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RESEARCH ARTICLE

ORAL APPLIANCE DESIGN FOR TREATMENT OF ORAL SLEEP APNEA- ADVANTAGES, SIDE EFFECTS, COMBINED THERAPY AND LATEST MODIFICATIONS - A REVIEW

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ABSTRACT

Although continuous positive airway (CPAP) pressure therapy is the most recommended treatment for patients with obstructive sleep apnea (OSA) not all patients are able to remain compliant with this form of treatment. Some complain of claustrophobia, dry nasal passages, skin irritation from masks, difficulty tolerating pressurized air, and accidentally removing the mask while tossing at night. For patients like these, an alternative to CPAP therapy may be recommended, and depending on the level of severity of their disorder, may benefit from a substitute treatment such as an oral dental appliance. Oral appliances (OA) have emerged as an alternative to continuous positive airway pressure (CPAP) for obstructive sleep apnea (OSA) treatment (Sutherland *et al.,* 2014). The most commonly used OA reduces upper airway collapse by advancing the mandible (OA_m). There is a strong evidence base demonstrating OA_m improve OSA in the majority of patients, including some with more severe disease. However OA_m are not efficacious for all, with approximately one-third of patients experiencing no therapeutic benefit. OA_m are generally well tolerated, although short-term adverse effects during acclimatization are common. Long-term dental changes do occur, but these are for the most part subclinical and do not preclude continued use. Patients often prefer OA_m to gold-standard CPAP treatment (1). Head-to-head trials confirm CPAP is superior in reducing OSA parameters on polysomnography; however, this greater efficacy does not necessarily translate into better health outcomes in clinical practice. Comparable effectiveness of OA_m and CPAP has been attributed to higher reported nightly use of OA_m, suggesting that inferiority in reducing apneic events may be counteracted by greater treatment adherence. Recently, significant advances in commercially available OA_m technologies have been made. Remotely controlled mandibular positioners have the potential to identify treatment responders and the level of therapeutic advancement required in single night titration polysomnography (Sutherland *et al.,* 2014). Objective monitoring of OA_m adherence using small embedded temperature sensing data loggers is now available and will enhance clinical practice and research. These technologies will further enhance efficacy and effectiveness of OA_m treatment for OSA (Sutherland *et al.,* 2014)

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INTRODUCTION

Obstructive sleep apnea (OSA) is a common sleep disorder characterized by recurring collapse of the upper airway during sleep, resulting in sleep fragmentation and oxygen desaturation (Marshall *et al.,* 2008). OSA is defined as the occurrence of 5 or more episodes of complete (apnea) or partial (hypopnea) upper airway obstruction per hour of sleep (apnea-hypopnea index [AHI]). and is estimated to occur in around 24% of middle-aged men and 9% of women. Daytime symptoms such as sleepiness, cognitive impairment, and effects on quality of life require appropriate treatment. Furthermore the association of OSA with increased risk of motor vehicle accidents, cardiovascular morbidity, and all-cause mortality emphasize the need for effective long-term treatment. The gold standard treatment for OSA is to pneumatically splint open the upper airway during sleep using continuous positive airway pressure

(CPAP). Although CPAP is highly efficacious in preventing upper airway collapse, patient acceptance, tolerance, and adherence is often low, thereby reducing effectiveness. Hence, there is a major need for effective alternative treatments. Oral appliances (OA) are designed to improve upper airway configuration and prevent collapse through alteration of jaw and tongue position. The most common mechanism of action is to hold the lower jaw in a more anterior position. These appliances are variously termed "mandibular advancement devices (MAD)," "mandibular advancement splints (MAS)," or mandibular repositioning appliances (MRA)." Imaging studies show that mandibular advancement with enlarges the upper airway space, most notably in the lateral dimension of the velopharyngeal region. Lateral expansion of the airway space is likely mediated through lateral tissue movement via direct tissue connections between the lateral walls and the ramus of the mandible (Young *et al.,* 2002). Various amounts of anterior tongue movement also occur with mandibular advancement. Alternative OA designs which protrude the tongue instead of the mandible (tongue-retaining device [TRD]) are also available. TRDs feature an extra-oral flexible bulb and hold the tongue forward by suction, preventing its collapse into the airway. TRDs may be poorly tolerated, with inadequate device retention a potential issue reducing effectiveness. TRD do not form part of the evidence base on which current recommendations for oral appliance treatment are made and are not further discussed in this review(14).Current practice parameters of the American Academy of Sleep Medicine (AASM) indicate OA_m as a first-line therapy in patients with mild-to-moderate OSA and in more severe OSA patients who fail treatment attempts with CPAP therapy.

