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Management of sleep apnea: a critical look at intra-oral appliances

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Abstract With so many disciplines of both medicine and dentistry involved in the treatment of obstructive sleep apnea (OSA), several forms of therapy are available. The orthodontist is rarely considered when the diagnosis of chronic obstructive sleep apnea (OSA) is delivered. However, the scope of orthodontic care today is much broader than the mere alignment of teeth. While the current gold standard for OSA care remains continuous positive air pressure (CPAP), the patient may be given a prescription for an intra-oral sleep appliance. When orthodontists work in concert with their medical colleagues to provide a sleep appliance, several considerations must be made including the evidence regarding oral appliance efficacy. For some patients, oral appliances are highly successful; however, even for responsive patients, there are risks associated with oral appliance therapy. The aim of the paper was to present a critical review of the current level of evidence for the use of oral appliances in the treatment of OSA. A substantial number of publications ranging from case reports, uncontrolled and controlled case series, prospective randomized studies, and even a small number of systematic reviews were available. The existing systematic reviews were based on either a limited number of prospective studies with limited numbers of patients or in some cases were based on subjective data only. As a result, a narrative review of the literature was performed that discusses objective clinically testable criteria and recent developments that may aid future research investigations.

Key words: efficacy; obstructive sleep apnea; oral appliance therapy; Orthodontics

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Introduction

Chronic obstructive sleep apnea (OSA) is a severe debilitating disorder affecting people of all ages characterized by periodic breathing cessation (apnea) or airflow reduction (hypopnea).

Overweight middle-aged adult men have the highest prevalence of the disease (1), yet women and an increasing number of children are also affected by OSA (2, 3). Several disciplines within dentistry are well equipped to provide successful treatment for patients with OSA due to their knowledge of facial growth and development and background in craniofacial and dentofacial anomalies. Patients who may not routinely see their physician may be unaware of their condition (4), and an observant dentist or dental specialist may pick up signs and symptoms of OSA during the dental visit, enabling them to make an appropriate referral to the physician and/or sleep team for definitive diagnosis. Once properly diagnosed, several treatment modalities are available (5–9) that lead to successful improvement in both the patient's subjective and objective assessment of their daytime sleepiness (10–13). The dental professional can provide some of the most highly successful treatments and provide a life-saving service and health benefit beyond improvement of the patients smile and self-esteem.

This study will present a critical review of the current evidence for the use of oral appliances in the treatment of OSA. A substantial number of publications are available, but the existing systematic reviews are based on either a limited number of prospective studies with limited numbers of patients or in some cases on subjective criteria. As a result, this critical review will discuss objective clinically testable criteria and recent developments that may aid future research investigations.

Diagnosis and classification of adult obstructive sleep apnea

The classic symptom of OSA is excessive daytime sleepiness, and the Epworth Sleepiness Scale (14) is an easy, inexpensive screening tool that assesses the patient's relative sleep health. Unfortunately, the test is extremely limited and is not able to distinguish OSA from the many other types of sleep-disordered breathing such as central sleep apnea, restless

leg syndrome, narcolepsy, and many other conditions.

The gold standard for proper diagnosis of obstructive sleep apnea is an overnight polysomnography (PSG)(15) which combines the results of electroencephalogram (EEG), electrocardiogram (EKG), electrooculogram (EOG), and electromyography (EMG) along with respiration rate, tidal volume, inspiration and expiration volumes, resulting in the patient's apnea–hypopnea index (AHI). An apnea is defined as a cessation in breathing for 10 s or more with an arterial oxygen desaturation of two to four percent (16). A hypopnea is defined as a fifty percent decrease in airflow for 10 s or more with a concomitant drop in arterial oxygen saturation (16).

