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Objectives. To determine whether a manually adjustable oral mandibular advancement titration appliance (EMA-T) predicts successful long-term treatment with an oral mandibular advancement appliance (MAA).
Study design. At an academic medical center, 21 adults with obstructive sleep apnea (AHI > 10 events/hr) performed baseline, titration, and MAA (Klearway) polysomnograms. During the titration polysomnogram with EMA-T, the mandible was advanced until apneas and hypopneas were eliminated or maximum tolerable advancement was reached. Participants then used the MAA at home and, once the mandible was advanced to the amount determined during the titration polysomnogram, a polysomnogram with MAA was performed.
Results. Mean AHI at baseline was 33.5 ± 18.3 (SD) events/hr. During the titration polysomnogram, 9 subjects achieved an AHI < 10 and at least a 50% reduction in AHI. None of the subjects met these criteria on the MAA polysomnogram.
Conclusions. EMA-T lowered the AHI to efficacious levels in 43% of patients but this acute response did not predict the efficacy of long-term MAA treatment.
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Intraoral devices that advance the mandible are used to treat patients with obstructive sleep apnea (OSA).[1,2] Like nasal continuous positive airway pressure treatment (CPAP), the appliances are worn only during sleep. Not all patients with OSA have an acceptable reduction in their apnea-hypopnea index (AHI) when treated with a mandibular advancement appliance (MAA).[3-10] In a recent study from our laboratory, only 32% of the patients with OSA using an elastic MAA had an AHI < 10 events/hr and at least a 50% reduction in AHI from baseline.[5] One of the factors limiting wider application of oral appliance treatment is the inability to identify those patients who will have a successful outcome prior to investing the time and resources necessary to implement this treatment. Studies report that younger age, lower body mass index, less severe OSA, previous uvulopalatopharyngoplasty, and positional OSA predict a successful response with MAA treatment.[7-9,11-14] However, the results are conflicting and no clear consensus exists about how to identify patients with OSA who will be successfully treated with an MAA.

Recent studies report that the amount of reduction in sleep disordered breathing using an adjustable mandibular advancement titration appliance during an overnight polysomnogram can predict the efficacy of subsequent MAA treatment.[15,16] The concept is analogous to the CPAP titration polysomnogram performed prior to initiating patients on CPAP treatment to identify the optimal pressure setting and demonstrate an acceptable reduction in AHI. Demonstrating the feasibility of this approach, Raphaelson and colleagues[17] reported that AHI on an overnight polysomnogram is reduced with progressive mandibular advancement using a manually adjustable mandibular advancement device. Pételle et al.[16] showed that the results of the titration polysomonogram using a remotely controlled hydraulic titration device to advance the mandible predicted the efficacy of an oral appliance with the same mandibular advancement on a polysomnogram performed the following night. Extending these findings, Tsai et al.[15] reported that successful elimination of respiratory events and oxygen desaturation during a polysomnogram using a remotely controlled mandibular positioner was highly predictive of MAA efficacy on a polysomnogram performed 4 ± 3 months following initiation of treatment.

The purpose of the current study was to determine if a polysomnogram with a manually adjustable mandibular advancement titration appliance would predict a patient's polysomnographic response to subsequent MAA treatment. Participants performed an overnight polysomnogram using a low-cost, quickly constructed, manually adjustable mandibular advancement titration appliance

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prior to starting regular MAA treatment. The study was designed to test the hypotheses that the results on a mandibular advancement titration polysomnogram would predict a patient's subsequent response to oral appliance treatment and identify the amount of mandibular advancement needed to achieve that response.

MATERIALS AND METHODS

Subject selection

Thirty-two patients seeking treatment for their OSA with an oral appliance were enrolled from the dental and sleep medicine clinics at the participating institutions. The protocol was approved by the Institutional Review Board of The University of Pennsylvania and the Philadelphia Veterans Affairs Medical Center, and each participant signed a detailed informed consent form. The criteria for enrollment in the study were an AHI $>$ 10 events/hr on a baseline full-night diagnostic polysomnogram and a dental evaluation by one of the dentists involved with the study (PG, LL, DS) indicating that the participant's dentition was suitable for oral appliance treatment. Exclusion criteria included insufficient number of teeth to anchor the oral appliance, oxygen saturation $<$ 85% for more than 20% of the total sleep time on the baseline polysomnogram, previous history of temporomandibular joint pain, central sleep apnea on baseline polysomnogram, or evidence on physical examination of right-sided congestive heart failure.

Dental evaluation

Subjects with excessive gag reflex or extremely loose teeth on the dental evaluation were excluded from participation. George gauge (Great Lakes Orthodontics, Tonawanda, NY) readings were obtained at centric occlusion and maximum voluntary mandibular advancement.[18] Plaster models of the upper and lower dental arches and bite registrations were constructed. To avoid damage to any bridge present, block-out material was used so the bridge would not be dislodged when the device was removed. The dental models were sent to a commercial vendor for manufacture of the MAA (Klearway, Great Lakes Orthodontics, Tonawanda, NY) that the participants used at home.

Protocol

Three nighttime polysomnograms were performed in the following order: polysomnogram 1 (baseline) established the baseline severity of OSA, polysomnogram 2 (titration) was performed with the patients using the mandibular advancement titration appliance, and polysomnogram 3 (MAA 1) was performed with the MAA that the participants were using at home advancing the mandible by the same amount achieved with the titration appliance. Those subjects who had an AHI $>$ 15 events/hr on the MAA 1 polysomnogram were reevaluated by one of the dentists and, if feasible, instructed to continue to advance the MAA to their maximum or maximum tolerable level. A fourth polysomnogram (MAA 2) was then performed with the MAA at this final position. Micrometer measurements (Bouley gauge) of the MAA's screw separating mechanism confirmed the amount of advancement at the time of the MAA polysomnograms. Subjects were not informed about the results of their titration study until they reached the end of the protocol or withdrew from the study.

