Effectiveness and Outcome of Oral Appliance Therapy

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KEYWORDS

- Oral appliances therapy • Obstructive sleep apnea
- Continuous positive airway pressure
- Mandibular advancement splints

Oral appliances (OAs) are indicated as a primary treatment option for snoring and mild to moderate obstructive sleep apnea (OSA)[1] and are also being implemented as a noninvasive alternative for patients with severe OSA who are unwilling or unable to tolerate continuous positive airway pressure (CPAP) for the management of their disease. CPAP is an effective treatment for the management of sleep-disordered breathing in both adults and children but has low adherence rates. Therefore, OAs play an important role in the therapy for patients with OSA. There is continued emergence of studies demonstrating the ability of OAs to eliminate or significantly reduce the symptoms of OSA and produce a measurable influence on the long-term health effects of the disease. Most studies have evaluated one type of OA, mandibular advancement splints (MAS). Therefore, this article describes the effectiveness and outcomes of MAS.

Over the past decade, several randomized controlled clinical trials have been conducted comparing the effects of MAS against both placebo devices[2–10] and CPAP.[2,3,11–22] The efficacy of MAS has been reviewed previously, including a Cochrane review[23] and a practice parameter update by the American Academy of Sleep Medicine[1]; all together, there is a considerable body of evidence toward the efficacy of MAS in the treatment of OSA. To summarize the efficacy studies, in randomized controlled trials comparing MAS with placebo, MAS have been shown to significantly improve objective sleep measurements, such as the apnea-hypopnea index (AHI), arousal index, snoring, and in some but not all studies, arterial oxygen desaturation. MAS have also been shown to significantly improve subjective and objective measurements of sleepiness, quality of life, and 24-hour blood pressure measurement devices.[2–10] A variety of randomized controlled trials have compared the efficacy of MAS with CPAP.[2,3,11–18] According to

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these trials, both CPAP and MAS improved objective sleep measurements, such as AHI, arousal index, and minimum arterial oxygen saturation. Although CPAP and MAS have similar improvements in cardiovascular outcomes and inflammatory markers,[24] the magnitude of improvements in AHI and oxygen saturation was significantly greater with CPAP. This contradiction may likely be related to a higher adherence to MAS compared with CPAP in terms of hours per night and nights per week of usage.[3] **Table 1** summarizes the outcomes of the most recent studies.

MAS increase the upper airway by preventing the tongue and soft tissues of the throat from collapsing into the pharynx while holding the mandible and attached soft tissues, including the tongue base forward, which enlarges the upper airway dimensions by specifically increasing the lateral dimensions of the velopharynx.[25]

FACTORS IMPACTING THE EFFECTIVENESS OF OSA TREATMENT WITH MAS

Adherence

Adherence has been defined by the World Health Organization as "the extent to which a person's behavior – taking medications, following a diet, and/or executing lifestyle changes, such as using CPAP or MAS every night – correspond with agreed recommendations from a heath care provider."[26] Poor adherence to long-term treatment is often a problem faced by health professionals, and unfortunately there is a paucity of specific training in adherence management for practitioners. To improve adherence, it is known that a patient-centered treatment approach is crucial and patient preferences and lifestyle has to be taken into account. The consequences of a nontailored method with poor patient adherence are related to poor health outcomes and increased health care costs.

The effectiveness of mandibular advancement device (MAD) therapy depends on patient adherence to wear the device comfortably, and appliances that are custom made and adjustable have been found to be more effective than the fixed, thermoplastic-type appliances.[27,28] Vanderveken and collaborators[27] have shown that prefabricated, off-the-shelf appliances are less effective and less accepted by patients and, therefore, should not be used either as a therapeutic option or as a screening tool to predict MAS responders.