What is an Oral Dental Appliance for Sleep Apnea?

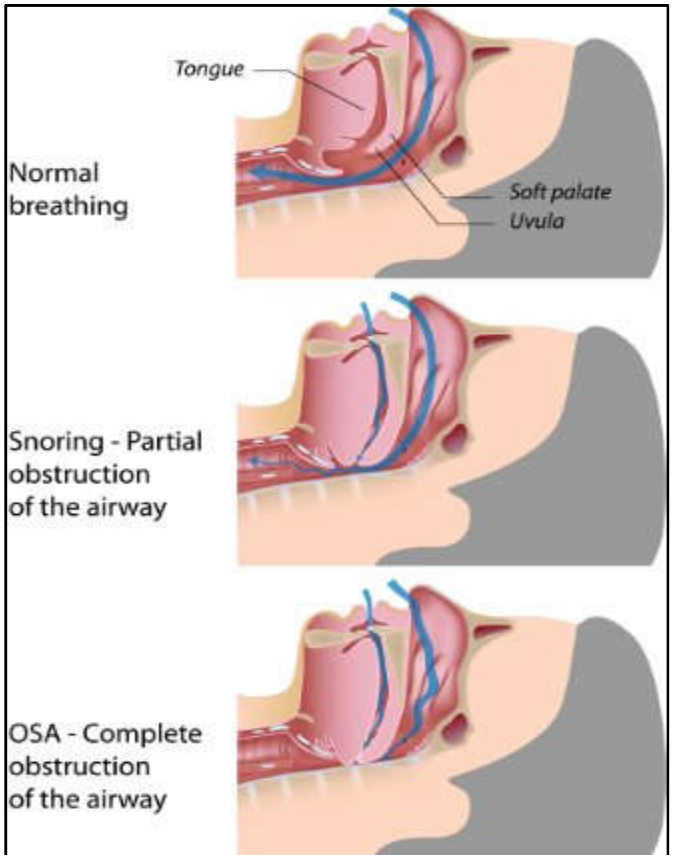
Before diving into how oral appliances work, lets have a brief recap on what sleep apnea is, and how it affects your sleep and health.

Obstructive Sleep Apnea

Obstructive sleep apnea is a sleep disorder in which a person stops breathing periodically throughout the night due to physical obstructions of the airway. These stops in breathing usually last for around ten seconds and are often followed by snorts, gasps, or choking sounds as a person's body fights to resume breathing again. When you sleep, the muscles in your body relax so they can begin to repair themselves to keep you healthy and active everyday (Kribbs, 1993). However, muscles in your mouth and throat also relax during sleep, and for some people (an estimated 18-20 million U.S. adults) these muscles along with soft fatty tissues relax to the point where they fall back into the upper airway and block the flow of oxygen from coming in.When you stop breathing during the night, your brain responds by partially waking to send signals to the respiratory system to work harder to get past the obstruction.

Side effects of obstructive sleep apnea include

- High blood pressure
- Heart arrhythmias
- Heart disease
- Heart attack
- Stroke
- Increased risk of diabetes
- And even death



