Remotely Controlled Mandibular Positioner Predicts Efficacy of Oral Appliances in Sleep Apnea

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Anterior mandibular positioners (AMPs) have become increasingly popular as alternatives to continuous positive airway pressure for the treatment of obstructive sleep apnea. However, widespread acceptance of AMP is limited by an efficacy rate of 50–80% and an inability to predict which patients will respond to therapy. We evaluated 23 patients with obstructive sleep apnea (respiratory disturbance index [RDI] $\geqslant$ 15 h^{-1}) with a remotely controlled mandibular positioner (RCMP), a temporary oral appliance that can advance or retract the mandible in a process analogous to changing the mask pressure during a continuous positive airway pressure titration study. We hypothesized that the elimination of respiratory events and significant nocturnal oxygen desaturation during an RCMP overnight study would predict AMP efficacy, as defined by an absolute reduction in RDI to less than 15 h^{-1}, a relative reduction in RDI of more than 30% from baseline, and a subjective improvement in symptoms. AMP compliance was 82%, and therapeutic efficacy was 53%. Among compliant patients, the positive and negative predictive value of an RCMP study in predicting AMP treatment success was 90% and 89%, respectively. An overnight RCMP study is highly predictive of AMP response.

Keywords: obstructive sleep apnea; treatment; oral appliance; diagnosis

Nasal continuous positive airway pressure (CPAP) is a highly efficacious treatment for obstructive sleep apnea (OSA); however, effectiveness is limited by compliance rates of between 60% and 80% (1–3). Oral appliances, such as anterior mandibular positioners (AMPs), may provide therapeutic alternatives to CPAP; however, treatment success rates range from between 50 and 80% (4–12). Unfortunately, the inability to predict prospectively which patients will benefit from treatment with AMP has limited its widespread use, as AMPs must be custom constructed for each patient.

Remotely controlled mandibular positioners (RCMPs) may provide a prospective means for predicting AMP treatment outcome. Such a device is applied during a sleep study, wherein the patient is fitted with a trial oral appliance. A stepping motor attached to the appliance protrudes or retrudes the mandible as directed by a remotely stationed technician. In a process analogous to a CPAP titration study, the mandible is progressively advanced during sleep until respiratory events are eliminated. We hypothesized that the successful elimination of respiratory events and oxygen desaturation by mandibular protrusion during sleep predicts AMP treatment response.

METHODS

Patients were recruited from the Alberta Lung Association Sleep Centre, which is the major referral center for southern Alberta. The sleep center draws from a wide variety of referral sources, including family physicians, internists, otolaryngologists, psychiatrists, and dentists.

As part of standard management, patients with newly diagnosed OSA are offered a variety of treatment options, including behavioral and lifestyle modification, CPAP therapy, uvulopalatopharyngeoplasty, or an oral appliance. All patients who had OSA and who were elected for therapy with an oral appliance (i.e., AMP) were approached for participation in the study. OSA was defined as a respiratory disturbance index (RDI) of 15 h^{-1} or more using a validated portable monitor (discussed later here).

Patients who agreed to participate underwent a baseline clinical evaluation and diagnostic testing with a portable monitor. An overnight RCMP study was then performed, followed by a referral to one of two dentists (L.D., B.R.) for fitting with the Klearway oral appliance (Space Maintainers, Calgary, AB, Canada). After an initial dental assessment and fabrication of the AMP, the dentist progressively advanced the mandible until the patient reported an improvement in OSA-related symptoms, snoring decreased as reported by the bed partner (optimal mandibular advancement), or maximally tolerated advancement was achieved. The rate of advancement was individualized according to patient tolerance. Once optimal mandibular advancement or maximally tolerated mandibular advancement was achieved, patients underwent a repeat clinical assessment and determination of their post-treatment RDI using the portable monitor. Both the dentist and patient were blinded to the results of the RCMP sleep study. Patients were also asked whether they experienced a qualitative improvement in OSA-related symptoms. A summary of the diagnostic and therapeutic process is outlined in Figure 1.