An area where MAS are described to excel compared with CPAP is the rate of patient adherence to the prescribed treatment regimen. Adherence is usually measured subjectively, and self-reported compliance with appliance use has been reported to be as high as 96% in patients using MAS for more than 75% of nights and 80% in patients using MAD more than 75% of each night.[12] The bias that can accompany self-reported adherence is highlighted by one study whereby a compliance monitor indicated that the MAD was worn for a mean of 6.8 hours per night.[29]

According to randomized controlled trials, CPAP therapy is consistently more effective at reducing sleep-disordered breathing events, but patients tolerate MAS better.[2,3,11–18] The superior patient satisfaction associated with the use of MAS reflects the relative simplicity and convenience of this form of treatment. Despite residual apneas with MAS, or a higher efficacy rate of CPAP in reducing the AHI, the similarities in treatment outcomes have been previously hypothesized to be related to the numbers of hours per night of use. MAS used for prolonged hours with partial efficacy may result in similar outcomes compared with CPAP being fully effective for only part of the night. A patient-tailored treatment is synonymous with good medicine, and life-long therapies are dependent on patients' cooperation and adherence. It is important to include patients in the decision of their treatment and offer more than

Table 1
Summary of some recent randomized controlled trials comparing MAS with CPAP

Author, Year, Reference Number of Patients	Measurements	Significant Changes Compared with Baseline	Significant Changes Compared with CPAP	Patients Who Preferred a Treatment (%)
Hoekema et al,[22] 2007 N = 20	PSG ESS Driving performance	MAS and CPAP improved AHI, min SaO2 Both improved ESS CPAP and MAS improved	MAS = CPAP MAS = CPAP MAS = CPAP	N/A Parallel study
Hoekema et al,[15] 2008 N = 28	NT-pro-BNP	MAS showed improvement	Only MAS improved NT-pro-BNP	N/A Parallel study
Gagnadoux et al,[14] 2009 N = 69	PSG Nottinham QoL Osler test	MAS and CPAP improved AHI Improvement Improvement	CPAP>MAS MAS = CPAP MAS = CPAP	71.2% MAS 8.5% CPAP 14.5% MAS = CPAP
Trzepizur et al,[20] 2009 N = 12	Microvascular reactivity PSG Blood pressure	MAS and CPAP Improvement AHI and ODI No difference	MAS = CPAP MAS = CPAP MAS = CPAP	Not described
Aarab et al,[19] 2011 N = 57	PSG ESS	Improvement AHI Improvement	MAS = CPAP MAS = CPAP	N/A Parallel study
Aarab et al,[2] 2011 N = 43	PSG after 1 y ESS	Stable AHI improvement Additional sleepiness improvement	CPAP>MAS MAS = CPAP	N/A Parallel study
Holley et al,[21] 2011 N = 378	PSG	Improved AHI	MAS = CPAP for mild to moderate CPAP>MAS severe OSA	Not described

Abbreviations: ESS, Epworth Sleepiness Scale; NT-pro-BNP, concentration of the amino-terminal fragment of pro- brain natriuretic peptide; ODI, oxygen desaturation index; PSG, polysomnogram.

one type of therapy for patients with OSA who are potentially good candidates for MAS therapy.

Titration

Analogous to the pressure of a CPAP mask, the amount of mandibular advancement produced by a MAD that will effectively reduce the number of apneas will vary from patient to patient. The amount of pressure required for each patient cannot be predetermined based on OSA severity or craniofacial characteristics; as such the magnitude of advancement needs to be determined through a titration procedure. Typically, the amount of advancement is initially set at 66% of maximum protrusion, and over a period of weeks, patients slowly increase the advancement by adjusting the appliance until there is resolution of subjective OSA symptoms. At this point, a follow-up polysomnogram (PSG) with the device worn is required to ensure adequate improvement to breathing during sleep. A schematic of the treatment protocol can be seen in **Fig. 1**.