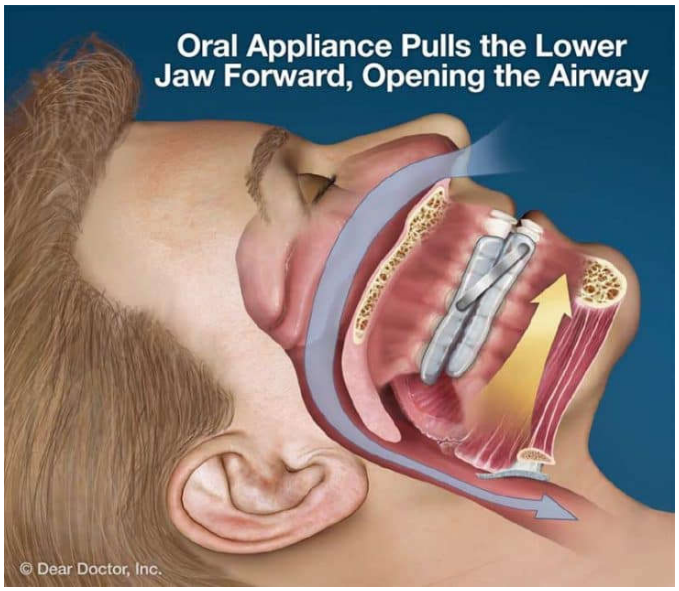
Pediatric OSA

Obstructive Sleep Apnea (OSA) is a potentially serious sleep disorder in which a child's breathing stops and starts during sleep. Child OSA is most commonly found in children between the ages of 2 and 6, but can occur at any age. There are a variety of treatments for OSA. Some of the most common devices to help are a Continuous Positive Airway Pressure machine (CPAP), mouth appliances, and specially designed pillows. Dentofacial orthopedics is another option for early treatment and even prevention of OSA. These orthopedics can open the airway 10mm or more by developing a facial profile to an optimum situation, which is a process to increase the airway space. Treatment can be started as young as 2 years old, and can help your child to reach the maximum sleep potential by reducing problems with breathing, swallowing, and sleeping. Other oral treatments include a Mandibular Repositioning device and a Tongue Retaining device. These devices open your airway by bringing your lower jaw forward during sleep (Chan *et al.,* 2010). They are acrylic and fit inside your mouth, much like an athletic mouth guard. Others may fit around your head and chin to adjust the position of your lower jaw as well. Dental devices are only effective for mild to moderate sleep apnea (Blanco *et al.,* 2005). There are also a number of possible troubling side effects from using the dental the devices to include soreness, saliva build-up, nausea, and damage or permanent change in position of the jaw, teeth, and mouth. It is very important to get fitted by a dentist specializing in sleep apnea. Also, see your dentist on a regular basis for any dental problems that may occur, and check with your sleep specialist to see if you are a proper candidate for OSA. Sleep apnea even leads to excessive daytime sleepiness because each time your brain has to "wake up" to tell your body to continue breathing, it's not spending enough time doing all of the other functions that are necessary of quality sleep. Being tired all day can cause poor performance

at work or school, memory and other cognitive troubles, depression, and even accidents while driving or while at work.

How severe one's sleep apnea is can be determined by the amount of apnea events (pauses in breathing):

- **Mild OSA**- The sufferer experiences 5-14 episodes of interruptions in breathing in an hour.
- **Moderate OSA-** The sufferer experiences 15-30 episodes of interruptions in breathing in an hour.
- **Severe OSA-** The sufferer experiences 30 or more interruptions in breathing in an hour.



Dental Appliances for sleep apnea

Before any treatment options can be determined, a sleep study must first be performed to determine the severity of one's symptoms as it can have a direct influence on the recommended therapy. The most common form of therapy is continuous positive airway pressure (CPAP) devices, which blow a steady stream of pressurized air through a mask into the respiratory system. For moderate to severe sleep apnea patients, most sleep professionals will recommend CPAP therapy as a first-line treatment option. For mild to moderate sleep apnea, a dental device is often the recommended therapy. Dental devices may also be recommended to be worn in conjunction a CPAP device to help lower high pressure needs (Brown *et al.,* 2013).

How do dental appliances work?

There are two major categories of dental devices:

1. Mandibular advancement devices (MADs)
2. Tongue Retaining Mouthpieces

MADs used to treat sleep apnea look very similar to sports mouth guards or orthodontic retainers. They fit into the mouth by snapping over the upper and lower dental arches and have metal hinges connecting the two pieces: one fits over the upper teeth, and the other fits over the lower teeth. MADs work by pushing the lower jaw and tongue slightly forward, which helps prevent throat muscles and issues (such as the pharynx) from collapsing back into the airways allowing for normal breathing during sleep. Most MADs are adjustable, allowing for dentists to fine-tune the position of the jaw for maximum effectiveness. Tongue retaining mouthpieces are similar in construction to the MAD, but has a small compartment that fits around the tongue using suction to keep it held forward, preventing it from collapsing back into the airway. These devices are mostly used in patients who cannot adequately have their jaw repositioned forward.

