm}) used in this study is made of soft SR-Ivocap Elastomer (Ivoclar, Vivadent AG; Schaan, Liechtenstein) and provides full occlusal coverage of both dental arches (Figure 1). The MAD_{cm} is totally tailor-made to the patient's dentition with a laboratory-controlled protrusion. The MAD_{cm} was fabricated at the dental laboratory of the Umeå University Hospital, Sweden, by a dental technician from individually made plaster casts of the teeth and a bite registration as taken by the hospital's dentist (Figure 1). The same MAD_{cm} has already been described and evaluated by Marklund and colleagues (5, 28, 29).

The thermoplastic MAD (MAD_{tp}) used in this study was the SomnoGuard Plus (Figure 2), a development product designed by Tomed Dr. Toussaint GmbH, Germany. The SomnoGuard Plus samples used in this study were supplied by the company. No changes were made to the SomnoGuard Plus units by the researchers. The MAD_{tp} was adapted to the individual patient according to the manufacturer's recommendations and instructions. The fitting of the MAD_{tp} starts from a prefabricated mold out of polymeric material, allowing for adjustment and advancement. After the MAD_{tp} is heated in hot water according to the instructions, the patient is asked to bite into the plastic moving the lower jaw forward to approximately half of maximal advancement. After this fitting procedure, the prefabricated mold has been adapted to the patient's dentition (Figure 2).

At the end of the study, the degree of advancement was reproduced and measured for both MADs of each patient, comparing the mandibular position with and without the MAD by putting the plaster casts in a dental articulator.

Study Design

The study design included a recent baseline overnight polysomnography followed by a single-center, randomized, controlled, cross-over trial design in which the two test treatments (MAD_{cm} vs. MAD_{tp}) were used for 4 months in randomized order, with a washout interval of 1 month between the two test conditions (Figure 3). The randomization procedure assured a balanced design. A follow-up sleep study, together with a structured interview, was conducted at the end of each treatment period.

Participants were randomly allocated (concealed randomization) to either treatment sequence A or B (see Figure 3). Half of the patients were randomized to the MAD_{cm} for 4 months, followed by a 1-month washout period. These patients were then treated with the MAD_{tp} for 4 months (sequence B). The remaining patients were randomized to the reversed treatment sequence of MAD_{tp}, followed by a 1-month washout period, and then treatment with MAD_{cm} for 4 months (sequence A).

Outcome Measures

Standard full-night polysomnography was performed (Medilog SAC; Oxford Instruments, Oxon, UK). Sleep recordings were scored manually in a standard fashion by a qualified sleep technician blinded to the subject's treatment status (30–32).

The AHI was the average number of respiratory events per hour of sleep.

To evaluate the status of snoring during sleep as assessed by the bed partner, a 10-point visual analog scale (VAS) ranging from 0 (no snoring noise) to 10 (extreme noise: bed partner has to leave the room or sleep in a separate room) was used as snoring index (16). The VAS was completed at baseline and at each follow-up evaluation. Heavy snoring was defined as a snoring index of at least 7. A decrease of at

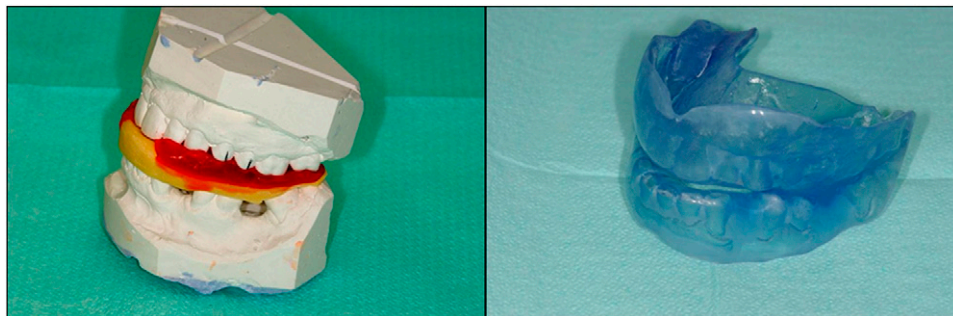


Figure 1. The custom-made mandibular advancement device (MAD_{cm}) evaluated in this study. First, plaster casts are made. A bite registration represents the individually determined advancement (left). Subsequently, the MAD_{cm} is fabricated at the dental laboratory using the individual data obtained with the plaster casts and the bite registration (right).

least 3 points after treatment was considered satisfactory. To be considered as an important reduction, snoring had to be reduced to a level that was no longer considered bothersome (i.e., to a snoring index of ≤ 3).