Portable Monitoring

The RDI was assessed at baseline and at study termination using a portable monitor, which digitally records oxygen saturation, snoring sounds, and body position. An offline algorithm analyzes the nocturnal oxygen saturation signal to determine the RDI. The monitor-derived RDI has excellent diagnostic performance characteristics for OSA and provides a close estimate of polysomnography-derived apnea hypopnea index (AHI) (13, 14). Using an AHI diagnostic criterion value of 15 h^{-1} or more, the analysis algorithm has a sensitivity and specificity of 98% and 88%, respectively (13).

Construction of the Temporary Appliance

A trial oral appliance was constructed by taking a bite registration using Polysil TransBite (SciCan, Alpenstrasse, Switzerland) and preformed upper and lower dental trays (Space Maintainers). The initial jaw position was obtained with the teeth in centric occlusion. The registration material is translucent and permits the operator to ensure that the incisor teeth are fully seated in each tray to reduce the amount of vertical opening. Construction of each trial appliance took approximately 10 minutes.

RCMP Study

A stepping motor was attached to a strut extending from the lower arch tray. Rotation of the motor extended the lower tray, thus advancing the mandible (Figure 2). A linear potentiometer provided feedback that quantified the protrusive distance from the initial centric occlusion position. The stepping motor was controlled remotely using a Windows (Microsoft, Redmond, WA)-based interface on a personal computer via a control wire.
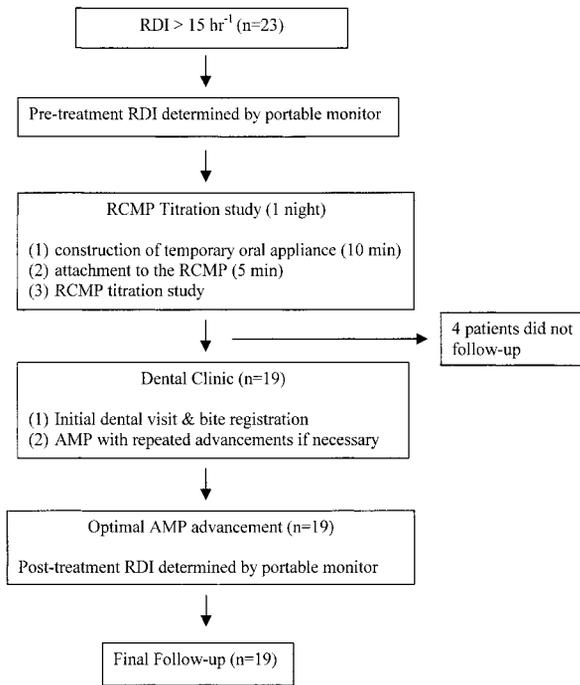
Figure 1. Diagnostic and therapeutic pathway for remotely controlled mandibular positioner (RCMP) titration and anterior mandibular positioner (AMP) treatment.

All polysomnography data were recorded by a computerized polysomnographic system (Sandman; Nellcor Puritan Bennett [Melville] Ltd., Ottawa, ON, Canada). The standard montage consisted of a single-channel electroencephalogram (C4/A1), an electrooculogram, a sub-mental electromyogram, an electrocardiogram, and digitally recorded snoring sounds. Airflow was qualitatively assessed using nasal prongs coupled to a pressure transducer (Valydyne, Northbridge, CA). Respiratory effort was detected by inductance changes on plethysmography (Respitrace, Ambulatory Monitoring, Ardsley, NY). Oxygen saturation was recorded using a finger oximeter (Model 3700; Ohmeda, Denver, CO).
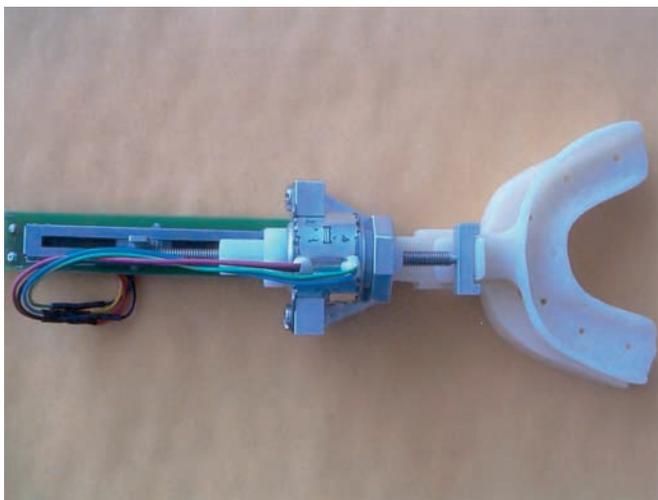
Figure 2. The RCMP. The arch trays (*far right*) are attached to a stepper motor (*left*), which is capable of advancing them via a connected rotating strut (*middle screw*). The trays do not have the bite registration material in place.