Polysomnogram

Using standard techniques,[19] the following signals were recorded during the polysomnograms with a computer data acquisition and analysis system (Mallinckrodt, Pleasanton, CA): C3A2 and O2A1 electroencephalograms, bilateral electrooculograms, chin muscle activity, bilateral anterior tibialis electromyogram, rib cage and abdominal movement (Pro-Tech, Woodinville, WA), nasal pressure and snoring (Pro-Tech), body position, and oxygen saturation by pulse oximetry (Ohmeda, Louisville, CO). The studies were scored manually by an unblinded certified polysomnographic technologist. Body position was not controlled during the polysomnograms.

Mandibular advancement titration appliance

The commercially available mandibular advancement titration appliance used in the study (EMA-T, Frantz Design Inc., Austin, TX) consists of plastic trays for the upper and lower dental arches (Fig. 1). When the appliance is in place, extensions protruding out of the mouth allow the mandible to be manually advanced in 3-mm increments by inserting a peg at the end of the maxillary projection into a hole in the mandibular projection. When the participants arrived at the sleep center for the titration polysomnogram, one of the investigators (STK) constructed the appliance by placing a fast-setting dental silicon putty material (Kerr, Orange, CA) in the dental trays and pushing the trays onto the patient's dental arches. After the silicone putty set, the appliance was removed and evaluated. Just prior to starting the polysomnogram recording, a fast-setting dental wash (Kerr, Orange, CA) was applied to the silicone putty impression and repositioned in the mouth in order to achieve greater retention. At the start of the titration polysomnogram, the appliance was initially set to advance the mandible by 3 mm beyond resting position except in one subject who was unable to tolerate advancement of the titration appliance beyond resting position. During the polysomnogram, the mandible was progressively advanced by the polysomnographic technologist in 3-mm increments until snoring, apneas,

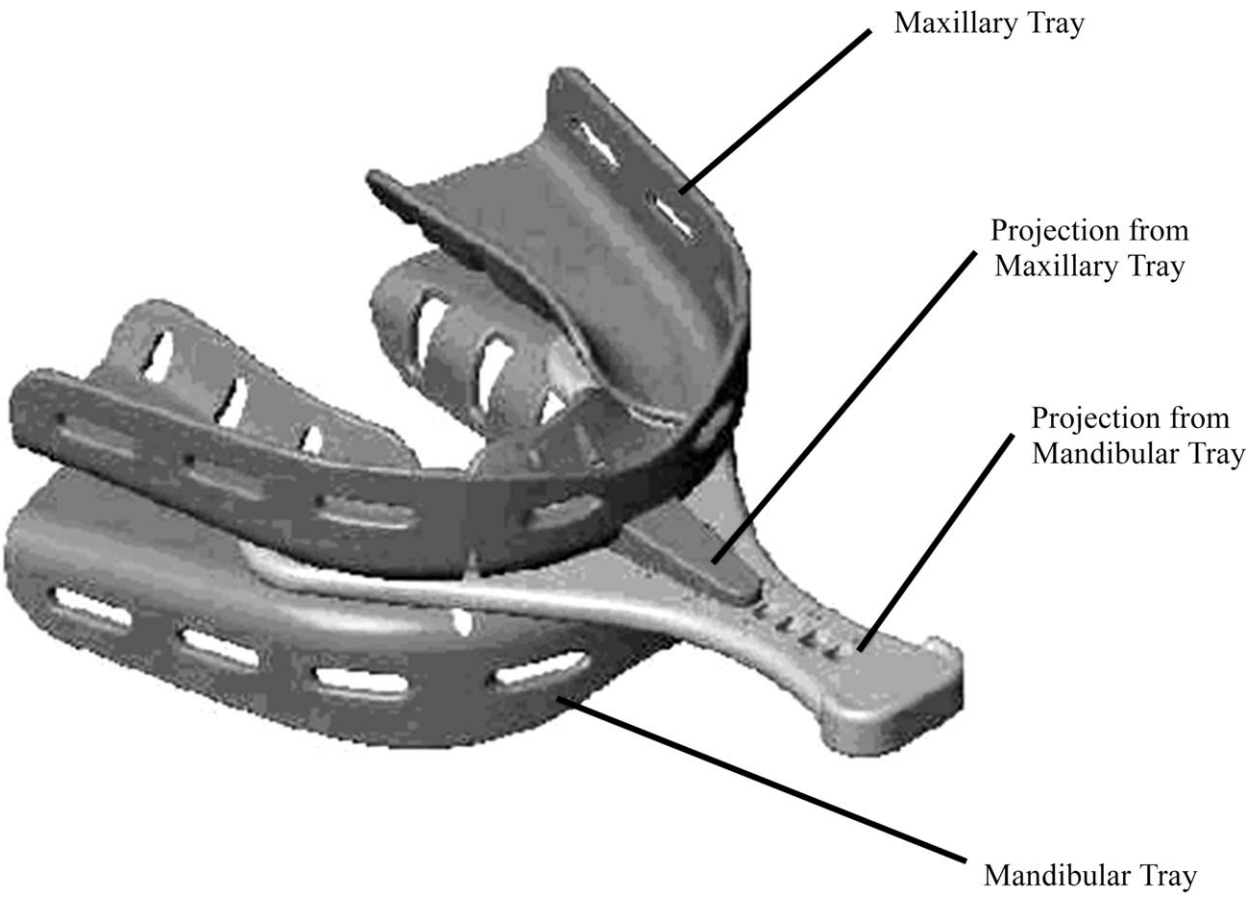

Fig. 1. Diagram of the titration appliance (EMA-T, Frantz Design Inc., Austin, TX). The appliance consists of plastic trays for the upper and lower dental arches. A custom-fitted appliance was constructed for each participant by placing fast-setting dental impression materials in the troughs of the trays. When the appliance is in place, the mandible is manually advanced by securing a peg (not shown) in the projection from the upper tray into one of the holes in the projection from the lower tray.