To assess daytime sleepiness, the subjects completed an ESS at each evaluation (33). EDS was defined as an ESS score of greater than 10.

Treatment Outcome

Complete response was defined as an important reduction of snoring plus a decrease in AHI to fewer than 5 events/hour. Partial response was defined as a satisfactory decrease of snoring plus a 50% or greater reduction in AHI. Treatment failure was defined as ongoing clinical symptoms and/or a less than 50% reduction in AHI. Compliance failure was defined as an inability of the patient to continue treatment.

Secondary outcomes included the effects of the tested MADs on polysomnographic parameters and on VAS and ESS. Compliance was assessed using a questionnaire filled out by the patient at each evaluation. At the end of the study, patients were asked about their preference.

Statistical Analysis

A database in Access (Microsoft Access 2002; Microsoft Corp., Redmond, WA) was developed in which all variables were collected. Data were manually checked for entry accuracy. Statistica 6.1 (StatSoft, Inc, Tulsa, OK) was used for statistical analysis. Quantitative variables were expressed as mean \pm SD. Normality of distribution was assessed using Kolmogorov-Smirnov. Treatment effects were compared by using analysis of variance (ANOVA) for repeated measures, followed by the Newman-Keuls multiple comparisons procedure or by Friedman's ANOVA and Wilcoxon's matched-pairs test, depending on the distribution of the variables. Categorical data were analyzed using chi-square tests. Carryover and period effects were assessed using ANOVA statistics (34).

A statistically significant difference was defined by a value of $P < 0.05$.

RESULTS

There were no period and carryover effects found in any evaluated variable studied. The patients' BMI did not change significantly during the study. The mandibular advancement

with the tested MAD_{cm} was $65 \pm 10\%$ of maximal protrusion; with the tested MAD_{tp}, the mean protrusion of the mandible amounted for $50 \pm 20\%$.

Primary Outcome

The MAD_{cm} resulted in either partial or complete response (= total treatment success) in 21 out of 35 patients (60%). Total treatment success with the MAD_{tp} was lower (31%) ($P = 0.02$) (Table 3). The number of treatment failures was not significantly different between both devices (34 vs. 37%), whereas compliance failure with the MAD_{tp} was more frequent as compared with compliance failure with the MAD_{cm} ($P = 0.006$) (Table 3).

The reasons for discontinuation with the respective MADs are summarized in Table 4.

Fifteen out of the 24 patients (63%) with total failure with the MAD_{tp} experienced treatment success with the MAD_{cm}.

Secondary Outcomes

Because 12 patients experienced compliance failure with one or both tested MADs (Table 4), polysomnography with both devices was obtained in 23 out of 35 patients. Therefore, statistical analysis regarding polysomnographic outcomes was performed only on these 23 subjects who completed both arms of the study (Table 5).

The MAD_{tp} had no significant effects on any of the polysomnographic parameters, whereas the MAD_{cm} resulted in a significant reduction in AHI compared with baseline ($P = 0.005$).

Overall, a reduction in snoring of a least 3 points on VAS was noted in 28 patients (80%) with the MAD_{cm} versus 18 patients (51%) with the MAD_{tp} ($P = 0.01$). Twenty-three patients (66%) reported an important reduction in snoring with the MAD_{cm} versus 13 patients (37%) with the MAD_{tp} ($P = 0.02$). The MAD_{cm} resulted in a significant reduction in VAS both compared with baseline and in comparison to MAD_{tp} (Table 5).

