SLEEP APNEA AND ORAL HEALTH - UNFOLDING THE LINK

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***Abstract*: Snoring and obstructive sleep apnea are typically caused by complete or partial obstruction of an individual's pharyngeal airway during sleep. Usually airway obstruction results from the apposition of the rear portion of the tongue or soft palate with the posterior pharyngeal wall. Obstructive sleep apnea is a potentially lethal disorder in which breathing stops during sleep for 10 seconds or more, sometimes up to 300 times per night. Snoring occurs when the pharyngeal airway is partially obstructed, resulting in vibration of the oral tissues during respiration. These sleep disorders tend to become more severe as patients grow older, likely due to a progressive loss of muscle tone in the patient's throat and oral tissues. Habitual snoring and sleep apnea have been associated with other potentially serious medical conditions, such as hypertension, ischemic heart disease and strokes. Accordingly, early diagnosis and treatment is recommended. One surgical approach, known as uvulopalato-pharyngoplasty, involves removal of a portion of the soft palate to prevent closure of the pharyngeal airway during sleep. However, this operation is not always effective and may result in undesirable complications, such as nasal regurgitation.**

***Keywords*: Oral cavity, Sleep, Obesity, Smoking, Obstructive sleep apnea**

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. OSA is a 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.[1]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.[2,3]

OSA is characterized by disordered breathing during sleep, resulting in sleep fragmentation and intermittent hypoxemia. Patients often suffer excessive daytime sleepiness and many are at increased risk for motor vehicle crashes [4]. Neurocognitive decline [5] and a lower self-reported quality of life (QOL) are also common. In addition, hypertension is highly prevalent and there is an increased incidence of cardiovascular mortality, stroke, and heart attack [6_8]. Hence, OSA is a major public health problem, imposing a financial burden on health systems [8,9]

Age

Snoring frequency increases with increase in age which is almost up to 50 to 60 years old and then decrease in both men and women [8,20,27,28] The prevalence of OSA also increases with age independent of other risk factors including obesity [5,10,29,30]. On the contrary to snoring, the prevalence of OSA still increases also after the age of 60 years [5,10,11,12].

Obesity

Obesity is a major risk factor for snoring and sleep apnea and a majority of patients with OSA are overweight [5,32-34]. Caloric restriction or bariatric surgery reduces the severity of sleep apnea [30,35-38]. One randomized controlled study reported a decrease

in AHI using very low calorie diet [39]. Another recent study reported that despite an effect of diet on AHI compared with continuous positive airway pressure (CPAP), patients were still better off with the combination of diet and CPAP than with CPAP alone [40]. Men are more likely than women to increase their AHI at a given weight gain regardless of starting weight, waist circumference, age, or ethnicity [41-43].

Smoking

Several cross-sectional epidemiological surveys observed significant associations between cigarette smoking and snoring or sleep apnea [20,21,44-48]. Possible underlying mechanisms include airway inflammation and sleep instability from overnight nicotine withdrawal [49,50]. Never-smokers who have been exposed to passive smoking on a daily basis display an increase in the odds of being a habitual snorer of 1.6 (95% CI, 1.2-2.1) after adjusting for age and BMI according to the Respiratory Health in Northern Europe Study [46]. In a Swedish longitudinal study, smoking predicted the development of snoring in men younger than 60 years old but not in older ones [27].

Alcohol

Alcohol intake reduces motor output to the upper airways with hypotonia of the oropharyngeal muscles as a result (51]. In studies performed in the laboratory, alcohol increases both the number of apneas and the duration of apnea [52,53]. The results did, however, diverge, when the relationship between chronic alcohol use and snoring or sleep apnea was analyzed in epidemiological studies and an association was found by some but not by others [15,27,32,54-56]. Svensson *et al*. reported that alcohol dependence was mostly related to snoring in lean women with a BMI of <20 kg/m2 [28]. It is thus possible that the alcohol-induced reduction in motor output to the upper airways is more important in lean women without compromised upper airways from fat deposits and overweight.

Oral Appliance Designs and Definitions of Treatment Success

There are various differences in the design features of commercially available OAm. Differences predominantly relate to the amount or degree of customization to the patient's dentition and one-piece (monobloc) designs (no mouth opening) versus two-piece design (separate upper and lower plates). Two-piece appliances also vary in permissible lateral jaw movement and in the coupling mechanisms which attach the plates together. Other variations include a wide range of degree of advancement, amount of vertical opening, fabrication material, and the amount of occlusal coverage.