and hypopneas were eliminated, or maximum tolerated advancement was reached. The patients had to be awakened in order to advance the mandible, but, in general, had little difficulty falling back to sleep. Recordings during stable sleep were obtained at each level of advancement for at least 15 min. The mandible was advanced to the next level in the presence of repetitive apneas and hypopneas.

Following completion of the titration polysomnogram, the patient's dental models were mounted on a Galletti articulator (Walter Lorenz Surgical, Jacksonville, FL) and fitted with his/her titration appliance. George gauge readings were obtained at centric occlusion without the appliance and at the maximum tolerated mandibular advancement achieved with the titration appliance during the titration polysomnogram. This measurement was used to determine the amount of advancement needed on the MAA for the MAA 1 polysomnogram.

Mandibular advancement appliance

The Klearway appliance used for home MAA treatment consisted of custom fabricated acrylic trays for the upper and lower dental arches.[20] The maxillary and mandibular trays are connected to each other by metal orthodontic struts positioned anteriorly on the appliance. A screw-separating mechanism located just below the hard palate allows the appliance to advance the mandible in 0.25-mm increments. When received from the manufacturer, the mandibular advancement on the Klearway appliance was already set at 50% of the patient's maximum voluntary anterior advancement from centric occlusion. The participants were instructed to wear the appliance whenever they slept and manually turn the advance screw in the separating mechanism by 0.25 mm every other day unless the appliance was causing temporomandibular or other discomfort. In this case, the amount of advancement was temporarily reduced or maintained at the current level until the

symptoms resolved. Adherence to treatment was not monitored.

Statistical analysis

A repeated measures analysis of variance (ANOVA) using SAS PROC.MIXED (SAS Institute, Cary, NC) software was used to determine whether there was an overall difference over time (baseline, MAA 1, and MAA 2) in the mean value of each of a series of polysomnographic outcome measures. If the overall test was significant, Tukey-adjusted post hoc comparisons were used to assess the significance of each pairwise comparison.

RESULTS

Subject recruitment

Of the 32 patients who performed the titration polysomnogram, 21 (17 men and 4 women) completed the MAA 1 polysomnogram. Eleven of the patients fitted with the MAA withdrew from the study prior to the MAA 1 polysomnogram due to: inability to tolerate the MAA (n = 7), development of a non-related medical condition (n = 2), and unwillingness to meet participant burden (n = 2). The most common side effects reported by subjects during MAA treatment included excessive salivation at the beginning of treatment, jaw and tooth discomfort, and temporomandibular joint discomfort.

The 21 patients who completed the MAA 1 polysomnogram had mean age 49.6 ± 11.1 (SD) years (range, 26-70 years), mean body mass index 29.3 ± 5.3 kg/m^2 (range, 21.8-37.2 kg/m^2), mean neck circumference 40.3 ± 4.2 cm (range, 31-48 cm), and mean Epworth sleepiness scale 11.9 ± 3.4 (range, 5-18).[21] There were no differences in these baseline measures between the 21 subjects completing the MAA 1 polysomnogram and the individuals who withdrew from the study. Of the 21 participants completing the MAA 1 polysomnogram, 6 had a previous uvulopalatopharyngoplasty at least one year prior to enrollment, 3 were using an oral appliance to treat their sleep apnea, and 12 patients were using CPAP. Participants who were using an oral appliance or CPAP at the time of enrollment were instructed to stop using these treatments at least one week prior to the baseline polysomnogram and to use only the MAA during the course of the study.

Eighteen subjects had an AHI > 15 events/hr on the MAA 1 polysomnogram. One of these subjects decided to withdraw from further participation. The remaining 17 subjects performed the fourth polysomnogram (MAA 2) with the MAA advancing the mandible to its maximum or maximum tolerable level.

Time intervals between polysomnograms

The time interval between the baseline and titration polysomnograms was 44.0 ± 40.1 days (range, 12-153 days). The time interval between the titration and MAA 1 polysomnograms was 131.8 ± 66.1 days (range, 42-298 days). In those subjects who performed the fourth polysomnogram, the time interval between the MAA 1 and MAA 2 polysomnograms was 131.2 ± 106.9 days (range, 27-464 days).

Baseline polysomnogram results

Polysomnographic results from the baseline and MAA polysomnograms are provided in Table I. The mean AHI at baseline was 33.5 ± 18.3 events/hr of sleep (range, 12.2-91.9 events/hr), 31.3 ± 20.9 events/hr in NREM sleep, and 34.1 ± 19.8 events/hr in REM sleep. Of the 19 participants with an AHI > 15 events/hr at baseline, mean AHI was 35.6 ± 17.9 events/hr (range, 16.1-91.9 events/hr).