Eleven patients had complaints of EDS at baseline. Of these, an elimination of EDS was observed in six patients (55%) with

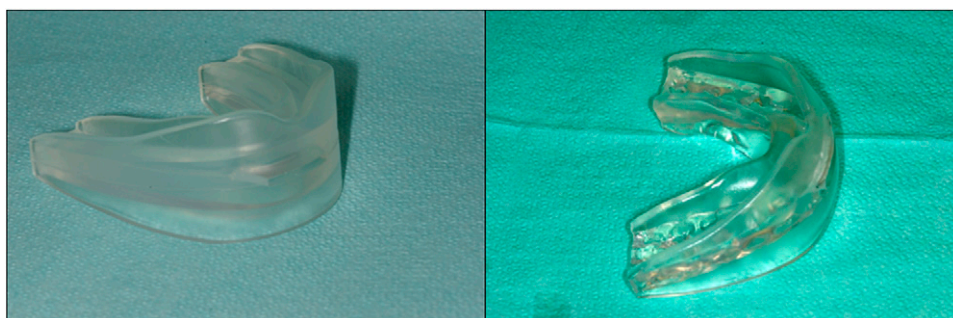


Figure 2. The thermoplastic mandibular advancement device (MAD_{tp}) evaluated in this study. The fitting procedure starts from a prefabricated mold made from thermoplastic material (left). Direct intraoral fitting is realized by heating the MAD_{tp} in hot water. Afterward, the patient is asked to bite into the plastic, moving the lower jaw forward to approximately 50% of maximal advancement. After the fitting procedure of the MAD_{tp}, the prefabricated mold has been adapted to the patient's dentition (right).

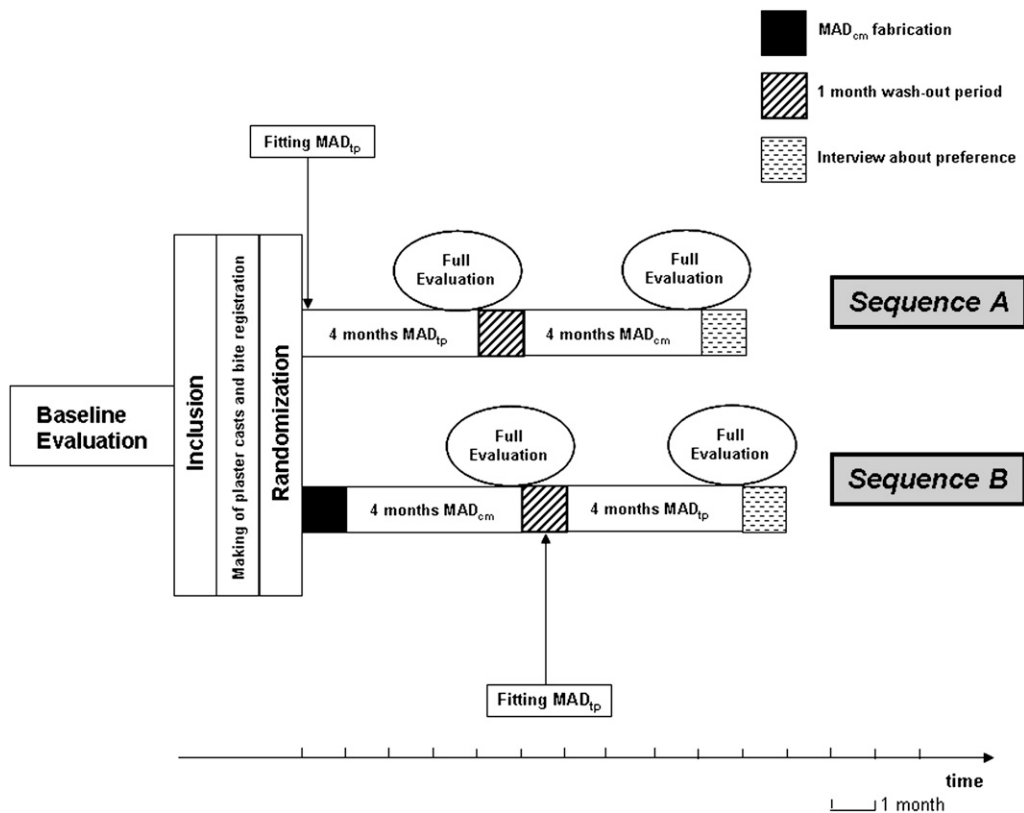


Figure 3. Schematic diagram summarizing the study design. MAD_{cm} = custom-made mandibular advancement device; MAD_{tp} = thermoplastic mandibular advancement device.

the MAD_{cm} compared with five patients (45%) with the MAD_{tp}.

Patients were using the MAD_{cm} on average for 6.4 nights per week (92%) and for 6.3 hours per night (92%). Compliance with the MAD_{tp} amounted to 4.5 nights per week (65%) and 4.6 hours per night (63%).