Patients with normal sleep have an AHI of 5 or less events per hour of sleep, mild sleep apnea patients have an AHI 5–15, moderate sleep apnea patients have an AHI 15–30 and severe sleep apnea patients have an AHI over 30 events per hour (16). To more critically assess severity, the AHI is subdivided into an apnea index (AI), a hypopnea index (HI), and respiratory event-related arousals (RERA). The subdivision of apnea alone and hypopnea alone helps refine the severity classification because patients with primarily apnea are more severely affected than patients with predominantly hypopneas. The difference may result in dramatically different treatment approaches. To further illustrate the biological impact of obstructive sleep apnea, one must understand that a patient with an AHI of 60 stops breathing or has a significant oxygen desaturation for at least 10 s every minute. The cumulative effect leads to significant reduction in oxygen perfusion to the brain causing an increased risk of stroke, myocardial infarction, and other cardiac anomalies (17). Central apnea is distinguished from obstructive apnea due to the lack of respiratory effort (documented by EMG) (18). This distinction is essential because treatment by the dental professional is mechanical and only effective for obstructive apnea.

The guidelines for what constitutes successful treatment vary widely, with the most stringent

criteria for success including achieving an AHI of less than 5. More conservative success criteria attempt to achieve $\geq 50\%$ reduction in the AHI or an AHI of less than 10. A recent report states that successfully treated patients have no increased morbidity or mortality (19), while untreated individuals have a 37% higher 5-year morbidity and mortality (12) resulting from higher incidence of heart attack, stroke, arrhythmia, hypertension, and motor vehicle accidents, with one study concluding that the incidence of motor vehicle accidents associated with obstructive sleep apnea is comparable to driving while intoxicated (20, 21).

Treatment modalities

The American Association of Sleep Medicine (AASM) describes continuous positive air pressure (CPAP) as the gold standard. The AASM also describes eight surgical treatment options and five conservative treatment options for the patient with OSA. The general surgical procedures most commonly include bariatric surgery (22) to assist with significant weight loss and pharyngeal surgery to remove adenotonsillar hypertrophy and/or to reduce the size of the uvula (23). The dental surgical procedures include genioplasty, mandibular advancement, and maxillomandibular advancement (MMA). Oral appliance therapy is among the conservative treatment options listed.

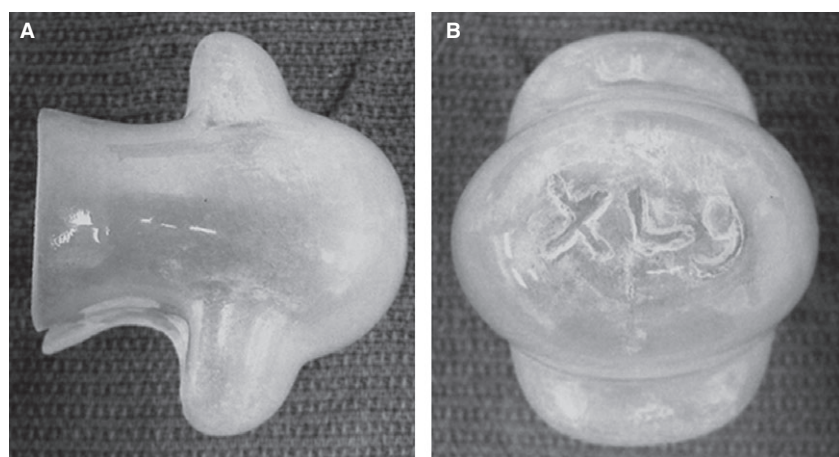
Oral appliance therapy rationale

The theoretical basis for the potential treatment effect is that in the supine position, all gravity-dependent tissue tends to fall posteriorly, including the tongue and lower jaw. If the oral appliance can prevent one or both, the airway will remain patent reducing the number of apneic and hypopneic events.

The first but smallest class of oral appliance is tongue-stabilizing appliances (Fig. 1). Normally, the tongue base is held anteriorly by muscles attached to the genial tubercles, but in the sleeping patient, this support may be insufficient resulting in airway occlusion. After measuring the tongue perimeter with a piece of dental floss, the appropriate size is selected, the appliance bulb is moistened and compressed, and the tongue is inserted. The negative pressure and the salivary adhesion act synergistically to maintain the tongue in a more forward position opening the oropharyngeal airway. The appliance comes in four sizes (S, M, L, and XL) and two versions (dentate and non-dentate).