Titration polysomnogram

Construction of the mandibular advancement titration appliance was performed without difficulty and usually took about 15 min. On initial insertion of the titration appliance, almost all patients commented on excessive salivation. Two participants requested that the amount of advancement be reduced from its maximum achievable level due to discomfort. One participant requested that the titration appliance be removed prior to the end of the recording due to inability to sleep further with the appliance in place. During the titration polysomnogram, mean sleep time at the maximum tolerated advancement achieved was 209.3 ± 106.0 min (range, 47.1-362.5 min). Based on the post hoc measurements on the Galletti articulator, maximum mandibular advancement achieved with the titration appliance was 7.8 ± 1.8 mm (range, 4.3-11.2 mm) (Table II). This amount of mandibular advancement was 85.2 ± 25.8% (range, 34-143%) of maximal voluntary advancement. At least some of the recording at the maximum tolerable advancement achieved with the titration appliance was obtained in the supine position in 18 subjects, in REM sleep in 16 subjects, and in both the supine position and REM sleep in 13 subjects. At the maximum tolerated advancement achieved with the titration appliance, the AHI was 16.4 ± 13.0 events/hr (range, 2.3-41.2 events/hr) or 59.7 ± 52.6% (range, 5-185%) of the baseline AHI ($P < .002$, Fig. 2). At the maximum tolerated advancement achieved during the titration polysomnogram, 13 subjects had at least a 50% reduction in AHI compared to that at baseline, and 9 of those subjects also had an AHI < 10 events/hr. Of the latter subjects, 1 had mild OSA on the baseline polysomnogram (5 < AHI < 15), 4 had moderate OSA (15 ≤ AHI < 30), and 4 had severe OSA (AHI ≥ 30).

Table I. Results of baseline, titration, and mandibular advancement appliance polysomnograms

Measure	*Baseline PSG**	*MAA 1 PSG*	*MAA 2 PSG*	*Titration PSG†*
AHI (total sleep)	33.5 ± 18.3	24.6 ± 17.1	24.9 ± 18.8	16.4 ± 13.0
AHI (NREM)	31.3 ± 20.9	22.1 ± 17.8	23.1 ± 20.3	15.3 ± 13.0
AHI (REM)	34.1 ± 19.8	30.2 ± 19.9	30.7 ± 25.7	20.5 ± 18.3
AHI (supine)	43.6 ± 23.8	31.2 ± 21.3	50.6 ± 69.1	22.5 ± 16.8
AHI (non-supine)	25.4 ± 21.5	16.1 ± 20.5	19.9 ± 17.3	12.3 ± 21.5
AI (total sleep)	4.1 ± 7.9	3.3 ± 4.9	6.8 ± 11.2	N/A
Time SaO_2 <90%	4.0 ± 12.7	4.4 ± 13.7	2.7 ± 6.8	N/A
Minimum SaO_2	84.1 ± 7.9	85.2 ± 9.3	85.4 ± 8.0	N/A
TST (min)	364 ± 64	340 ± 55	363 ± 43	209 ± 101
Sleep efficiency	79.8 ± 9.3	78.6 ± 10.2	82.2 ± 9.7	N/A
NREM time (min)	289 ± 84	269 ± 93	292 ± 77	171 ± 83
REM time (min)	71.5 ± 28.3	69.9 ± 24.5	68.4 ± 29.9	45.4 ± 32.3
Time supine (min)	74 ± 117	192 ± 96	190 ± 102	N/A

AHI, apnea-hypopnea index (events/hr); *AI,* apnea index (events/hr); *Time SaO_2 < 90%,* time during sleep that oxygen saturation < 90%; *Minimum SaO_2,* minimum oxygen saturation; *TST,* total sleep time; *Sleep efficiency,* total sleep time as a percent of total recording time; *Time supine,* sleep time spent in the supine position; *N/A,* not available; *PSG,* polysomnogram; *MAA,* mandibular advancement appliance.
*All values are for 21 participants except the MAA 2 PSG (n = 17).
†Results of titration polysomnogram (PSG) represent values at maximum or maximum tolerated advancement achieved with titration appliance.

Table II. Amount of mandibular advancement during the polysomnograms with the titration appliance and MAA

	Amount of mandibular advancement			
Appliance	*Mean ± SD (mm)*	*Range (mm)*	*Mean ± SD (% of maximum voluntary)*	*Range (% of maximum voluntary)*
Titration appliance† (n = 21)	7.8 ± 1.8	4.3-11.2	85.2 ± 25.8	34-143
MAA 1 (n = 21)	7.9 ± 2.1	4.25-13.0	86.8 ± 24.0	54-150
MAA 2 (n = 17)	10.1 ± 2.1*	7.25-15.0	115 ± 42*	60-225

MAA, mandibular advancement appliance.
*$P < .001$ on repeated measures ANOVA comparing the three conditions.
†The maximum advancement achieved during the manual titration.

Amount of mandibular advancement with Klearway appliance

During the MAA 1 polysomnogram, the mean mandibular advancement was 7.9 ± 2.1 mm (range, 4.25-13.0 mm) (Table II). This amount of mandibular advancement was 86.8 ± 24% (range, 54-150%) of maximal voluntary advancement. There was no difference in the amount of advancement on the MAA 1 polysomnogram compared to the maximum amount of advancement achieved during the titration polysomnogram ($P = 0.495$). The 17 subjects who performed the MAA 2 polysomnogram advanced the MAA another 2.2 ± 1.2 mm (range, 0.25-5.0 mm) beyond its position at the MAA 1 polysomnogram for a mean mandibular advancement from centric occlusion of 10.1 ± 2.1 mm (range, 7.25-15.0 mm) or 115 ± 42% (range, 60-225%) of maximal voluntary advancement (Table II). The final advancement achieved with the MAA in 7 of the participants was greater than their maximal voluntary advancement determined at the beginning of the study.