No serious side effects were noted with either MAD during this study.

At the end of the study, 19 out of the 23 subjects (82%) who completed both arms preferred the custom-made device, whereas two patients (9%) had no preference ($P < 0.0001$).

DISCUSSION

MAD therapy has become a routine treatment modality for patients with SDB (18). MADs may be custom-made devices or prefabricated, thermoplastic boil-and-bite devices. Custom-made devices are fabricated by the dentist in coordination with a dental laboratory based on plaster models and a bite registration (16, 17, 22). Direct intraoral fitting of prefabricated devices can be done at the outpatient clinic, without need for

plaster casts or bite registrations, which results in reduced costs and significant savings in the number of clinic visits (16, 22). This advantage had led to the suggestion to use prefabricated, thermoplastic devices as trial devices to screen for responders to the therapeutic principle of MADs, and thus candidates for a more expensive, custom-made MAD (22, 35). To date, this screening hypothesis remains speculative because no studies have addressed this issue.

The present study is the first report to compare the efficacy of two MADs that differ in mode of fabrication and degree of customization. In this randomized controlled cross-over trial, MAD_{cm} and MAD_{tp} were compared.

The first aim of the study was to determine the efficacy of MAD_{tp} compared with that of MAD_{cm} in the treatment of snoring and mild sleep apnea. The success percentages as listed in Table 3 favor the MAD_{cm}. The reduction of AHI with the MAD_{cm} compared with baseline is highly significant, whereas no significant drop in AHI is noted with the MAD_{tp} (Table 5).

Two independent effects are responsible for the inferior performance of the MAD_{tp} in terms of efficacy, compliance, and patient preference. First, as shown in Table 3, the MAD_{tp} compliance failure rate was unambiguously higher than that of MAD_{cm} (31 vs. 6%). Of all compliance failures with MAD_{tp},

TABLE 3. SUCCESS PERCENTAGES

	MAD _{cm} n (%)	MAD _{tp} n (%)
Complete response	17 (49)	6 (17)
Partial response	4 (11)	5 (14)
Total treatment success	21 (60)	11 (31)
Treatment failure	12 (34)	13 (37)
Compliance failure	2 (6)	11 (31)
Total failure	14 (40)	24 (69)

Definition of abbreviations: MAD_{cm} = custom-made mandibular advancement device; MAD_{tp} = thermoplastic mandibular advancement device. Total n = 35.

TABLE 4. NUMBER OF COMPLIANCE FAILURES WITH CORRESPONDING REASON FOR DISCONTINUATION

Reasons for Discontinuation	MAD _{cm}	MAD _{tp}
Lack of device retention	—	8
Pain from TMJ or teeth	2	1
Sleeping problems	—	1
Discomfort at night	—	1
Total number of compliance failures (n = 12)*	2	11

* One patient experienced compliance failure with both devices. TMJ = temporomandibular joint.

TABLE 5. STUDY DATA

Variable	Baseline	MAD _{cm}	MAD _{tp}
Polysomnographic variables			
AHI, per h of TST	14 ± 12	6 ± 8*	11 ± 9
Sa _O ₂ mean, %	95 ± 1	95 ± 1	95 ± 2
Sa _O ₂ min, %	83 ± 7	82 ± 8	82 ± 6
TST, min	349 ± 60	325 ± 81	352 ± 60
Sleep efficiency, %TST/TIB	78 ± 11	80 ± 11	81 ± 12
Symptom scores			
VAS snoring (0–10)	8 ± 2	2 ± 3*†	4 ± 3*
ESS (0–24)	7 ± 5	5 ± 4	6 ± 4
Anthropometric variable			
BMI, kg/m ²	28 ± 4	28 ± 3	28 ± 3

Definition of abbreviations: AHI = apnea–hypopnea index; BMI = body mass index; ESS = Epworth Sleepiness Scale; MAD_{cm} = custom-made mandibular advancement device; MAD_{tp} = thermoplastic mandibular advancement device; TIB = time in bed; TST = total sleep time; VAS = visual analog scale.

Total n = 23.

* Significantly different from baseline ($P < 0.01$).

† Significantly different from MAD_{tp} at the corresponding measurement ($P < 0.05$).