Definitions of treatment success in reports of OAm efficacy also vary. Treatment success is predominantly defined by a reduction in AHI with or without requirement for symptomatic improvement. Treatment success in terms of AHI are expressed as a reduction in treatment AHI below a specified value, such as < 5 (resolution of OSA) or < 10 (very mild disease), or by a percentage reduction in AHI from baseline which is deemed to be clinically significant (typically 50% AHI reduction).

EFFICACY AND EFFECT OF ORAL APPLIANCE TREATMENT FOR OSA

There is now a large body of research that demonstrates efficacy of OAm in terms of reducing snoring and obstructive breathing events as well as showing beneficial effects on associated health outcomes such as daytime sleepiness.

Oral Appliances Compared to Inactive Appliances

Randomized controlled studies have established OAm efficacy by comparison to placebo or inactive appliance (does not provide mandibular advancement).[57-63] Four parallel group randomized controlled trials have compared a monobloc appliance (75% of maximum mandibular advancement) to the control device over treatment periods from 2 weeks to 3 months. All studies found in favor of the active appliance in reduction in AHI[57,58,60,63] and arousal index,[15] and improving oxygen saturation.20 Three crossover studies of active and inactive (single dental plate) OAm also confirm OSA improvement specific to the mandibular advancement device[58,59,60] with reductions in both NREM and REM AHI,[64] and improvement in arousal index, oxygen saturation, and REM sleep time. Reduced snoring was also found to be specifically related to the action of mandibular advancement both by objective measurement using a sound meter[58,61] and by subjective bed partner assessment.[58,60] These inactive-device controlled studies confirm that OAm that jaw protrusion by OAm is the key mechanism by which treatment is delivered.

Effects of Oral Appliance Treatment on Health Outcomes

Subjective daytime sleepiness, assessed by the Epworth Sleepiness Score (ESS), improves with OAm compared to inactive appliances in the majority of studies, although a placebo effect on ESS has been reported.[59,61] Objectively measured sleepiness by the multiple sleep latency test (MSLT) was improved only with active OAm.[59]

There are three placebo-controlled OAm studies that have included health related quality of life questionnaires in assessment of OAm effectiveness. The Medical Outcome Survey Short Form 36 (SF-36) outcomes did not differ between OAm and inactive device in one study,[58] although the vitality domain improved in another.[63]A large effect of OAm therapy in improvements on The Functional Outcomes of Sleep Questionnaire (FOSQ) has been reported.[58] OAm treatment also improved assessment on the Profile of Mood States (POMS) questionnaire, Vigor-Activity and Fatigue-Inertia scales.[64]

INFLUENCE OF ORAL APPLIANCE DESIGN FEATURES

Customization of Appliance

OAm are 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 cost efficient 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 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 OAm 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 OAm.[66]The thermoplastic device also showed a much lower rate of treatment success (60% vs. 31%). Lower adherence to the thermoplastic appliance was evident, attributable to insufficient retention of the appliance during sleep. The overwhelming majority of patients (82%) preferred the customized OAm at the end of the study. Hence customization to a patient's dentition is an important component of treatment success.

Degree of Mandibular Advancement

Generally greater level of advancement gives a better 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).[67]Assessment of pharyngeal collapsibility during mandibular advancement has also shown a dose-dependent effect in improvement of upper airway closing pressures.[67] In a study of mild-to-moderate OSA patients were 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%).[68]However in severe OSA, more patients achieved treatment success with 75% compared to 50% maximum advancement (52% vs. 31%),[69]suggesting maximizing advancement may be more important in severe disease. A dose-dependent effect of mandibular advancement method 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%.[70]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.[71] 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.[71]A newly available remotely controlled mandibular titration device provides an objective mechanism to determine the 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 OAm in an initial study. Identification of therapeutic protrusion level by this method may help reduce side effects produced by further unnecessary titration. Optimizing mandibular advancement in individual patients is important for successful treatment, although no standardized titration procedure currently exists.[71]In the clinical setting, a follow-up sleep study to objectively verify satisfactory treatment is often not conducted; this is an area to improve clinical outcomes.