Polysomnogram results with the mandibular advancement appliance

Comparison of the baseline, MAA 1, and MAA 2 polysomnograms found no significant differences in total sleep time, sleep efficiency, time in each stage of NREM sleep, time in REM sleep, time during sleep in the supine position, or body weight (Table I). In addition, there were no differences in time spent below 90% oxygen saturation, minimum oxygen saturation, or arousal index.

On the MAA 1 polysomnogram, during which the mandible was advanced by the same amount achieved with the titration appliance, the AHI was reduced to 24.6 ± 17.1 events/hr (range, 6.3-88.8 events/hr) ($P = .01$ compared to baseline AHI, Fig. 2). AHI with the MAA was 80 ± 39% (range, 32-177%) of baseline AHI. Eight subjects had at least a 50% reduction in AHI with the MAA. AHI was < 10 events/hr in only one of these subjects.

Of the 9 subjects who had both an AHI < 10 events/hr and a 50% or greater reduction in AHI from baseline on

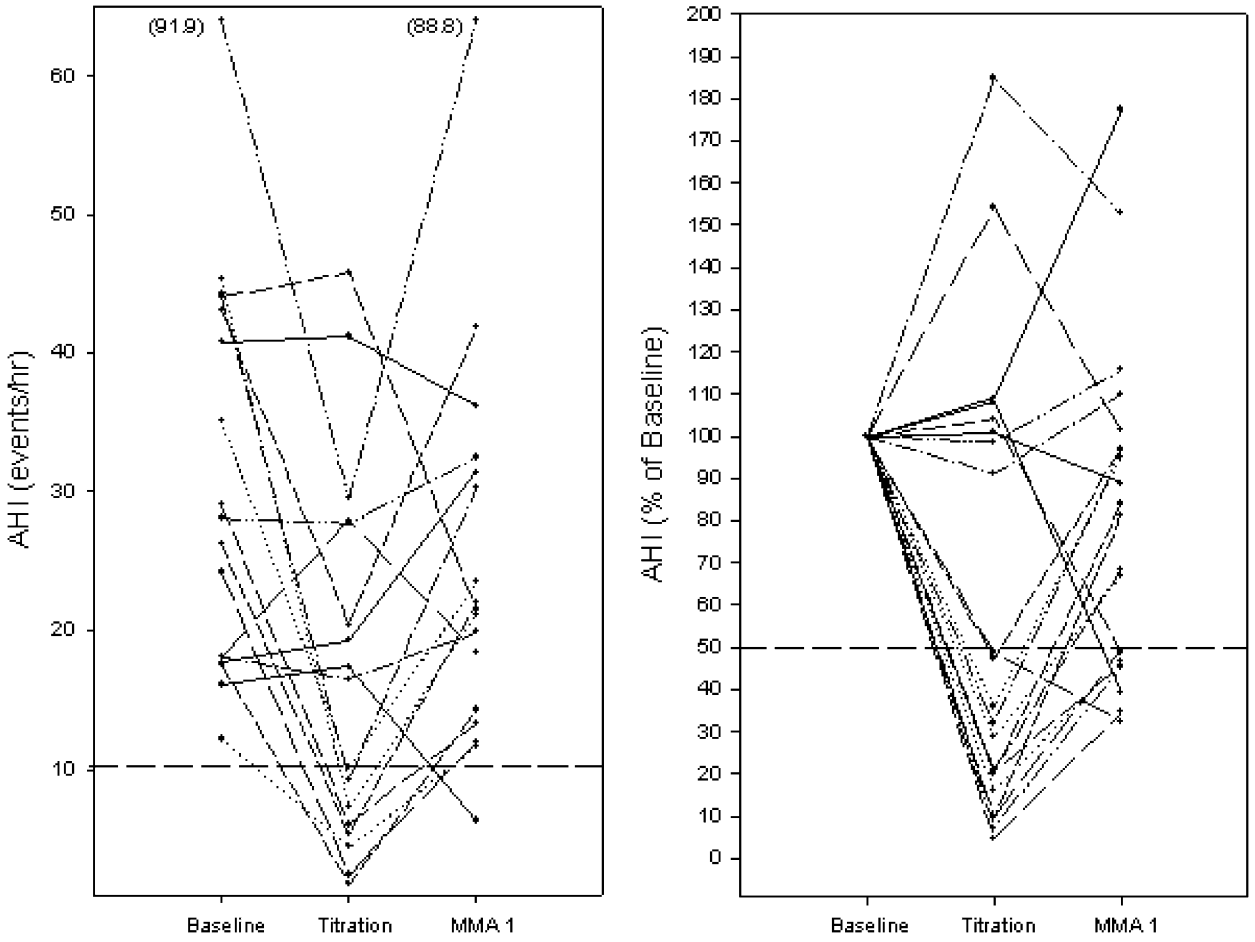

Fig. 2. Apnea-hypopnea index (AHI) in events/hr (*left*) and as a percent of baseline (*right*) in each participant on the baseline, titration and MAA 1 polysomnograms. The horizontal lines in each panel represent an AHI of 10 events/hr and an AHI that is 50% of baseline respectively.

the titration polysomnogram, none met both of these criteria on the MAA 1 polysomnogram. None of the 9 subjects who had an AHI < 10 on the titration polysomnogram had an AHI < 10 on the MAA 1 polysomnogram. Of the 13 subjects who had a 50% or greater reduction in AHI from baseline on the titration polysomnogram, only 6 had a comparable result on the MAA 1 polysomnogram. Two of the 8 subjects who had either an increase or less than a 50% reduction in AHI from baseline on the titration polysomnogram had a reduction in AHI of 50% or greater on the MAA 1 polysomnogram. Of the 12 subjects with an AHI ≥ 10 on the titration polysomnogram, one had an AHI < 10 on the MAA 1 polysomnogram.