Influence of oral appliance design features

Customization of Appliance: OA_m are generally customized devices fabricated from dental casts of a patient's dentition and bite registrations by a dentist, which is associated with expense and time. A lower cost alternative is a thermoplastic or "boil and bite" appliance. These devices are a thermoplastic polymer material, which becomes moldable when heated in boiling water. A patient bites into the softened material and advances the lower jaw to approximately 50% of maximum, and the device will set in this configuration with cooling. Direct comparison of the efficacy of thermoplastic and customized OA_m devices in a crossover study of 35 patients over 4 months of each device found post-treatment AHI was reduced only with the custom-made OA_m. The thermoplastic device also showed a much lower rate of treatment success (60% vs. 31%). Lower adherence to the thermoplastic appliance was also evident, attributable to insufficient retention of the appliance during sleep. The overwhelming majority of patients (82%) preferred the customized OA_m at the end of the study. Hence customization to a patient's dentition is a key component of treatment success (Sutherland *et al.,* 2014).

Degree of mandibular advancement: Generally the greater the level of advancement, the better the treatment effect, although this must be balanced against potential increase in side effects. A study of 3 levels of advancement (2, 4, and 6 mm) found dose dependence in improvement of overnight oximetry (25%, 48%, and 65% of patients showing improvement [> 50%] in desaturation, respectively). Assessment of pharyngeal collapsibility during mandibular advancement has also shown a dose-dependent effect in improvement of upper airway closing pressures. In a study of mild-to-moderate OSA patients randomized to either 50% or 75% of maximum advancement, there was no difference between these levels in treatment AHI or proportion of patients successfully treated (79% vs. 73%). However in severe OSA, more patients achieved treatment success with 75% compared to 50% maximum advancement (52% vs. 31%), suggesting maximizing advancement may be more important in severe disease (Dort *et al.,* 2008). A dose-dependent effect of mandibular advancement was demonstrated using 4 randomized levels of advancement (0%, 25%, 50%, and 75% maximum), with the efficacy of 50% to 75% advancement greater than 25%, and 25% greater than 0%. However above 50% of maximum advancement there was an associated increase in reported side effects. A titration approach to determine optimal level of advancement with gradual increments over time is thought to optimize treatment outcome. Titration can be guided by a combination of both subjective symptomatic improvement and objective monitoring by overnight oximetry to find the optimally effective advancement level. A newly available remotely controlled mandibular titration device provides an objective mechanism by which to determine the maximal therapeutic level of mandibular protrusion during sleep. The target treatment protrusion identified by this method of sleep titration was found to result in effective treatment in 87% of patients

predicted to be successfully treated OA_m in an initial study. Identification of therapeutic protrusion level by this method may help reduce side effects produced by further unnecessary titration (Sutherland *et al.,* 2014). Optimizing mandibular advancement in individual patients is important for successful treatment, although no standardized titration procedure currently exists. In the clinical setting, a follow-up sleep study to objectively verify satisfactory treatment is often not conducted; this is an area by which to improve clinical outcomes.

Degree of Vertical Opening: Opening of the bite occurs during OA_m treatment as all appliances have a given thickness causing vertical jaw displacement. A crossover trial compared 2 levels of vertical opening (4 mm and 14 mm, equivalent advancement), found no detrimental impact on AHI, although patient preference was in favor of the smaller degree of mouth opening. However, increased vertical mouth opening has an adverse effect on upper airway patency in the majority of OSA patients (Sutherland *et al.,* 2014). Therefore amount of bite opening should be minimized to improve patient tolerance and increase the beneficial effect on upper airway dimensions.

Getting dental devices

You will have to have your dentist make a custom fitted oral device to suit your particular needs. Over-the-counter options are available, but not recommended. Over-the-counter devices may be appealing because of their reduced prices, but can actually complicate sleep apnea (Higurashi *et al.,* 2002). Many patients who order oral devices without consulting with a dentist, find that their snoring symptoms went away, but were unaware that it was not preventing apnea events leading to complications down the road as only the snoring symptom was prevented but the disorder itself was not.

