Evaluation of the Effects of Mandibular Advancement Device in Obstructive Sleep Apnea Patients

A research protocol

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Contents

Introduction

Sleep-related breathing disorders (SRBDs) constitute a diagnostic entity of disease that encompasses obstructive phenomena, including primary snoring, and Obstructive sleep apnea-hypopnea syndrome (OSAHS), along with the related disorders of central sleep apnea and sleep-related hypoventilation. [1]

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is characterized by the occurrence of abnormally frequent episodes of partial (hypopnea) or complete obstruction (apnea) of the upper airway during sleep.[2]
The importance of addressing this disorder lies in the fact that it has significant medical, psychological, and social consequences.[3]
OSA can be a serious, even life-threatening disorder. Interrupted episodes of sleep result in excessive daytime sleepiness which, in turn, increases the risk of motor vehicle accidents and diminishes quality of life. The chronic decrease in oxygen saturation along with the heightened sympathetic activity result in increased risk of endothelial damage to the blood vessels. This in turn may lead to coronary artery disease, congestive heart failure, myocardial infarction, hypertension, stroke, cardiac arrhythmia, and sudden cardiac death.[1]

Prevalence:

OSA is commonly thought to involve 2% of middle-aged women and 4% of middle-aged men.[4] A higher prevalence rate was mentioned in another study, stating that 14% of men and 5% of women suffer from OSA.[1]

Pathogenesis:

OSA results from sleep related narrowing of the upper airway. Both anatomical and neuromuscular factors play a role in the increased collapsibility of the upper airway . [5]

The pharyngeal critical closing pressure (Pcrit) is the pressure at which the upper airway collapses. When the airway becomes constricted during sleep, respiratory effort increases to maintain airflow, accompanied by relative increase in serum

carbon dioxide (hypercarbia) and decrease in serum oxygen (hypoxemia). The increased work of breathing causes arousal from sleep, which in turn raises sympathetic neural activity, leading to increased heart rate and blood pressure and a tendency for cardiac arrhythmia. Arousal from sleep helps to increase the airway patency once again and resumes the normal airflow. However, when subjects return to sleep subsequently, the sleep-related upper airway collapsibility recurs.[1]

Risk factors:

Individuals with certain characteristics appear to be predisposed to OSA. Conditions that may be risk factors for the development of OSA in adults include obesity (body mass index [BMI] >30 kg/m), menopause, male sex, and increasing age.[1]

Etiology:

The etiology of OSA is multifactorial. Many factors related to the anatomical craniofacial structures and the neuromuscular tone are the main reasons. The most common predisposing craniofacial morphologies are retrognathia, dolichocephalic facial type, narrow and deep palate, steep mandibular plane angle, anterior open bite, midface deficiency, and lower hyoid position. Regarding the functional etiological factors, collapsibility of the upper airway is influenced by hormonal fluctuation (eg, pregnancy or menopause), obesity, rostral fluid shifts,.[1]

Diagnosis:

The gold standard for diagnostic confirmation of OSA is an in-center overnight sleep study (**polysomnography [PSG**]) or out-of-center sleep testing (OCST). Polysomnography is performed by a sleep medicine specialist. Home sleep apnea testing (HSAT) is a type of OCST. The overnight polysomnography includes at least 7 channels of recording, including electroencephalography (EEG), electrocardiography, and monitoring of sleep, airflow through the nose and mouth, pulse oximetry, respiratory effort, and leg movement. [1]

Two main indices are important for determining the severity of OSA. These are the respiratory disturbance index (RDI) and the apnea-hypopnea index (AHI). The respiratory disturbance index includes the number of apneas, hypopneas, and respiratory effort–related arousals RERAs per hour of sleep. The apnea-hypopnea index (AHI) includes the number of apneas and hypopneas per hour of sleep.[1]

Classification of OSA:

OSA can be categorized into mild (AHI or RDI >5 and <15), moderate (AHI or RDI >15 and <30), and severe (AHI or RDI >30).[1]

OSA lines of treatment:

1. **Surgical treatment:**

A common staged protocol involves utilizing uvulopalato-phayngoplasty with tongue suspension or with genioglossus advancement and hyoid myotomy (Phase I) and maxillary and mandibular advancement osteotomy (Phase II). Several new techniques of upper airway surgical modifications have recently been described. Submucosal lingualplasty in combination with palatal surgery was found to be effective in improving sleep apnea symptoms.[6]

2. **Non-Surgical treatment:**

A. Continuous Positive airway pressure (CPAP) therapy is the gold standard treatment for OSA in adults. CPAP acts as a high pressure splint that maintains patency of the upper airway. It is delivered through a mask interface.[5]