A second class of appliances actively protrudes the mandible and maintains this forward position during sleep (Fig. 2A and B). Several types of appliances are available including the Klee-way (24) developed by orthodontists, and the Tap (25) developed by a prosthodontist and many others. Each is removable and allows the patient to insert at night and remove upon wak-

Fig. 1. Tongue-stabilizing appliance A: sagittal view and B: frontal view. The interior of the bulb is moistened with water, the bulb compressed, and then tongue inserted. The negative pressure created by compressing the bulb maintains the tongue in a more forward position.



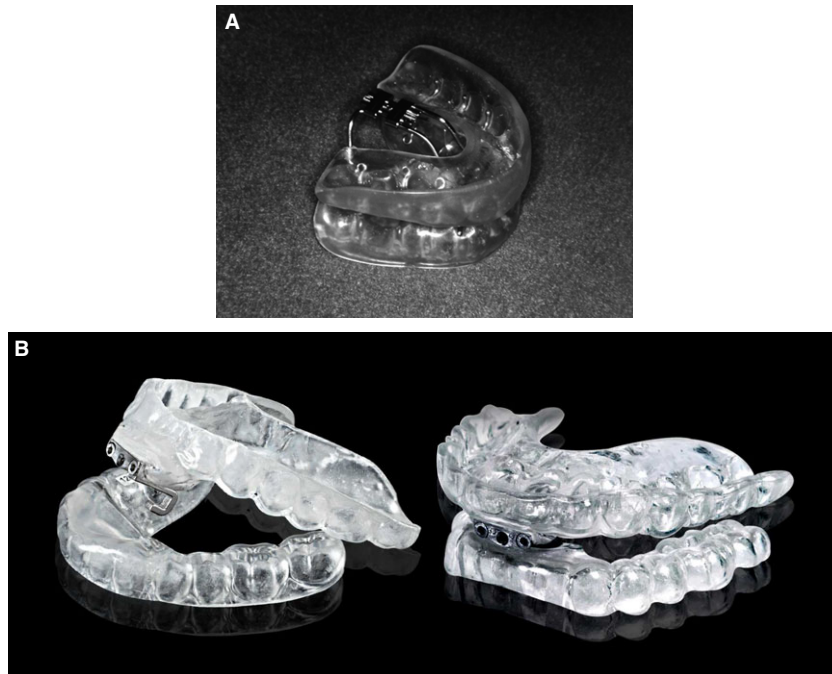


Fig. 2. A: Kleeerway appliance developed by orthodontist Dr. Lowe and B: TAP appliance developed by Dr. Thornton. Both fit intimately against the maxillary and mandibular dental arches. Each uses a screw type design to titrate the final advanced mandibular position for maximum treatment effect.

ing. The oral appliances are small, transportable, and relatively inexpensive and reversible; that is, there are no permanent dental changes in the short-term if treatment is unsuccessful. Selection of the specific advancing appliance can be made using multiple factors including cost, convenience, durability, adjustability, and patient comfort giving the patient the freedom to individually select the appliance, potentially aiding compliance.

Oral appliance fabrication and treatment

Prior to appliance fabrication, records should be taken to document the patient's oral health status. The records should minimally consist of photographs, dental casts, and on a case-by-case basis, appropriate imaging (including lateral cephalometric, panoramic radiograph, periapicals, or cone beam computed tomography (CBCT)). For some, the oral health and particularly periodontal status will be poor resulting in recommendation not to proceed. For others, the records will serve as a baseline indicator for assessment of dental or skeletal changes.

To fabricate, upper and lower dental impressions and pre-treatment range of motion

including maximum opening, lateral excursions, and maximum protrusion are obtained. The appliance is constructed approximately one-half to two-thirds of the patient's maximum protrusion and several millimeters open. A George gauge (Fig. 3) can be helpful in stabilizing the patient in the construction bite position. The impressions and bite registrations are then sent to a commercial laboratory for fabrication or made in-house. At delivery, appliance fit and comfort are assessed and titrated to meet the patient's specific needs.

Efficacy

Dental practitioners who provide treatment for OSA must be in compliance with the AASM treatment parameters for oral appliances, first established in 1995 (26). The best evidence available at that time was a limited number of case series investigations. Since then, higher levels of evidence including prospective randomized clinical trials have become available resulting in the 2005 AASM revised practice parameters (27). The AASM's strongest parameter is a *practice standard*, established only after well-designed prospective randomized clinical studies demonstrate that treatment is beneficial and safe.