During the MAA 2 polysomnogram, the AHI was reduced to 24.9 $\pm$ 18.8 events/hr (range, 3.9-72.9 events/hr, $P < .012$ when compared to baseline) or 70 $\pm$ 35% (range, 16-138%) of baseline AHI (Fig. 3). Three subjects had an AHI < 10 events/hr, and 4 subjects had at least a 50% reduction in AHI compared to baseline. Two subjects had both an AHI < 10 events/hr and a 50% or greater reduction in AHI on the MAA 2 polysomnogram. One individual had mild OSA and the other had severe OSA on the baseline polysomnogram. Both subjects had an AHI < 10 events/hr and a 50% or greater reduction in AHI at the maximum advancement on the titration polysomnogram.

Using different criteria to define successful treatment

The results were also examined using an AHI < 15 events/hr and at least a 50% reduction from baseline as the criteria for successful treatment. Of the 19 participants with an AHI > 15 at baseline, 13 subjects had a 50% reduction in AHI on their titration polysomnogram and 9 of those subjects had an AHI < 15 events/hr. Of the 9 participants who met both criteria on the titration polysomnogram, 2 subjects met the same criteria on the MAA 1 polysomnogram and 3 subjects met these criteria on the last MAA polysomnogram. The same

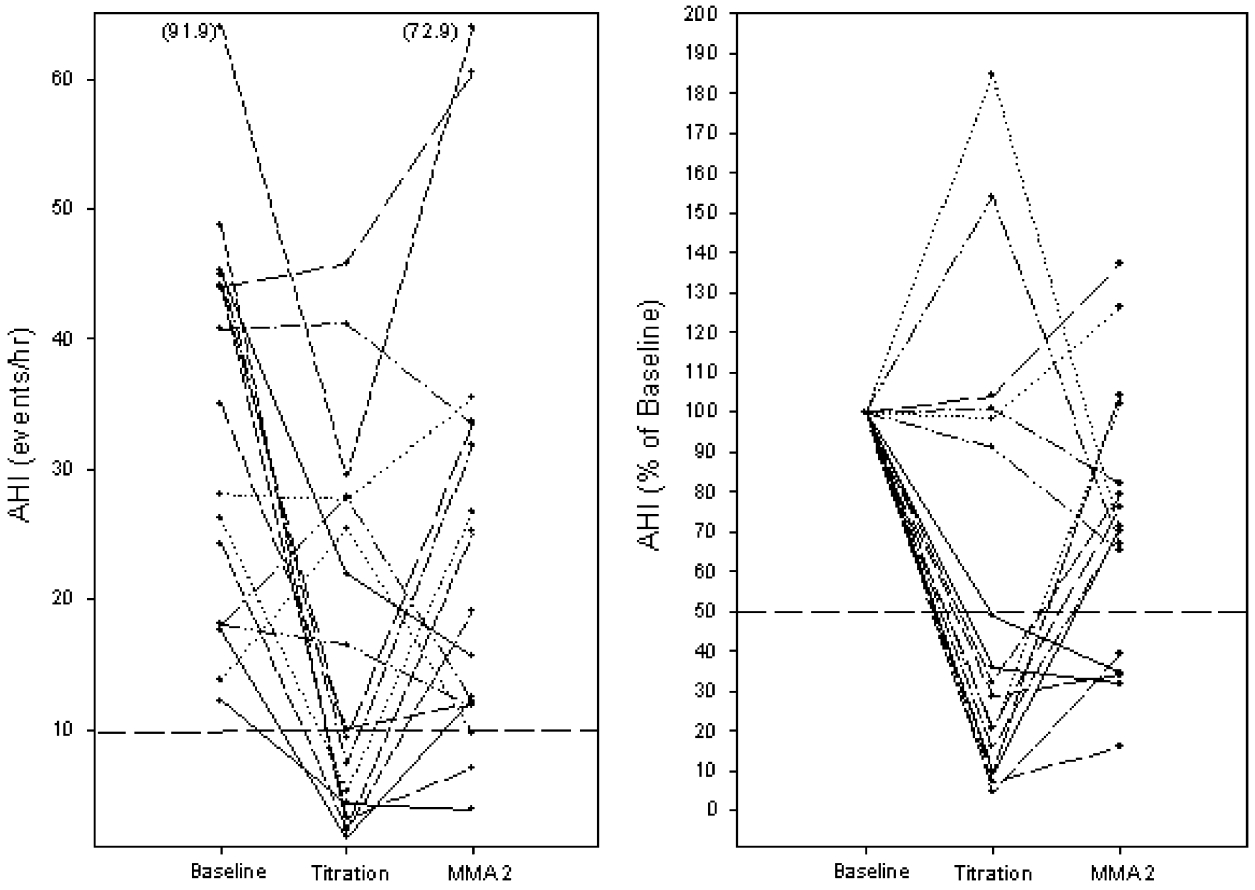

Fig. 3. Apnea-hypopnea index (AHI) in events/hr (*left*) and as a percent of baseline (*right*) in each participant on the baseline, titration, and MAA 2 polysomnograms. The horizontal lines in each panel are similar to those in Fig. 2.

results were obtained when the criteria were reduced to an AHI < 15 events/hr and at least a 30% reduction from baseline.