Additional advancement of the appliance by titration carried out during this follow-up PSG has been shown to further increase the success rate of OA therapy.[30,31] This advancement is achieved by simply having the sleep technologist wake and ask the patient to increase the protrusion of the appliance should there be persistent snoring or events related to adverse breathing. Several studies have evaluated whether a titration of mandibular advancement during polysomnography could be used as a predictor and accelerate MAS treatment, similar to CPAP titration.[30,32–35] These studies had mixed results in predicting the amount of mandibular advancement needed for successful MAS therapy, and overnight titration of MAS at appliance delivery remains an experimental approach.

The importance of titration to enhance the efficacy of MAS therapy is highlighted by a closer examination of randomized controlled trials (see **Table 1**) comparing CPAP to MAS. Most of these studies have found that MAS and CPAP have a similar impact on daytime sleepiness and quality of life.[2,3,12–15,17,18,35] In 2 other studies, Engleman[11] and Lam[16] have reported an inferiority of MAS compared with CPAP; however, it is important to note that fixed, nontitratable, single-jaw position appliances were used for their patients. Previous reports on effective single-jaw positioners have proposed that, if this type of appliance is used, there should be the opportunity to remake these devices with further mandibular advancement, which represents titration with multiple appliances.[36] Also, the increased likelihood of providing successful therapy with adjustable compared with fixed appliances is especially evident in cases of moderate and severe OSA.[37] It is clear in the literature that customizing the fit of the MAS, with the use of a custom-made appliance to the patient's specific oral anatomy, and determining the ideal anterior position of the mandible via titration of the amount of advancement are crucial to optimizing the effectiveness of therapy.

APPLIANCE DESIGN

There are a multitude of MAS designs with various methods of adjustment and retention mechanisms available on the marketplace today. As such it is easy to imagine these differences contributing to some of the variability observed in the results of clinical studies investigating MAS effectiveness. The possible influence of various MAS design features on the management of subjective symptoms during OSA treatment was recently examined in a systematic review.[38] The results suggest that an appliance with titratable mandibular advancement that is found acceptable by patients because of greater comfort and retention, and being custom made (not prefabricated), will be