Side effects of oral appliance treatment

In initial acclimatization to OA_m therapy, adverse side effects are commonly experienced. Adverse effects primarily include excessive salivation, mouth dryness, tooth pain, gum irritation, headaches, and temporomandibular joint discomfort. Reported frequencies of side effects vary greatly, potentially related to differences in device design. However adverse symptoms are usually transient, lasting around 2 months. Temporomandibular disorder symptoms of pain and impairment in the initial treatment period tend to decrease over time and resolve after 6 to 12 months in the majority of patients. Long-term persistence of side effects such as mouth dryness and tooth or jaw discomfort may lead to discontinuation of treatment. Assessment of dental changes with OA_m primarily relate to decreases in overbite and overjet, retroclination of the upper incisor and proclination of the lower incisors, changes in anterior-posterior occlusion, and reduction in the number of occlusal contacts (Sutherland *et al.,* 2014). Overbite and overjet changes are evident 6 months after initiation of treatment. Duration of OA_m use is reported to correlate with dental changes such as decreased overbite, suggesting progressive changes to the dentition over time. However generally occlusal changes are negligible and in over half of patients actually represent an improvement on baseline occlusion. The initial type of bite, degree of mandibular advancement, adherence, and oral health will influence the amount of bite changes and discomfort produced during longer term treatment. Skeletal changes relating to prolonged OA_m use on lateral cephalometry, primarily report an increase in lower face height and a downward rotation of the mandible. Skeletal changes are probably a result of the changes in dentition that occur with wear of the OA_m (Higurashi *et al.,* 2002) Many patients are unaware of any changes in their bite and the majority of patients concur that positive effects of OSA treatment far outweigh any adverse effects related to dental changes.

Pros of Dental devices

- Many patients find dental devices to be more comfortable and tolerable to wear as opposed to CPAP masks.
- Patients on CPAP often complain of dry, itchy noses from the air pressure drying out their sinuses. Oral devices do not have this problem.
- There is less equipment to become entangled with during sleep, or knock off during slumber, for patients who are active movers during sleep.
- There is a lot less equipment involved, and therefore easier to travel with.

Cons of Dental devices

- Jaw pain, soreness, or tension
- Sore teeth and/or gums
- Excessive salivation or even dry mouth
- Possible damage or permanent change to jaw position/bite
- Loosening of dental restorations (crowns, bridges, etc)

Who qualifies for dental appliances?