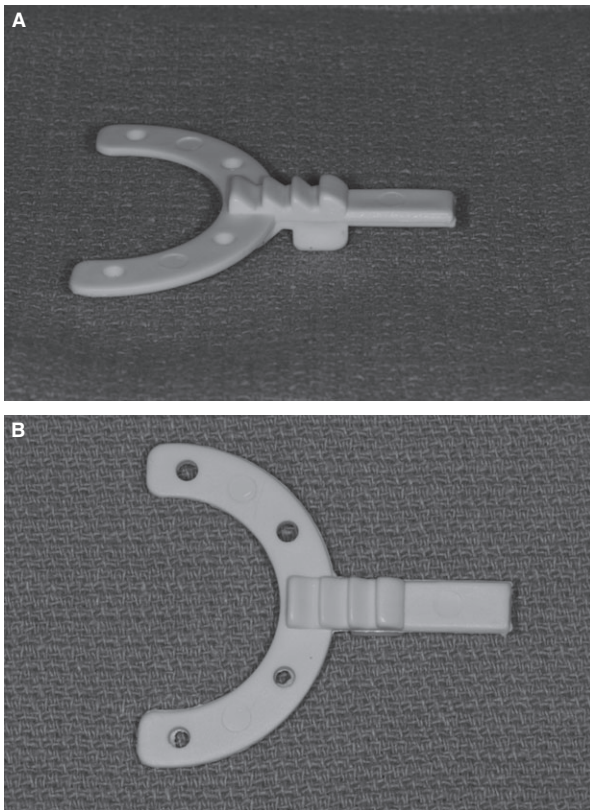


Fig. 3. The George gauge is applied to the maxillary arch and used to help the patient stabilize his/her mandible as they protrude. A: sagittal view and B: occlusal view of the George gauge. Many clinicians will use this 'upside down' placing the mandibular incisors into the single slot and the maxillary incisors into the slot that will provide a construction bite that is 50–60% of the patient's maximum mandibular protrusion.

Practice guidelines are developed from lower levels of evidence such as case series or prospective studies with high potential bias and *practice parameters* list treatment options with minimal literature support. The underlying goal of establishing practice guidelines and parameters was to highlight the current evidence and illustrate the necessary future research directions required for improved outcomes (28).

Given the significant morbidity and mortality associated with unresolved OSA, it is essential to quantify the treatment effect following oral appliance delivery. Surveys and other subjective measures nearly universally report positive changes (29). Other indirect forms of assessment include either two-dimensional lateral cephalometric radiographs (30) or three-dimensional imaging using cone beam computed tomography (CBCT) to demonstrate airway size and shape changes.

The gold standard assessment requires PSG, and this has been performed in case reports, case series, and prospective non-randomized studies. Limited sample sizes, high dropout rate, lack of controls, short study duration, and other factors make interpretation and application of these investigations difficult (31, 32).

More recently, higher levels of evidence using PSG in prospective randomized control studies have emerged. Okuno (33) demonstrated that oral appliances improved AHI more than control appliances, although less than CPAP. Contrary to previous investigators (34, 35), their study group demonstrated similar compliance rates with oral appliances or CPAP. In a short-term prospective randomized cross-over study (36), Phillips compared the results of CPAP and a mandibular advancing device (MAD). With over 100 patients completing both arms of the study, the MAD achieved complete resolution in 40% and partial resolution in another 25% of patients in contrast to CPAP which achieved complete resolution in 75% and partial in 15% of patients. Of note, patients preferred the MAD over CPAP by a 2:1 margin and reported compliance was 6.5 ± 1.3 h for the MAD vs. 5.2 ± 2 h per night for CPAP. For long-term results, Ghazal compared two oral appliances, a modified Herbst appliance (IST) and a prosthodontic (TAP) appliance over several years (25). The study utilized 103 consecutively enrolled and randomly assigned middle-aged adults. At 6 months, both appliances improved the AHI, with the TAP having a higher percentage of success. By study end (42 months), both appliance groups showed similar results. Caution must be taken with these results as there was significant patient drop out and loss to follow-up leaving less than half the original study population. Of note, this group was among the first to examine not only the AHI, but also the effects of oral appliances on blood pressure, an important consideration given the recent concern that controlling blood pressure (BP) may be more important than AHI in reducing the adverse health effects of OSA (37, 38).