DISCUSSION

The results indicate that a quickly and easily constructed oral mandibular titration appliance lowered the AHI to efficacious levels in 43% of the participants, but this acute response did not predict the efficacy of long term MAA treatment. Using an AHI < 10 and a 50% or greater reduction in AHI from baseline as the criteria for treatment efficacy, 9 of the 21 subjects met these criteria on the titration polysomnogram, but none of the 21 subjects met both criteria on a subsequent polysomnogram when the MAA advanced the mandible to the same extent achieved with the titration appliance. Even when the MAA was subsequently advanced to extend the mandible to maximum tolerable levels ($115 \pm 42\%$ of maximal voluntary advancement), only 2 subjects achieved the prescribed reductions in AHI. Both subjects had a successful response with the titration appliance. Despite these negative results, the study provides some potentially interesting findings concerning oral appliance treatment.

The unexpected result of the study was the disappointing response in AHI to Klearway MAA treatment. This appliance was specifically chosen because previous studies have reported a treatment efficacy ranging from 50% to 80%.[12,15,20,22,23] Direct comparisons across studies are difficult due to the different polysomnographic criteria used to define treatment success. However, the lower success rate in the current study does not appear to be explained by differences in the baseline polysomnographic severity of sleep apnea, body mass index, age, or amount of mandibular advancement. Lowe et al.[20] report that Klearway treatment in 38 patients with OSA (mean age 44 years, mean BMI 30.3 kg/m^2) reduced the mean AHI from 32.6 (SEM 2.1) to 12.1 (SEM 1.7). The AHI was reduced to less than 15 events/hr in 80% of the 20 patients with moderate OSA and in 61% of the 18 patients with severe OSA. Mean mandibular advancement was 11.3 mm (range, 9-14 mm). In a subsequent study by these investigators of 47 patients (mean age 49 years, mean BMI 29.6 kg/m^2)

with OSA, the mean AHI of 40.3 ± 16.6 events/hr at baseline was reduced to 17.1 ± 12.3 events/hr with the Klearway appliance.[12] The Klearway appliance reduced the AHI to < 10 events/hr in 59.1% of subjects. Ferguson et al.[22] performed a crossover study comparing nasal CPAP and Klearway treatment in patients with OSA (mean age 44 years, mean BMI 32 kg/m^2, mean AHI 25.3 events/hr). Eleven (55%) of the 20 patients who used the MAA were treatment successes defined as a reduction in AHI to less than 10 events/hr and relief of symptoms. Tsai et al.[15] reported a 53% therapeutic efficacy with the Klearway appliance based on a reduction in AHI to less than 15 events/hr, a relative reduction in AHI of more than 30% from baseline, and a subjective improvement in symptoms. Based on studies using the Klearway appliance and the known night-to-night variability in AHI,[24-26] the current study was designed to obtain data on 30 patients in order to be adequately powered. However, we decided to discontinue subject recruitment prior to reaching that desired level given our less favorable results with the Klearway appliance. The results demonstrate the importance of obtaining a follow-up polysomnogram once a patient is on oral appliance treatment to evaluate its efficacy.

We speculate that the relatively prolonged time interval between the baseline and MAA polysomnograms may explain our failure to reproduce the Klearway results of previous investigators. When initiating oral appliance treatment, standard practice is to advance the mandible slowly over time in order to allow bone and soft tissue structures to adjust to the displacement. This normally results in a relatively prolonged time interval from the start of treatment to when the desired amount of mandibular advancement is achieved. The time intervals from baseline to the MAA polysomnograms in the current study were higher than those reported by previous studies in which adjustment intervals ranging from 3 months to over 12 months.[22,27,28]

The prolonged adjustment interval may be of importance because long term use of the oral appliance has been shown to result in anatomic changes. Bondemark[29] performed cephalograms in centric occlusion in 30 individuals before and following 2 years of oral appliance treatment and found forward and downward changes in mandibular position. These changes may alter the polysomnographic efficacy of oral appliance treatment over time at a given level of advancement. Rose et al.[30] studied the long-term efficacy of an oral appliance (Karwetzky activator) on respiratory and sleep parameters in 26 patients with mild to moderate OSA. The mean AHI decreased from 17.8 events/h at the baseline to 4.2 events/hr at 6 to 12 weeks of treatment, 8.2 events/hr after 6 to 12 months of treatment and 8.3 events/hr 18 to 24 months later. In most patients, therapeutic efficacy was maintained at the 2-year follow-up, although there was a tendency for effectiveness to fall over time. These results raise the possibility that changes in tissue characteristics with use of the oral appliance over time may have contributed to the relatively poor outcome to treatment with the mandibular advancement device. Additional studies are needed to determine the long term efficacy of oral mandibular advancement appliance treatment.

We do not believe that different results would have been obtained if a different MAA device had been selected. Despite the wide variation in their designs, commercially available MAA devices have similar efficacies reported on polysomnographic testing.[28,34-36] Studies using other MAAs also report similar amounts of mandibular advancement as that tested in the current study, generally at or above 80% of maximum voluntary advancement. We excluded the possibility that our MAA results might have been due to the polysomnographic criteria we selected to define successful treatment.[36] There are no uniformly applied polysomnographic criteria defining successful treatment with a MAA. Some studies use a certain percent reduction in AHI as the sole criterion while others also include a reduction in AHI below a certain number of events/hr. However the exact cut-offs for both percent reduction and reduction in events/hr often vary from study to study. The results of our study did not change even when we analyzed our data using several different criteria reported in the literature.