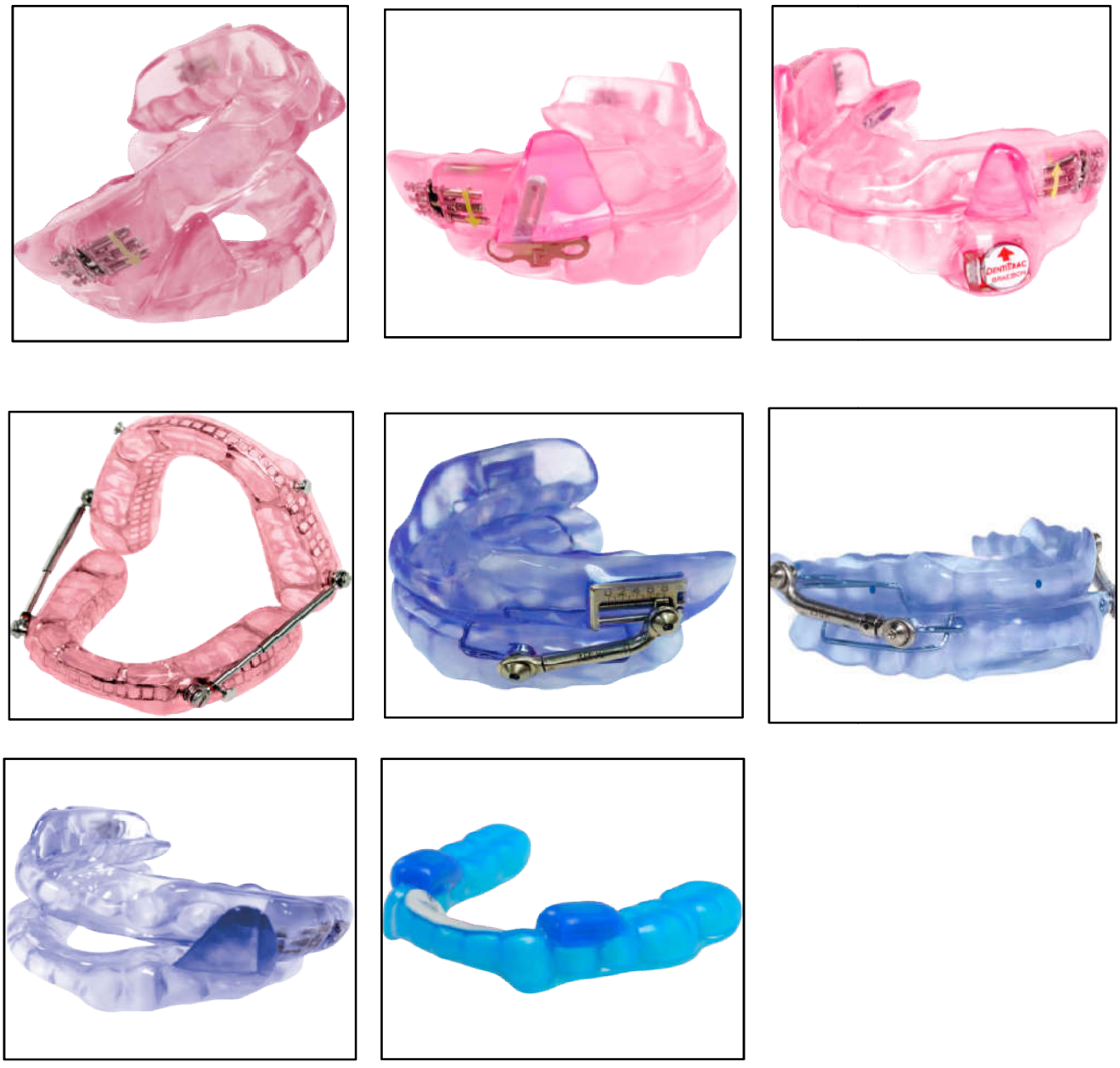
- Patients with mild to moderate sleep apnea (not recommended for moderate to severe sleep apnea)
- Patients with primary snoring (in absence of sleep apnea)
- Patients who have tried and failed at CPAP therapy may qualify
- Patients who were unsuccessful with or refused surgeries such as tonsillectomy, adenoidectomy, craniofacial operations, or tracheostomy.
- In combination with CPAP device to help lower patient's apnea/hypopnea index for more tolerable air pressure settings.

Combined Oral Appliance and CPAP Therapy: Although OA_m and CPAP have been considered as alternative treatment pathways, there is scope for a patient to alternate between them as needed in situations such as travel when CPAP may be inconvenient. Additionally there are some recent lines of evidence suggesting combining the 2 treatment modalities simultaneously may be of additional benefit. The effect of OA_m in opening the upper airway has been explored as a means to reduce CPAP pressure, as high pressure requirement can lead to intolerance and reduced adherence in some patients. A pilot study of 10 patients partially treated by OA_m but who failed CPAP due to intolerance to prescribed pressure, found auto-titration of CPAP pressure while wearing an OA_m reduced average pressure requirement from 9.4 to 7.3. A physiological study of upper airway mechanics at various CPAP pressures delivered under conditions of (Sutherland *et al.,* 2014) oronasal mask, (Marshall *et al.,* 2008) nasal mask and combined OA_m, and (Young *et al.,* 2002) nasal mask

showed that velopharyngeal resistance was reduced in the OA_m/nasal mask condition compared to CPAP alone. OA_m may prove to be a useful adjunct to CPAP therapy in reducing pressure requirements and preventing issues of mouth opening, leaks and chin retrusion which variously result from different CPAP masks (Sutherland *et al.,* 2014).