Supraglottic pressure was assessed using a 5F water-filled pediatric feeding tube (Med-Rx; Benlan Inc., Oakville, ON, Canada) coupled to an arterial line pressure transducer (Medex Inc., Hilliard, OH). The supraglottic catheter was introduced intranasally and positioned with the tip just above the epiglottis.

Graduated mandibular advancement was initiated after visualization of baseline obstructive respiratory events and stable stage 2 sleep. An obstructive event was defined as a 10-second or more discernible reduction in either airflow or thoracoabdominal effort, associated with a 3% or more drop in oxygen saturation and increased pressure deflections in supraglottic pressure. The supraglottic catheter was used primarily to exclude patients with central sleep apnea (> 75% of respiratory events lacking increased pressure deflections in supraglottic pressure), in addition to use in another study. It was not used for titration.

The mandible was advanced in 1-mm increments until optimal advancement (i.e., elimination of majority of obstructive apneas, hypopneas, and nocturnal oxygen desaturation) was achieved. The vertical dimension was kept closed as much as possible to prevent clockwise rotation of the mandible. If a protrusive step appeared to induce an awakening on the electroencephalogram, further advancement was forestalled until stable sleep (at least three epochs of sleep without arousals) returned. In the event that the patient awoke from sleep and was unable to fall asleep again within 10 minutes, the mandible was retracted to the neutral or centric occlusion position (0-mm advancement). The advancement process was then reinitiated after stable sleep. Once optimal advancement was achieved, no further adjustments were made.

Quantitative sleep staging was unavailable because technical limitations (channel availability) allowed only a single EEG channel to be used.

RCMP Scoring Criteria

An RCMP study was deemed predictive of AMP treatment success if the majority of apneas, hypopneas, and oxygen desaturations were eliminated with a total mandibular advancement of less than 15 mm. The cut-off value of 15-mm mandibular protrusion was prospectively selected based on the observation that many patients do not tolerate mandibular advancement beyond 15 mm. Ideally, the patient was evaluated in supine and nonsupine body positions, but this was not consistently feasible.

AMPs

The patient was subsequently referred to a dentist (B.R., L.D.), who fitted the patient with a permanent AMP. The oral appliance is a screw adjustable prosthesis that allows for progressive mandibular protrusion over time. Previous generation oral appliances were permanently fixed at a prespecified mandibular advancement, thus rendering it impossible to change the settings in the event of poor patient tolerance or insufficient advancement to achieve therapeutic results. The combination of a thermoelastic acrylic resin to increase retention and the ability to advance progressively the mandible over a several week period are reported to increase patient compliance (10). In a randomized control trial comparing Klearway to CPAP, therapeutic efficacy was determined to be 71% (11).

Assessment of AMP Treatment Efficacy

Therapeutic efficacy was defined as the success rate among patients who agreed to the therapeutic intervention and were available for post-treatment evaluation. AMP therapy was deemed successful if the patient was at optimal mandibular advancement or maximally tolerated mandibular advancement and if all of the following criteria were met: the RDI was reduced to an absolute value of less than 15 h^{-1}, the RDI was reduced by more than 30% from the baseline RDI, and a subjective improvement in symptoms was reported. A 30% reduction in RDI was included in the outcome criteria to prevent small reductions in RDI close to diagnostic threshold levels from being considered a treatment success (e.g., a reduction in RDI from 17 to 14 h^{-1}). Because a number of criteria for evaluating treatment success have been employed in the research literature, for comparison purposes, AMP success was also assessed using a reduction in RDI of less than 15 h^{-1} alone, symptom reduction alone, and very rigid criteria (RDI < 15 h^{-1}, ⩾ 50% reduction in RDI from baseline, and improved quality of life).

The clinician assessing clinical efficacy was blinded to the results of the RCMP study. Furthermore, the RDI was determined using an automated analysis algorithm, thus providing blinded objective scoring of RDI. Compliance was defined as self-reported nightly use of the AMP at the time of trial follow-up.