B. Other treatment options include positional therapy (avoidance of sleeping on back) and body weight reduction. Drug therapy may be indicated for cases of nasal congestion or allergic rhinitis.[1]

C. **Oral appliances:**

Oral appliances are indicated, and may be a first-line therapy for patients with mild to moderate OSA and primary snoring. Oral appliances may also be a second line of therapy for patients with severe OSA who do not respond to or are unable or unwilling to tolerate positive airway pressure (PAP) therapies.[7]
Several studies have demonstrated that OAs and PAP therapy were comparable in improving daytime somnolence, hypertension, neurocognitive function, quality-of-life indices, and cardiovascular mortality.[6, 8]

The **Advantages** of oral appliances are silent, portable, noninvasive, and well tolerated. Most side effects tend to be transient, though permanent dental consequences may occur.[7]

Types of Oral appliances:

i. The most commonly used oral appliances are the Mandibular Advancement Devices (**MADs)** which advance the mandible and the genio-glossus muscles thus enlarging the airway.[1]

ii. **Tongue-stabilizing devices** may also be used in controlling mild to moderate OSA cases. Tongue-stabilizing devices use suction to protrude the tongue forward, however it is less tolerated than mandibular advancement devices[6] TDs are used in patients with large tongues, or when there are contraindications to use of an MRA. Some TDs are custom made for the patient (e.g., tongue retaining device (TRD) but some devices are prefabricated. To use the TRD the patient advances the tongue into the bulb while squeezing the bulb to create negative suction. The patient experiments with the amount of forward Positioning of the tongue that is required to decrease snoring and symptoms[9]

iii. A third, less commonly used device is the **soft palate lifters**.

Regarding the Mandibular advancement devices (MADs), they may be **custom-made or ready-made.** Traditionally, MADs have been individually fabricated by a dental technician from plaster casts of patients' teeth and construction bites obtained by the dentist. Potential disadvantages of this custom-made method are the costs and time required to construct the device. Prefabricated MADs made of thermoplastic material, also called boil and bite appliances, could provide a reasonable alternative to custom-made devices to reduce the costs as well as the fabrication time. [10]

MADs may also be **dual-arch or monobloc**. In the Two-arch appliances, a locking mechanism is inserted to lock the appliance in a protruded position. Regarding the advancement mechanism of MADs, they may be constructed at a **single fixed protruded position, or they may be titrable**, having an adjustment screw to adjust the degree of advancement.[4]
Custom, adjustable dual-arch OAs have been shown to be highly efficacious for treating primary snoring and mild-moderate OSA.[6]

The target degree of protrusion of the mandible is defined as the final and most effective protrusion, that yields the most successful outcome.[4] It varies from 50 to 75% of the maximum protrusion of the patient.[9]
Some studies have demonstrated a dose-dependent effect of mandibular advancement on OSA, i.e., more protrusion yielding larger improvements in OSA. However, an exaggerated mandibular protrusion can cause temporomandibular joint problems, and/or muscle discomfort. This suggests that the target protrusion is an individual variable for every patient.[4]
According to Ferguson etal, the most commonly used definition of success of MADs is a reduction to less than five respiratory events per hour of sleep while the

most liberal definition was a reduction of 50% or more from the baseline apnea-hypopnea index (AHI).[11]

Mehta and coworkers compared the patients' response to 2 devices, one that protruded the mandible and the other did not. The placebo device did not improve the AHI suggesting that it is protrusion that is necessary for the OA to be effective.[12]

Walker-Engström etal compared two different degrees of mandibular protrusion 50% or 75% of maximum using the same device in both groups. The success rate of the 75% protrusion proved to be higher than that of the 50% protrusion. Additionally, they did not find increased side effects with more protrusion.[13]

Therapeutic Mechanism of MADs:

The mandibular advancement device acts by displacing oropharyngeal tissues forward that results in a patent airway.[10]

According to **Haekema etal**, three different mechanisms may explain the efficacy of oral appliances in improving sleep respiration. First, mandibular advancement moves the suprahyoid and genioglossus muscles anteriorly, enlarging the airway, thus lessening the likelihood of its collapse. Second, downward movement of the mandible accompanies advancement, thereby exerting tension across the soft palate via the palatoglossal and palatopharyngeal arches, thereby preserving the velopharyngeal airway space. Third, the oral appliance maintains a forward position of the mandible and hyoid bone during sleep, preventing backward rotation of the jaw and retrolapse of the tongue into the airway.[14]

Effects of MADs on airway dimensions:

Many imaging modalities were used for assessing the effects of MADs on the airway. Initially studies used two dimensional lateral cephalograms and demonstrated significant changes in the antero-posterior airway dimensions.[3]] Later on, three dimensional studies using CBCT demonstrated an additional increase in transverse airway dimensions, which exceeded the increase in the anteroposterior dimension.[15]

Haskell et al used Cone beam Computed tomography to detect changes in airway volume caused by the mandibular advancement devices. They found that the largest changes occurred in the lateral rather than AP dimension, particularly at the level of the C2 vertebra; where the airway acquired a more elliptical cross-sectional shape.[16]

Shete and Bhad used a titrable twin block appliance and evaluated its effect on the airway using Cone beam computed tomography. They found greater

increases in transverse dimensions than in anteroposterior dimensions of the smallest crossctional area in all patients irrespective of initial small or large transverse dimensions of the smallest cross section area. These findings are similar to those of Haskell etal.[15]

Zhao etal used Magnetic Resonance Imaging and demonstrated similar results.[17]

Side effects of MADs:

1. **Effects on occlusion and alignment:**

Tooth movement , specifically occlusal changes represented by incisor changes, position of canines, decreased overjet/overbite, and altered occlusal contacts/bite changes is a concern during the treatment of OSA using MADs.

Vranjes etal assessed the effect of a mandibular advancement device using scanned digital models. Eighteen patients were recruited in this study. They showed that a rigid MAD demonstrated no significant change in tooth position during the test period, or in bite changes per maximum intercuspation, as measured by overjet and overbite. The mean change in Little Irregularity Index for the lower anterior teeth was 0.007 mm which was not statistically significant. Moreover, patients were highly satisfied with the device and considered it beneficial.[18]

A systematic review by **Araie etal** performed a meta-analysis on 12 studies to detect occlusal changes associated with MAD use. They demonstrated that MAD use was associated with a significant decrease of overjet (OJ) and overbite (OB), and it was suggested that both parameters decreased along with the duration of treatment. Meta-analysis also demonstrated a significant increase of L1-MP. However, there were no significant changes of skeletal modifications or mandibular rotation. Changes of incisor inclination were suggested to make a contribution to reduction of OJ and OB. The mean decrease in overjet and overbite during the first year of use of MADs was 0.7 mm and 0.6 mm respectively. [19]

Fransson etal in 2020 conducted a 10-year prospective cephalometric study to evaluate the influence of a mandibular protruding device (MPD) in people with obstructive sleep apnea and snoring. At baseline and after 10 years, a lateral cephalogram was taken in the upright position.They showed that long-term nocturnal MPD use causes retroclination of the maxillary incisors and proclination of the mandibular incisors with consequent decreased overjet and overbite. Both MPD and MPD-stopped users obtained increased mandibular length and lower position of the hyoid bone, which can be a normal physiological change with age.[20]

2. **Effects on Temporomandibular joint**

Martinez-Gomis performed a study to assess Temporomandibular disorders (diagnosed according to the Research Diagnostic Criteria for TMD), overjet, overbite, occlusal contacts, subjective side effects, and technical complications before and after 14, 21, and 58 months of treatment using MADs. They found no significant variation in TMD prevalence. Subjective side effects were common, and a significant reduction was found in overjet, overbite, and in the number of occlusal contacts.[21]

A 2019 systematic review aimed to evaluate the effects of MADs on prevalence of TMD signs and symptoms in adult OSA patients. Twelve studies were included. The meta-regression analysis showed that patients with pre-existing signs and symptoms of TMD do not experience significant exacerbation of symptoms using the MAD. Moreover, the presence of TMD does not appear to be routine contraindication for the use of MAD used for the management of OSA.[22]

Orthodontists role in OSA management:

The orthodontist is involved in 2 main roles regarding OSA management:

1. **Screening for obstructive sleep apnea (OSA).** In the adult population, the Epworth Sleepiness Scale and Berlin and STOP-BANG questionnaires are examples of questionnaires that collectively focus on subjective and objective criteria and are valuable tools for the initial screening process.[23]
2. **As part of the team involved in the multidisciplinary management of OSA in both children and adults.**

Being experts in the science of facial growth and development, combined with their knowledge of mandibular advancing appliances , orthodontists are well suited to collaborate with physicians in the treatment of OSA.[1]

No clinical trials have been carried out previously to evaluate the effects and side effects three dimensionally on Egyptian population, thus came the idea of this study.

Aim of the study

The aim of this study is to investigate the effects of mandibular advancement device in obstructive sleep apnea patients.