Oral Appliances Compared to Surgery: There is currently only one prospective randomized trial of OA_m compared to surgical treatment for OSA. The surgical procedure used in this study was uvulopalatopharyngoplasty (UPPP), which involves removal of upper airway soft tissues including the uvula, soft palate, tonsils, and adenoids. Ninety-five mild-moderate (apnea index > 5 and < 25 events/h) OSA male patients were randomized to receive either UPPP or OA_m treatment set to 50% of the patient's maximum level of mandibular advancement (Sutherland *et al.,* 2014). Both treatments significantly reduced sleep disordered breathing events on polysomnography at 6 and 12 months, although at 12 months the OA_m group showed a greater reduction in AHI. Complete treatment response (AHI ≥ 10 events/h) also occurred in a greater proportion of patients using OA_m compared to the UPPP group (78% **vs**. 51%)(1). At 4-year follow-up, AHI remained lower in the OA_m group, with a complete response sustained in 63% compared to 33% of the UPPP treated group. In terms of symptoms, both surgical and OA_m treatment reduced subjective daytime sleepiness assessed at 6 and 12 months. Greater reduction in sleepiness was initially observed with OA_m treatment at 6 months, but this was not sustained at 12 months (10). Quality of life assessment performed before treatment and at 1-year follow-up found improvement in all 3 quality of life domains (quality, vitality, and contentment) with both treatments; however, the UPPP-treated group showed significantly more contentment than the OA_m group. Maxillomandibular advancement (MMA) surgery, to enlarge the pharyngeal space by expanding the skeletal boundaries of the maxilla and mandible, is currently considered the most efficacious surgical procedure for treatment of OSA, particularly severe OSA. Although there are no randomized trials of MMA and OA_m(1) A French study

Latest designs of mandibular advancement appliances BY SomnoDent



offered MMA to 102 non-obese, severe OSA patients and treated those who refused surgery with an OA_m. Polysomnography at 3 months found MMA reduced AHI with a 74% surgery success rate (AHI < 10/h). OA_m also reduced the AHI with a lower success rate (30%), although a significant number of OA_m patients did not complete the 3-month assessment. Hoekema and colleagues offered MMA to OSA patients who were successfully treated with an oral appliance (> 50% reduction in AHI). Four (of 43) patients completed the surgery; AHI was significantly reduced, with a complete response (AHI< 5/h) in 3 of these patients (Kushida *et al.,* 2005). The authors suggest response to OA_m therapy may be a predictor of success of MMA surgery for OSA. Overall, studies comparing OA_m with surgical treatment for OSA are extremely limited. Such comparisons of effectiveness should also take into account adherence factors. Surgery, as an irreversible intervention, has 100% adherence over all hours of sleep, whereas device therapy is dependent on patient adherence to be effective. Therefore treatment comparisons need to take into account not only efficacy on treatment but the percentage of sleep time for which a removable device is used, as a high proportion of sleep time not on treatment will reduce the overall effectiveness, even in a highly efficacious device (Sutherland *et al.,* 2014)

Oral Appliances Compared to CPAP: To our knowledge there are currently 11 published randomized controlled trials which compare efficacy of OA_m treatment with CPAP with polysomnographic outcomes (8 crossover trials, 3 parallel group trials) and variously evaluate aspects of clinical effectiveness with subjective and objective health outcome measures(9).Most studies have been limited to patients with mild-moderate OSA, although some did not include an upper AHI limit or allowed inclusion of patients with an AHI ≤ 60. The most recent study specifically enriched the sample with moderate-severe patients. Refer table 1 below-

Conclusion

OA_m are an effective treatment for OSA, not only improving AHI but also a variety of physiologic and behavioral outcomes. Recent comparative effectiveness trials have shown health outcomes between CPAP and OA_m treatments are equivalent, even in severe OSA, despite greater efficacy of CPAP in reducing AHI. This likely reflects greater nightly adherence to OA_m compared to CPAP therapy. Recent advances in technologies related to OA_m treatment have the potential to further improve their efficacy and effectiveness in clinical practice. Selection of appropriate patients who will respond to OA_m treatment is an ongoing barrier to use (Vanderveken *et al.,* 2013; Remmers *et al.,* 2013). The now commercially available remotely controlled mandibular positioner offers a means to predict response from a single-night mandibular titration study and has shown good positive predictive value in initial testing (Gotsopoulos *et al.,* 2002). The advent of new adherence monitoring technology that can be routinely incorporated into OA_m devices to objectively monitor treatment usage represents another advance in OSA treatment, which will be beneficial in practice and research. This will further help clarify the role of OA_m in OSA treatment next to CPAP. Establishing best quality devices that are objectively validated in terms of both efficacy and durability in combination with recent advances in patient selection and treatment monitoring, will continue to optimize OA_m as an effective and even first-line treatment for OSA (Hans *et al.,* 1997).

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