Statistics

Descriptive analysis was performed, and non-normally distributed variables were geometrically transformed for the purpose of summary statistics. Pretreatment and post-treatment RDI were compared using the paired t test. Two-by-two frequency tables were constructed, cross-tabulating RCMP predicted success rates against AMP treatment outcome. Positive and negative predictive values were determined. Simple logistic regression was employed to identify potential clinical predictors of treatment success. Baseline RDI, body mass index, neck size, Epworth sleepiness score, and age were used as independent variables. The study was approved by the Conjoint Ethics Committee, University of Calgary.

RESULTS

Patient Characteristics

Twenty-three patients agreed to participate in the study. Table 1 outlines patient characteristics. Patients tolerated the RCMP study well. In no case was an RCMP study terminated because of an inability to tolerate the trial oral appliance. Four patients underwent RCMP studies but either declined AMP therapy or did not return for scheduled advancement of the AMP (Figure 1). Two of these patients were predicted to be treatment successes, and two were predicted to be treatment failures. Consequently, 19 patients went on to be fitted with a permanent AMP.

All 19 patients reported using the oral appliance nightly for more than 4 hours (reported compliance of 82%). The dentist progressively advanced the mandible until the patient reported an improvement in OSA-related symptoms, snoring decreased as reported by the bed partner, or maximally tolerated protrusion was achieved. This process took 4 ± 3 months. A repeat determination of the RDI was then obtained.

Treatment Effects

Mean RDI was significantly reduced from 34 ± 4.9 to $17 \pm 4.7\ h^{-1}$ after treatment with the Klearway AMP at optimal advancement ($p < 0.0001$). Ten patients were considered treatment successes, as defined by an absolute RDI reduction of less than $15\ h^{-1}$, an RDI reduction of more than 30% from baseline, and a subjective improvement in symptoms. AMP effectiveness was thus 53%.

RCMP predictive ability is summarized in Table 2. If the RCMP predicted treatment success, the chance of a successful AMP treatment outcome (positive predictive value) was 90%. With an unfavorable RCMP study, the chance of AMP treatment failure (negative predictive value) was 89%. Table 3 summarizes RCMP predictive ability using a variety of criteria for defining AMP success. Figure 3 graphically summarizes AMP treatment outcome against RCMP predicted outcome.

TABLE 1. SUMMARY OF PATIENT CHARACTERISTICS (n = 19)

Patient Characteristics	Mean ± SE	Range
Age, yr	47.0 ± 2.14	30–64
Sex, male:female		19:1
Body mass index, kg/m²	32.0 ± 1.28	25.0–45.4
Neck circumference, cm	42.0 ± 1.04	38–51
Epworth sleepiness scale	14.0 ± 1.44	4–21
Baseline RDI, h⁻¹	34.0 ± 4.88	15–89

Definition of abbreviation: RDI = respiratory disturbance index.

TABLE 2. REMOTELY CONTROLLED MANDIBULAR POSITIONER PREDICTION OF ANTERIOR MANDIBULAR POSITIONER TREATMENT SUCCESS

	AMP Treatment Outcome	
RCMP Prediction	Success	Failure
Success	9	1
Failure	1	8
Total	10	9

Definition of abbreviations: AMP = anterior mandibular positioner; RCMP = remotely controlled mandibular positioner.

Adverse Effects

In the 19 patients who completed the study, adverse effects included jaw discomfort (four patients), repetitive breakage of the oral appliance (one patient), and initial difficulties with gagging (one patient).

Assessment of Clinical Predictors

Baseline RDI, body mass index, neck size, Epworth sleepiness score, and age were not predictive of Klearway treatment success. As such, no attempt was made to combine clinical variables with RCMP results in a prediction model.

It was not possible to determine whether the RCMP could predict final protrusion with the permanent oral appliance. The average protrusion at the end of the study was 11.4 ± 2.4 mm, whereas the RCMP predicted optimal advancement was 11.0 ± 3.1 mm. Although the average protrusions appeared similar, the number of patients was small. Moreover, the individual protrusion values determined by the RCMP and those at the end of the study displayed extensive scatter; thus, no meaningful correlations could be made.