The different effects of the manual titration and MAA in the current study may have been due to differences in the design of the appliances that led to different mechanical effects on the pharyngeal airway.[33] The two appliances in the current study use different mechanisms to advance the mandible. The MAA appliance has metal struts located in the anterior oral cavity and under the hard palate that may crowd the tongue. In contrast, the titration appliance has projections extending out of the mouth that were used to manually advance the mandible. The titration appliance has greater bulk than the custom molded trays of the MAA, but has no hardware in the oral cavity. The two appliances may also have had different effects on the amount of bite opening. Bite opening with the appliances was not quantified, but attempts were made in the construction of the titration appliance to minimize bite opening by firmly pressing the trays into the upper and lower arches when making the dental impressions. Mouth opening is reported to affect pharyngeal collapsibility.[37] However, Pitsis et al.[38] recently reported that altering the amount of bite opening of a mandibular advancement device did not alter its polysomnographic effects in patients with OSA.

The EMA-T appliance was easy to construct and generally well tolerated by the participants. Its simple design gives it the potential advantage of easy access and wide applicability. The more complicated designs of the titration appliances used by two previous studies allowed these appliances to be adjusted remotely allowing changes in mandibular position to be made without waking the subject.[15,16] In contrast, the EMA-T appliance requires manual adjustment necessitating the awakening of the patient with each change in position. In the current study, total sleep time was shorter on the titration compared to the baseline and MAA polysomnograms. This may have resulted from the awakenings needed to adjust the appliance as well as participants adapting to using an oral appliance for the first time. Nevertheless, the shortened total sleep time did not prevent adequate titration. In general, the maximum tolerated advancement was achieved relatively early in the recording and the mean sleep time at the maximum tolerated advancement was 209.3 ± 106.0 min (range, 47.1-362.5 min).

The other difference between EMA-T and previous reported titration appliances is that changes in mandible position with EMA-T are limited to 3-mm increments as opposed to the 1-mm increments that could be achieved with the previously reported titration appliances.[15,16] The smaller incremental changes would be advantageous if, as demonstrated by the study of Pételle et al.[16] the level of advancement determined on the titration night was the same as that needed for long-term treatment efficacy. However, the study of Tsai et al.[15] had a 4 ± 3 month interval between the titration and the Klearway polysomnogram and reported that a single night titration procedure did not determine the optimum amount of advancement. Most studies report that the mandible needs to be advanced to maximum or near maximum to achieve an acceptable reduction in AHI. This is supported by the current study in which mandible was advanced to 85.2 ± 25.8% of maximum voluntary advancement to obtain a successful outcome with the titration appliance. These findings suggest that the goal of MAA treatment should be to advance the mandible to maximum tolerable levels and that fine increments in mandibular advancement with a titration appliance may not be required.

Although the current study and that of Tsai et al.[15] failed to show a role for the titration of a precise amount of mandibular advancement, other studies have demonstrated a dose-dependent effect on mandibular advancement on sleep-disordered breathing.[17,31,32] These latter studies report that progressive advancement of the mandible is associated with a progressive improvement in sleep disordered breathing. During a single overnight polysomnogram in 6 patients with OSA, Raphaelson et al.[17] progressively advanced the mandible using a Silencer appliance (John's Dental, Terre Haute, IN) and showed a relationship between mandibular advancement and AHI. As in the current study, the subjects were awakened during the night to adjust the device and advance the mandible. Kato et al.[31] demonstrated a dose dependent reduction in closing pressure with mandibular advancement in anesthetized, paralyzed patients with OSA who also performed 3 home overnight oximetry recordings with a fixed oral appliance advancing the mandible by 2, 4, and 6 mm. Each 2-mm advancement of the mandible was associated with a 20% improvement in oxygen desaturation index. De Almeida et al.[32] found a progressive decrease in AHI when serial polysomnograms were performed in 6 patients with OSA wearing a Klearway appliance at progressive amounts of mandibular advancement. Given the above findings reporting a dose-dependent effect of mandibular advancement on sleep disordered breathing in overnight or consecutive night recordings, additional long-term studies are needed to determine if a precise amount of advancement should be identified with the titration appliance prior to initiating oral appliance treatment.

The study had a number of limitations that may have influenced the results. First, the study had a relatively high participant attrition rate. However, no differences in demographics or severity of OSA could be identified between the individuals withdrawing from or completing the study. One would predict that the attrition rate might have improved outcomes, since it is probable that non-responders would be more likely to withdraw. Another limitation of the study was the heterogeneity of the population studied in terms of exposure to other treatments (other oral appliances, CPAP, UPPP). We did not exclude individuals who had received previous treatment for their OSA as this is the most common type of patient presenting for oral appliance therapy. The lower success rate in the current study is particularly surprising as 6 of the 21 subjects were status postuvulopalatopharyngoplasty. Millman et al.[14] report that these individuals are more likely to have a successful response to oral appliance treatment. Based on this observation, one can speculate that MAAs may have a greater dilating and stiffening effect in the retroglossal as opposed to the retropalatal region of the pharynx. Indeed, our two subjects who had an acceptable response on their MAA polysomnogram had had this surgery.

In summary, the current study demonstrates the feasibility of performing an overnight mandibular advancement titration polysomnogram using a manually adjusted oral appliance in patients with OSA. The titration appliance was well tolerated and reduced the AHI to acceptable levels in 43% of the subjects. These acute results, however, were not borne out on subsequent

polysomnographic testing with the oral appliance that the patients had used for long-term treatment at home. It is possible that results were affected by the prolonged time intervals between testing and the specific oral appliance used for home treatment. Although this method of titration may be helpful in determining the correct amount of advancement from a research perspective, its use from a clinical, practical, and economic standpoint may not be warranted. Although the results do not support the initial hypotheses, they nevertheless raise some interesting questions regarding the design and long term efficacy of oral appliances that need to be addressed in order to better understand the role of oral appliance therapy in patients with OSA.

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