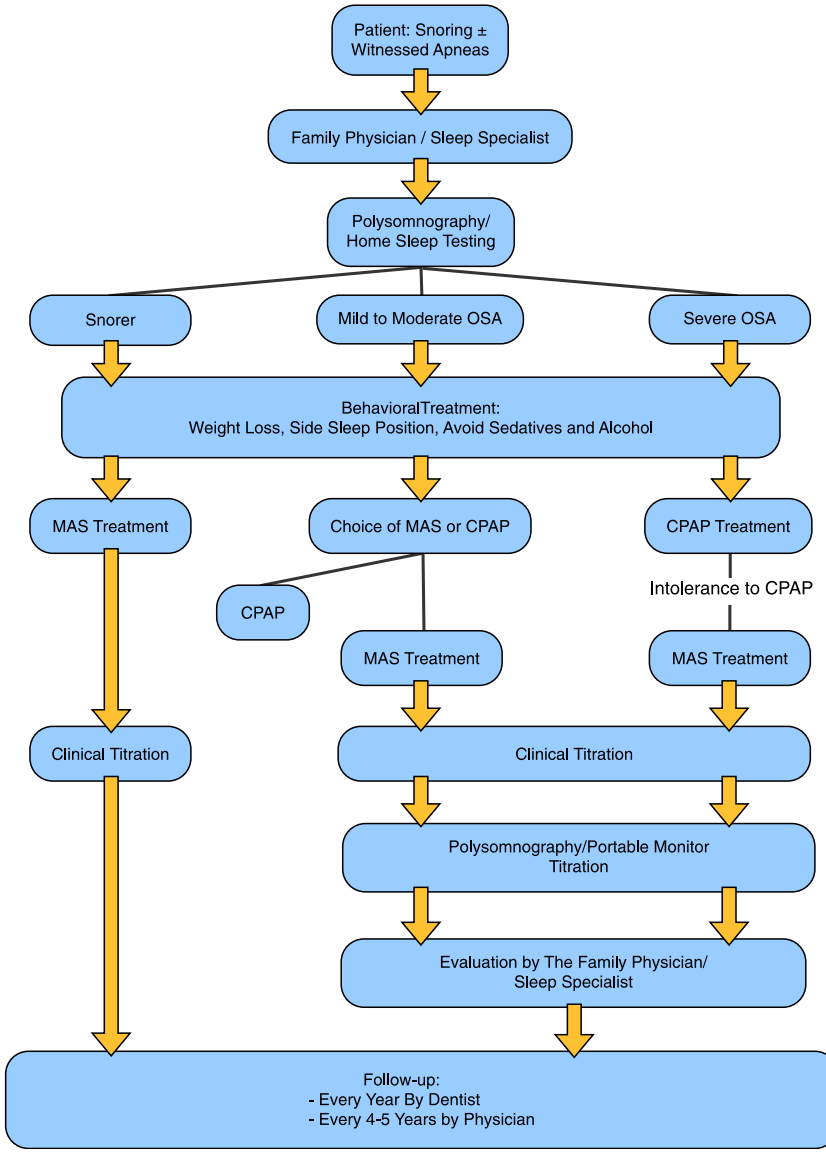


Fig. 1. Treatment algorithm for the management of OSA with an oral appliance.

successful at improving sleep-disordered breathing signs and symptoms. It is also noted that the optimum amount of advancement might not necessarily be the maximum achievable forward position of the mandible. The investigators also reported that the amount of vertical opening did not impact significantly on the appliance design. Isono and collaborators[39] found that an increase in jaw opening would decrease the upper airway area. Pitsis and colleagues[40] found that a 10-mm increase in the jaw opening did not make significant differences in the AHI, but a highest percentage of patients developed temporomandibular joint symptoms with the greater jaw opening. More recently Nikolopoulou and collaborators[41] evaluated an increase in

vertical dimensions without mandibular advancement. They concluded that without mandibular protrusion an increase in vertical dimension was associated with an aggravation of OSA. In summary, there is no preferred MAD design, as long as it is properly custom made for the patient, patient comfort is achieved, it has good retention, and most importantly allows for mandibular advancement and titration to optimize treatment outcome.

MAS EFFECTS ON SLEEPINESS AND QUALITY OF LIFE

MAS have been shown to be effective in improving subjective and objective daytime sleepiness in patients with OSAS when compared with placebo and improves sleepiness to the same degree as the CPAP.[23,42] Aarab and colleagues[2] examined the effects of MAS and CPAP treatment 12 months following initial titration for patients with mild to moderate OSA. They found that CPAP reduced AHI slightly better than MAS and that the improvements in AHI were stable over the 12-month time period; however, subjective sleepiness progressively improved for all patients in the same time frame. They concluded that a lack of long-term differences in improvements in sleepiness between the MAS and the CPAP groups may indicate that the larger improvements in AHI values in the CPAP group are not clinically relevant. Johal and collaborators[42] found that MAS therapy significantly improved the energy/vitality domain of quality of life and reduced subjective sleepiness in a group of patients with OSA preselected for a favorable treatment outcome using sleep nasendoscopy. Similar improvements were not seen in a conservatively managed group. There were some interesting findings in a study from Gagnadoux and colleagues[14] whereby MAS showed a greater improvement compared with CPAP in a variety of profiles of quality of life (Nottingham Health Profile), such as physical mobility, social isolation, pain, emotional function, and sleep. MAS treatment may not improve AHI as much as CPAP, but consistently throughout various studies, does significantly improve their quality of life. For patients to adhere to treatment, it is crucial that patients feel better and acknowledge the importance of treatment.

MAS INFLUENCE ON LONG-TERM HEALTH EFFECTS OF OSA

OSA is considered a risk factor for cardiovascular disease, including systemic hypertension, congestive heart failure, arrhythmias, and stroke[43]; and recent studies have demonstrated a significant increased risk of fatal cardiovascular events in patients with untreated sleep apnea.[44] There is currently initial evidence demonstrating that MAS therapy can play a role in reducing the risk of these adverse health effects associated with OSA.