DISCUSSION

Twenty-three patients were evaluated with an RCMP study, followed by treatment with AMP. The AMP compliance rate was 82%, with a treatment efficacy rate of 53%. The RCMP study had positive and negative predictive values of 90% and 89%, respectively, for predicting AMP treatment outcome.

In a randomized controlled trial involving 34 patients with mild OSA (RDI = $5–15\ h^{-1}$), patients experienced an improvement in daytime performance with CPAP, but only 14 preferred CPAP to oral placebo (15). As such, identifying therapeutic alternatives to CPAP for the treatment of OSA would be beneficial. AMPs provide such an option, but are limited by therapeutic efficacy rates ranging from 50–80% (4–9). In this study, the AMP efficacy rate of 53% is consistent with the existing literature. Despite being less efficacious than CPAP, some patients prefer AMP to CPAP (11). However, this is not consistently the case (16). Widespread acceptance of AMPs is limited by an inability to identify prospectively patients who will benefit from AMP therapy.

A number of attempts have been made to predict AMP treatment success. Clinical predictors, cephalometry, and computerized tomography have been used with varying results (17). In a series of 19 patients who were unable to tolerate CPAP and were subsequently treated with an oral appliance, Eveloff and colleagues identified four cephalometric measurements that were predictive of post-treatment AHI (8). A linear regression model was developed using baseline AHI and the cephalometric measurements as independent variables. However, from a practical standpoint, the need to combine weighted coefficients in a linear regression model is cumbersome. More importantly, no

TABLE 3. REMOTELY CONTROLLED MANDIBULAR POSITIONER PREDICTION OF ANTERIOR MANDIBULAR POSITIONER TREATMENT SUCCESS USING DIFFERENT OUTCOME CRITERIA

RCMP Diagnostic Characteristics	Criteria 1	Criteria 2	Criteria 3	Criteria 4
PPV	90	90	90	60
NPV	89	67	78	89
Sensitivity	90	75	81	86
Specificity	89	86	88	67

Definition of abbreviations: NPV = negative predictive value; PPV = positive predictive value; RCMP = remotely controlled mandibular positioner.

Criteria 1: respiratory disturbance index < 15 h^{-1}, respiratory disturbance index reduction $> 30\%$ from baseline, improved symptoms. Criteria 2: respiratory disturbance index < 15 h^{-1}. Criteria 3: symptom improvement. Criteria 4: respiratory disturbance index < 15 h^{-1}, respiratory disturbance index reduction $> 50\%$ from baseline, improved symptoms.

attempt was made to predict symptomatic improvement. Furthermore, the predictive value of cephalometric measurements has not been supported by other researchers (17).

Simple measurements such as body mass index and baseline capacity for mandibular protrusion do not correlate with AHI reduction (7). However, several studies suggest that treatment with an oral appliance is less effective in patients with a high baseline AHI (7, 8, 12). Marklund and colleagues suggested that treatment success may correlate inversely with disease severity (18). Similarly, O'Sullivan and colleagues (7) reported that the best predictor of treatment response is an untreated AHI between 20 and 60 h^{-1}. In contrast, these results failed to demonstrate baseline RDI, body mass index, neck size, Epworth sleepiness score, or age as being predictive of AMP treatment outcome.

A more recent study evaluated 26 patients with OSA (AHI $\geq$ 15 h^{-1}) (19). Treatment success was defined by a reduction in AHI to less than 10 h^{-1}. The AHI was only mildly predictive of treatment success (odds ratio of 7.5 for patients with a baseline AHI < 20 h^{-1}). However, patients with supine-dependent OSA (supine AHI ≥ 10 h^{-1} and a lateral AHI < 10 h^{-1}) had an odds ratio of 30 for AMP treatment success.

Currently, the use of clinical predictors to determine AMP treatment outcome prospectively has produced conflicting results. The lack of consistent or even clearly defined inclusion criteria or treatment outcomes explains some of this variability. Additionally, the small sample sizes in existing studies have resulted in most studies being of insufficient statistical power. Most studies tested a large number of measurement variables on a small number of patients, thus raising concerns with respect to the validity of high-order statistical modeling. The predictive value of supine-dependent sleep apnea is compelling but needs to be reproduced in larger population samples.