Objectives:

The following parameters will be assessed:

- Respiratory sleep parameters.
- Occlusion (Inter-arch parameters)
- Dental parameters (Intra-arch parameters)
- Skeletal parameters
- Airway dimensions.

Material and Methods

This clinical study will be performed on ten patients referred from the outpatient clinics of Demerdash hospital, Ain Shams university.

The subjects will be selected to fulfill the following inclusion criteria:

1. Mild, moderate obstructive sleep apnea (OSA) as diagnosed on pre-treatment polysomnography. (measured by AHI or RDI) between 5 and 30 events per hour.
2. Age: adults aged above 18 years.
3. Sex: males and females
4. Subjects having a sufficient set of teeth to hold an appliance.
5. Subjects capable of giving informed consent.

Exclusion criteria:

1. Central sleep apnea.
2. Patients with severe periodontal disease
3. Patients with severe somatic or psychiatric disease
4. Pregnant females
5. Patients who are allergic to the appliance materials.

Methods:

Subjects in this study will receive a Mandibular advancement device (MAD).

The Mandibular advancement device that will be used in this study will be a custom-made, two-piece titrable appliance. The appliance consists of an upper and a lower compartment. Two acrylic flanges are constructed bilaterally on the buccal surface of the lower appliance in the molar region. These fit against a slot on the upper appliance in the same region, thus allowing engagement and locking of the

two appliances. The flanges are constructed at an angle to guide the mandible forward and maintain advancement. Two screw devices are incorporated posteriorly on each side in the upper appliance to enable advancement of the slots to permit incremental protrusion of the mandible.
Alginate impressions, as well as wax construction bites taken at 65% mandibular advancement will be taken to each patient for the purpose of appliance construction.
After appliance delivery, patients will be instructed to wear the appliance just before sleep and take it off in the morning after they wake up.

After acclimatization to wearing the appliance, the patients will be instructed to further advance the appliance by turning the screw forward two times per week (to achieve an advancement of 0.5 mm per week). Titration will be performed until subjects report improvement in their apnea symptoms, or until they cannot tolerate any further advancement.

Acclimatization to wearing the appliance will take 2 weeks, after which titration will be started.

The patients will be followed up on a weekly basis during the titration period, and then they will be followed up every 3 months for the rest of the study period.

Outcomes:

- Respiratory sleep parameters measured by Polysomnography.
- Occlusion (Overbite, overjet, molar relation) measured on digital study models.
- Dental parameters (incisors inclination, inter-molar width, inter-canine width, incisors irregularity, curve of spee) measured on digital study models and lateral cephalogram.
- Skeletal parameters measured on lateral cephalogram.
- Three-dimensional airway changes measured on Cone beam CT.

Measuring tools:

- Polysomnography test will be done before treatment and after 6 weeks of wearing the appliance (after titration is done) to detect improvement in respiratory sleep parameters.

- 3D Digital study models will be acquired for every patient before treatment and after one year of appliance use to detect changes in occlusion and alignment of teeth.
- Cone beam computed tomography scans will be taken before and after 6 weeks of wearing the appliance to measure three dimensional changes in airway. A lateral cephalogram will be derived from the pre-treatment CBCT.
- Lateral cephalogram will be taken after one year.
- Epworth sleepiness scale questionnaire will be used to evaluate the subjective improvement of OSA symptoms.

Data management:

All personal information about the participants will be confidential. Access to the final dataset will be limited to the investigators and the supervisors of this clinical trial.

Statistical Methods:

The study outcomes will be statistically analyzed to evaluate the changes brought by the appliance.

Informed consent and Adverse Event Reporting

Each participant will sign an informed consent describing in full details the interventions carried out in this clinical trial. Each participant has the right to withdraw from the study at any time without any penalty or loss of benefit. Available data to the time of the participant's withdrawal might be included in the final data analysis.

Risks to Study Participants and Adverse Events Reporting:

Risks to study participants include temporomandibular joint symptoms and changes in occlusal relationship. Participants will be followed up for these side effects and will be managed accordingly.

Benefits to Study Participants and to the Community:

Benefits to the Study participants:

Treatment of OSA using oral appliances will improve the patients sleep which will in turn improve their quality of life. Also this will prevent the serious consequences of untreated OSA such as cardiac diseases, Diabetes, and Stroke. Moreover, day-time sleepiness will decrease with the consequent improvement in the patients' occupational performance.

Benefits to the Community:

Decreased day-time sleepiness will lead to better occupational performance, and more subjects' productivity. Also the decreased sleepiness may lead to decreased motor vehicle accidents.

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