MAS treatment has been shown to reduce systemic blood pressure in several studies, including 2 randomized controlled trials with intention-to-treat analysis[3,45] and 3 nonrandomized prospective studies.[46–48] Compared with a placebo, the management of OSA with MAS can significantly reduce systolic and diastolic pressure, while lowering the mean blood pressure measurements by 3.6 mm Hg.[45] Barnes and colleagues[3] examined nocturnal blood pressure levels and demonstrated no change in blood pressure with CPAP treatment, whereas MAS treatment significantly improved the nocturnal diastolic blood pressure and increased the proportion of patients with a normal nighttime dip in blood pressure. Improvements in blood pressure levels have been observed to persist for at least 3 years with continued MAS therapy.[48] A correlation between the improvement in AHI and decrease in blood pressure after MAS treatment has also been found.[46]

In an examination of biomarkers of oxidative stress and inflammation, the endothelial function in a MAS treatment group normalized compared with a reference non-OSA group of patients.[24] Interestingly these changes were observable after 12 months of treatment despite residual sleep-disordered breathing (average AHI of 19 per hour). Treatment effects of MAS have also been found on the autonomic nervous system with improvements in cardiovascular variability.[49]

PREDICTORS OF MAS TREATMENT SUCCESS

There are various studies on the prediction of MAS treatment success. Treatment success may be inversely related to pretreatment severity, but this relationship may be a function of the definition of treatment success, although one study has shown that the higher AHI pretreatment, the greater decrease in AHI could be achieved.[35] In an evaluation of the literature, there is a common agreement that MAS is likely to be more effective in patients that are younger[50,51]; have a lower body mass index[14,51]; have a smaller neck circumference[8]; and have positional OSA,[36,50,52] whereby patients have a higher number of respiratory events in the supine compared with the lateral sleep position. Women also have shown a higher percentage of success.[36] Despite these findings, further prospective studies are required to better predict which patients will experience a greater level of success through OA therapy.

SIDE EFFECTS OF MAS

Although effective and well tolerated, MAS have known side effects, including dry mouth, increase in salivation, dental discomfort, transitory temporomandibular dysfunction, and most commonly, unwanted dental movement. Previous studies have shown a significant decrease in overbite (OB) and overjet (OJ) after long-term appliance use.[53–55] Martinez and colleagues[53] found a mean OB reduction of 0.81 mm and OJ reduction of 1.1 mm from 15 patients with OSA with 4.8 years of MAS use. Similarly, Marklund[54] found reduction of both OB and OJ by 0.6 mm from a 5-year follow-up of 155 patients with OSA. In the longest follow-up period published to date, Almeida and colleagues[55] demonstrated that the use of an adjustable MAD for a mean period of 7.3 years has a significant impact on the occlusion, with a mean reduction of 1.9 mm and 1.2 mm for OB and OJ respectively. In that study, many changes were described as favorable changes to the patient's occlusion, as seen in **Fig. 2**. It is important to emphasize that these changes are mainly related to dentoalveolar

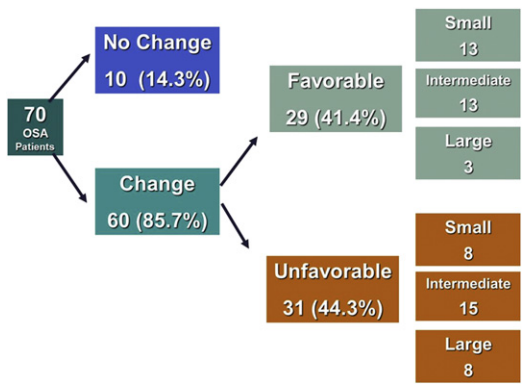
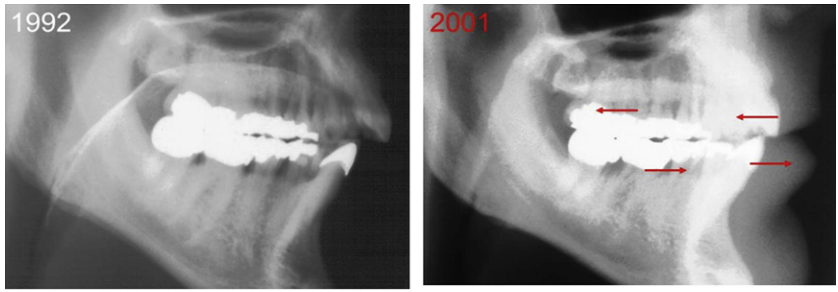