Recently, in a small pilot study (n = 6), Petelle and colleagues demonstrated that mandibular advancement titration could predict dental appliance efficacy on a second treatment night (20). The AHI reduction using a single-night mandibular advancement study, using a temporary dental appliance, demonstrated a similar AHI to that seen on a follow-up evaluation using a permanent dental appliance.

The Petelle and colleagues study supports the possible use of RCMP as an alternative to clinical prediction rules or cephalometry. In this pilot study, the RCMP had a high positive and negative predictive value for prospectively determining AMP treatment outcome among compliant patients. Although we evaluated only a small number of patients, the results are impressive, particularly given the physiologic basis for the RCMP's predictive ability. Moreover, the RCMP platform provides an excellent research tool for evaluating the effects of mandibular advancement on upper airway physiology.

Nevertheless, criticism could be raised with respect to the criteria used to determine AMP treatment efficacy. However, the primary criteria (an absolute RDI reduction, a relative reduction in RDI of 30% from baseline, and symptom relief) were more rigid than those employed in other efficacy studies. Most oral appliance studies used a fall in RDI below a specific threshold to define success but did not necessarily link it to a percentage fall in RDI or symptom relief. A 50% reduction in RDI has been cited in some surgical studies evaluating uvulopalatopharyngeoplasty, but these studies employed either an RDI reduction below a certain threshold or a 50% reduction in RDI. This is a much more liberal interpretation of success.

Similarly, criticism could be directed toward the choice of an RDI of 15 h^{-1} to determine treatment success. This cut-off was selected because the receiver operating characteristics of the portable monitor are optimal at this point. The problem with small differences in RDI markedly changing the prevalence of disease (or operating characteristics of device) has been well illustrated in other studies (21, 22). In both studies, variability in the prevalence of disease was less pronounced at an AHI of 15 h^{-1} than at lower values. In other words, a difference of 3 h^{-1} is not considered clinically significant, but if most patients have AHIs close to the diagnostic cut-off level, the prevalence of disease may change substantially. This is illustrated in Figure 1, where a single patient had a substantial drop in the RDI, but if an RDI of 10 h^{-1} was chosen to determine success, they would be considered a therapeutic failure.

Our study based symptomatic improvement on the subjective impression of the patients, rather than a validated health-related
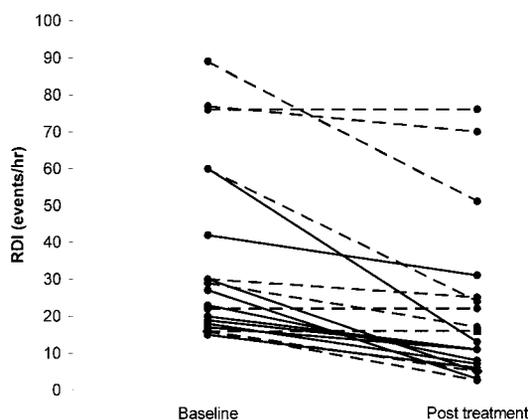
Figure 3. Respiratory disturbance index (RDI) at baseline and after treatment with AMP. The *dotted lines* represent patients in whom the RCMP predicted failure, whereas the *solid lines* represent patients in whom the RCMP predicted success.

quality-of-life instrument. Unfortunately, such tools were unavailable at the time of study initiation. Since this time, at least two such instruments have become available (23, 24). Given that most patients treated with oral appliances have a relatively low RDI and are thus treated for alleviation of daytime hypersomnolence, objective measurement of health-related quality of life is of at least equivalent importance to RDI reduction as an outcome measure.

Finally, RCMP prediction of AMP treatment outcome requires overnight admission to a sleep center. Moreover, although the RCMP predicted treatment outcome, at an individual level, the RCMP-predicted advancement was not the same as dentist-determined advancement. It remains to be determined whether the RCMP proves more cost-effective than simply engaging in an empiric AMP trial or alternatively using a temporary device at maximally tolerated advancement during the study night.

Conclusions

In summary, AMP has a therapeutic efficacy rate of approximately 50%. Currently, the use of clinical measurements to predict AMP treatment outcome has produced variable results. The RCMP is promising, both as an instrument for predicting AMP treatment outcome, as well as a platform for investigation of upper airway physiology in OSA. Nevertheless, larger clinical outcome trials and an assessment of cost-effectiveness are necessary.

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