73% discontinued treatment due to lack of retention, whereas with MAD_{cm} no compliance failures were noted due to lack of retention (Table 4). Indeed, the design of the MAD_{tp} limits the coverage of upper and lower teeth, whereas the MAD_{cm} completely covers all teeth and even part of the gums. Therefore, the design of the MAD itself is reflected directly in the outcome results. Second, there is the difference in mean advancement found for both MADs evaluated in this study, with a higher advancement for MAD_{cm}. In the literature, it remains unclear whether there is a dose-dependent relationship between the degree of advancement and treatment outcome with MADs (10, 13, 36, 37). However, the degree of advancement must be reproducible. Because MAD_{tp} is directly fitted intraorally, the mandibular advancement has to be determined and controlled during the fitting procedure itself. Unfortunately, the determination of the advancement during the fitting procedure is hampered by the intraoral presence of the MAD_{tp} itself. This aspect is reflected in the high standard deviation of the mean advancement of MAD_{tp} as compared with MAD_{cm}. Therefore, the fitting procedure of MAD_{tp} should be considered as a method with an inherent uncontrollable degree of mandibular advancement. This method is in contrast to the fabrication process of MAD_{cm}, in which the degree of advancement is controlled to a much higher degree during the laboratory procedure, resulting in a more consistent and reproducible mean advancement with a lower standard deviation.

A second aim of this study was to test the hypothesis suggested in previous reports that the prefabricated, thermoplastic, boil-and-bite devices could be used to screen for candidates for MAD treatment, before adaptation of a more expensive, custom-made MAD.

In the present study, an exceptionally high total failure rate of 69% with the MAD_{tp} was noted (Table 3). The fact that a majority of these patients experienced treatment success with the MAD_{cm} despite failure with MAD_{tp} clearly demonstrated that the outcome with MAD_{tp} was not related to treatment outcome with MAD_{cm}. These data provide convincing evidence to abandon this screening hypothesis.

The primary strength of the present study is the use of definitions for successful treatment that include both objective parameters and subjective complaints (38, 39). This is of paramount importance because the goal of therapy in the treatment of SDB is not only to lower the number of respiratory events, thereby reducing cardiovascular and other health-re-

lated risk, but also to relieve symptoms, or vice versa. Therefore, we mainly used definitions for success that included both effect on AHI and changes in subjective complaints.

Another strength of the study is the cross-over design, which offers the advantage of a clear comparison of the differences in efficacy, acceptance, and patient preference between both types of MADs. Moreover, in this study in particular, the cross-over design required the creation of plaster casts for every study patient because plaster casts are required in the fabrication process of MAD_{cm}. With these plaster casts available, we were also able to quantify the degree of advancement obtained with MAD_{tp} at the end of the study. In routine clinical practice, as explained previously, the practitioner is not aware of the exact degree of advancement when fitting the MAD_{tp}. This study is the first study to report on the quantification of the protrusion obtained by direct intraoral fitting of an MAD_{tp}. From our data, it is clear that the overall degree of mandibular advancement obtained with this procedure is uncontrollable and lacks reproducibility in the absence of plaster casts and a bite registration.

The present study has its limitations, which underline the complexity in comparing treatments. First, two independent factors inherent to the structural characteristics and the fabrication philosophy of thermoplastic MADs, believed to be responsible for the inferior performance of MAD_{tp}, were discussed previously. However, it was the distinct aim of the present study to compare a custom-made with a thermoplastic MAD in their original way of fabrication and customization according to their recommended use in clinical practice. On the basis of the results of this study, the tested MAD_{tp} cannot be recommended for treatment of snoring and mild sleep apnea in routine clinical practice. Second, another limitation of the present study includes the heterogeneous patient population evaluated. Patients who were enrolled were either snorers or had mild OSAHS. Some of the patients had a history of CPAP intolerance or UPPP failure before participation. We believe, however, that the performance of MAD_{cm} versus MAD_{tp} in daily clinical practice is adequately reflected in this heterogeneous study population with respect to the different indications for MAD treatment (15, 18).

In conclusion, this randomized controlled cross-over trial provides primary evidence that a custom-made MAD is more efficacious than a prefabricated MAD made from thermoplastic material in the treatment of snoring and mild sleep apnea. In addition, on the basis of these results, a screening trial with a prefabricated MAD that is directly fitted intraorally cannot be recommended as a convenient low-cost screening strategy to predict success with custom-made MADs.

Conflict of Interest Statement: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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