With the increasing number of prospective randomized studies, systematic reviews and meta-analyses have now been performed exam-

ining different aspects of treatment. Using 14 of a possible 1475 studies that met their initial search criteria, Ahrens and Hagg evaluated oral appliances (one or two piece) vs. control appliances and each other (39). They concluded that MAD appliances performed better than controls with two-thirds of treated patient's AHI improving. There was no difference between one-piece MAD designs and also no difference for 50% or 75% maximum protrusion. Comparing one- or two-piece design, there was no clearly superior appliance. Using 7 separate studies with a pooled 399 patients, Iftikhar evaluated oral appliances and their effect on BP demonstrating a modest decrease in systolic, diastolic, and mean arterial pressure (40), although there was no correlation between the reduced blood pressure and the decreased AHI. Finally, Li performed a systematic review using 14 prospective randomized trials comparing the gold standard CPAP with oral appliance therapy (41). The results indicated CPAP was significantly more effective in reducing AHI and AI and increasing the minimum oxygen saturation (SpO_2) than oral appliances, and there was no compliance difference between the two treatment approaches. Their conclusion was that while CPAP was better, oral appliances are appropriate to prescribe to patients who are unable or unwilling to wear CPAP.

Treatment limitations and side effects

One must consider both the treatment limitations (i.e., some patients do not respond to either CPAP or OA) and potential side effects of any prescribed treatment (42, 43). In addition with oral appliances, concern arises regarding possible dental changes (44, 45). In one study over a seven-year period, 14.3% of oral appliance patients showed no dental change, conversely 41.4% experienced favorable change, and 44.3% experienced unfavorable bite changes. Favorable change was described as patients with Class II who improved; unfavorable change was observed in Class I patients who became Class III. A more

recent two-year prospective randomized study evaluated potential dental changes in both CPAP and oral appliances. The oral appliance group demonstrated a 1.1 mm decrease in overbite, a 1.5 mm decrease in overjet, and a reduced number of posterior contacts with CPAP demonstrating smaller occlusal changes (albeit smaller and not statistically significant due to patient drop out). CPAP also demonstrate a higher number of moderate-to-severe side effects such as nasal congestion, rhinorrhea, eye irritation, and sense of suffocation that must be considered.

In an attempt to reduce dental side effects through skeletal anchorage and to better treat patients with excessive numbers of missing teeth, a novel micro-implant retained device was attempted in a small number (10) of patients (46). All patient's AHI improved over the 6-month study period with 80% of TADs remaining stable, and 'no dental side effects were seen' (46).

New developments

The data above indicates that oral appliances completely resolve some, partially treat others, with approximately one-third of users experiencing no treatment effect. Using upright and alert lung function tests of 35 patients, (25 responders and 10 non-responders) Chan attempted to predict who would respond to oral appliance therapy (47). The study group was able to correctly assess patient's 48.6% of the time, but with only 36% sensitivity. This failure led other investigators to perform remote-controlled activation of a simulate oral appliance during a PSG prior to prescribing one (48). The results are promising but imperfect with a predictive accuracy of 83–94%. Some subjects were anticipated to be 'responders' during the remote activation test but did not experience a treatment effect from oral appliance therapy and vice versa.

Conclusion

Oral appliance therapy has been investigated and demonstrates one successful form of treat-

ment that the dentist and dental specialist can provide. CPAP remains the most effective form of therapy, but may suffer from reduced patient preference and compliance. While less effective in reducing AHI, blood pressure, and increasing SpO₂, oral appliance therapy remains a viable treatment options for patients unable to tolerate or unwilling to wear CPAP. While the evidence appears to be improving, additional stringent long-term study methodology must be applied to provide the highest levels of evidence in the treatment of adult OSA.

Clinical relevance

The level of evidence in the treatment of obstructive sleep apnea varies tremendously ranging from clinical case reports to systematic reviews and meta-analyses. With the ever-increasing numbers of people affected by this disease, it is essential to constantly review and where needed add to the existing literature to assure that people are treated with the most efficacious intervention possible.

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