Fig. 2. The occlusal changes in 70 patients after an average of 7.4 years of MAS use.



- Retroclination of the maxillary incisors
- Distal tipping of the maxillary molars
- Proclination of the mandibular incisors
- Mesial tipping of the mandibular molars
- NO Changes in condyle position

Fig. 3. Dentoalveolar changes after 9 years of MAS use.

changes and not condylar remodeling (**Fig. 3**). Because MAS are a life-long treatment and changes do continue overtime, it is crucial to advise patients before initiation of treatment that some type of occlusion changes are likely to happen, and the dentist should ideally collect cephalometric radiographs, dental models, and intraoral photographs over the course of the treatment. MAS are an important treatment option for OSA, which is a life-threatening disease that requires long-term treatment. Changes in the occlusion should not stop patients from using MAS, unless patients are willing to start using CPAP. If patients are willing to use CPAP, they should be advised not to use the nasal masks because these also change the occlusion.[56]

ORAL APPLIANCES FOR THE TREATMENT OF SLEEP-DISORDERED BREATHING IN CHILDREN AND ADOLESCENTS

The use of MAS, which can be highly effective in the treatment of adult OSA, has more limited applications in younger patients. In a growing child or adolescent, such an appliance can result in dramatic skeletal and dentoalveolar changes, as observed with the use of functional orthodontic appliances. Such concerns over bite alterations preclude widespread use. However, in class II retrognathic patients, these occlusal changes are favorable, and functional appliance treatment has been proposed as a means to treat retrognathic children suffering from sleep-disordered breathing. In a randomized controlled study of 7-year-old children suffering from OSA, Villa and colleagues[57] observed a mean reduction in AHI of 7.1 $\pm$ 4.6 to 2.6 $\pm$ 2.2, whereas no reduction in AHI was seen in the control group. Similar positive outcomes were demonstrated in an older cohort of retrognathic adolescents with sleep-disordered breathing in the absence of tonsillar hypertrophy, where Schutz and colleagues[58] effectively normalized the respiratory disturbance index with orthopedic correction of mandibular deficiency.

An equally common appliance in orthodontic treatment, the use of a rapid maxillary expander has been shown to be effective in reducing sleep respiratory disturbances in patients with[59] and without[60] tonsillar hypertrophy. Furthermore, these results have been shown to remain up to 36 months following the expansion protocol.[61] However, the greatest utility of this protocol may be as an adjunctive therapy for children who

have incomplete resolution of their symptoms following the removal of enlarged tonsils and adenoids. Guilleminault and colleagues[62] compared adenotonsillectomy surgery with palatal expansion in a crossover study design of young children diagnosed with OSA by PSG. In their sample of 31 children who had tonsillar hypertrophy and a narrow and high palate, an equal level of improvement to AHI and reported symptoms was found after treatment with either intervention; however, both the surgical and orthodontic treatments were required for complete resolution of symptoms and normalization of AHI, which occurred in 29 of the 31 children.

There is emerging evidence that treatment with oral appliances for maxillary expansion or mandibular advancement can be an effective therapy in children suffering from sleep-disordered breathing, particularly if a craniofacial discrepancy plays a significantly role in the patient's disease. However, further research is needed to elicit in which patients this treatment will be most effective and when such treatment can act as an adjunct or as the first line of therapy for children and adolescents with sleep-disordered breathing.

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