Degree of Vertical Opening

Opening of the bite occurs during OAm treatment as all appliances have a thickness that can cause vertical jaw displacement. A crossover trial that 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.[72] However, increased vertical mouth opening has an adverse effect on upper airway patency in the majority of OSA patients. Therefore amount of bite opening should be minimized to improve patient tolerance and increase the beneficial effect on upper airway dimensions.

COMPARISONS OF DIFFERENT CUSTOMIZED APPLIANCES

Differences in previously reported OAm treatment efficacy potentially relate to different design features. There are a relatively few number of trials which compare customized appliance designs for efficacy. However existing studies suggest different OAm designs are similarly effective in treating OSA. Two-piece appliances are thought to improve comfort and wearability as lateral movement and jaw opening is possible, however monobloc appliances can be cheaper and easier to manufacture. A comparison of a monobloc and 2-piece OAm found there was no significant difference in AHI reduction, improved sleepiness, or reported side effects, although patient preference in this study favored the monobloc appliance.[73] A recent retrospective analysis of 805 patients using either an adjustable OAm (n = 602) or a fixed device (n = 203) found a higher treatment response rate for the adjustable device (56.8% *vs.* 47.0%).[73] A comparison of 2 adjustable OAs with different retention mechanisms (one with occlusal coverage and firm dental retention, the other more passive retention with a looser attachment to the dental arches) found no differences in subjective symptoms, but the passive appliance resulted in greater reduction in treatment AHI, although the difference is unlikely clinically significant.[74]Two crossover studies have compared 2-piece adjustable appliances with different advancement mechanisms and found similar improvements in AHI, symptomatic improvements, and side effects.75,76

New variations in customized OAm designs may enhance effectiveness in the future. A recent cohort study tested the addition of tongue protrusion, via an anterior tongue bulb on an OAm device and showed greater AHI reduction compared to mandibular advancement alone.77 Simultaneous advancement of both the tongue and mandible, for example, may prove to increase therapeutic effect.

SIDE EFFECTS OF ORAL APPLIANCE TREATMENT

In initial acclimatization to OAm therapy, 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,78 potentially related to differences in device design. However adverse symptoms are only transient, lasting around 2 months. Temporomandibular disorder which has 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.79,80 Long-term persistence of side effects such as mouth dryness and tooth or jaw discomfort may lead to discontinuation of treatment.81

Assessment of dental changes with OAm primarily relate to decreases in overbite and overjet,[82-87] retroclination of the upper incisor and proclination of the lower incisors,43,46 changes in anterior-posterior occlusion, and reduction in the number of occlusal contacts.[82,85,86] Overbite and overjet changes are evident 6 months after initiation of treatment. Duration of OAm use is reported to correlate with dental changes such as decreased overbite,[88]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.82 The initial type of bite, degree of mandibular advancement, adherence, and oral health will influence the degree of bite changes and the discomfort produced during longer term treatment. Skeletal changes relating to prolonged OAm use on lateral cephalometry, primarily report an increase in lower face height and a downward rotation of the mandible.[89-90] Skeletal changes are probably a result of the changes in dentition that occur with wear of the OAm.[91] Many patients are unaware of any changes in their bite and the majority of patients concur about the positive effects of OSA treatment far outweigh any adverse effects related to dental changes.

CONCLUSION

OSA is highly prevalent in the population. It is related to age and obesity. Only a group of subjects with OSA in the population have symptoms in the form of daytime sleepiness. The prevalence of OSA and OSA syndrome has been increasing in epidemiological studies. Differences and the increase in the prevalence of sleep apnea is mostly due to diagnostic equipment, study design, definitions and characteristics of subjects included. OAm is 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 OAm treatments are equivalent, even in severe OSA, despite greater efficacy of CPAP in reducing AHI. This reflects greater nightly adherence to OAm compared to CPAP therapy. Recent advances in technologies related to OAm treatment have the potential to further improve their efficacy and effectiveness in clinical practice. Selection of appropriate patients who will respond to OAm treatment is still barrier to use. 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. The advent of new adherence monitoring technology that can be routinely incorporated into OAm 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 OAm 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 prove OAm as an effective and even first-line treatment for OSA.

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